American Journal of Obstetrics and Gynecology

SOCIETY FOR MATERNAL—FETAL MEDICINE

2000 20TH ANNUAL MEETING
Postgraduate Courses/Scientific/Clinical Meeting
(jointly sponsored by The American College of Obstetricians and Gynecologists)

January 31-February 5, 2000
Miami Beach, Florida
In accordance with the wishes of the majority of the SMFM membership, we ask that our members and guests refrain from smoking in the meeting rooms. This conforms to the spirit of our society and the written procedures of our parent organization.
## Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organization</td>
<td>III</td>
</tr>
<tr>
<td>Letter from the Program Chair</td>
<td>IV</td>
</tr>
<tr>
<td>Program Committee</td>
<td>V</td>
</tr>
<tr>
<td>List of Reviewers</td>
<td>VI</td>
</tr>
<tr>
<td>Acknowledgments</td>
<td>VII</td>
</tr>
<tr>
<td>Map of Meeting Areas - Fontainebleau Hilton</td>
<td>VIII</td>
</tr>
<tr>
<td>Program</td>
<td>IX</td>
</tr>
<tr>
<td>Scientific Forums/Special Focus Groups</td>
<td>X</td>
</tr>
<tr>
<td>Masters' Series Luncheon Roundables</td>
<td>XIV</td>
</tr>
<tr>
<td>Scientific Sessions Program</td>
<td>XV</td>
</tr>
<tr>
<td>Oral Session I (Plenary)</td>
<td>SII</td>
</tr>
<tr>
<td>Concurrent Oral Sessions</td>
<td>S15</td>
</tr>
<tr>
<td>Session A</td>
<td>S15</td>
</tr>
<tr>
<td>Session B</td>
<td>S19</td>
</tr>
<tr>
<td>Oral Session II (Plenary)</td>
<td>S23</td>
</tr>
<tr>
<td>Concurrent Oral Sessions</td>
<td>S27</td>
</tr>
<tr>
<td>Session C</td>
<td>S27</td>
</tr>
<tr>
<td>Session D</td>
<td>S31</td>
</tr>
<tr>
<td>Concurrent Oral Sessions</td>
<td>S35</td>
</tr>
<tr>
<td>Session E</td>
<td>S35</td>
</tr>
<tr>
<td>Session F</td>
<td>S39</td>
</tr>
<tr>
<td>Poster Session I</td>
<td>S43</td>
</tr>
<tr>
<td>Poster Session II</td>
<td>S75</td>
</tr>
<tr>
<td>Poster Session III</td>
<td>S107</td>
</tr>
<tr>
<td>Poster Session IV</td>
<td>S139</td>
</tr>
<tr>
<td>Poster Session V</td>
<td>S169</td>
</tr>
<tr>
<td>Subject Index</td>
<td>S203</td>
</tr>
<tr>
<td>Author Index</td>
<td>S207</td>
</tr>
<tr>
<td>Academic Institution Index</td>
<td>S221</td>
</tr>
</tbody>
</table>

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20th Annual Clinical, Scientific, & Business Meeting

of the

Society For Maternal-Fetal Medicine

January 31 - February 5, 2000

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Dear Colleagues:

The 2000 Annual Meeting of the Society for Maternal-Fetal Medicine marks the 23rd anniversary of the Society formerly known as the Society of Perinatal Obstetricians. There were 1,074 abstracts submitted for consideration this year: 68 were selected for oral presentation and 600 for poster presentation. The quality of the abstracts was superb and the balance of clinical and basic research portends an outstanding meeting. As a quick glance at the academic institutions represented will attest, our meeting has truly become an international one.

I want to thank everyone who submitted an abstract, as well as all the reviewers. Each abstract was graded by four reviewers, after which the top 128 were sent out for secondary evaluation. I would particularly like to thank the senior reviewers who had to work on a tight schedule in order for the program to be put together on time. This year I tried to implement a more standardized means of judging the abstracts and I welcome feedback.

Once again, the review process was conducted at the Society’s office in Washington, D.C. Our Executive Director, Pat Stahr, did a phenomenal job organizing and coordinating this project. We all owe her and her staff -- Jill Reese, Nanette Irby, Barbara Ohlstein, and Mimi Mullin -- a hearty thanks for their dedication and hard work.

A few special acknowledgments are also in order. Haywood Brown, Poster Chair, Jay Iams, Postgraduate Course Chair, Katharine Wenstrom, Scientific Forums and Special Focus Groups Chair, and Dibe Martin, Local Arrangements Chair were instrumental in organizing this year’s meeting. Past efforts of James Martin and Susan Cox have ensured our ability to receive CME credits. Lastly, I want to personally thank our Past President Mary D’Alton, current President Peter VanDorsten, and the Board of Directors for their encouragement, support, and vote of confidence.

Finally, thanks to the membership of the Society for its continued support and submission of scientific work, making our annual meeting a successful educational forum for everyone.

Sincerely,

Michael L. Socol, MD
2000 Program Chair

American Journal of Obstetrics and Gynecology

IV January 2000
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  Postgraduate Course Chair

Katharine D. Wenstrom, MD
  Coordinator, Scientific Forums

Dibe Martin, MD
  Local Arrangements Chair
Reviewers for 2000 SMFM Abstracts

The Program Chair, on behalf of the Society, is most grateful to the following people who so conscientiously and promptly judged the abstracts for this meeting.

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ACKNOWLEDGMENTS
The Society for Maternal-Fetal Medicine extends sincere thanks and appreciation to the following organizations for their generous support. As per the SMFM’s Board of Directors policy that corporate contributions no longer go to directly support the Annual Meeting, the funds donated by these organizations will be used to support such SMFM activities as the Foundation Fellowship Award and the Fellows Retreat.

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| Mallinckrodt |
| Matria Healthcare |
| OB Scientific |
| Obstetrix |
| Sheridan Healthcorp |
| Siemens Medical Systems |
| Vision Chips |
| Friends of the SMFM |
| Contributions of $2,500-4,999 |
| Magella Healthcare |
| Ortho-McNeil |
ILLUSTRATION OF FUNCTION SPACE

Illustrations on this and all following pages have been scaled to differing proportions.
Program

Monday, January 31
6:00pm-8:00pm Registration Grand Gallerie
4:00pm-8:00pm Speaker Ready Room Imperial III

Tuesday, February 1
7:00am-6:00pm Registration Grand Gallerie
7:00am-7:00pm Speaker Ready Room Imperial III
7:00am-8:00am Continental Breakfast Grand Ballroom West
8:00am-5:00pm Postgraduate Course I
"Preconceptional Counseling"
Course Director: Ronald J. Wapner, MD
Fontainebleau Ballroom A/B
8:00am-5:00pm Postgraduate Course II
"Controversies in the Management of Hypertension and Diabetes in Pregnancy"
Course Director: Mark B. Landon, MD
Fontainebleau Ballroom C/D
10:00am-10:30am Coffee Break Grand Ballroom West
Noon-1:00pm Lunch Grand Ballroom
3:00pm-3:30pm Coffee Break Grand Ballroom West
4:00pm-7:00pm Board of Directors Meeting I Imperial V

Wednesday, February 2
7:00am-6:00pm Registration Grand Gallerie
7:00am-7:00pm Speaker Ready Room Imperial III
7:00am-8:00am Continental Breakfast Grand Ballroom West
8:00am-3:00pm Postgraduate Course III
"Obstetric Intensive Care"
Course Director: Michael R. Foley, MD
Fontainebleau Ballroom A/B
8:00am-3:00pm Postgraduate Course IV
"Use of Diagnostic Tests in Obstetrics"
Course Director: M. Kathryn Menard, MD
Fontainebleau Ballroom C/D
10:00am-10:30am Coffee Break Grand Ballroom West
Noon-1:00pm Lunch Grand Ballroom
Noon-3:00pm Board of Directors Meeting II Imperial V
3:00pm-various Scientific Forums (see page XIII for locations)
6:00pm-7:00pm Program Directors Meeting Imperial I
6:30pm-8:00pm Opening Reception Great Lawn
Backup: Fontainebleau

Thursday, February 3
7:00am-5:00pm Registration Grand Gallerie
7:00am-7:00pm Speaker Ready Room Imperial III
7:00am-7:45am Continental Breakfast Grand Ballroom West
7:45am-8:00am Welcome & Announcements
Michael L. Socol, MD
2000 Program Chair
Welcome
J. Peter VanDorsten, MD
President, SMFM
Grand Ballroom East

8:00am-10:00am Oral Plenary Session I
Moderators:
Mary E. D’Alton, MD
J. Peter VanDorsten, MD
Grand Ballroom East

10:00am-noon Poster Session I & Coffee
Moderators:
J. Peter VanDorsten, MD
Fontainebleau Ballroom A/B

12:00-1:00pm Masters’ Series Luncheon
Roundtables
(See page XIV)

1:15pm-3:30pm Oral Concurrent Session A:
Moderators:
Lindsey Allan, MD
Ronald J. Wapner, MD
Grand Ballroom East

1:15pm-3:30pm Oral Concurrent Session B:
Moderators:
W. Patrick Duff, MD
Daniel F. O’Keeffe, MD
Fontainebleau Ballroom C/D

3:30pm-5:30pm Poster Session II & Coffee
Fontainebleau Ballroom A/B

Friday, February 4

7:00am-5:00pm Registration
Grand Gallerie

7:00am-7:00pm Speaker Ready Room
Imperial III

7:00am-8:00am Continental Breakfast
Grand Ballroom West

7:00am-8:00am Oral Plenary Session II
Moderators:
Ronald S. Gibbs, MD
Valerie M. Parisi, MD
Grand Ballroom East

8:00am-10:00am

10:00am-noon Poster Session III & Coffee
Moderators:
Haywood L. Brown, MD
Kenneth J. Moise, Jr., MD
Fontainebleau Ballroom A/B

12:00-1:00pm Masters’ Series Luncheon
Roundtables
Vendor Luncheon
(See page XIV)

1:15pm-3:30pm Oral Concurrent Session C:
Moderators:
Fontainebleau Ballroom A/B

1:15pm-3:30pm Oral Concurrent Session D:
Moderators:
Susan M. Cox, MD
Katharine D. Wenstrom, MD
Fontainebleau Ballroom C/D

3:30pm-5:30pm Poster Session IV & Coffee
Fontainebleau Ballroom A/B

5:30pm-6:15pm Annual SMFM Business Meeting
(Regular Members Only)
Grand Ballroom East
5:30pm-6:15pm  
**Associate Members Meeting**  
(Fellow-in-Training Members and other Associate Members of SMFIM)  
Fontainebleau Ballroom C/D

6:30pm-9:30pm  
Cocktail Reception  
Annual Banquet  
Awards Presentation  
Grand Ballroom

9:30pm-midnight  
After-Banquet Entertainment  
Grand Ballroom

**Saturday, February 5**

7:00am-noon  
Registration  
Grand Gallerie

7:00am-1:00pm  
Speaker Ready Room  
Imperial III

7:00am-8:00am  
Continental Breakfast  
Grand Ballroom West

8:00am-10:00am  
**Concurrent Oral Session E:**  
Moderators:  
Michael P. Nageotte, MD  
Susan M. Ramin, MD  
Fontainebleau Ballroom C

8:00am-10:00am  
**Concurrent Oral Session F:**  
Moderators:  
James T. Christmas, MD  
Jay D. Iams, MD  
Fontainebleau Ballroom D

10:00am-noon  
**Poster Session V & Coffee**  
Presentation of Saturday Oral and Poster Awards  
Fontainebleau Ballroom A/B

Adjourn
ACCME Accreditation
This activity has been planned and implemented in accordance with the Essentials and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine. The American College of Obstetricians and Gynecologists is accredited by the ACCME to provide continuing medical education for physicians and takes responsibility for the content, quality and scientific integrity of this CME activity.

AMA CME Credit Hours in Category 1 and ACOG Cognate Hours
ACOG designates the postgraduate course “Preconception Counseling” for up to 7 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association and up to 7 cognate hours in Category I (Formal Learning) of the ACOG Program for Continuing Professional Development. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
ACOG designates the postgraduate course “Controversies in the Management of Hypertension and Diabetes in Pregnancy” for up to 7 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association and 7 cognate hours in Category I (Formal Learning) of the ACOG Program for Continuing Professional Development. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
ACOG designates the postgraduate course “Obstetric Intensive Care” for up to 6 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association and up to 6 cognate hours in Category I (Formal Learning) of the ACOG Program for Continuing Professional Development. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
ACOG designates the postgraduate course “Use of Diagnostic Tests in Obstetrics” for up to 6 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association and up to 6 cognate hours in Category I (Formal Learning) of the ACOG Program for Continuing Professional Development. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

20th Annual Meeting
ACOG designates the Annual Meeting for up to 27 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association and up to 27 cognate hours in Category I (Formal Learning) of the ACOG Program for Continuing Professional Development. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
The following is a breakdown of credit hours awarded each day: Wed., Feb. 2 = 2 hours; Thurs., Feb. 3 = 10 hours; Fri., Feb. 4 = 10 hours; Sat., Feb. 5 = 5 hours.

Learning Objectives
At the conclusion of the postgraduate courses and the annual meeting, the participant will be able to:
- Discuss the relevant science and appropriate clinical application for the topics in maternal-fetal medicine including issues relevant to prematurity, perinatal infectious diseases, hypertensive disorders, diagnostic ultrasound, genetics, prenatal diagnosis, fetal therapy, clinical obstetrics, other major problems of pregnancy, pharmacology, maternal-fetal physiology, and perinatal outcomes based research.
- Identify concepts and therapeutic approaches to aspects of maternal-fetal medicine which have been displaced by newer ones that will immediately impact clinical practice.

Disclosure of Faculty and Industry Relationships
In accordance with ACOG policy, all faculty members have signed a conflict of interest statement in which they have disclosed any significant financial interests or other relationships with industry relative to topics they will discuss at this program. At the beginning of the program, faculty members are expected to disclose any such information to participants. Such disclosure allows you to evaluate better the objectivity of the information presented in lectures. Please report on your evaluation form any undisclosed conflict of interest you perceive. Thank you.

SMFM POLICY REGARDING AUDIO AND VIDEO RECORDING
As a courtesy to faculty, presenters and registrants, it is the general policy of the Society for Maternal-Fetal Medicine that there shall be no audio/video recording or any type of photographic reproduction of any material presented at a SMFM-sponsored postgraduate course or the annual scientific meeting. [This does not preclude taking pictures of your poster presentation for personal use.]
In special circumstances, a presenter or participant can petition the Program Chair and the SMFM Board of Directors by written request at least 30 days in advance of the meeting to have this policy waived for a specific reason if the presenter(s) is (are) in agreement and if the recording or photography can be arranged without disruption to the other meeting participants.
### SCIENTIFIC FORUMS/SPECIAL FOCUS GROUPS
#### WEDNESDAY, FEBRUARY 2, 2000

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Computer Usage in Perinatal Medicine</td>
<td>3:00-5:30 pm</td>
<td>Burgundy</td>
</tr>
<tr>
<td>Critical Care in Perinatal Medicine</td>
<td>3:00-6:00 pm</td>
<td>Pasteur</td>
</tr>
<tr>
<td>Diabetes Mellitus in Pregnancy</td>
<td>3:00-6:00 pm</td>
<td>Bordeaux</td>
</tr>
<tr>
<td>Genetics</td>
<td>3:00-TBA</td>
<td>Voltaire</td>
</tr>
<tr>
<td>Hypertension in Pregnancy</td>
<td>3:00-5:30 pm</td>
<td>Le Mans</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>3:00-5:30 pm</td>
<td>Lafayette</td>
</tr>
<tr>
<td>Perinatal Epidemiology and Health Services Research</td>
<td>3:00-TBA</td>
<td>Monaco</td>
</tr>
<tr>
<td>Preterm Labor</td>
<td>3:00-TBA</td>
<td>Champagne</td>
</tr>
<tr>
<td>Ultrasound in Perinatal Medicine</td>
<td>3:00-TBA</td>
<td>Brittany</td>
</tr>
</tbody>
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### THURSDAY, FEBRUARY 3, 2000

<table>
<thead>
<tr>
<th>Event</th>
<th>Time</th>
<th>Room</th>
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<tbody>
<tr>
<td>Women In Perinatology Special Focus Group Box Lunch</td>
<td>11:30 am-1:00 pm</td>
<td>Club Atlantic</td>
</tr>
<tr>
<td>Research Support Personnel Special Focus Group Box Lunch Meeting</td>
<td>11:30 am-1:00 pm</td>
<td>Pasteur</td>
</tr>
<tr>
<td>International Society of Perinatal Obstetricians Scientific Forum</td>
<td>6:30 pm-8:30 pm</td>
<td>Imperial II</td>
</tr>
</tbody>
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### FRIDAY, FEBRUARY 4, 2000

<table>
<thead>
<tr>
<th>Event</th>
<th>Time</th>
<th>Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>International Society of Perinatal Obs. (Breakfast/Annual Business Meeting)</td>
<td>7:00 am-8:00 am</td>
<td>Imperial II</td>
</tr>
<tr>
<td>Community Practice Management</td>
<td>7:00 am-8:00 am</td>
<td>Imperial IV</td>
</tr>
</tbody>
</table>

Other Special Focus Group Meetings:
- Education**
- Fetal Surgery**
- Pro-Life MFM's**

**Check with Meeting Registration Desk for specific dates, times and locations.
MASTERS’ SERIES LUNCHEON ROUNDTABLES

THURSDAY, FEBRUARY 3, 2000  Noon to 1:00 pm

First Trimester Screening for Aneuploidy  
Mary E. D’Alton, MD  
Room: Brittany

Non-surgical Fetal Therapy  
Mark I. Evans, MD  
Room: Champagne

Alloimmune/Idiopathic Thrombocytopenic Purpura  
Richard L. Berkowitz, MD  
Room: Monaco

Biochemical Markers of Prematurity  
Thomas J. Garite, MD  
Room: Le Mans

HIV in Pregnancy  
Howard L. Minkoff, MD  
Room: Bordeaux

Management of the Isoimmunized Gravida  
Kenneth J. Moise, Jr., MD  
Room: Burgundy

FRIDAY, FEBRUARY 4, 2000  Noon to 1:00 pm

Second Trimester Screening for Aneuploidy  
Ray Bahado-Singh, MD  
Room: Brittany

Fetal Surgery  
Mark P. Johnson, MD  
Room: Champagne

Antiphospholipid Antibody Syndrome  
Charles J. Lockwood, MD  
Room: Monaco

Endocervical Sonography and Preterm Birth Prevention  
Jay D. Iams, MD  
Room: Le Mans

Non-aneuploidy Antenatal Genetic Screening  
Katharine D. Wenstrom, MD  
Room: Bordeaux

Antibiotics and Preterm Birth Prevention  
Robert L. Goldenberg, MD  
Room: Burgundy
# Schedule of Oral Presentations

**Thursday, February 3, 2000**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:45-8:00</td>
<td>WELCOME AND ANNOUNCEMENTS</td>
</tr>
<tr>
<td>8:00-8:15</td>
<td>1 A MULTICENTER RANDOMIZED TRIAL OF FETAL PULSE OXIMETRY</td>
</tr>
<tr>
<td>8:15-8:30</td>
<td>2 TOWARD A MULTIPLE MARKER TEST FOR SPONTANEOUS PRETERM BIRTH (SPB)</td>
</tr>
<tr>
<td>8:30-8:45</td>
<td>3 MULTICENTER RANDOMIZED TRIAL OF SINGLE VERSUS WEEKLY COURSES OF ANTENATAL CORTICOSTEROIDS (ACS): INTERIM ANALYSIS</td>
</tr>
<tr>
<td>8:45-9:00</td>
<td>4 PRETERM DELIVERY AND MATERNAL INTERLEUKIN-1 POLYMORPHISMS</td>
</tr>
<tr>
<td>9:00-9:15</td>
<td>5 MATRIX METALLOPROTEINASE-9 IN THE RAT CERVIX FOLLOWING TREATMENT TO INDUCE RIPENING</td>
</tr>
<tr>
<td>9:15-9:30</td>
<td>6 UNILATERAL UTERINE ISCHEMIA/REPERFUSION INDUCES OXIDATIVE STRESS WITH FETAL GROWTH RESTRICTION IN BOTH HORN IN THE RAT</td>
</tr>
<tr>
<td>9:30-9:45</td>
<td>7 METRONIDAZOLE TREATMENT INCREASED THE RISK OF PRETERM BIRTH IN ASYMPTOMATIC WOMEN WITH TRICHOMONAS</td>
</tr>
<tr>
<td>9:45-10:00</td>
<td>8 A RANDOMIZED TRIAL OF CERCLAGE VS NO CERCLAGE IN PATIENTS WITH SONOGRAPHICALLY DETECTED 2ND TRIMESTER PREMATURE DILATATION OF THE INTERNAL OS</td>
</tr>
</tbody>
</table>

Moderators: Mary E. D'Alton, MD, Immediate Past President
J. Peter VanDorsten, MD, President

- Dildy GA, Garite TJ, McNamara H, Nageotte MP, Swedlow DB, Mallickrodt Fetal Oximetry Research Group
- Goldenberg RL, NICHD MFMU Network, Bethesda, MD
- Guinn Da, BMZ Study Group Loyola Univ., Maywood, IL
- Lewis R, Abokas R, Sibai B, Dept. of Ob/Gyn, Univ. of Tennessee, Memphis, TN
- Casey LC, Klebanoff M, NICHD MFMU Network, Bethesda, MD
- Rust O, Atlas R, Jones K, Benham B, Balducci J, Dept. of Ob/Gyn, Lehigh Valley Hospital, Allentown, PA
Thursday, February 3, 2000

1:15 p.m. to 3:30 p.m. Oral Concurrent Session A Grand Ballroom East

Fetus Ultrasound

Moderators: Lindsey Allan, MD, 2000 Honorary Member
Ronald J. Wapner, MD

1:15-1:30  9  HEAD CIRCUMFERENCE AND VENTRICULAR SIZE FOLLOWING IN UTERO CLOSURE OF MYELOMENINGOCELE
Walsh DS, Johnson MP, King M, Flake AW, Crombleholme TM, Sutton LN, Bar M, Jr., Adzick NS, Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia and Univ. of Michigan, Philadelphia, PA, and Ann Arbor, MI

1:30-1:45  10  TREATMENT OF SEVERE CONGENITAL DIAPHRAGMATIC HERNIA BY FETAL TRACHEAL OCCLUSION: CLINICAL EXPERIENCE WITH FIFTEEN CASES
Flake AW, Crombleholme TM, Johnson MP, Howell L, Adzick NS, Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia, PA

1:45-2:00  11  LATE TRACHEAL OCCLUSION IN A FETAL RABBIT MODEL FOR CONGENITAL DIAPHRAGMATIC HERNIA ACHIEVES NORMAL PULMONARY DEVELOPMENT AND MATURATION

2:00-2:15  12  ASSESSMENT OF FETAL LUNG VOLUMES AND LIVER HERNIATION WITH MAGNETIC RESONANCE IMAGING IN CONGENITAL DIAPHRAGMATIC HERNIA
Walsh DS, Hubbard AM, Olotuyee OO, Crombleholme TM, Flake AW, Johnson MP, Adzick NS, Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia, PA

2:15-2:30  13  THE DOPPLER ASSESSMENT IN MULTIPLE PREGNANCY STUDY (DAMP) AND META-ANALYSIS OF DOPPLER AND TWINS
Giles W, Bisits A, O’Callaghan S, Discipline of Reproductive Medicine, University of Newcastle, Australia

2:30-2:45  14  THE TEMPORAL SEQUENCE OF CHANGES IN FETAL VELOCIMETRY INDICES FOR GROWTH-RESTRICTED FETUSES
Ferazzi E, Bellotti M, Bozzo M, Riganò S, Pardi G, Battaglia F, Galan H, Depts. of Ob/Gyn at DMCO San Paolo Univ. at Milan, and UCHSC at Denver, CO

2:45-3:00  15  PREVENTION OF FETAL DEATH WITH NOVEL PEPTIDES IN FETAL ALCOHOL SYNDROME
Spring CT, Abebe DT, Gozes I, Brenneman DE, Hill JM, SDMP, NICHD, NIH, Bethesda, MD and Sackler School of Med., Tel Aviv Univ., Tel Aviv, Israel

3:00-3:15  16  SUCCESSFUL ENGRAP-TMENT AFTER IN UTERO TRANSPLANTATION OF HUMAN CORD BLOOD STEM CELLS IN NOD/SCID MICE
Sturrock DV, Schatt S, Hahn S, Burk M, Holzgrewe W, Dept. of Ob/Gyn, Univ. of Basel, Switzerland

3:15-3:30  17  IN VITRO HEMATOPOIESIS IS INHIBITED IN HUMAN AND NON-HUMAN PRIMATES BY RECOMBINANT PARVO VIRUS CAPSID
Shields LE, Andrews RG, Westgren M, Brolinden K, University of Washington, Seattle, WA and Karolinska Institute, Huddinge, Sweden
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:15-1:30</td>
<td>Oral Concurrent</td>
<td>THE EFFECT OF A CHANGE IN REMUNERATION ON OBSTETRIC INTERVENTION</td>
<td>Bland E., Oppenheimer L., Shi Wu Wen, Division of MFM, University of Ottawa, Laboratory Centre for Disease Control Ottawa, ON, Canada</td>
</tr>
<tr>
<td></td>
<td>Session B</td>
<td>CERVICAL INCOMPETENCE PREVENTION RANDOMIZED CERCLAGE TRIAL, PRELIMINARY RESULTS</td>
<td>Althuisius SM., Dekker GA., van Geijn HP., Bekedam DJ., Hummel P., Depts Ob/Gyn, Free University Hospital, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands</td>
</tr>
<tr>
<td>1:30-1:45</td>
<td></td>
<td>OUTPATIENT MANAGEMENT OF PROLONGED PREGNANCY WITH MISOPROSTOL (MP): A RANDOMIZED DOUBLEBLIND, PLACEBO-CONTROLLED STUDY, PRELIMINARY DATA</td>
<td>Ascher-Walsh C., Burke B., Baxi L., Columbia University, New York Presbyterian Medical Center, NY, NY</td>
</tr>
<tr>
<td>1:45-2:00</td>
<td></td>
<td>DOES EXPOSURE TO ANTENATAL MAGNESIUM SULFATE PREVENT CEREBRAL PALSY?</td>
<td>Mittendorf R., Bents L., Borg M., Roizen N., University of Chicago, Chicago, IL</td>
</tr>
<tr>
<td>2:00-2:15</td>
<td></td>
<td>TIMING OF ANTENATAL STEROIDS AND NEONATAL PULMONARY MECHANICS</td>
<td>Maher J., Collins J., Bowling S., Williamson K., Tolaymat L., McEvoy C., Pensacola, FL</td>
</tr>
<tr>
<td>2:15-2:30</td>
<td></td>
<td>REPEATED ANTENATAL BETAMETHASONE AND PERINATAL OUTCOME</td>
<td>Thorn JA., Yeast JD., Cohen GR., Wickstrom EA., D'Angelo LJ., St. Luke's Hospital of Kansas City, MO</td>
</tr>
<tr>
<td>2:30-2:45</td>
<td></td>
<td>MANAGEMENT OF ISOLATED OLIGOYDRAMNIOS IN THE TERM PREGNANCY: A RANDOMIZED CLINICAL TRIAL</td>
<td>Conway DL., Groth S., Adkins WB., Langer O., Dept. of Ob/Gyn, UTHSCSA, San Antonio, TX</td>
</tr>
<tr>
<td>2:45-3:00</td>
<td></td>
<td>NON-INVASIVE ALTERNATIVE TO CORDOCENTESIS FOR DETECTION OF FETAL ANEMIA - A PROSPECTIVE MULTINATIONAL TRIAL</td>
<td>Mari G., and the Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses: Baylor College of Medicine, Houston, TX, Berne and Zurich, Switzerland, Pennsylvania Hospital, Philadelphia, PA, Riyadh, Saudi Arabia, Santiago, Chile, Univ. of NC, Chapel Hill, NC, Yale University, New Haven, CT, Wayne State, Detroit, MI</td>
</tr>
<tr>
<td>3:00-3:15</td>
<td></td>
<td>UMBILICAL ARTERY END-DIASTOLIC VELOCITY IN INTRAUTERINE GROWTH RESTRICTION - RELATIONSHIP TO HEMATOLOGIC PARAMETERS AT BIRTH</td>
<td>Baschat AA., Reiss J., Gortner L., Weiner CP., Harman CR., Gembruch U., Depts. OB/Gyn, Univ. of Maryland, Baltimore, MD, Pediatrics &amp; Ob/Gyn Med. Univ. Lübeck, Germany</td>
</tr>
</tbody>
</table>

American Journal of Obstetrics and Gynecology January 2000 XVII
Friday, February 4, 2000

Oral Plenary Session II

Moderators: Ronald S. Gibbs, MD
Valerie M. Parisi, MD

8:00-8:15 27 MULTIPLE COURSES OF ANTENATAL STEROIDS ARE ASSOCIATED WITH A DELAY IN LONG-TERM PSYCHOMOTOR DEVELOPMENT IN CHILDREN WITH BIRTH WEIGHTS ≤ 1,500 GRAMS

8:15-8:30 28 NEONATAL SEPSIS AND DEATH AFTER MULTIPLE DOSES OF ANTENATAL BETAMETHASONE

8:30-8:45 29 PLACENTAL APOPTOSIS IN PREECLAMPSIA

8:45-9:00 30 HINDBRAIN HERNIATION DEVELOPS IN SURGICALLY CREATED MYELOMENINGOCLE AND IS PREVENTED BY PRENATAL REPAIR IN FETAL LAMBS

9:00-9:15 31 EVALUATION OF ALLOIMMUNIZATION TO PATERNAL LEUKOCYTES AS A TREATMENT FOR HEMOLYTIC DISEASE OF THE FETUS/NEWBORN IN A RABBIT MODEL

9:15-9:30 32 THE EFFECTS OF CERVICAL APPLICATION OF iNOS, COX-1, AND COX-2 INHIBITORS ON DELIVERY IN RATS

9:30-9:45 33 AMNIOTIC CYCLOOXYGENASE-2 EXPRESSION AND ACTIVITY ARE ENHANCED IN PREGNANCIES COMPLICATED BY PRETERM DELIVERY OF WOMEN WITH TWINS OR POLYHYDRAMNIOS

9:45-10:00 34 MATERNAL AND FETAL GENETIC THROMBOPHILIAS ARE NOT ASSOCIATED WITH SEVERE PREECLAMPSIA

FRIDAY, FEBRUARY 4, 2000

Oral Concurrent Session C

Physiology/Endocrinology
Epidemiology

Moderators: Haywood L. Brown, MD
Kenneth J. Moise, Jr., MD

1:15-1:30 35 GESTATIONAL AGE COMPARISON OF HUMAN UTERINE Ca2+ L-CHANNEL FUNCTION AND SENSITIVITY TO ENDOGENOUS Ca2+ L-CHANNEL INHIBITOR (ECCI)

1:30-1:45 36 CHORION RELEASES A FACTOR THAT INHIBITS OXYTOCIN INDUCED MYOMETRIAL CONTRACTILITY IN PREGNANT GUINEA PIG

1:45-2:00 37 LEPTIN TREATMENT PREVENTS GESTATIONAL DIABETES IN HETEROZYGOUS C57BL/KSJ LEPTIN RECEPTOR (DBA/+) MICE

Grand Ballroom East
INCREASED EXPRESSION OF HEAT SHOCK PROTEIN 70 IN HUMAN DECIDUA WITH ADVANCING GESTATION MAY REGULATE GLUCOCORTICOID ACTION IN THIS TISSUE

THROMBIN: THE UTEROTONIN RESPONSIBLE FOR THE INCREASED MYOMETRIAL CONTRACTIONS OBSERVED WITH INTRAUTERINE BLEEDING

ELVATED NUCLEATED RED BLOOD CELLS DIFFERENTIATE THE PATHOLOGICALLY GROWTH RESTRICTED FETUS FROM THE HEALTHY BUT SMALL FOR GESTATIONAL AGE FETUS

CEREBRAL PALSY IN PRETERM INFANTS: A POPULATION BASED ANALYSIS OF ANTENATAL RISK FACTORS

MAGNESIUM PREVENTS SEIZURE INDUCED REDUCTION IN EXCITATORY AMINO ACID RECEPTOR (NON-NMDA) BINDING IN PREGNANT RAT BRAIN

SEVERE PLACENTAL INSUFFICIENCY AND A RISE IN SYSTEMIC VENOUS PRESSURE IN THE FETUS ARE ASSOCIATED WITH INCREASED CARDIAC TROPOIN-T LEVELS IN NEWBORNS

Friday, February 4, 2000

1:15 p.m. to 3:30 p.m. Oral Concurrent Session D

Prematurity

Moderators: Susan M. Cox, MD
Katharine D. Wenstrom, MD

Fontainebleau Ballroom C/D

1:15-1:30 44 VAGINAL FETAL FIBRONECTIN (V-fFN) LEVELS AT 8-22 WEEKS AND SUBSEQUENT SPONTANEOUS PRETERM BIRTH (SPB)

Goldenberg RL, for the NICHD MFMU Network, Bethesda, MD

1:30-1:45 45 MID-TRIMESTER THRESHOLD VAGINAL pH AND GRAM STAIN SCORES PREDICTIVE OF SUBSEQUENT PRETERM BIRTH

Hauth JC, for the NICHD MFMU Network, Bethesda, MD

1:45-2:00 46 REASSESSING THE RELATIONSHIP BETWEEN CERVICAL DIMENSIONS AND PRETERM DELIVERY

Gustilo-Ashby T, Hartman K, Thorp J, Savitz D, McDonald T, Depts. Public Health & Ob/Gyn, Univ. of North Carolina, Chapel Hill, NC

2:00-2:15 47 SELF-PERCEIVED SYMPTOMS TO PREDICT PRETERM BIRTH

Jams ID, for the NICHD MFMU Network, Bethesda, MD

2:15-2:30 48 EFFECTIVENESS OF ANTENATAL BETAMETHASONE AFTER PRETERM PREMATURITY RUPTURE OF THE MEMBRANES

Vermillion S, Soper D, Bland M, Newman R, Dept. of Ob/Gyn, Medical Univ. of SC, Charleston, SC

2:30-2:45 49 SECOND TRIMESTER MATERNAL SERUM INTERLEUKIN-6 IN PATIENTS WHO DELIVER EXTREMELY PRETERM

Skinner V, Greig P, Nichols K, Blackhurst D, Stewart K, Johnson B, Dept. of Ob/Gyn, Greenville Memorial Hospital, Greenville, SC, Greenwood Genetics Center, Greenwood, SC, R&D Systems, Minneapolis, MN

2:45-3:00 50 INTERLEUKIN-6 DETERMINATIONS IN CERVICAL FLUID HAVE DIAGNOSTIC AND PROGNOSTIC VALUE IN PRETERM PREMATURITY RUPTURE OF THE MEMBRANES

Yoon BH, Romero R, Kim MH, Park JS, Ki SH, Kim T, Kim GJ, Dept. of Ob/Gyn, Seoul National University College of Medicine, Seoul, Korea
FURTHER OBSERVATIONS ON THE FETAL INFLAMMATORY RESPONSE SYNDROME: A POTENTIAL HOMEOSTATIC ROLE OF THE SOLUBLE RECEPTORS OF TUMOR NECROSIS FACTOR

USE OF ANTENATAL MAGNESIUM SULFATE DOES NOT SEEM TO PREVENT INTRAVENTRICULAR HEMORRHAGE

Saturday, February 5, 2000

8:00 a.m. to 10:00 a.m.

Oral Concurrent Session E

Fontainebleau Ballroom C

Moderators: Michael P. Nageotte, MD
Susan M. Ramin, MD

8:00-8:15 53 PREDICTION OF PARTURITION IN HUMANS USING TRANSABDOMINAL UTERINE ELECTROMYOGRAPHIC ACTIVITY RECORDING

Garfield R, Maner W, Martin E, Saade G, Dept. of Ob/Gyn, The Univ. of Texas Medical Branch, Galveston, TX

8:15-8:30 54 EVIDENCE FOR INCREASED ACTIVITY OF A POTENT MATRIX DEGRADING ENZYME IN PRETERM AND TERM LABOR


8:30-8:45 55 THE OPTIMISATION OF INTRAVAGINAL MISOPROSTOL DOSING IN SECOND-TRIMESTER PREGNANCY TERMINATION

Dickenson JE, Evans SF, University of Western Australia and The Women and Infants Research Foundation, King Edward Memorial Hospital, Perth, Western Australia

8:45-9:00 56 FOLEY BULB FOR PREINDUCTION CERVICAL RIPENING IN THE OUTPATIENT VERSUS THE INPATIENT SETTING


9:00-9:15 57 A RANDOMIZED TRIAL ON THE INFLUENCE OF INCREASED INTRAVENOUS HYDRATION ON THE COURSE OF NULLIPAROUS LABOR

Garite TJ, Weeks J, Peters-Phair K, University of California, Irvine, Orange, CA

9:15-9:30 58 COMPARISON OF IMMEDIATE AND DELAYED PUSHING IN SECOND STAGE OF LABOR ON ANAL SPINCHTER INTEGRITY AND MODE OF DELIVERY

Fitzpatrick M, O'Brien C, McQuillan K, O'Connell PR, O'Herlihy C, Dept. of Obstetrics, National Maternity Hospital and Univ. College Dublin, Ireland

9:30-9:45 59 MATHEMATICAL MODELING OF FORCES ASSOCIATED WITH SHOULDER DYSTOCIA: A COMPARISON OF ENDOGENOUS AND EXOGENOUS SOURCES

Gonik B, Walker A, Grimm M, Depts. of Ob/Gyn and Mech Eng., Wayne State Univ., Detroit, MI

9:45-10:00 60 A RANDOMIZED CONTROLLED TRIAL OF PRIMARY REPAIR OF THIRD DEGREE PERINEAL TEARS, COMPARING OVERLAP AND APPROXIMATION TECHNIQUES

Fitzpatrick M, Behan M, O'Connell PR, O'Herlihy C, Depts. of Obstetrics, Surgery and Radiology, National Maternity Hospital and Univ. College, Dublin, Ireland
Saturday, February 5, 2000

Oral Concurrent Session F

Fontainebleau Ballroom D

Medical/Surgical Complications
Infectious Diseases

Moderators: James T. Christmas, MD
Jay D. Iams, MD

8:00-8:15

THE CLINICAL IMPLICATIONS OF DETECTING UREAPLASMA UREALYTICUM FROM THE AMNIOTIC CAVITY WITH THE POLYMERASE CHAIN REACTION


8:15-8:30

COST-EFFECTIVENESS OF A RECOMMENDATION FOR ELECTIVE CESAREAN SECTION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTED PREGNANT WOMEN ON ZIDOVUDINE THERAPY TO REDUCE VERTICAL TRANSMISSION

Chen KT, Tuomala RE, Sell RL., Dept. of Ob/Gyn, Brigham and Women’s Hospital, Boston, MA and Div. of Sociomedical Sciences, Columbia School of Public Health, New York, NY

8:30-8:45

HEPARIN USE IN PREGNANCY FOR WOMEN WITH A HISTORY OF VENOUS THROMBOEMBOLISM: A DECISION ANALYSIS

Walker M, Ta M, Detsky A, Univ. of Toronto, Mount Sinai Hospital, Toronto, ON, Canada

8:45-9:00

MECHANISMS OF CELLULAR INSULIN RESISTANCE IN ADIPOCYTES DURING LATE HUMAN PREGNANCY


9:00-9:15

EFFECTS OF L-NAME (A NITRIC OXIDE INHIBITOR) ON GROWTH AND FERTILITY IN 2ND-GENERATION RATS

Witten A, Gangula PR, Yallampalli C, Dept. of Ob/Gyn, Univ. of Texas Medical Branch at Galveston, Galveston, TX

9:15-9:30

INTERLEUKIN-10 ADMINISTRATION PREVENTS INFECTION MEDIATED PRETERM BIRTH IN A RAT MODEL

Terrone DA, Rinehart BK, Barrilleaux PS, Martin JN Jr., Granger JP, Bennett WA, Dept. of Ob/Gyn, Univ. of Mississippi Medical Center, Jackson, MS

9:30-9:45

LIPOPOLYSACCHARIDE INDUCED CERVICAL RIPENING IN PREGNANT RATS IS PREVENTED BY NITRIC OXIDE INHIBITION

Shi L, Shi SQ, Saade G, Garfield R, Dept. of Ob/Gyn, The Univ. of Texas Medical Branch, Galveston, TX

9:45-10:00

PLASMA LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND PLACENTAL GROWTH FACTOR ARE REDUCED IN WOMEN WITH SEVERE PREECLAMPSIA

Livingston JC, Chin R, McKinney ET, Haddad BR, Sibai BM, Dept. of Ob/Gyn, Univ. of Tennessee, Memphis, TN
ORAL PLENARY SESSION I

Thursday, February 3, 2000
8:00 am - 10:00 am

Moderators: Mary E. D’Alton, MD
Immediate Past
President, SMFM

J. Peter VanDorsten, MD
President, SMFM

Judges: Patrick M. Catalano, MD
Sarah J. Kilpatrick, MD
Philip Samuels, MD

Grand Ballroom East
Abstract Numbers 1-8
A MULTICENTER RANDOMIZED TRIAL OF FETAL PULSE OXIMETRY.


OBJECTIVE: Intrapartum fetal oxygen saturation (FSpO2) monitoring has the potential to overcome some of the disadvantages of electronic fetal monitoring (EFM). A prospective randomized clinical trial was conducted in 9 centers to test the hypothesis that the addition of FSpO2 monitoring to EFM lowers the cesarean (CS) rate for non-reassuring fetal status (NRFS), without adversely affecting neonatal outcome.

STUDY DESIGN: Term patients who developed pre-defined abnormal EFM patterns were randomized to receive either EFM alone (Control Group = CG) or EFM plus FSpO2 monitoring (Study Group = SG). In the CG, intervention by CS for NRFS was for defined abnormal EFM patterns, and in the SG intervention was for abnormal EFM plus with an FSpO2 < 50% for the entire interval between two contractions. Sample size provided adequate power to show a 50% reduction in CS for NRFS. All comparisons were for intent to treat.

RESULTS: 1019 patients were randomized, 502 in the CG and 508 in the SG. Pre-randomization variables were similar except for a higher rate of labor induction in the SG (56% vs 49%; P = 0.05). There was a > 50% reduction in CS for NRFS in the SG (4.5% vs 10.2%; OR = 0.42, 95% CI = 0.24 - 0.72, P < 0.001), however, there was a higher CS rate for dystocia in the SG (18.5% vs 8.6%; OR = 2.15, 95% CI = 1.6 - 2.4, P < 0.001) resulting in no overall difference in CS rate. Purtogram analysis confirmed similar rates of arrested labors with CS for dystocia in both groups. Analysis of CS for NRFS revealed statistically significant higher sensitivities and specificities in the CG for endpoints of low 1-minute (< 4) and 5-minute (< 7) Apgar scores, low umbilical artery pH (< 7.15, < 7.10, or < 7.05), low base excess (< -12 mEq/L), NICU admissions and neonatal resuscitation. There were no overall differences in neonatal outcomes between the two groups.

CONCLUSIONS: The addition of fetal pulse oximetry to EFM in patients with abnormal EFM patterns resulted in a > 50% reduction in CS for NRFS with no increase in adverse neonatal outcome. The use of fetal pulse oximetry also improved the sensitivity and specificity of intervention by CS for dystocia and acidotic newborns. An unexplained increase in CS for dystocia offset the reduction in CS for NRFS, resulting in no overall reduction in CS. Nonetheless this new modality shows great promise for improving our ability to more accurately assess fetal status and intervene more appropriately for the fetus truly in distress.

TOWARD A MULTIPLE MARKER TEST FOR SPONTANEOUS PRETERM BIRTH (SPB).

Richard Goldberg for the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: The NICHD MFMU Preterm Prediction Study evaluated 30 potential biologic markers for SPB in asymptomatic women at 24 weeks GA. This analysis compares those markers singly and in combination for association with SPB <32 and <35 GA.

STUDY DESIGN: Using a nested-case-control design from an original cohort study of 2929 women, results of tests from 45 women with a SPB <32 wk, and 113 women with a SPB of <35 wks were compared to results from matched term controls.

RESULTS: In the univariate analysis, the most potent markers associated with SPB <32 wks by odds ratio (OR) were cervical-vascular fetal fibronectin (fFN) (OR 32.7) and short cervical length (OR 5.8), and in plasma, α-fetoprotein (αFP) (OR 8.3), alkaline phosphatase (AP) (OR 6.8), and granulocyte colony stimulating factor (GCSF) (OR 5.5). Results for SPB <35 wks were generally similar but not as strong. Univariate and multivariate regression analyses demonstrated little interaction among the tests in their association with SPB. Adjusting for fFN and Cx length did not substantially reduce the association of αFP, AP, and GCSF with SPB. Combinations of the 5 markers evaluated for their association with SPB <32 wk had at least one positive test vs 15/45 (33%) controls (OR 16.0 (5.2-48.9)). Among the cases, 28/45 (62%) had 2 or more positive tests vs 2/45 (4.4%) controls (OR 35.4 (7.6-160)). If a cutoff of 5 positive tests was used, 11/45 (24%) cases and 0/45 controls were positive (p=0.007). A positive fFN or short Cx identified 24/45 (53%) cases vs. 6/45 (13%) controls (OR 7.4 (2.6-21.0)). Using only the 3 plasma tests, AP, αFP and GCSF, any positive test identified 34/45 (76%) cases vs 10/45 (22%) controls (OR 10.8 (4.1-28.8)). For SPB <35 wks, any 2 positive tests identified 48/113 (43%) cases vs 7/113 (6%) controls (OR 11.2 (4.8-26.2)).

CONCLUSION: Overlap among the strongest biologic markers for SPB is small suggesting that adding tests such as maternal plasma αFP, AP, and GCSF to fFN and cervical length may enhance our ability to predict SPB, and that developing a multiple marker test for SPB is feasible. In fact, the combination of the 3 maternal plasma tests may outperform fFN and cervical length for predicting SPB <32 wks. The predictive value of a multiple marker test will need to be tested in a prospective cohort study.

MULTICENTER RANDOMIZED TRIAL OF SINGLE VERSUS WEEKLY COURSES OF ANTENATAL CORTICOSTEROIDS (ACS): INTERIM ANALYSIS. Gauthier DA and BMZ study group. Loyola Univ., Maywood IL.

OBJECTIVE: To compare rates of neonatal morbidities in women exposed to a single course versus weekly courses of ACS.

STUDY DESIGN: After their first course of standard ACS therapy, women at high-risk for preterm delivery between 24 0/7-31 6/7 weeks' gestation, were randomly assigned to receive Betamethasone (12 mg IM q 24 hr x 2) or placebo injections weekly until 34 0/7 weeks. The primary outcome measure was the rate of composite morbidity (any of; severe RDS, BPD, severe (grade III or IV) IVH, PVL, proven sepsis, NEC, neonatal death). Latency was defined as the time from the first course of ACS to delivery. The primary analysis was based on intent to treat.

RESULTS: From 3/96 to 12/98, 308 women were enrolled in 12 centers. Indications for receiving ACS were PTL (n=174), PPROM (n=71), maternal (n=47) and fetal (n=16) complications. The blinded results of this interim analysis are presented as mean ± SD, or % in the Table.

<table>
<thead>
<tr>
<th>Group A (N=161)</th>
<th>Group B (N=147)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA randomization (wk)</td>
<td>29.2±2.8</td>
<td>28.8±3.5</td>
</tr>
<tr>
<td>Latency interval (wk)</td>
<td>4.5±3.6</td>
<td>6.0±6.2</td>
</tr>
<tr>
<td>GA delivery (wk)</td>
<td>32.4±1.4</td>
<td>33.5±4.8</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>1945±552</td>
<td>2157±867</td>
</tr>
<tr>
<td>Composite Morbidity (%)</td>
<td>26.7</td>
<td>27.3</td>
</tr>
</tbody>
</table>

There were no significant differences between groups in the rates of severe RDS, BPD, proven sepsis, NEC, or neonatal death. Group A had a shorter latency period and a trend toward higher rates of severe IVH (6 versus 1, p=0.08) and PVL (5 versus 0, p=0.08). If the current trend continues, this study will be terminated with delivery of the 500th patient in October 1999.

CONCLUSION: Weekly doses of ACS apparently do not reduce composite neonatal morbidity.

PRETERM DELIVERY AND MATERNAL INTERLEUKIN-I POLYMORPHISMS. AP Marthai1, WNP Herbert1, S. Lieff2, K. Kornman3, C. Knobelman2, K. Stephenson3, GW DuPP, and S. Offenberg4x.

The purpose of this investigation was to determine whether maternal polymorphisms, within the IL-1 gene cluster are associated with an increased risk for preterm delivery.

STUDY DESIGN: Oral Conditions and Pregnancy (OCAP) is a prospective study to examine the role of oral and vaginal infection and maternal cytokine responses on prematurity. Genotyping for the four IL-1 gene polymorphisms has been completed on the first 60 subjects. Prevalence of the various genotypic patterns for each locus was determined on this initial group of subjects. The purpose of this investigation was to determine whether maternal polymorphisms, within the IL-1 gene cluster are associated with an increased risk for preterm delivery.

RESULTS: Among Caucasians, there was no pattern of IL-1 gene cluster within functional variants of IL-1 bioactivity include IL-1A(+4845), IL-1B(+3954), IL-1B(-511) and IL-1RN(+2018). The purpose of this investigation was to determine whether maternal polymorphisms, within the IL-1 gene cluster are associated with an increased risk for preterm delivery.

OBJECTIVE: The NICHD MFMU Preterm Prediction Study evaluated 30 potential biologic markers for SPB in asymptomatic women at 24 wks GA. This analysis compares those markers singly and in combination for association with SPB <32 and <35 GA.

RESULTS: Among Caucasians, there was no pattern of IL-1 gene cluster within functional variants of IL-1 bioactivity include IL-1A(+4845), IL-1B(+3954), IL-1B(-511) and IL-1RN(+2018). The purpose of this investigation was to determine whether maternal polymorphisms, within the IL-1 gene cluster are associated with an increased risk for preterm delivery.

CONCLUSION: There were no significant differences between groups in the rates of severe RDS, BPD, proven sepsis, NEC, or neonatal death. Group A had a shorter latency period and a trend toward higher rates of severe IVH (6 versus 1, p=0.08) and PVL (5 versus 0, p=0.08). If the current trend continues, this study will be terminated with delivery of the 500th patient in October 1999.

CONCLUSION: Weekly doses of ACS apparently do not reduce composite neonatal morbidity.
METRONIDAZOLE TREATMENT INCREASED THE RISK OF PRETERM BIRTH IN ASYMPTOMATIC WOMEN WITH TRICHOMONAS.

J.C. Carey*, M. Kirkland+ for the NICHD MFMU Network, Bethesda MD.

OBJECTIVE: To determine whether treatment of asymptomatic pregnant women with Trichomonas vaginalis (TV) reduces preterm births (PTB).

STUDY DESIGN: In this multicenter, double-blind, placebo-controlled trial, women with positive TV culture were randomized at 16-23 weeks to metronidazole (ME, n=320) or placebo (PL, n=297). Women took 2 grams of ME or PL in the clinic and were given another dose to take 48 hours later. Sex partners were prescribed ME. The regimen was repeated at 24-29 weeks. The primary outcome was PTB (<37 weeks); other outcomes included PTB after preterm labor (PTL), PTB after preterm PROM (PPROM), birth <32 weeks, birth wt <2500 grams and <1500 grams.

RESULTS: The two groups did not differ significantly on baseline characteristics. Outcomes were present for 604 (92.7%) women, 315 ME and 289 PL. The occurrence of adverse outcomes is shown in the table.

<table>
<thead>
<tr>
<th></th>
<th>METRO</th>
<th>PLACEBO</th>
<th>RR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PTB</td>
<td>19.0%</td>
<td>10.7%</td>
<td>1.78</td>
<td>1.19-2.66</td>
</tr>
<tr>
<td>PTB-PTL</td>
<td>10.0%</td>
<td>5.5%</td>
<td>1.97</td>
<td>1.43-2.75</td>
</tr>
<tr>
<td>PTB-PPROM</td>
<td>4.5%</td>
<td>2.1%</td>
<td>2.08</td>
<td>0.51-2.30</td>
</tr>
<tr>
<td>Birth &lt;32 weeks</td>
<td>5.1%</td>
<td>5.8%</td>
<td>0.93</td>
<td>0.63-1.35</td>
</tr>
<tr>
<td>&lt;2500 grams</td>
<td>11.5%</td>
<td>11.9%</td>
<td>0.98</td>
<td>0.92-1.07</td>
</tr>
<tr>
<td>&lt;1500 grams</td>
<td>5.5%</td>
<td>5.8%</td>
<td>0.93</td>
<td>0.65-1.49</td>
</tr>
</tbody>
</table>

The risk of PTB in the ME group was elevated among women with a prior PTB (RR=1.99, 0.93-3.88); women who had both bacterial vaginosis and TV (RR=1.86, 1.32-2.62); women who had vaginal meconium in the meconium (ME=1.79, 1.12-2.85); and more compliant women (RR=1.81, 1.13-2.92). At 24-29 weeks, TV persisted in 66% of the PL and 70% of the ME groups.

CONCLUSION: In asymptomatic women with TV, ME treatment increased the risk of PTB. Routine screening and treatment of asymptomatic pregnant women with TV cannot be recommended.

A RANDOMIZED TRIAL OF CERCLAGE VS NO CERCLAGE IN PATIENTS WITH SONOGRAPHICALLY DETECTED 2ND TRIMESTER PREMATURE DILATION OF THE INTERNAL OS

OBJECTIVE: To compare the perinatal outcome of patients with sonographic evidence of premature dilation of the internal os (funnelling) in 2nd trimester pregnancies treated with cervical cerclage to those without cerclage.

STUDY DESIGN: From May 1998 to June 1999 patients with ultrasound evidence of funnelling between 16-24 wk were randomly assigned to receive a McDonald cerclage or expectant management. Prior to randomization, all patients received 48 hr of indocin (100 mg po, then 50 mg po Qd) and antibiotic (clindamycin 900 mg IV Qhr) therapy. All patients received an aminocentesis and multiple urogenital cultures to rule out active infection. After 48-72 hr of hospitalization, each patient had indocin and antibiotic therapy discontinued then was treated as an outpatient with modified bed rest at home and weekly sonographic evaluation of the lower uterine segment. A rescue cerclage procedure was offered to any patients <24 weeks that had membranes prolapsed past the external os. Any cerclage was removed with PFROM, PTL, unresponsive to tocolysis, or at 36 wk gestation.

RESULTS: Of the 61 patients, 51 randomized to cerclage and 30 randomized to no cerclage. The results are summarized in the following table:

<table>
<thead>
<tr>
<th>Cerclage (n = 51)</th>
<th>No Cerclage (n = 30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (wk)</td>
<td>20.2 + 2.1 21.2 + 2.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Funnell Width (cm)</td>
<td>1.5 + 0.7 1.6 + 0.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Funnell Depth (cm)</td>
<td>1.9 + 1.3 1.7 + 1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Distal Cx (cm)</td>
<td>2.1 + 1.1 2.1 + 1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Gest at Del (wk)</td>
<td>35.5 + 6.3 34.7 + 4.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Delivery &lt;40 wk</td>
<td>38.7 30.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Delivery &lt;28 wk</td>
<td>22.6 13.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Perinatal Death (%)</td>
<td>14.1 11.4</td>
<td>0.9</td>
</tr>
</tbody>
</table>

CONCLUSION: The treatment of 2nd trimester premature dilation of the cervix with McDonald cerclage does not improve perinatal outcome.
ORAL CONCURRENT SESSION A

Fetus
Ultrasound

Thursday, February 3, 2000
1:15 pm - 3:30 pm

Moderators: Lindsey Allan, MD, 2000 Honorary Member
Ronald J. Wapner, MD

Judges: Barbara V. Parilla, MD
Richard K. Silver, MD
Jerome Yankowitz, MD

Grand Ballroom East
Abstract Numbers 9-17
HEAD CIRCUMFERENCE AND VENTRICULAR SIZE FOLLOWING IN UTERO CLOSURE OF MYELOMENINGOCELE. DS Waldt, MF Johnson, M. King, AW Flake, TM Cromptonholm, LN Sutton, M. Bar, Jr, NS Adzick. Center for Fetal Diagnosis and Treatment, Children’s Hosp. of Philadelphia and Univ of Mich., Philadelphia, PA and Ann Arbor, MI.

OBJECTIVE: Previous reports on prenatal brain development in myelomeningocele (MMC) have demonstrated progressive ventriculomegaly with disproportionately small head circumference (HC) measurements. The purpose of this study is to assess the impact of fetal MMC repair on HC and ventricular diameter (VD).

STUDY DESIGN: Nineteen MMC fetuses underwent MMC closure at 22-25 weeks gestation and remained in utero for at least 30 days postoperatively. Serial sonograms with measurements of HC and lateral VD were performed in the pre- and postoperative period by two experienced examiners HC measurements were compared to a group of age-matched normal fetuses HC percentile was plotted on normograms established by Hadlock. VD was taken as the average of the left and right atria. Cystic index (CI) at each time point was calculated as HC divided by the average VD.

RESULTS: Preoperatively, all patients had HC below the 50th%, with 4 of 9 (44%) below the 2.5th%. Postoperatively gestational day 30, 7 of 9 (78%) had HC above the 50th%. Average increase in HC was 25.3% for the MMC group and 17% for the normals. The increase in HC was significantly more than the increase in VD (p<0.0001). Mean VD preoperatively was 10.3mm (range 7-14mm) and postoperatively 12.3mm (range 7.5-18.5mm), with an average increase of 2.2mm (range 0.3 to 4.7 mm). Average increase in CI was 10.3%. This was not significantly different than the change in CI for normal fetuses.

CONCLUSION: HC measurements increase significantly following fetal closure of MMC. This contrasts with the persistently small HC measurements previously reported in fetal MMC. While VD increases modestly following fetal repair, CI increases much like normal fetuses. Previous reports demonstrate no increase in CI in untreated MMC fetuses. Thus, the increase in HC and CI are not solely due to ventriculomegaly. Rather, head growth following MMC repair is at least partly due to brain growth. Midgestational closure alters the natural history of fetal head growth in MMC.


OBJECTIVE: To investigate prenatal growth and maturation after tracheal occlusion (TO) performed at different gestational ages, using a fetal rabbit model of congenital diaphragmatic hernia (CDH).

STUDY DESIGN: In 36 fetal rabbits, CDH was created at 23 out of 31 days gestation, i.e., in the pseudoglandular phase of lung development. TO was performed on 6 fetuses at either 26 (during the canalicular phase of lung development) or 28 (saccular phase) days (CDH+TO). Controls were either 6 fetuses that underwent a sham operation (+CDH+sham), or 6 non-operated littersmates (CTR). All were delivered by cesarean section at 30 days to assess fetal response by lung-to-body-weight ratio (LBWR), morphometric measures such as mean terminal bronchial density (MTBD) and linear intercept (Lm), and density of type II pneumocytes using immunohistochemistry to identify surfactant protein-A. Statistics were done with ANOVA for multiple comparison (Tukey’s test).

RESULTS: Table; *<0.01 compared to normal controls (CTR).

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Intervention (n=6 per group)</th>
<th>Lung-Body Weight-Ratio</th>
<th>Mean Terminal Bronchial Density</th>
<th>Linear Intercept</th>
<th>Density of type II pneumocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 days</td>
<td>CDH+TO</td>
<td>0.055±0.04*</td>
<td>0.92±2.10</td>
<td>10.7±9.9</td>
<td>120.5±24.6*</td>
</tr>
<tr>
<td></td>
<td>CDH+sham</td>
<td>0.015±0.03*</td>
<td>1.81±25*</td>
<td>107.9±11.3</td>
<td>137.0±38.3*</td>
</tr>
<tr>
<td></td>
<td>CTR</td>
<td>0.034±0.05</td>
<td>0.91±13</td>
<td>100.6±13</td>
<td>239.0±64.5</td>
</tr>
<tr>
<td>28 days</td>
<td>CDH+TO</td>
<td>0.030±0.08*</td>
<td>0.88±24</td>
<td>93.8±6.3</td>
<td>216.4±40.8</td>
</tr>
<tr>
<td></td>
<td>CDH+sham</td>
<td>0.015±0.03*</td>
<td>1.79±34*</td>
<td>100.6±1</td>
<td>149.4±20.10</td>
</tr>
<tr>
<td></td>
<td>CTR</td>
<td>0.026±0.06</td>
<td>0.91±9.1</td>
<td>98.7±5.8</td>
<td>208.1±29.3</td>
</tr>
</tbody>
</table>

CONCLUSION: The exact time point when TO is carried out throughout gestation is critical to the pulmonary effects. In a rabbit model of CDH, delaying TO till 28 days of GA achieves normal lung growth, normal morphometry and density of type II pneumocytes, in contrast to earlier TO, which causes pulmonary overgrowth and type II pneumocyte depletion.

TREATMENT OF SEVERE CONGENITAL DIAPHRAGMATIC HERNIA BY FETAL TRACHEAL OCCLUSION: CLINICAL EXPERIENCE WITH FIFTEEN CASES. AW Flake, TM Cromptonholm, MF Johnson, L. Howell, and NS Adzick. The Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia, Philadelphia, PA.

OBJECTIVE: To determine if prenatal tracheal occlusion (TO) improves survival, relative to standard postnatal treatment, in a selected population of fetuses effected by severe Congenital Diaphragmatic Hernia (CDH).

STUDY DESIGN: Fetuses with isolated CDH were selected as candidates for fetal intervention by specific criteria designed to predict a 10% survival with conventional postnatal treatment including extracorporeal membrane oxygenation (ECMO). Eligible patients were offered TO as one option for treatment during non-directive counseling. The TO procedure was performed via maternal hysterotomy at 27-28 weeks gestation in the first 9 patients and at 25-26 weeks gestation in the last 6 patients in the series. Postoperative care and tocolysis were standardized throughout the study. Delivery was performed by the EXIT procedure for controlled establishment of the airway.

RESULTS: Fifteen fetuses underwent TO with 5 survivors (33%). Two fetuses were lost to early preterm labor, 2 days and 5 days following the TO procedure. Of the remaining 13 mothers, postoperative gestation ranged from 19 days to 98 days with a mean duration of pregnancy following TO of 28 days and a mean gestational age at delivery of 32 weeks. The 5 survivors were hospitalized from 37 days to 145 days with an average length of stay of 76 days. One survivor required ECMO for salvage. Lung growth after tracheal occlusion was documented by serial ultrasound and MRI assessment and was more consistent after TO performed at 25-26 weeks gestation. Despite dramatic lung growth in some fetuses after TO, intensive ventilatory management was uniformly required, and most deaths were due to respiratory insufficiency or its secondary consequences.

CONCLUSION: Prenatal TO can result in impressive lung growth in a subset of fetuses with severe CDH. However, survival remains compromised by pulmonary function and the consequences of prematurity.


OBJECTIVE: Predictive survival in congenital diaphragmatic hernia (CDH) remains difficult. We evaluated the utility of fetal magnetic resonance imaging (MRI) in predicting outcomes following ultrasound diagnosis of left-sided CDH.

STUDY DESIGN: From March 1996-July 1999 69 pregnant women carrying fetuses with CDH underwent MRI scans. Patients were excluded from consideration for right CDH=3, bilateral CDH=1, absence of the ventral chest wall=1, elective termination=8, treatment with fetal tracheal occlusion=13, no follow-up=1 and poor quality scans=1. Two patients were scanned at two different gestational ages yielding 43 scans for inclusion. Images were obtained with a 1.5 Tesla magnet on a half-fourier single shot turbo spin-echo (HASTE) sequence. Lung volumes (LV) were calculated by summing the volumes on 6mm axial sections through the chest. A LV to gestational age (GA) ratio was obtained using LV/GA. The presence or absence of liver herniation into the left chest was noted. The left liver diaphragm (LD) ratio was obtained using the distances from the superior aspect of the liver to the apex of the left chest and left liver diaphragm. Statistical analysis was performed with either Student’s t-test or chi square test.

RESULTS: Mean GA was 26 weeks (range 20-39). Overall survival was 61%. Neither absolute right, left, or total LV nor the LV:GA ratio were predictive of outcome. The presence of liver herniation into the left chest was predictive of outcome at p<0.05. Survival with liver down was 75% while survival with liver up was 41%. The LD ratio was also predictive of outcome at p<0.04.

CONCLUSION: Fetal MRI permits calculation of LV, but the absolute volumes are not predictive of outcome. However, both the presence of liver herniation and the ratio of liver in the chest as expressed by the LD ratio help predict outcome in left-sided CDH.
**THE DOPLER ASSESSMENT IN MULTIPLE PREGNANCY STUDY (DAMP) AND METAANALYSIS OF DOPPLER AND TWINS.** W Gite, A. Barts1, S. O’Callaghan1. Discipline of Reproductive Medicine, University of Newcastle, Australia

**OBJECTIVE:** To assess the impact on fetal death in utero of the introduction of umbilical artery Doppler ultrasound waveform analysis in the management of twin pregnancies.

**STUDY DESIGN:** This was a prospective, multicentre, randomised controlled trial (RCT). 526 women with twin pregnancies were randomised to either standard ultrasound imaging (N=262) or without umbilical artery Doppler waveform studies (N=264) at 25, 30 and 35 weeks gestation in fetal medicine units in Australia, New Zealand, Singapore and Malaysia. Women were randomised at 25 weeks gestation and had repeat studies at 30 and 35 weeks gestation if otherwise indicated. Interventions were considered abnormal if abnormal umbilical artery Doppler or biometry results were found. Results were analysed by non-parametric testing for continuous outcomes and Odds Ratios for categorical outcomes.

**RESULTS:** The two groups were demographically equal. There were 3 unexplained stillbirths in the control group and none in the Doppler group (2 stillbirths in the Doppler group were due to a cord prolapse in labour and a fetomaternal haemorrhage both very unlikely to be influenced by Doppler surveillance) this gave an Odds Ratio of 0.14 (95% CI 0.01 to 1.31). Otherwise there were no significant differences between the two groups with respect to antenatal, peripartum and neonatal outcomes. Metaanalysis of two other RCTs of the use of Doppler in high risk pregnancies shows a significant reduction in unexplained fetal death in utero (Odds Ratio 0.15, 95% CI 0.03 to 0.63).

**CONCLUSION:** Close surveillance of twin pregnancies in the latter part of pregnancy from 25 weeks is associated with lower fetal mortality. The addition of Doppler ultrasound improves this outcome. Firsty assessment of these results shows that to prevent 1 fetal death in utero 48 (25-500) twin pregnancies need to be studied with Doppler surveillance. Secondly uncomplicated twin pregnancies do not need to be studied more frequently than every 5th week from 25 weeks gestation.

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**PREVENTION OF FETAL DEATH WITH NOVEL PEPTIDES IN FETAL ALCOHOL SYNDROME.** CY Speng, DT Abebe, I Gozes, DE Brenneman, JM Hiji, SDMP, NICHD, NIH, Bethesda MD and Sackler School of Med, Tel Aviv Univ, Tel Aviv, Israel

**OBJECTIVE:** An increase in free radical formation has been implicated in the pathogenesis of alcohol-induced dysfunction in fetal alcohol syndrome (FAS). Two peptides (NAPPSIPQ and SALLRS1PA) with anti-oxidative properties, derived from proteins related to vasoactive intestinal peptide (a known embryonic growth regulator) were tested for their ability to prevent FAS.

**STUDY DESIGN:** In a well-characterized FAS mouse model, peptides were given either pre or post alcohol on gestational day 8. Litter size, viability, and fetal weights were obtained on day 18. To understand the mechanism of peptide action, glutathione levels [conversion of GSH (reduced) to GSSG (oxidized)] was widely recognized as a reliable index of oxidative stress] were simultaneously determined and quantitated with capillary electrophoresis in the embryo 8h after treatment. Radioencoded peptide was administered and analyzed chromatographically on a size exclusion column at gestational day 8 to determine if intact peptide is present in the embryo.

**RESULTS:** The fetal demise rate was higher in the alcohol (n=35, 35%) than control (n=30, 4%, P<0.001). Peptide treatment reduced the demise rate to control (n=19, 10%, P=4). Peptide treatment also prevented the alcohol-induced fetal pup and brain weight reduction (P<0.05).

**CONCLUSIONS:** These peptides prevented fetal demise and growth abnormalities in FAS, a model for conditions of severe oxidative stress. Thus, these peptides may be of therapeutic value in the treatment of conditions due to oxidative stress.

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**THE TEMPORAL SEQUENCE OF CHANGES IN FETAL VELOCIMETRY INDICES FOR GROWTH RESTRICTED FETUSES.** E Ferrazz, M Belloti, M Bocca, S Rigan, G Pardis, F Battaglia, H Galan. Deps. Ob/Gyn at DCMO San Paolo Univ, Milan, and SUCS/DU as Denver, CO.

**OBJECTIVE:** To describe the temporal sequence of Doppler velocimetry changes in peripheral and central vessels of the intrauterine growth restricted (IUGR) fetus.

**STUDY DESIGN:** The series includes 34 IUGR fetuses delivered between 27-35 weeks gestation with longitudinal Doppler observations starting 21 days prior to delivery. Timing of delivery was based on non-Doppler clinical information. The following fetal vessels were scored as normal or abnormal: PI >2sd, absent end-diastolic flow (UA AF), and UA reverse diastolic flow in the DV were scored separately: S/a aortic peak velocity. The measurements were considered abnormal only if the abnormality persisted. Observations are presented as mean days ± SEM prior to delivery and then compared by ANOVA and Student Newman Keuls pairwise multiple comparison.

**RESULTS:** Data was not normally distributed, therefore, the square root of the data was determined and found to have equal variance and a normal distribution. The graph depicts the temporal relationship of Doppler changes in vessels prior to delivery. The mean number of days prior to delivery at which an abnormal UA PI was observed was significantly different from the timing of abnormal findings in all other vessels (p<0.001). Earliest changes were seen in the UA PI and MCA while later changes included UA and DV reverse flows, and abnormal aortic peak velocity.

**CONCLUSION:** This is the first study using longitudinal data in a single population showing the composite temporal changes in Doppler indices occurring in IUGR fetuses. Vascular indices followed a consistent sequence of changes The reverse flow in the DV and UA, and the reduced Ao peak velocities were the final events of this cascade prior to delivery of the most severely affected IUGR fetuses. (Supported in part by the MOD 69-FY97-0174 and AAOGF)

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**SUCCESSFUL ENGRAFTMENT AFTER IN UTERO TRANSPLANTATION OF HUMAN CORD BLOOD STEM CELLS IN NOD/SCID MICE.** B.V. Srodek, S.Schott, S.Hahlm, M. Brüke, W. Holzgreve. Department of Obstetrics & Gynecology, University of Basel, Switzerland

**OBJECTIVE:** To assess the feasibility of an in utero transplantation model using human cord blood hematopoietic stem cells in NOD/SCID mice, known to be deficient of functional B and T cells (SCID background), as well as NK cell activity and APC (antigen presenting cell) function.

**STUDY DESIGN:** Cord blood mononuclear cells from term deliveries were separated by Ficoll gradient centrifugation. Inbred NOD/1.8e-scid mice were used as recipients. At 13.5 days gestational age (post plug), the uterine horns were exposed by lower abdominal incision during general anesthesia, and 1-2x10^5 cells in 5µL fluid were injected intraperitoneally into murine fetuses. Fluorescence-activated cell sorting with human anti-CD45 MoAbs was used for analysis of engraftment in peripheral blood from recipients 6-8 weeks post delivery.

**RESULTS:** A total of 286 fetuses from 39 pregnant mice were transplanted in utero. Fetal wastage exceeded 30%, showing a learning curve with increasing experience. A total of 41.6% of the remaining mice, which were available for analysis, were chimeric. The level of engraftment (proportion of human cells among nucleated cells from recipients) ranged from 0.4 to 2% in peripheral blood.

**CONCLUSION:** Our study shows that human cord blood cells engraft successfully in a large proportion of recipient fetal mice after in utero transplantation. Thus, in utero human-NOD/SCID mouse model seems appropriate for the study of prenatal stem cell transplantation and gene therapy using human cord blood cells, provided that the fetal wastage rate can be lowered by specific measures.
IN VITRO HEMATOPOIESIS IS INHIBITED IN HUMANS AND NON-HUMAN PRIMATES BY RECOMBINANT PARVO VIRUS CAPSID. LE Shwlds, RG Andrews*, M Westgren, K Brolinden*. University of Washington, Seattle, WA and Karolinska Institute, Huddinge, Sweden

OBJECTIVE: The purpose of this study was to determine if in vitro hematopoiesis could be inhibited by recombinant parvo virus B19 capsid proteins.

STUDY DESIGN: Hematopoietic progenitor cells (HPC) were obtained from human umbilical cord blood (HUCB) and bone marrow from non-human primates (M. nemestrina and P. papio). HPC were incubated with decreasing concentrations (8μg/ml → 0.008 μg/ml) of capsid protein, or saline as control. The cells were then incubated for 14 days in soft agar supplemented with multiple growth factors. The number of colony-forming cells (CFC) [colony forming units granulocyte (CFU-GM) and Burst forming unit-erythroid (BFU-E)] were then determined. The data, as a percentage of control, were analyzed by ANOVA.

RESULTS: Recombinant parvo virus B19 capsid protein inhibited total CFC formation from HUCB in a dose-dependent fashion. Total CFC formation was reduced by 48 ±1.7% (p<0.01) at the highest concentration of capsid protein. Nearly equal reductions were noted in erythroid (BFU-E, 55.6±3.5%, p<0.01) and CFU-GM colonies (49.6±11%, p<0.01). Colony formation was similarly inhibited in HPC from non-human primates. Total CFC's (43.1±1.7%, p<0.01), BFU-E (45.7±3.8%, p<0.01) and CFU-GM (49.1±1.0, p<0.01). There was no difference in the inhibitory effect noted in HUCB and BM from non-human primates.

CONCLUSIONS: This data suggest that the in vivo effect of parvo virus B19 capsid protein should be testable in non-human primates. If in vivo hematopoiesis can be inhibited then recombinant parvo virus B19 may offer a non-toxic method of fetal hematopoietic suppression as an adjunct to in utero stem cell transplantation.
ORAL CONCURRENT SESSION B

Clinical Obstetrics

Thursday, February 3, 2000
1:15 pm - 3:30 pm

Moderators:  W. Patrick Duff, MD
              Daniel F. O'Keeffe, MD

Judges:      M. Kathryn Menard, MD
              Brian M. Mercer, MD
              Dwight J. Rouse, MD

Fontainebleau Ballroom C/D
Abstract Numbers 18-26
18
THE EFFECT OF A CHANGE IN REMUNERATION ON OBSTETRIC INTERVENTION E. Blandix, L. Oppenheimer1, Shi Wu Wen2, Division of Maternal-Fetal Medicine, University of Ottawa, 1Laboratory Centre for Disease Control Ottawa, ON, Canada.

OBJECTIVE: To test the hypothesis that a change in an obstetric call group's remuneration from individual fee-for-service billing to equal sharing of the pooled group income, would result in reduced rates of obstetric interventions, specifically rates of induction of labor and cesarean delivery.

STUDY DESIGN: On July 1st 1997 the call group at the Ottawa General Hospital changed its remuneration method from individual billing to revenue sharing. Using information from the obstetric data management system, intervention rates were compared for the 12 months prior to (PRE) and the 12 months subsequent to (POST) the change. Only those physicians who were in the group for the entire time period were studied. Data was collected on onset of labor, indication for induction of labor and mode of delivery and statistical analysis performed using chi-squared and the two-tailed t-test.

RESULTS: There were 8 eligible physicians who delivered 1601 patients in the PRE year and 2002 in the POST year.

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<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
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<tbody>
<tr>
<td>Elective Induction</td>
<td>37.1%</td>
<td>29.0%</td>
<td>0.001</td>
</tr>
<tr>
<td>Operative del</td>
<td>34.4%</td>
<td>30.9%</td>
<td>0.03</td>
</tr>
<tr>
<td>Length of labor (min)</td>
<td>540±93</td>
<td>585±415</td>
<td>0.002</td>
</tr>
<tr>
<td>2nd stage (min)</td>
<td>57±65</td>
<td>66±75</td>
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CONCLUSION: The change in remuneration was associated with a significant, and clinically important, decrease in rates of labor induction and operative delivery. This suggests that physicians in call groups where individual billings have an incentive to be more interventionist.

19
CERVICAL INCOMPETENCE PREVENTION RANDOMIZED CERCLAGE TRIAL, PRELIMINARY RESULTS. Albabuis MPS, Dekker GA1, van Geijn HP1, Bekedam HJ, Hunnek P1, Deps OB/GYN, Free University Hospital1, Onze Lieve Vrouwe Gasthuis2, Amsterdam, the Netherlands.

OBJECTIVE: To compare the incidences of preterm delivery (PTD) and neonatal survival (NS) rates between prophylactic cerclage and transvaginal ultrasound follow-up in the cervix with randomization for therapeutic cerclage versus no cerclage when cervical length ≤ 25 mm was found in 18 patients (41%) of the ultrasound group at a mean gestation age of 19 0/7 weeks. PTD before 34 weeks' gestation was significantly higher in the group with a short cervix 6/18 versus 1/26 (p=0.01; OR 200 vs 100 mcg MP; P=0.001; Table 1).

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<tr>
<td>200mcg MP</td>
<td>0.066</td>
<td>0.02</td>
<td>0.582</td>
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<tr>
<td>200 vs Placebo</td>
<td>0.14</td>
<td>0.025</td>
<td>0.825</td>
</tr>
<tr>
<td>Birth wt</td>
<td>0.065</td>
<td>0.006</td>
<td>0.901</td>
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<tr>
<td>Ind.c42w</td>
<td>0</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperstim.</td>
<td>1</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Ave. doses</td>
<td>1</td>
<td>1.11</td>
<td>NS</td>
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CONCLUSION: There was a trend towards a decrease in pain med. requirement, a decrease in length of labor and a decrease in PTD before 34 weeks' gestation in patients with symptoms of cervical incompetence. There were no stat. signific. diff. in the APGAR scores, Uv or Ua pH between any groups. Patients with hyperstimulation were treated w/o complication by terbutaline.

20
OUTPATIENT MANAGEMENT OF PROLONGED PREGNANCY WITH MISOPROSTOL (MP): A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY, PRELIM. DATA. C. Ascher-Walsh1, B. Burke2, L. Baxi1, Columbia University, New York Presbyterian Medical Center, NY, NY.

OBJECTIVES: Both vaginal and oral MP are efficacious in cervical ripening. Because of the increased risk of adverse perinatal outcome in pregnancies >42wk, induction of labor is considered. Cesarean section rate in inductions at 42 weeks gestation approaches 40%. This study attempts to: 1. determine the optimal dose of misoprostol combining ripening and augmentation of labor, 2. decrease % of failed inductions. 3. evaluate the safety of outpatient administration of MP.

STUDY DESIGN: In a double blind randomized placebo-controlled study, 30 women, 40-41 weeks gestation, Bishop score <7, BP>28 received 1 oral dose of 200mcg or 100 mcg MP, or placebo, with FHR and uterine monitoring for 2 or 3 hrs if contractions. If no labor, procedure repeated every 3rd day until 42 weeks. Bishop score >5, BP>28, oligohydramnios or another indication for induction. At this time, labor was induced by standard labor room protocol using oxytocin and/or vaginal dinoprostone. Outcomes variables: time to mode of delivery; indication for induction, length of labor, need for tocolysis, use of pain meds, fetal wt., APGAR scores, Ua & Uv gases, maternal and fetal complications.

RESULTS: There were 8 eligible physicians who delivered 1601 patients in the PRE year and 2002 in the POST year.

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CONCLUSION: The change in remuneration was associated with a significant, and clinically important, decrease in rates of labor induction and operative delivery. This suggests that physicians in call groups where individual billings have an incentive to be more interventionist.

21
DOES EXPOSURE TO ANTENATAL MAGNESIUM SULFATE PREVENT CEREBRAL PALSY? R. Mittendorf, L. Bento, R. Borg, N. Rizen, University of Chicago, Chicago, IL.

OBJECTIVE: To determine whether the use of magnesium sulfate in the mother with preterm labor will prevent the occurrence of cerebral palsy (CP) in her child.

STUDY DESIGN: The MAGnet Trial, a randomized controlled trial funded by the United Cerebral Palsy Research and Educational Foundation, consisted of two mutually-exclusive parts. In the tocolytic part, mothers in preterm labor were randomized to either MgSO4 or placebo.

RESULTS: There were 1080 women randomized to the tocolytic part of the trial. A total of 1052 women were followed to age 18-months. Of those children who survived to age 18-months, there is a suggestion—but only one that does not reach customary significance—in our data that use of IV MgSO4 in the mother with preterm labor may prevent CP.
MANAGEMENT OF ISOLATED OLIGOHYDRAMNIOS IN THE TERM PREGNANCY: A RANDOMIZED CLINICAL TRIAL.

**BACKGROUND/OBJECTIVE:** To determine if expectant management is an acceptable alternative to labor induction for oligohydramnios in the otherwise normal term pregnancy.

**STUDY DESIGN:** Our randomized clinical trial included women between 37 and 41+6/7 wks with AFI ≤ 5 cm. We excluded patients with hypertension, ruptured membranes, abnormal fetal testing, fetal growth restriction, fetal anomaly, or late entry to prenatal care. Participants were randomized to immediate labor induction (INDUCE) or expectant management with twice-weekly fetal testing (EXPECT). Maternal hydration was not used before enrollment, and amniocentesis was not used in labor. The groups were compared for adverse neonatal outcomes (e.g., meconium aspiration), fetal growth characteristics, route of delivery, reason for cesarean, and maternal complications. Additionally, the anecoopel course of the EXPECT group was examined in terms of need for intervention, AFI trend, and interval to labor.

**RESULTS:** Sixty-one women were randomized (mean AFI 3.3±0.9, GA 40.6 wk±1.0). Fetal/neonatal compromise was rare in both groups: 1) no perinatal deaths, neonatal sepsis, or meconium aspiration occurred; 2) no infants required mechanical ventilation or oxygen >24 hrs; 3) two cesareans were performed for fetal distress (INDUCE group); 4) two infants had 5-min Apgar <7 (INDUCE group); 5) no cord pH was <7.10. No difference was found between groups in fetal growth characteristics (birth weight percentile distribution, ponderal index). Delivery was by cesarean in 17.6% of the EXPECT group and 16.0% of the INDUCE group (p=0.85).

Spontaneous labor developed in 97% of the EXPECT group; this occurred within 3 days of enrollment in 83%. No one in the EXPECT group was induced for evidence of fetal compromise.

**CONCLUSIONS:** Data from this pilot randomized trial suggest that when oligohydramnios (AFI ≤ 5) occurs in the otherwise normal pregnancy at term, expectant management appears to be a reasonable alternative to labor induction. The majority of women managed expectantly will enter spontaneous labor within 3 days.

**NON-INVASIVE ALTERNATIVE TO CORDOCENTESIS FOR DETECTION OF FETAL ANEMIA—A PROSPECTIVE MULTINATIONAL TRIAL.**

**BACKGROUND/OBJECTIVE:** Cordocentesis requires significant technical expertise, is expensive, and poses significant risk to the fetus. The middle cerebral artery peak systolic velocity detects fetal anemia with a high sensitivity and specificity. The objective of this study was to prospectively test the feasibility of the middle cerebral artery peak systolic velocity for prediction of anemia and to minimize the frequency of cordocenteses in red blood cell alloimmunized pregnancies.

**STUDY DESIGN:** Eighty fetuses at risk for anemia because of red blood cell alloimmunization (maternal antibody titer ≥1:16) were studied. The middle cerebral artery was assessed at intervals of one to four weeks. Cordocentesis was performed only when the trend of the middle cerebral artery peak systolic velocity deviated from the trend of the reference range obtained in non-anemic appropriate for gestational age fetuses. Anemia was defined as a value of hemoglobin below the 5th percentile for gestational age. No fetal deaths, neonatal seizures, or meconium aspiration occurred; 2) no one in the INDUCE group (p=0.85).

**RESULTS:** Gestational age at the first Doppler study ranged from 19 to 34.7 weeks. A total of 448 Doppler studies were performed. A cordocentesis was performed in only 10 fetuses, and none of them were anemic. In 71 fetuses (87%) any invasives were avoided. Antibody titers did not change significantly over time in any fetus at birth with a hematocrit below 30% (24.3%) (Sensitivity = 90%; Specificity = 98%) without any complications.

**CONCLUSIONS:** Cordocentesis is an invasive procedure that is associated with risks to both the fetus and mother. The middle cerebral artery peak systolic velocity appears to be a sensitive non-invasive marker for fetal anemia in red blood cell alloimmunized pregnancies. This method will minimize fetal complications associated with cordocenteses and will significantly lower health care costs and prove more convenient and acceptable to alloimmunized patients.
UMBILICAL ARTERY END-DIASTOLIC VELOCITY IN INTRAUTERINE GROWTH RESTRICTION - RELATIONSHIP TO HEMATOLOGIC PARAMETERS AT BIRTH


OBJECTIVE: Polycythemia, increased nucleated red blood cell (NRBC) count and thrombocytopenia are features of intrauterine growth restriction (IUGR). Our aim was to examine the relationship between umbilical artery (UA) end-diastolic flow and these hematologic parameters.

STUDY DESIGN: 111 anatomically normal singleton fetuses with UA pulsatility index (PI) >2SD above the gestational age mean and birthweight <10th percentile were studied. A complete peripheral blood count obtained within two hours of birth was compared between fetuses with positive - (group 1) and absent or reversed UA end-diastolic velocity (=AREDV, group 2). The deviation of the PI from the gestational age mean was calculated (Δ-PI). Multiple regression with Δ-PI, gestational age, birthweight percentile and cord blood gas as independent variables and hematologic parameters as dependent variables was performed. Anemia and polycythemia and thrombocytopenia were defined according to gestational age specific cutoffs.

RESULTS: There was a 14-fold rise in the incidence of thrombocytopenia and significantly elevated NRBC count in group 2 (Table). Multiple regression revealed that hemoglobin and hematocrit were gestational age dependent (r²=0.18 p<0.05 respectively), while NRBC count was related to cord bicarbonate (r=0.18 p=0.05). The platelet count was predominantly related to the UA Δ-PI (r²=0.22 p<0.005) and therefore placental resistance.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 n=63</th>
<th>Group 2 n=48</th>
<th>p value</th>
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<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>16.4 (12.8-22.1)</td>
<td>15.1 (8.1-21.6)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>51.4 (39.8-68.4)</td>
<td>47.7 (28.2-71.5)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Anemia (n,% )</td>
<td>0 (0%)</td>
<td>2 (4.2%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Polycythemia (n,% )</td>
<td>33 (52.4%)</td>
<td>16 (33.3%)</td>
<td>0.07</td>
</tr>
<tr>
<td>WBC/mm³ (x1000)</td>
<td>10.1 (2.1-17.1)</td>
<td>9.5 (2.6-15.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Platelets/mm³ (x1000)</td>
<td>208 (26-418)</td>
<td>102 (32-568)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Thrombocytopenia (n,%)</td>
<td>2 (3.2%)</td>
<td>21 (43.8%)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>NRBC/100 WBC</td>
<td>13 (0-595)</td>
<td>168 (2-3180)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CONCLUSION: Fetal Doppler examination in IUGR indicates hematologic status with important neonatal implications. Absent umbilical artery end-diastolic velocity in IUGR strongly predicts neonatal thrombocytopenia, while polycythemia is less frequent. Paradoxically, despite higher NRBC counts, anemia may be observed in the worst cases.
ORAL PLENARY SESSION II

Friday, February 4, 2000
8:00 am - 10:00 am

Moderators:  Ronald S. Gibbs, MD
Valerie M. Parisi, MD

Judges:  T. Murphy Goodwin, MD
John Owen, MD
Mark Phillippe, MD

Grand Ballroom East
Abstract Numbers 27-34
MULTIPLE COURSES OF ANTENATAL STEROIDS ARE ASSOCIATED WITH A DELAY IN LONG-TERM PSYCHOMOTOR DEVELOPMENT IN CHILDREN WITH BIRTH WEIGHTS ≤ 1,500 GRAMS. S. England, MB, S. Gans, MB, S. Smith, BT, Oshio, TF, Porter, DW, Branch and MW. Van Ryn: Univ. Of Utah, SLG, UT.

OBJECTIVE: To compare mental and psychomotor development of low birth weight infants who were exposed to ≥ 2 courses of antenatal steroids with those that were exposed to a single course or no antenatal steroids.

METHODS: Infants born between 1993 and 1998 with a birth weight ≤ 1,500 gms were identified in the State Neonatal follow-up clinic. Infants treated with ≥ 2 courses of antenatal steroids (at least 3 weeks more than one week apart) were included in the multiple course group. Control groups consisted of infants exposed to one course of antenatal steroids and infants who had no exposure. Groups were compared with respect to EGA at delivery, birth weight, and other possible confounding variables. Performance on the Bayley Scales of Infant Development, including the Mental Developmental Index (MDI) and the Psychomotor Developmental Index (PDI), also were compared. The mean age at testing for all three groups was 2.5 months. Adjusted age.

RESULTS: There were 429 infants included in the study (Multiple course group: 71; Single course group:201; No steroid group:157). The multiple course group had a slightly higher EGA at delivery (28.2 ± 2.5 wks vs single course; 27.5 ± 2.6 wks single course, 27.1 ± 2.5 wks no steroids; p = 0.061). There was no difference in birth weight when controlled for EGA (p=0.06). There was no difference in the mean MDI scores between the three groups (87.3 ± 12.9 multiple courses; 89.1 ± 12.1 single course, 88.4 ± 12.9 no steroids; p=0.98). The mean PDI scores were 76.9 ± 22.4 for the multiple course group, 83.7 ± 21.6 for the single course group, and 80 ± 22.1 for the no steroid group (p=0.05). When controlled for EGA at delivery, birth weight, multiple gestation, PTL, PROM, preclampsia, EGA at delivery, birth weight, multiple gestation, and presence of CP, the use of multiple courses of steroids was independently associated with an abnormal PDI (< 85) score (p=0.0173).

CONCLUSION: Exposure to multiple courses of antenatal steroids was independently associated with an abnormal PDI, suggesting psychomotor delay, compared to infants who received a single course or no antenatal steroids. Prospective analysis is needed to confirm this association. These findings suggest caution with the routine use of multiple courses of antenatal steroids.

PLACENTAL APOPTOSIS IN PRE-ECLAMPSIA. A. D. Alam*, K.A. Ballenger*, S R Wells, B.A. Lessey*. Dept Ob/Gyn, Univ of NC, Chapel Hill, NC.

OBJECTIVE: To determine if the number of apoptotic nuclei is increased and if the immune mediators of apoptosis, Fas and Fasl, are differentially expressed in placentas from pre-eclamptic pregnancies compared to controls.

STUDY DESIGN: Placental samples from 31 pre-eclamptic and 31 gestational age-matched controls were frozen in liquid nitrogen immediately after delivery. Six micrometer crosssections were then analyzed using TUNEL (terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end labeling) staining. The apoptotic index (apoptotic nuclei/total number of nuclei x 100) was calculated by analyzing 10 high power fields (mean of 3608 cells counted per subject) per subject. Rabbit polyclonal anti-Fas and Fasl (Fasl) antibodies were used followed by avidin-biotin immunoperoxidase staining to evaluate expression in the placental villus trophoblast, stroma, and endothelial cells. Intensity of staining was quantified by calculating an H-score (a continuous scale of 0-4). Observers were blinded to the study group of each subject during analysis. The Wilcoxon signed rank test was used for statistical analysis.

RESULTS: The median apoptotic index was 0.49 (inter-quartile range (IQR) = 0.00, 0.84) for the study group and 0.19 (IQR 0.10, 0.32) for the control group; p=0.001. The median apoptotic index for the trophoblast nuclei was 0.33 (IQR 0.16, 0.58) for the study group and 0.09 (IQR 0.03, 0.28) for the control group; p<0.01. Fasl expression in the villus trophoblast was less in the study subjects compared to the control subjects: median H-score 1.40 (IQR 0.00, 1.80) and 2.90 (IQR 2.0, 3.20); p<0.001. Fasl expression in the villus trophoblast was greater in the study subjects compared to the control subjects. median H-score 2.40 (IQR 1.80, 2.90) and 1.80 (IQR 1.20, 2.10); p<0.01. There was no difference in apoptotic index or Fas and Fasl expression in stroma and endothelium between groups.

CONCLUSION: Altered expression of Fas and Fasl in trophoblast may play a role in the pathogenesis of pre-eclampsia through the alteration of the maternal immune response and subsequent increase in placental apoptosis.


OBJECTIVE: The vast majority of children with myelomeningocele develop hindbrain herniation. The purpose of this study was to create a surgically induced animal model of myelomeningocele with hindbrain herniation in fetal sheep. Furthermore, we hypothesized that prenatal coverage of myelomeningocele can prevent hindbrain herniation in the sheep model.

STUDY DESIGN: A myelomeningocele was surgically created in 19 fetal sheep at 75 days of gestation (term 145 days). The animals were divided into three groups: one group was delivered without prenatal repair, in the other two groups, two methods of in utero repair were employed at 95 days gestation. One set of animals was repaired using standard postnatal techniques, the second group by tissue coverage with Alloderm®. After delivery, brain specimens were assessed for the presence of a hindbrain herniation. The brains of all lambs that had undergone creation of a defect.

RESULTS: Ten pregnancies continued to term and were available for pathological evaluation. All three lambs that had not undergone repair of the myelomeningocele developed a severe hindbrain herniation when compared to normal control lambs (n=4). The brains of all lambs that had undergone fetal repair either by primary closure (n=5) or Alloderm® coverage (n=5) were grossly normal.

CONCLUSION: Mid-gestation surgical creation of myelomeningocele induces hindbrain herniation in the fetal sheep model similar to spontaneous myelomeningocele in humans. Prenatal repair of myelomeningocele prevents development of the hindbrain herniation in the lamb.
EVALUATION OF ALLOIMMUNIZATION TO PATERNAL LEUKOCYTES AS A TREATMENT FOR HEMOLYTIC DISEASE OF THE FETUS/NEOBRN. IN A RABBIT MODEL. J. Hudon, A. Graham*, K. Dorman*, LS Rodkey*, KL Mohle, JR. Dept. Ob/Gyn., Baylor College of Medicine, Houston, TX. Dept. Pathology, Univ. of Texas, Houston, TX. Dept. Ob/Gyn., Univ. of North Carolina School of Medicine, Chapel Hill, NC.

OBJECTIVE: The primary hypothesis of this study is that maternal alloimmunization to paternal antigens is an effective treatment for hemolytic disease of the fetus/newborn (HDN) in a rabbit model.

STUDY DESIGN: DNA extraction and Southernblot were used to ascertain the class I and class II rabbit leukocyte antigen (RLA) of our rabbit colony. Six virgin does entered the protocol. We compared the fetal and neonatal hematologic parameters of a compatible litter (unaffected), an affected litter (after alloimmunization to RBC antigens) and an incompatible litter after allogeneic transfer to paternal antigens. Immunization of the does to RBC antigens was performed using subcutaneous injections of RBC with and without an adjuvant alternating with intravenous injections. All litters were evaluated with ultrasound guided fetal intracardiac blood sampling to determine fetal hematologic values on day 28. The does were induced on day 50. The liveborn neonates were euthanized and cardiac sampling under direct visualization was performed to document hematological parameters. RBC antibody titers were assessed at the time of breeding and sampling. A litter of 1:320 consistently produces severe HDN. Alloimmunization of the does to paternal leukocytes was achieved by successive intradermal injections of paternal leukocytes with and without an adjuvant followed by intravenous injections. A complement fixation assay was used to determine the presence of anti-RAL antibodies in the does.

RESULTS: Successful immunization of does to paternal RLA antigens proved difficult due to the low circulating white cell pool. Significant immunization in one doe resulted in a marked improvement in fetal hemoglobin: control litter hgb 9.9 gm/dl; incompatible litter hgb 6.8 gm/dl; post-antibodies incompatible litter hgb 8.3 gm/dl. A more modest improvement in hemolytic disease was noted in a second doe with a moderate titer to RLA antigens.

CONCLUSION: When sufficient titers of anti-RAL antibodies were achieved, a decrease in the severity of the hemolytic disease was observed in some animals.

THE EFFECTS OF CYCLOOXYGENASE INHIBITORS ON DELIVERY IN RATS. R. Bukowskzx, M. Kukowskzx, K. Dormanx, G. Saude, R. Garfieldx. Dept. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To investigate the effect of cyclo-oxygenase inhibition on parturition in rats.

STUDY DESIGN: In a series of experimental protocols, timed-pregnant Sprague-Dawley rats (length of pregnancy 22 days) were randomly allocated to 4 different cyclo-oxygenase treatments: [I] L-NIL, 0.04mg (n=6), 0.4mg (n=6), 4mg (n=13), 40mg (n=12) or vehicle (n=19) on days 19-22 of pregnancy; [II] L-NIL 4mg (n=5), L-NIL 40mg (n=5), L-NIL 4mg plus INDO 3mg (n=9), INDO 3mg (n=5) or vehicle (n=6) on days 19-22; [III] AG 50mg (n=6), NM 50mg/kg (n=5), AG 50mg plus NM 50mg/kg (n=6) or vehicle (n=6) on days 14-22. The following variables were evaluated: proportion of animals which delivered on day 23, time to delivery of the first pup (midnight on day 22 to 6 hour), percentage of stillborn and average pup weight of each litter.

RESULTS: Neither L-NIL nor INDO significantly increased proportion of animals delivered on day 23 alone or in combination. AG and NM did not change the proportion of deliveries on day 25 and only non-significantly increased the time to delivery of the first pup by 6.7 (p=0.158) and 23.3 h (p=0.056), respectively. Simultaneous administration of AG and NM induced prolongation of pregnancy by 4.5 days (p=0.019). Treatment with L-NIL, AG or NM did not cause any significant change in the percentage of stillborn pups nor in their birthweight. Compared with control, significantly more pups in the INDO group died in utero (p=0.019) and surviving animals had lower birthweight (p=0.001).

CONCLUSIONS: NOX or COX-2 inhibitors applied singly in the dosages used and for the specific treatment period do not significantly extend the duration of pregnancy. Inhibition of both iNOS and COX-2, however, significantly delays delivery. Non-specific inhibition of COX by INDO increases fetal mortality and morbidity.

AMNIOTIC CYCLOOXYGENASE-2 EXPRESSION AND ACTIVITY ARE ENHANCED IN PREGNANCIES COMPLICATED BY PRETERM DELIVERY OF WOMEN WITH TWINS OR POLYHYDRAMNIOS. G. Leguzamox, JR Barton, V Park*, B Haddad*, R Chahine*, O Phillips*, and BM Sibai, University of Tennessee-Memphis, TN and Central Baptist Hospital, Lexington, KY.

OBJECTIVE: We have previously shown that term or iatrogenic preterm delivery is associated with enhanced expression and activity of cyclo-oxygenase (COX)-2, but not COX-1. Here we tested the hypothesis that preterm delivery secondary to multiple gestation or polyhydramnios, both associated with uterine over-distention, is associated with increased expression and activity of amniotic COX-2.

STUDY DESIGN: Samples of amnion were obtained from women undergoing preterm delivery complicated by twins (n=12) or polyhydramnios (n=3), as well as from women undergoing preterm cesarean delivery without labor (n=6). Samples were analyzed for COX-1 and COX-2 expression by western blot using tissue-specific antibodies. COX-2 content was measured using ELA. COX-1 and COX-2 activity were selectively inhibited in the presence of amniotic acid using either SC-236 or SC-296, respectively.

RESULTS: Preterm delivery complicated by twins or polyhydramnios was associated with enhanced expression of amniotic COX-2 (4- and 5-fold, respectively). In contrast, COX-1 expression was unchanged. The enhanced expression of COX-2 was associated with an increase in amniotic PGE2 production in twins (3.5-fold, p<0.05) and in polyhydramnios (12-fold p<0.05). Pre-incubation of amnion samples with indomethacin (50µM) in vitro effectively reduced PGE2 production (4.5-fold, p<0.05). We observed a similar reduction in PGE2 production (5-fold, p<0.05) with the selective COX-2 inhibitor SC-236 (10µM). In contrast, the selective COX-1 inhibitor SC-560 had no effect.

CONCLUSION: Preterm delivery, secondary to multiple gestation or polyhydramnios, is associated with increased expression and activity of amniotic COX-2. This increase is likely attributed to uterine over-distention.

MATERNAL AND FETAL GENETIC THROMBOPHILIAS ARE NOT ASSOCIATED WITH SEVERE PREECLAMPSIA. JR Barton, JS Hoekstra, Y Saperston*, Y Schneider*, G Legutzamox, JR Barton, V Park*, B Haddad*, R Chahine*, O Phillips*, and BM Sibai, University of Tennessee-Memphis, TN and Central Baptist Hospital, Lexington, KY.

OBJECTIVES: Thrombophilias may predispose patients to the development of preeclampsia (PRE) (N Engl J Med 1999). The purpose of this study was to determine whether maternal (M) or fetal (F) genotype frequencies of the inheritable thrombophilic gene mutations (Factor V Leiden (FV), prothrombin (PT), methylenetetrahydrofolate reductase (MTHFR), and protein C (PC) deficiency are altered in severe PRE.

STUDY DESIGN: We performed a prospective cross-sectional study to compare the M and F genotype frequencies of FV, MTHFR, and PC. Patients with severe PRE (n=114) were matched for gestational age to normotensive pregnancies (n=94). Umbilical cord blood was obtained from 88 controls and 80 preeclamptic patients. DNA was extracted from leukocytes and PCR performed. PCR products were digested with the appropriate restriction enzyme and fractionated by gel electrophoresis. Chi-square test was performed to determine statistical significance.

RESULTS: No differences were found in severe PRE and control patients in the frequency of maternal FV G/506/A mutation (4.4% vs 4.3%, p=0.96), MTHFR C1298/T1298/T mutation (9.5% vs 6.3%, p=0.54), or PC G20210A mutation (4% vs 1.1%, p=0.92). No statistical difference could be found between fetal thrombophilias and the development of PRE. Findings were similar in both Caucasian (n=79) and African American (n=129) subsets. There was no association between either maternal or fetal genetic polymorphisms and the incidence of HELLP (n=27), eclampsia (n=9), IUGR (n=9), abortion (n=11), recurrent PRE (n=12), or onset of PRE at <28 weeks' gestation. Table below describes frequency of all M and F genotypes.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>MTHFR</th>
<th>FV G/506/A</th>
<th>PC G20210A</th>
<th>FV C1298/T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.96</td>
<td>0.04</td>
<td>0.03</td>
<td>0.06</td>
</tr>
<tr>
<td>Severe PRE</td>
<td>0.06</td>
<td>0.04</td>
<td>0.51</td>
<td>0.1</td>
</tr>
<tr>
<td>Control</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
<td>1.00</td>
</tr>
<tr>
<td>Severe PRE</td>
<td>0.98</td>
<td>0.03</td>
<td>0.24</td>
<td>0.10</td>
</tr>
</tbody>
</table>

CONCLUSION: Contrary to previous reports, genetic thrombophilias are not associated with severe preeclampsia in our population.
ORAL CONCURRENT SESSION C

Physiology/Endocrinology
Epidemiology

Friday, February 4, 2000
1:15 pm - 3:30 pm

Moderators: Haywood L. Brown, MD
Kenneth J. Moise, Jr., MD

Judges: Kimberly K. Leslie, MD
George R. Saade, MD
Yoel Sadovsky, MD

Grand Ballroom East
Abstract Numbers 35-43
GESTATIONAL AGE COMPARISON OF HUMAN UTERINE Ca2+-L-CHANNEL FUNCTION AND SENSITIVITY TO ENDOGENOUS Ca2+-L-CHANNEL INHIBITOR (ECCI).

P.L. Collins, R.I. Karlman. Dept.Ob/Gyn, Loyola University Medical Center, Maywood, IL.

OBJECTIVE: To determine if 1) human uterine vasocontractile response to Bay K 8644, a Ca2+-L-channel agonist, is age-regulated and 2) sensitivity of human uterine tissue to human ECCI decreases with advancing gestation as seen in pregnant guinea pig.

STUDY DESIGN: A uterine biopsy was obtained from women undergoing Ca2+-L-channel agonist-stimulation of Ca2+-L-channel antagonist, Bay K 8644. Uterine slices were cut to a .5x.5 cm template and anchored into the maternal side of a Plexiglas chamber. Chambers consist of a fetal compartment and a maternal compartment divided by fetal membranes in a removable cassette. Uterine strips were attached to a strain gauge, maintaining orientation in order to measure longitudinal force. After an equilibration, the patient's uterus was exposed to her own fetal membranes or to Parafilm in control chambers. Bay K 8644 was added to the maternal side of chambers in 5 minute cumulative doses from 100 pM to 5gM. Data are displayed as force in millinewtons. Comparisons are made at EC50 dose of Bay K 8644 for term uterus.

RESULTS: Uterine contractions increase in response to Bay K 8644 with advancing gestation, maximal at term. When the patient's uterine sample was exposed to ECCI produced by her own fetal membranes, Bay K 8644 induced uterine contractions were inhibited at all gestational ages (18%, 39%, 57%, 54% inhibition at 24, 34, 34 1/2 and Term, respectively). CONCLUSION: There is an up-regulation of function of the Ca2+-L-channel with advancing gestation in the human uterus which is similar to that seen in the pregnant guinea pig. In contrast to guinea pig, human uterus maintains sensitivity to ECCI through term. Supported by NICHD and MOD.

CHORION RELEASES A FACTOR THAT INHIBITS OXYTOCIN INDUCED MYOMETRIAL CONTRACTILITY IN PREGNANT GUINEA PIG.

JA Carvajal1, I Buhimschi2, I.P. Thompson3, K Aguana3 and CP Weiner. Department of Ob/Gyn and Reproductive Sciences, University of Maryland School of Medicine, Baltimore, MD.

OBJECTIVE: To test the hypothesis that chorion (CHO) releases a substance necessary for the maintenance of uterine quiescence during pregnancy. A decrease in the release of this inhibitory substance would render the myometrium (MYO) susceptible to uterotonic agents, such as oxytocin (OXT) and prostaglandin.

STUDY DESIGN: Myometrial samples and fetal membranes (FM) were obtained from timed pregnant Duncans-Harley guinea pigs at pre-term (40-45 days gestation, n=5) and term not in labor (55-60 days gestation, n=10; term = 65 days). Full thickness myometral strips were placed in organ baths for isometric tension measurement. Contractile activity was induced with a sub-maximal concentration of OXT (10-8 M). After a pattern of regular myometrial activity was observed, FM or conditioned medium (CM) were placed with Krebs solution at (C=30 ml) and strips were added to the organ bath. Temporal controls were run in parallel. Contractility was recorded during the 10 min before (basal) and 30 min after the addition of CM and measured in 10 min intervals.

RESULTS: Term CM and term chloron CM produced a time dependent decrease in the OXT induced contractile activity. Term CHO significantly (p<0.05) reduced the contractile activity from basal to 58 % and 39 % at 15 and 25 min respectively. The relaxing capability of preterm CHO was greater than term CHO, since preterm CHO decreased the contractile activity to 41 % and 28 % of the basal activity at 15 and 25 min respectively (p< 0.05 from term CHO). However, neither CM nor term amnion (AMN) has no effect on the contractile activity. Further CHO induced relaxation was independent of the gestational age of the MYO, i.e. relaxation induced by the same CHO was similar in preterm or term MYO.

CONCLUSION: We have shown that the CHO, but not the AMN, is able to decrease the myometrial contractile activity. This is the first demonstration of the ability of CHO to inhibit oxytocin induced contractions in MYO. The action is gestational age, time dependent, and not affected by the gestational age of the MYO. Further it is mediated by a substance (s) transmitted to the CM. Thus, the CHO may release a substance or substances that modulate myometrial contractility and may be involved in the maintenance of uterine quiescence during pregnancy. A decrease in this substance would be necessary for the initiation of parturition.


Department of Nutrition, Case Western Reserve University, Cleveland, Ohio.

OBJECTIVE: Mice heterozygous for the leptin receptor (db/+ ) develop spontaneous gestational diabetes during pregnancy and the offspring are macrosomic compared to offspring of wild-type mice. The objective of this study was to evaluate the effect of human recombinant leptin-IGF administration on maternal glucose metabolism in db/+ mice and the effect on fetal growth.

STUDY DESIGN: Beginning on day 10 of pregnancy, human recombinant leptin-IGF-I fusion protein or vehicle was administered daily for up to seven days by intraperitoneal injection (1 mg/kg/day in 100ul saline). The body weight and food intake of each mouse was recorded every day. Glucose tolerance tests were performed prior to pregnancy and on day 19 of pregnancy. Insulin stimulated tyrosine phosphorylation of insulin receptor (IR), insulin receptor substrate-1 (IRS-1), and p85α were evaluated in the muscle. Comparison between groups were made using Student t-test, except for glucose tolerance data, which was analysed by analysis of variance for repeated measures using Prism. Statistical significance was set at p<0.05.

RESULTS: Leptin treatment suppressed food intake to levels similar to pregnant wild type mice and led to significant lower maternal weight gain in pregnant db/+ mice (p<0.01). However, leptin treatment reduced maternal weight gain and fat mass significantly beyond that found in pair-fed db/+ mice (p<0.05). During the glucose tolerance test, glucose levels were markedly lower (p<0.001) in leptin treated db/+ mice relative to pregnant db/+ and pair-fed controls. There was a mean 26% higher insulin secretion in leptin treated db/+ mice compared to pregnant db/+ controls (p<0.001), and this response was significantly improved relative to pair-fed mice (p<0.01). Leptin treatment resulted in significant improvement of insulin-stimulated IRS-1 and p85α expression in skeletal muscle. In contrast, leptin induced insulin resistance in neonatal skeletal muscle and did not affect insulin receptor substrate-1 (IRS-1) expression significantly. CONCLUSION: Leptin treatment significantly decreased maternal weight gain, improvedβ-cell function, and decreased skeletal muscle insulin resistance in pregnant db/+ mice. However maternal leptin treatment appeared to have no significant impact on fetal growth.

INCREASED EXPRESSION OF HEAT SHOCK PROTEIN 70 IN HUMAN DECIDUA WITH ADVANCING GESTATION MAY REGULATE GLUCOCORTICOID ACTION IN THIS TISSUE. W. Usheb and M. Sun3. Division of Maternal-Fetal Medicine, Dept. of Ob/Gyn, University of Ottawa, Ottawa, ON, Canada.

OBJECTIVE: The human fetal membranes appear to be important sources of prostaglandins involved in human labor and glucocorticoids have been shown to be involved in the regulation of prostaglandin production by these tissues. Heat shock protein 70 (HSP 70) is involved in the regulation of glucocorticoid receptor (GR) function by binding to the unliganded glucocorticoid receptor in the cytoplasm and preventing nuclear translocation. The purpose of this study was to examine the expression of HSP 70 protein and mRNA in human fetal membranes and decidua throughout gestation and to localize the active GR, GRα.

STUDY DESIGN: Tissues were obtained following vaginal delivery and C-section from 30 to term and frozen in liquid N2. Frozen sections were examined by immunohistochemistry (IHC) for HSP 70 protein expression and by in situ hybridization (ISH) for HSP 70 mRNA expression. The localization of GRα was also examined by IHC at term.

RESULTS: HSP 70 protein and mRNA were expressed in amnion, chorion and decidua at all weeks of gestation examined. In amnion and chorion there was no change in mRNA or protein expression with advancing gestation. In contrast, in the decidua there was a marked increase in HSP 70 protein and mRNA expression in term tissues compared to preterm tissues. In term tissues GRα was localized in the nuclei of cells in the amnion and chorion whereas in decidua it was more diffusely expressed throughout the cell. CONCLUSION: We suggest that the increased expression of HSP 70 in decidua with advancing gestation may be involved in regulating glucocorticoid action in this tissue by limiting translocation of GR to the nucleus.
40 ELEVATED NUCLEATED RED BLOOD CELLS DIFFERENTIATE THE PATHOLOGICALLY GROWTH RESTRICTED FETUS FROM THE HEALTHY BUT SMALL FOR GESTATIONAL AGE FETUS Minow VK,1,8 Shatzkin E2x, Divon M3,2, Long Island Jewish Medical Center1, Albert Einstein College of Medicine2, Lenox Hill Hospital2, New York, New York.

OBJECTIVE: To evaluate the utility of the neonatal nucleated red blood cell (NRBC) count in differentiating the growth restricted fetus from the small but otherwise healthy fetus.

STUDY DESIGN: Perinatal outcome was evaluated prospectively in all neonates admitted to the NICU in 1997. Non-anomalous, genetically normal neonates with a CBC drawn within the first 6 hours of life were included in the study. Fetal growth restriction (FGR) was defined as birthweight <10th%ile for gestational age. NRBCs were considered elevated when they were >90th%ile for gestational age. Neonates were divided into four groups: 1. FGR with elevated NRBCs, 2. FGR with normal NRBCs and 3. AGA with normal NRBCs. ANOVA and stepwise regression were used for statistical analysis.

RESULTS: 237 neonates met the inclusion criteria. 18% were FGR. A comparison of groups with regard to major adverse outcomes is as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>FGR (%)</th>
<th>AGA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRBC elevated</td>
<td>7.11</td>
<td>0.01*</td>
</tr>
<tr>
<td>NRBC normal</td>
<td>7.11</td>
<td>0.01*</td>
</tr>
</tbody>
</table>
| Neonatal Death | 2 (22%) | 0 (0%)

*Independent of gestational age in stepwise regression analysis.

42 MAGNESIUM PREVENTS SEIZURE INDUCED REDUCTION IN EXCITATORY AMINO ACID RECEPTOR (NON NMDA) BINDING IN PREGNANT RAT BRAIN. M Haluk, JW Hotra*, D Custodio*, ML Krueger1, Departments of Ob/Gyn, Ben Gurion University/Soroka Medical Center, Beer Sheva, Israel and Wayne State University School of Medicine, Detroit, Michigan.

OBJECTIVE: To evaluate the effect of seizures on excitatory amino acid receptor (Kainate & AMPA) binding in maternal rat brain, and whether peripheral administration of magnesium sulfate (MgSO4) can decrease this effect.

STUDY DESIGN: Rats were stereotaxically implanted with a bipolar electrode into the hippocampus. One week of recovery was allowed prior to breeding. Pregnant rats were randomly assigned to one of four groups: 1. Saline & no seizure (n=5), 2. MgSO4 & no seizure (n=5), 3. Saline & seizure (n=8), and 4. MgSO4 & seizure (n=9). Subcutaneous doses of saline or MgSO4 were administered every 20 minutes for 4 hours (loading-maintenance-loading) to all rats on gestational days (GD) 9, 11, 13, 15, 17, and 19. Study groups 3&4 were subsequently stimulated and seizures induced after each injection session. At GD 20, rats were perfused and brains dissected. Cryostat sections were taken, labeled in-vitro and mounted on Hyperfilm for 4 weeks. The ligands used were [3H]Kainate - agonist, Kainate binding site; [3H]AMPA - agonist, and [3H]CNQX - antagonist, both at the AMPA binding site. Optical density measurements of binding in 15 brain regions on each section were performed. Statistics included one and two way ANOVA.

RESULTS: Seizure activity was associated with decreased, and magnesium administration with increased, AMPA receptor binding of [3H]AMPA in pregnant rat brains (p<0.01). The same trend was seen with the Kainate receptor in the hippocampus and hypothalamus, with significant interaction effect between seizure and magnesium (p<0.05). No seizure/treatment effects were seen in the binding of CNQX. *p<0.01

AMPA Receptor & ligand Seizure/No seizure Magnesium/Saline values in fmole/mg tissue effect

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindbrain</td>
<td>25.9±4.2/44.5±4.7*</td>
<td>44.9±2.5/25.3±3.7*</td>
</tr>
<tr>
<td>Forebrain</td>
<td>92.6±4.3/110.7±5.0*</td>
<td>110.4±4.5/92.9±4.8*</td>
</tr>
</tbody>
</table>


OBJECTIVE: To identify antenatal risk factors for spastic forms of cerebral palsy (CP) in preterm infants in an area with a low incidence of perinatal infections.

STUDY DESIGN: A population based case-control study was performed. All infants born (n=296) at 23-37 gestational weeks during the period 1988-1990 in the western region that developed cerebral palsy (n=152) were included. For each case, 2 controls were matched according to gestational age, gender, multiple pregnancy and delivery unit. All 456 records were found and scrutinized by one of us (BJ). Four cases were excluded because of known CMV infections (n=2) or a corrected gestational age ≤27 weeks. More than 150 antenatal variables were collected for each case/control and related to the occurrence of CP. The results were given as Odds Ratio (OR) estimates with 95% confidence intervals (CI). Continuous variables were analyzed with Wilcoxon rank sum test. Adjusted OR were also calculated to correct for minor differences in gestational age between case and control.

RESULTS: Hypertensive disease (preeclampsia, idiopathic and gestational hypertension), antenatal corticosteroids, cervical insufficiency, clinical chloroammoniosis (including prelabyrinthis) and histological chloroammoniosis were all significantly associated with CP (Table).

<table>
<thead>
<tr>
<th>CP cases</th>
<th>Controls</th>
<th>OR (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive disease</td>
<td>14/18 (9.5%)</td>
<td>48/296 (16.2%)</td>
</tr>
<tr>
<td>Antenatal corticosteroids</td>
<td>9/15 (6.4%)</td>
<td>35/296 (11.5%)</td>
</tr>
<tr>
<td>Cervical insufficiency</td>
<td>10/28 (35.7%)</td>
<td>6/45 (13.3%)</td>
</tr>
<tr>
<td>Cerebral palsy (CP)</td>
<td>2/18 (1.4%)</td>
<td>16/296 (5.5%)</td>
</tr>
<tr>
<td>Fever before delivery</td>
<td>12/146 (8.2%)</td>
<td>11/289 (3.8%)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: CP in preterm infants was higher in cases complicated by antenatal infections. Non-inflammatory factors (hypertension, cervical insufficiency) or antenatal corticosteroids on the other hand, were associated with a lower occurrence of CP. The results implicate inflammatory factors in the etiology of CP in a region with a low incidence of preterm birth (5.0%) and perinatal infections.
SEVERE PLACENTAL INSUFFICIENCY AND A RISE IN SYSTEMIC VE-NOUS PRESSURE IN THE FETUS ARE ASSOCIATED WITH INCREASED CARDIAC TROPOIN-T LEVELS IN NEWBORNS. R. Makaliho*, P. Jouppila*, J. Kaski*, Dept Ob/Gyn, University of Oulu, Finland.

OBJECTIVE: To test the hypothesis that severe placental insufficiency and a rise in fetal systemic venous pressure are associated with fetal myocardial cell damage leading to increased newborn troponin-T levels.

STUDY DESIGN: Sixty-six newborns with uncomplicated pregnancy and delivery were included in the control group. Study group 1 consisted of 32 newborns with maternal hypertensive disorder with normal intra-abdominal umbilical venous blood flow pattern by pulsed Doppler ultrasonography during fetal life, and study group 2 of five newborns with atrial pulsations in the intra-abdominal portion of the umbilical vein during fetal life indicating increased systemic venous pressure. Immediately after delivery umbilical artery blood samples were collected and newborn cardiac troponin-T concentrations were measured by using commercially available ELISA kits (Enzymun-Test Tropomin-T, Boehringer Mannheim Diagnostics). A clinically significant troponin-T level was set at 0.10 ng/ml.

RESULTS: Umbilical artery pH-values did not differ between the groups.

<table>
<thead>
<tr>
<th>GA (w) mean (SD)</th>
<th>Birthweight (g) mean (SD)</th>
<th>Apgar 5min mean (SD)</th>
<th>Troponin-T (ng/ml) median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>40.0 (1.2)</td>
<td>3713 (408)</td>
<td>9.1 (0.6)</td>
</tr>
<tr>
<td>Study 1</td>
<td>37.6 (3.4)*</td>
<td>2794 (988)*</td>
<td>8.7 (1.2)</td>
</tr>
<tr>
<td>Study 2</td>
<td>29.8 (3.0)†</td>
<td>660 (269)†</td>
<td>5.0 (2.6)†</td>
</tr>
</tbody>
</table>

*p<0.001 (comparing to control group), †p<0.0001 (comparing to control group and study group 1)

CONCLUSION: In normal pregnancies and in pregnancies complicated by maternal hypertensive disorder with normal fetal umbilical venous return, newborn troponin-T levels are not clinically significantly increased. If these pregnancy complications are associated with abnormal umbilical venous return, newborn troponin-T concentrations are significantly increased, indicating myocardial cell damage.
ORAL CONCURRENT SESSION D

Prematurity

Friday, February 4, 2000
1:15 pm - 3:30 pm

Moderators:  Susan M. Cox, MD
             Katharine D. Wenstrom, MD

Judges:      Dru E. Carlson, MD
             Michael R. Foley, MD
             Carol A. Major, MD

Fontainebleau Ballroom C/D
Abstract Numbers 44-52
44 VAGINAL FETAL FIBRONECTIN (V-fFN) LEVELS AT 8-22 WEEKS AND SUBSEQUENT SPONTANEOUS PRETERM BIRTH (SPB).  JF. Goldenberg for the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: In the late 2nd and early 3rd trimesters, a positive V-fFN test is strongly associated with subsequent SPB. Our goals were to define gestational age (GA) specific V-fFN distributions from 8-22 wks, to determine factors associated with high values, and to evaluate whether high values in specific GA periods were associated with SPB.

STUDY DESIGN: V-fFN values were quantitatively determined in a prospective cohort study of 13,166 women at 8-22 wks. V-fFN values were correlated with GA at screening, race, bacterial vaginosis and with SPB defined as <28 wks, <32 wks, <35 wks, and <37 wks GA.

RESULTS: At each GA, V-fFN values ranged from 0 to 100 ng/ml with median values declining from 8 ng/ml at <9 wks to 1 ng/ml at >21 wks. 90th %ile values declined from 320 ng/ml at <9 to 23 ng/ml at >21 wks. African American and multiparous women, and those with bacterial vaginosis had significantly higher levels of V-fFN. V-fFN values >90th %ile obtained at 8-12 wks did not predict losses <20 wks or SPB, while values >90th %ile obtained at 13-18 wks predicted <20 wk losses (4.2 vs 1.0%, OR 4.5, P<0.001). Overall, from 13-22 weeks, values >90th %ile were associated with a 2-fold and statistically significant increased risk of SPB <32, <35 and <37 wks and a 4-fold increased risk of SPB <28 wks. V-fFN values >90th %ile at 19-22 wks were associated with a nearly 8-fold increased risk of <28 wk SPB (OR 7.6 (3.9-15.1)).

CONCLUSION: GA-specific elevated V-fFN levels from 13-22 wks, defined as >90th %ile, are associated with a significantly increased risk of SPB, with later vs earlier testing enhancing the predictive value of V-fFN for SPB. From 13 to 22 wks, a high V-fFN is a better predictor of earlier vs later preterm birth.


OBJECTIVE: The biology and predictors of preterm birth remain unclear. Traditionally studies have not distinguished between two classes of preterm birth, premature rupture of membranes (PPROM) and preterm labor (PTL), but recent work suggests that they should be evaluated as separate entities with potentially important differences in their etiologic pathways. The purpose of this study was to determine if cervical dimensions at 24-29 weeks estimated gestational age (EGA) are differentially associated with PPROM versus PTL.

STUDY DESIGN: A prospective cohort of 1,986 asymptomatic women enrolled in the Pregnancy, Infection and Nutrition Study in North Carolina underwent screening cervical examinations between 24 and 29 weeks EGA. They were then followed until delivery. Relative risks for discrete clinically discernable categories of cervical length, dilatation and cervicovaginal score (length minus dilatation) were calculated for the two main outcomes, PPROM and PTL. Confounding was assessed by analysis of covariance and included: prior pregnancy history, maternal demographics, social factors and history of infections during the current pregnancy.

RESULTS: There were 142 spontaneous preterm births, 48 associated with PPROM and 94 associated with PTL. Cervical length less than 3 cm was associated with PPROM but not PTL. Thus, the cervical length categories of 2-3 cm, 3-4 cm, and <1 cm were associated with relative risks of 1.0 (0.7-2.8), 5.3 (2.1-15.0) and 9.8 (1.1-85.6) for PPROM but for PTL, these relative risks were 0.8 (0.5-1.3), 1.9 (0.9-4.2) and indeterminate (no subjects). Multivariate analysis did not appreciably change these estimates. A dose response relationship between increasing dilatation and increasing risk for both PPROM and PTL was also noted; again, multivariate analysis did not alter these associations.

CONCLUSIONS: The differential relationship in the strength of the relationship between shortened cervical length and the risk of PPROM and PTL suggests that there may be important biological and clinical differences between these two types of premature delivery. Further work focusing on these differences may prove enlightening for understanding their etiologies and developing predictive models and possible interventions.

45 MID-TRIMESTER THRESHOLD VAGINAL pH AND GRAM STAIN SCORES PREDICTIVE OF SUBSEQUENT PRETERM BIRTH.  J C. Haush for the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: To identify mid-trimester vaginal markers predictive of subsequent preterm birth (PTB).

STUDY DESIGN: During the NICHD MFMU Network Bacterial Vaginosis (BV) Trial, 21,554 women were screened with a vaginal pH and 12,041 had a vaginal Gram stain score of 0 to 10. Nugent criteria were used to determine a vaginal Gram stain score of 0 to 10.

RESULTS: Delivery at <37, <35, or <32 weeks GA was similar for women with a vaginal pH of 4.4 or 4.7 (P=NS), but was increased in women with a pH of 5.0 (P=0.04, 0.02, 0.03, respectively) or with a pH >5.0 (at each GA P<0.001). The effect of pH >5.0 was similar for a spontaneous PTB at each GA (P<0.001), or birthweight <2500 or <1500 g (P<0.005). Women with a Gram score of 9-10 compared to <9 had increased PTB rates at <37, <35, and <32 weeks GA (P<0.006), and birthweights <2500 (P<0.004) or <1500 g (P<0.01). Women with a score of 4-6 had a similar occurrence of PTB and/or birthweight <2500 or <1500 g compared to women with a score of 7-10. Women whose vaginal pH was >5.0 had a higher prevalence of vaginal FFN >250 ng/ml (P<0.001), but the proportion of women with a vaginal FFN >250 did not differ by Gram score.

CONCLUSION: Women with a vaginal pH >5.0 and/or a Gram stain score of 9-10 had significantly increased PTB's at <37, <35, and <32 weeks GA (and/or a birthweight <2500 or <1500 g). Inclusion of a pH >5.0 or a Gram score >9 may obscure potential benefits in antimicrobial trials to prevent PTB.

47 SELF PERCEIVED SYMPTOMS TO PREDICT PRETERM BIRTH.  Iams JD for the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: To determine the ability of self-perceived symptoms (Sx) to predict preterm birth (PTB) and to compare Sx to monitored contractions (MC), Bishop score (BS), cervical length (CL) and fibrinectin (FFN) as tests to predict PTB in singleton pregnancies.

STUDY DESIGN: 295 women (246 with risk factors for PTB) enrolled in a multicenter prospective observational study of predictors of PTB and recorded the occurrence of self perceived Sx (contractions, pelvic pressure, vaginal discharge, menstrual cramps, abdominal pain, backache) and MC electronically at least twice/day and twice/week from 22-24 weeks until delivery or 36 weeks. BS, CL by transvaginal ultrasound, and FFN were assessed every 4 weeks. Multivariate logistic regression was used to relate the frequency of individual and multiple (≥2 by ROC curve) Sx, MC≥4/hr, BS≥4, CL≥25 mm, and FFN≥200 ng/ml with PTB <32, 30, and 37 weeks.

RESULTS: 28,660 symptom assessment sessions were recorded. 78% and 92% of subjects noted one or > symptoms at 22-24 and ≥ 25 weeks, respectively. No single symptom was consistently associated with PTB. Women with ≥ 3 symptoms at 25-32 weeks were more likely to deliver < 37 but not < 35 or < 32 weeks. The sensitivity (range 62.9% to 75.8%) and positive predictive value (range 33.7% to 41.6%) of ≥ 3 Sx were low. Odds ratio and 95% confidence intervals from the multivariable analysis are shown in the table for PTB < 37 weeks.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC≥4/hr</td>
<td>1.49 (1.12-1.98)</td>
</tr>
<tr>
<td>BS≥4</td>
<td>1.49 (1.07-2.05)</td>
</tr>
<tr>
<td>CL≥25 mm</td>
<td>2.16 (1.24-3.75)</td>
</tr>
<tr>
<td>FFN≥200 ng/ml</td>
<td>2.18 (1.06-4.47)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Self perceived Sx are poor predictors of PTB. After adjustment for CL, FFN, MC, and BS, the occurrence of multiple Sx was related to PTB only at ≥31-32 weeks and only for PTB < 37 weeks.
EFFECTIVENESS OF ANTENATAL BETAMETHASONE AFTER PRETERM PREMATURE RUPTURE OF THE MEMBRANES

Objective: To determine the effect of antenatal betamethasone on the incidence of intraventricular hemorrhage (IVH) and respiratory distress syndrome (RDS) in patients with preterm premature rupture of the membranes (PPROM).

Study Design: We performed a prospective observational analysis of 407 singleton infants with PPROM delivered between 24 and 32 weeks gestation. Patients were subdivided into two groups based on betamethasone exposure: (1) none (controls), and (2) two 12 mg doses over a 24 hour interval on admission (single course). Patients receiving >2 doses of betamethasone were excluded. All patients received broad-spectrum prophylactic antibiotics. Data were analyzed by the Student’s t-test, chi square test, and Fischer’s exact test. Multiple logistic regression analysis was performed incorporating multiple variables considered risk factors for RDS and grades 3-4 IVH with p < 0.05 considered significant.

Results: A total of 302 patients were included with 203 in the control group and 99 in the single course group delivering at 31.0 ± 3.0 (S.D.) weeks of gestation. The groups were similar with respect to selected demographics, latency until delivery, mode of delivery, birthweight, and maternal GBS status. Univariate analysis demonstrated a significant decrease in the frequency of both RDS and grades 3-4 IVH without an increase in infectious morbidity/mortality in the betamethasone group (p < 0.01). Multiple logistic regression analysis demonstrated a significant decrease in the frequency of RDS and grades 3-4 IVH with a p < 0.05.

Conclusions: These data support the hypothesis that an asymptomatic chronic intratamotic inflammatory process may be associated with some early cases of preterm delivery that could be identified at the time of routine MSAFP screening.

INTERLEUKIN-6 DETERMINATIONS IN CERVICAL FLUID HAVE DIAGNOSTIC AND PROGNOSTIC VALUE IN PRETERM PREMATURE RUPTURE OF THE MEMBRANES

R.H. Youn, R. Romero, M.J. Kim, S. Park, S.H. Ko, T. Kim, G.J. Kim

Objective: To determine the behavior of interleukin-6 (IL-6) concentrations in cervical fluid samples of women who delivered an amniotic cavity, prediction of the duration of the latency period and assess the risk for developing serious neonatal complications.

Study Design: A cohort study was performed in 81 patients with preterm PROM. Amniotic fluid and cervical fluid were collected. Amniotic fluid was cultured for aerobic and anaerobic bacteria as well as Mycoplasmas. IL-6 was measured by a sensitive and specific immunoassay. Receiver operating characteristic curve analysis, logistic regression and survival techniques were used for analysis.

Results: 1) Patients with a positive amniotic fluid culture had a significantly higher median cervical fluid IL-6 than those with a negative amniotic fluid culture (median 528 [range 174-825] pg/ml vs median 168 [range 9261 pg/ml; p<0.001]. 2) Cervical fluid IL-6 concentration of >350 pg/ml had a sensitivity of 92% and a specificity of 74% in the identification of a positive amniotic fluid culture. 3) Patients with a cervical fluid IL-6 of >350 pg/ml had a significantly shorter median interval to delivery, higher rate of spontaneous preterm delivery within 2 days, 3 days and 7 days and the occurrence of significant neonatal morbidity/mortality than those with a cervical fluid IL-6 of <350 pg/ml (p<0.05 for each). 4) The increased perinatal morbidity remained significant after adjusting for gestational age (p<0.05). 5) There was a strong correlation between cervical fluid IL-6 concentrations and amniotic fluid concentrations of IL-6 (r=0.01).

Conclusion: Cervical fluid IL-6 determinations are of value in the identification of patients with microbial invasion of the amniotic cavity, those at risk for impending preterm delivery and the occurrence of significant neonatal complications in the setting of preterm PROM.

FURTHER OBSERVATIONS ON THE FETAL INFLAMMATORY RESPONSE SYNDROME: A POTENTIAL HOMEOSTATIC ROLE OF THE SOLUBLE RECEPTORS OF TUMOR NECROSIS FACTOR.

R. Romero, L. Maymon, M. Mazor, R. Gonzalez, B.H. Yoon, S.M. Berry

Objective: The fetal inflammatory response syndrome (FIRS) is a clinical condition frequently present in preterm labor and preterm premature rupture of membranes (PPROM) and is associated with increased perinatal morbidity/mortality. We propose that FIRS is part of a spectrum of disease that can progress from systemic fetal inflammation, multiple organ dysfunction and septic shock to fetal death in the absence of timely birth (spontaneous or induced). Tumor necrosis factor (TNFα) is a mediator of septic shock and death. This cytokine exerts its biological effects by interacting with two receptors: TNF-R1, which induces programmed cell death and TNF-R2, which activates nuclear factor kappa B (NFκB). Soluble TNF receptors are thought to buffer the biological effects of TNFα. The purpose of this study was to determine the behavior of soluble TNF receptors in fetal blood samples with and without FIRS.

Study Design: Fetal blood samples were obtained at an average of 16.5 weeks gestation in patients with preterm labor (n=95) and PPROM (n=46). Control samples were obtained from fetuses undergoing blood sampling for clinical indications who had normal uneventful pregnancies. The level of TNFα-R1 and TNFα-R2 concentrations were determined using sensitive and specific immunoassays. ANCOVA was used for statistical analysis.

Results: 1) TNF-R1 and TNF-R2 were detectable in all samples and concentrations increased with advancing gestational age (r=0.77 and r=0.65; p<0.0001 and p<0.003, respectively) 2) The mean fetal plasma TNF-R1 and TNF-R2 concentrations were significantly higher in fetuses with FIRS than those without FIRS after adjusting for gestational age and fetal membrane status. TNF-R1 (n=48) mean 130.4 pg/ml, SE 7.9 pg/ml vs. FIRS mean 197.9 pg/ml, SE 17.4 pg/ml; p<0.0003). TNF-R2 (n=48) mean 6604 pg/ml, SE 705.2 pg/ml vs. FIRS mean 7785 pg/ml, SE 342.8 pg/ml; p<0.0001). 3) Fetuses of patients who delivered within 72 hours of labor had coagulopathy which had significantly higher concentrations of TNF-R1 and TNF-R2 than those with longer latency periods (p<0.005 for each).

Conclusions: We propose that the increased concentration of soluble TNF receptors in the human fetus with FIRS attenuate the deleterious effects of TNF.
USE OF ANTENATAL MAGNESIUM SULFATE DOES NOT SEEM TO PREVENT INTRAVENTRICULAR HEMORRHAGE. R. M. Mittendorf, L. Bentz, J. Kohn, R. Covert. University of Chicago, Chicago, IL.

OBJECTIVE: To learn whether using tocolytic or small prophylactic doses of intravenous magnesium sulfate (MgSO4) in the mother with preterm labor will prevent intraventricular hemorrhage (IVH), or periventricular leukomalacia (PVL) in her infant.

METHODS: The Magnesium and Neurologic Endpoints (MAGnet) Trial, a randomized controlled trial funded by the United Cerebral Palsy Research and Educational Foundation, consisted of two mutually-exclusive sections. In the tocolytic section, mothers in preterm labor who were candidates for tocolysis were randomized to either MgSO4 or another tocolytic. In the other section of the trial, mothers in active preterm labor who could not be tocolyzed because they were dilated >4 cm, were randomized to receive either MgSO4 4 g IV or saline control. We used this amount of MgSO4 as a bolus because the drug had never been used before in the U.S. as a possible neuroprotectant against IVH, or PVL. Thus, the IRB approved the same loading dose of MgSO4 (4 g) that our hospital uses for eclampsia prophylaxis. After delivery, to diagnose IVH and PVL, we did neuroimaging on at least 3 occasions: once in the first 3 days of life, once at the end of the first week, and lastly, at 1 month of age.

RESULTS: In the tocolytic arms, 17% (8/47) of fetuses exposed to MgSO4 were later diagnosed as having IVH (2 of 8, Grades III-IV), whereas 14% (6/42) of those exposed to “other” tocolytics got IVH (1 of 6, Grades III-IV) (overall 2-sided Fisher’s exact test, p=.78). In the preventive arms, 14% (4/29) exposed to MgSO4 had IVH (0 of 4 had Grades III-IV), whereas 14% (4/28) exposed to saline control had IVH (1 of 4, Grades III-IV) (overall 2-sided Fisher’s exact test, p=1.0). One child, exposed to MgSO4 in the preventive sections, got PVL.

CONCLUSION: Our data findings do not support the hypothesis that MgSO4 is a neuroprotectant against IVH. Further, despite any limitations of size, the profundity of the findings do not suggest that a type II statistical error could be evoked to explain the absence of a neuroprotective effect.
ORAL CONCURRENT SESSION E

Labor

Saturday, February 5, 2000
8:00 am - 10:00 am

Moderators: Michael P. Nageotte, MD
Susan M. Ramin, MD

Judges: Helen H. Kay, MD
Howard T. Strassner, MD
James A. Thorp, MD

Fontainebleau Ballroom C
Abstract Numbers 53-60
**PREDICTION OF PARTURITION IN HUMANS USING TRANSABDOMINAL UTERINE ELECTROMYOGRAPHIC ACTIVITY RECORDING.**

**STUDY DESIGN:** Pregnant women presenting to the labor and delivery area to rule out labor were evaluated. Those in whom the differentiation between true and false labor could not be made clinically with certainty (confections present but no definitive cervical change) were included (n=17; 27 to 42 weeks gestation). Uterine electrical activity in a frequency range of 0.05-50 Hz was recorded for about 30 minutes using bipolar electrodes placed on the abdominal surface. The EMG signals were stored and analyzed using a 12-bit Lab Recording System. For those patients which exhibited significant activity during the record, each EMG “burst” was analyzed by Fast Fourier Transform at a resolution of 9128 FFTs to obtain its power density spectrum (PDS). For each burst, the PDS peak frequency (Hz) and mean values for the burst were calculated for each patient. The mean PDS peak was plotted against the measurement-to-delivery interval. Receiver operating characteristics (ROC) curves were used to predict delivery within 24, 12 or 8 hours.

**RESULTS:** PDS peak frequency increased as the time from measurement to delivery (tune of 0) decreased (Fig. 1). ROC curve analysis showed that PDS peak was predictive of delivery within 24, 12 or 8 hours, thereby allowing for improved management of patients in whom the diagnosis of true labor is not clear.

**CONCLUSIONS:** Transabdominal recording of uterine EMG activity can predict delivery within 24, 12 or 8 hours, thereby allowing for improved management of patients in whom the diagnosis of true labor is not clear. (Supported by NIH HD37480)

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**EVIDENCE FOR INCREASED ACTIVITY OF A POTENT MATRIX DEGRADING ENZYME IN PRETERM AND TERM LABOR.**

**OBJECTIVE:** Degradation of extracellular matrix is a central event of the mechanisms responsible for membrane rupture: MMP-9 and MMP-2.

**STUDY DESIGN:** To determine if parturition can be predicted using uterine electromyographic (EMG) activity recorded transabdominally.

**RESULTS:** PDS peak frequency increased as the time from measurement to delivery within 24 (Fig. 2: r=0.38, p<0.0001), 12 (r=0.34, p=0.001) and 8 (r=2.9, p=0.002) hours. Best cutoffs and sensitivity (Sens), specificity (Spec) and predictive values (PVA), and (NPV) for each measurement-to-delivery interval shown:

<table>
<thead>
<tr>
<th>Delivery within</th>
<th>Cutoff (Hz)</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hours</td>
<td>3.496</td>
<td>92.3</td>
<td>83.3</td>
<td>85.7</td>
<td>90.9</td>
</tr>
<tr>
<td>12 hours</td>
<td>3.510</td>
<td>88.9</td>
<td>75.0</td>
<td>66.7</td>
<td>92.5</td>
</tr>
<tr>
<td>8 hours</td>
<td>3.510</td>
<td>100</td>
<td>65.0</td>
<td>41.7</td>
<td>100</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Transabdominal recording of uterine EMG activity can predict delivery within 24, 12 or 8 hours, thereby allowing for improved management of patients in whom the diagnosis of true labor is not clear. (Supported by NIH HD37480-01)

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**THE OPTIMISATION OF INTRAVAGINAL MISOPROSTOL DOSE IN SECOND-TRIMESTER PREGNANCY TERMINATION**

**STUDY DESIGN:** Prospective randomized double-blind controlled clinical trial of pregnancy termination between 14 and 30 weeks gestation. Three intravaginal misoprostol dosage regimens were compared: 200 μg misoprostol 6-hourly (Group 1), 400 μg misoprostol 6-hourly (Group 2), and a loading dose of 600 μg misoprostol followed by 200 μg 6-hourly (Group 3). A sample size of 150 women was required for equivalence of the three groups.

**RESULTS:** 150 women were randomised: 51 to Group 1, 50 to Group 2 and 49 to Group 3. There was no difference in maternal age, race, parity or prior uterine surgery between groups. Indications for termination: 21% fetal death, 63% severe fetal anomaly and 16% maternal reasons. There were significantly more women in Group 1 with a fetal death compared to Groups 2 and 3 (35.5% vs 18% vs 18.4%, p=0.001). Median gestation at recruitment was identical: Group 1:19.0 weeks (IQ 16.2-20.7 weeks), Group 2: 18.4 weeks (IQ 17.4-19.7 weeks), Group 3: 18.7 weeks (IQ 17.7-19.9 weeks); p=0.46.

There was a significant difference in the median time to achieve delivery between the group; Group 1: 18.2 hours (IQ 13.8-29.5) vs Group 2: 15.1 hours (IQ 10.9-26.7) vs Group 3: 13.2 hours (IQ 11.26-21.7); p=0.0005. 56% of women in Group 1, 76% in Group 2 and 80% in Group 3 delivered within 24 hours (p=0.015, 7.8% in Group 1, 0% in Group 2 and 2.1% in Group 3 were undelivered at 48 hours (p=0.05). The median delivery interval was very similar to those cases with a live fetus for all groups (15.3 hours vs 18.2 hours); p=0.60. There was a significant increase in the incidence of maternal side effects (nausea, diarrhea, vomiting and pain) for Group 3 compared to Groups 1 and 2 (p=0.038). The incidence of vomiting within 3 hours of the initial dose was increased in Group 3 compared to Groups 1 and 2 (p=0.018). There was no significant difference in nausea, diarrrhea, vomiting and pain scores for Groups 1 and 2.

**CONCLUSION:** Intravaginal misoprostol 400 μg 6-hourly appears to be the preferred dosage regimen for second trimester pregnancy termination with a shorter commencement to delivery interval than the 200 μg dosage regimen and less maternal side-effects than the 600 μg loading dose regimen.

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**FOLEY BULB FOR PREINDUCTION CERVICAL RIPENING IN THE OUT-PATIENT VERSUS THE INPATIENT SETTING**

**OBJECTIVE:** To compare the clinical efficacy and side effects of three dosage regimens for cervical ripening in the inpatient (IP) vs. the outpatient (OP) setting. The use of the Foley bulb has been previously shown to be safe and effective for preinduction cervical ripening. The potential benefits of OP cervical ripening includes a lower cost, a decreased burden on busy obstetric units, and increased patient comfort and convenience.

**STUDY DESIGN:** A randomized prospective trial was conducted from May 1998 to August 1999. Women with a term gestation in the vertex presentation, a reactive non-stress test, an amniotic fluid index >5th percentile, and a Bishop score of <7 with a reacUve non-stress test, an amniotic fluid index > 5th percentile, and a Bishop score of <7 were included in the study. Fifty women were randomized into the OP group and 44 into the IP group. Maternal age, gravidity, previous Cesarean delivery, and gestational age were not different between the groups. The mean Bishop score at entry was 2.5 for each group (p=0.58). The mean change in Bishop score was not different between the IP and OP groups (2.4 vs. 2.5; p=0.48).

There was no significant difference in discomfort during preinduction cervical ripening between the groups. The maximum dose of pethidine, time on pethidine, epidural rate, duration of epidural, and time to first dose of pethidine and cord pH were not significantly different. There was no significant difference in the rate of Cesarean delivery between the IP and OP groups (43 % vs. 4% P=0.19). The OP group on average avoided 9.6 hours of hospitalization. Furthermore, there was a 30% reduction in hospital charges in the OP group (p<0.001). There were no adverse events or maternal morbidity in either group.

**CONCLUSIONS:** The Foley bulb is as effective in the OP as the IP setting for preinduction cervical ripening. The use of the Foley bulbs in the OP setting resulted in a significant decrease in hospital costs. Furthermore, less time spent in the hospital may result in an increase in patient satisfaction with the preinduction ripening process.
A RANDOMIZED TRIAL ON THE INFLUENCE OF INCREASED INTRA-VEOUS HYDRATION ON THE COURSE OF NULLIPAROUS LABOR

T.J. Weeks, M.D., J. Weeks, M.D., K. Peters-Pirhr, R.N.† University of GA, Irvine, Orange, CA

OBJECTIVE: The adequacy of maternal hydration has the potential to affect the course of labor, but has not been evaluated clinically. Typical practice allows only 125 cc/hr of IV fluids; yet many such laboring patients have evidence of inadequate hydration. Exercise physiology studies suggest increased hydration improves muscle performance. This study was designed to determine if increased IV fluids affect the course of labor.

STUDY DESIGN: Uncomplicated nulliparas at term in spontaneous labor between 2 and 5 cm of dilation with a cephalic presentation were eligible. Consentted patients were randomized to receive either 125cc or 250 cc/hr of Lactated Ringer's via infusion pump.

RESULTS: At study conclusion, there were 94 patients in the 125cc and 101 in the 250cc groups. Pseudorandomization variables were well matched between the two groups including variables known to affect labor such as maternal age, birthweight, dilation at entry, frequency of and dilation at amniotomy, frequency of epidural, station and dilation at epidural placement. The means of total IV fluids administered were significantly different both for total fluids (1880 cc in 125cc vs. 2357 in the 250 cc groups, P<0.01) as were the hourly fluids (152 cc/hr vs. 254 cc/hr, P<0.01). Caesareans were more frequent (17% - 125cc vs. 9.9% - 250cc) but not statistically significant (P=0.2). The mean duration of the first stage and total labor (randomization to complete dilation and to vaginal delivery), although longer in the 125cc group by 52 and 51 min, respectively, also did not achieve statistical significance (P=0.2), although laborers longer than 15 hours were greater in the 125cc group (23/78 vs. 15/91, P<0.05).

CONCLUSION: Although not definitive, the suggestion of longer labors and more frequent cesarean sections, and the trends for higher C-section rates, would suggest that insufficient hydration in labor may be a contributing factor to higher rates of dysfunctional, less efficient labors. Consideration of this factor in future studies considering variables which affect labor is warranted.

A RANDOMIZED CONTROLLED TRIAL OF PRIMARY REPAIR OF THIRD DEGREE PERINEAL TEARS, COMPARING OVERLAP AND APPROXIMATION TECHNIQUES


OBJECTIVE: Delayed pushing in the second stage of labor has been recommended to reduce increased instrumental delivery rates associated with epidural analgesia. However injury to the anal sphincter mechanism may be associated with prolonged second stage. We report the outcome of a prospective, randomized, controlled trial comparing immediate and delayed pushing after full cervical dilation.

STUDY DESIGN: 114 nulliparous patients, all with epidural analgesia, were randomized at full cervical dilation, but before the fetal head had reached the pelvic floor, to either immediate pushing (IP) or one hour delayed pushing (DP). In addition to labor outcome analysis, all women who had a normal delivery underwent postpartum assessment of anal sphincter function, including manometry and neurophysiology.

RESULTS: 60 (53%) women were randomized to IP and 54 (47%) to DP. The spontaneous vaginal delivery rate was 62% (37/60) in the IP group and 60% (32/54) in the DP group. Labor was significantly longer with DP compared to IP (490 mins vs. 386 mins, P<0.05). Fetal outcome did not differ with either practice. 18 of 64 women (28%) who had a normal delivery noted some alteration in fecal continence postpartum (19% IP and 41% DP). Neither anorectal manometry nor neurophysiology differed significantly between the IP and DP groups. Pudendal nerve sensory threshold was prolonged in 5 IP and 8 DP patients. Pudendal nerve EMG did not differ with either practice but pudendal nerve demyelination was identified in 50% following normal delivery.

CONCLUSION: Delayed pushing in second stage of labor with epidural analgesia does not seem beneficial in reducing instrumental deliveries and leads to significantly longer labors. Altered fecal continence was more frequent, but not significantly so, following delayed pushing. Postpartum anal manometry and EMG did not differ with either practice but pudendal nerve demyelination was identified in 50% following normal delivery.

MATHEMATICAL MODELING OF FORCES ASSOCIATED WITH SHOULDER DYSTOIA: A COMPARISON OF ENDOGENOUS AND EXOGENOUS SOURCES

R. Gohda, A. Walker, R. Grinnan, Dept. Obst/Gyn and Mech Eng, Wayne State Univ, Detroit, MI.

OBJECTIVE: A model was developed to estimate the compression pressure exerted on the fetal neck overlying the brachial plexus by the symphysis pubis (SP) during a shoulder dystocia event. The induced pressure (P) was calculated for both exogenous (EXO) (clinician applied) and endogenous (ENDO) (maternal/neonate) forces (F) during the 2nd stage of labor.

STUDY DESIGN: A free body diagram was constructed using standard engineering principles. Representative uterine (UT) and SP geometric data were transformed to match the data presented from the literature. For END10, the area (A) of the SP evaluated on the basis of the maximum uterine pressure (P) on the uterine end. The induced compression pressure at the site of fetal impaction compared to the END0 related forces.

RESULTS: As the areas (A) of the UT and fetal impaction site behind the SP were approximated using the formulas for an ellipsoid and animal, respectively, any deviations were extrapolated using existing intrauterine pressure measurements, according to the equation: $F_{END0} = P_{UT} \times A_{UT}$. Tracturation related $F_{EXO}$ were obtained from previously established in situ data. Impact pressures behind the SP were then derived using the equation: $F_{EXO} = F_{END0} - F_{UT}$.

RESULTS: The calculated areas for the transverse cross-section of the UT and the contact area of the SP were 0.0549 m² and 0.00437 m², respectively. $F_{END0}$ ranged from 986-884 Newtons (N). $F_{EXO}$ were previously determined to range between 48-100 N. When the model was applied to determine the impact pressure between the base of the fetal neck and the SP, values ranged from 91-229 kPa for $F_{END0}$. In contrast, the clinician generated $F_{EXO}$ resulted in compression pressures of 11-23 kPa (p<0.01). Using the highest estimated traction forces, this still represents only 1/15th to 1/4th the compression pressure at the site of fetal impaction compared to the END0 related forces.

CONCLUSION: These are the first data to examine 2nd stage of labor delivery forces and their potential relationship to impaction site brachial plexus compression injury. Significant endogenous forces, much in excess of those generated by the delivering clinician’s traction efforts, may be a contributing factor to this type of injury. Neonatal brachial plexopathy is not a priori explained by iatrogenically induced excessive traction applied by the clinician.

VENOUS HYDRATION ON THE COURSE OF NULLIPAROUS LABOR

A RANDOMIZED TRIAL ON THE INFLUENCE OF INCREASED INTRA-VEOUS HYDRATION ON THE COURSE OF NULLIPAROUS LABOR


OBJECTIVE: To compare anal sphincter approximation with overlap primary repair after third degree tear in a prospective, randomised controlled trial.

STUDY DESIGN: 112 primiparous women who sustained a third degree tear during a one year period were randomized, upon diagnosis, to an overlap or approximation repair. Obstetric personnel, trained in both methods, carried out the repairs immediately following delivery. Overlap repair was performed in 55 women and approximation repair in 57. Follow-up at three months postpartum consisted of symptom questionnaire, anal manometry and endoanal ultrasound. Data were analysed using Mann-Whitney U and Chi-square tests.

RESULTS: Obstetric factors, including mode of delivery, birthweight, length of labour and episiotomy rate, did not differ significantly between the two repair cohorts. Status of operator, analgesia used and place of repair were similar in both groups. Median incontinence scores were 0 after overlapping and 3 after approximation repairs. 11(20%) women complained of a fecal sensation following overlap repair compared with 17 (30%) following approximation. There was no significant difference in either anal manometry or endoanal ultrasonography or symptoms between the two groups. 6 (11%) of women had a significant (>1 quadrant) anal sphincter defect following overlap repair compared with 3(5%) following approximation repair. Overall, 66% of women had ultrasonic evidence of a residual full thickness defect in the external anal sphincter following primary repair.

CONCLUSION: In this randomised trial, overlap repair of the anal sphincter following third degree tears was not superior to approximation repair in terms of postpartum continence symptoms, manometry or ultrasound. Overall symptomatic outcome was good, although two-thirds of women had evidence suggesting some residual damage on endoanal ultrasound irrespective of the method of repair.
ORAL CONCURRENT SESSION F

Medical/Surgical Complications
Infectious Diseases

Saturday, February 5, 2000
8:00 am - 10:00 am

Moderators:  James T. Christmas, MD
Jay D. Iams, MD

Judges:      Stanley M. Berry, MD
Maureen P. Malee, MD
George D. Wendel, MD

Fontainebleau Ballroom D
Abstract Numbers 61-68

OBJECTIVE: Ureaplasma urealyticum (U urealyticum) is the most common microorganisms isolated from the amniotic fluid (AF) with standard microbiologic techniques (i.e., culture) in patients with preterm premature rupture of the membranes (PROM) and preterm labor. Recently, the polymerase chain reaction (PCR) has been an excellent, sensitive and rapid method for the detection of microorganisms. The high sensitivity of PCR may result in the identification of patients who are colonized with a small number of microorganisms but not at risk for the adverse pregnancy outcome observed in patients with a positive microbial cultures. The objective of this study was to determine the clinical significance of a positive PCR for U urealyticum in the AF of patient with preterm PROM.

STUDY DESIGN: Ameioticosis was performed in 154 patients with preterm PROM. AF was cultured for aerobic and anaerobic bacteria as well as Mycoplasma. U urealyticum was detected by PCR. Patients were divided into three groups according to the results of AF culture and PCR for U urealyticum: 1) those with negative AF culture and negative PCR (n=99), those with negative AF culture but positive PCR (n=18), and those with positive AF cultures (n=37). Survival techniques were used for analysis.

RESULTS: 1) U urealyticum was isolated by PCR in 27% (42/154) of cases and by culture in 16% (25/154), 2) Of the 42 cases with positive PCR for U urealyticum, AF culture was negative in 42% (18/42), 3) Patients with negative AF culture and positive PCR for U urealyticum had significantly shorter median amnioticosis-to-delivery interval and higher AF white blood cell than those with negative AF culture and negative PCR (interval to delivery: median 55 range 0-3535 hours vs median 1141; 0.005, AF WBC count: median 513 [1295] cells/mm3 vs median 1 [7056] cells/mm3, p=0.001); 4) Patients with positive PCR for U urealyticum but negative AF culture had a higher rate of significant neonatal morbidity than those with negative culture and negative PCR (p=0.05). 5) No significant differences in perinatal outcome were observed between patients with negative culture and positive PCR and those with positive AF culture.

CONCLUSION: 1) Standard culture for Mycoplasmas missed 49% of patients with macroscopic invasion with U urealyticum; 2) Patients with positive PCR but negative AF culture are at risk for adverse maternal and neonatal outcomes; 3) The use of molecular microbiologic techniques will increase the detection of infection in patients with obstetrical complications.

62 COST-EFFECTIVENESS OF A RECOMMENDATION FOR ELECTIVE CESAREAN SECTION OF HIV-INFECTED PREGNANT WOMEN ON ZIDOVUDINE THERAPY TO REDUCE VERTICAL TRANSMISSION. J. T. Chye, RE Tsuama, RL Sell, Dept Obst/Gyn, Brigham and Women's Hospital, Boston, MA and Div of Somatic Medical Sciences, Columbia School of Public Health, New York, NY.

OBJECTIVE: To evaluate the clinical and economic outcomes of a recommendation for elective cesarean section of HIV-infected pregnant women on zidovudine (ZDV) therapy.

STUDY DESIGN: A decision analysis model was constructed to compare two strategies. 1) usual care where HIV-infected pregnant women on ZDV therapy undergo delivery according to obstetrical indications and 2) recommendation for elective cesarean section. The model followed a hypothetical cohort of 7000 HIV-infected pregnant women only on ZDV therapy in the United States for one year. The number of each delivery method (with and without complications), the number of maternal deaths, and the number of HIV-infected neonates resulting from each strategy were calculated. Costs of delivery method (with and without complications), age-specific work-loss costs from death due to delivery method, and lifetime care costs for HIV-infected children were considered.

RESULTS: Compared to usual care, recommendation for elective cesarean section strategy would result in an additional 3485 cesarean sections (50% with complications) occurring each year, present 53% (184 of 343) of vertical transmission cases each year, cost $39,000 per case prevented, and result in net savings of $345 million in discounted medical costs if lifetime care costs for HIV-infected children were considered. The recommendation for elective cesarean section strategy would result in only one maternal death after 2.93 years as compared to after 4.8 years in the usual care strategy.

CONCLUSION: The recommendation for elective cesarean section of HIV-infected pregnant women only on ZDV therapy could prevent more than half of vertical transmission cases, and is cost-saving. It should be considered for prevention of vertical transmission in this select population.

63 HEPARIN USE IN PREGNANCY FOR WOMEN WITH A HISTORY OF VENOUS THROMBOEMBOLISM: A DECISION ANALYSIS. M. M. Tai, A. Deeks, Univ. of Toronto, Mount Sinai Hospital, Toronto, ON, Canada.

OBJECTIVE: Heparin prophylaxis for all pregnant women with a history of Venous Thromboembolism (VTE) remains controversial. Heparin, although potentially decreasing the risk of VTE, may lead to osteoporosis, thrombocytopenia, and bleeding. With the use of a decision analysis model, we propose to use explicit, quantitative methods to compare the expected consequences of the following strategies: 1) heparin prophylaxis for all pregnant women with a history of VTE; 2) test pregnant women with a history of VTE for a hereditary thrombophilia and give heparin prophylaxis to those with a positive test; or 3) no heparin prophylaxis; just clinical follow-up.

STUDY DESIGN: Our base case is a thirty year old woman who would be expected to live 46 years. Probabilities for each outcome are derived from extensive literature searching. The payoffs are Quality adjusted life years (QUALY'S). Utilities are derived from patient interviews. Osteoporosis is modelled as a health state with its own utility. Bleeding, HIT, VTE, and heparin use are all modelled as disutilities. The utilities for each health state are developed by the composite method. Disutilities are subtracted from the utilities.

RESULTS: In the base case analysis the test strategy was favoured over the treat none and treat all. The test strategy was superior to the treat all by 0.14 QUALY'S. The model was sensitive to the recurrence risk of VTE and to the specificity of the thrombophilia test.

CONCLUSION: We conclude from our model, that for women who have a history of VTE who become pregnant, that it is best to use heparin prophylaxis only for those who test positive for a thrombophilia. Our sensitivity analysis indicates that more research is necessary to determine the recurrence risk of VTE in pregnant women and to determine the prevalence of thrombophilias in this population.

OBJECTIVE: Lipopolysaccharide (LPS) and other products of infection stimulate inducible nitric oxide synthase (iNOS) and increase nitric oxide (NO) production. Our objective was to determine if LPS promotes cervical ripening in pregnant rats and whether its effect is NO dependent.

STUDY DESIGN: Timed-pregnant Sprague-Dawley rats were sacrificed on gestational day 17 after treatment with L-arginine-methyl ester salts (L-NME, 50mg/day/rat for 48hrs via osmotic minipumps), LPS (40μg/kg intraperitoneal at 39.5), LPS plus L-NME, or vehicle control (CTR). The cervix was isolated from each animal and suspended between two hooks in organ baths containing physiologic solution. The hooks were connected to a cervometer that stretched the cervical tissues in incremental steps of 0.5 mm at 1 minute intervals. This procedure produced force versus displacement curves. The slope of the regression line through the linear portion of the curve was taken as a measure of the cervical extensibility or resistance to stretch. A steeper slope indicates more resistance to stretch and a more rigid cervix.

RESULTS: Cervical resistance was significantly lower in the LPS treated animals compared to control (CTR). L-NME (LN) alone significantly increased cervical resistance. The combined treatment of LPS plus L-NME were significantly higher than LPS alone, and similar to CTR. Values with common superscripts in the figure are not significantly different (p>0.05).

CONCLUSIONS: LPS softens the cervix and this effect is NO mediated. Infection-induced cervical ripening may be prevented by NOS inhibition.

PLASMA LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND PLACENTAL GROWTH FACTOR ARE REDUCED IN WOMEN WITH SEVERE PREECLAMPSIA. JC Livenson, R. Chin*, FT McKinney, BR Haddad, and BM Sibai, Department of Ob/Gyn, University of Tennessee, Memphis, TN.

OBJECTIVE: Placental growth factor (PlGF) and vascular endothelial growth factor (VEGF) are homologous protein members of the endothelial growth factor family with potent angiogenic and mitogenic activity resulting in enhanced permeability. The purpose of this study was to determine whether plasma levels of the VEGF and PlGF are altered in women with severe preeclampsia.

STUDY DESIGN: Plasma levels of VEGF and PlGF were measured in 21 women with severe preeclampsia and in 21 normotensive women admitted for delivery. VEGF and PlGF were measured by a specific antigen captured enzyme-linked immunosorbent assay. Comparisons were made using the Student's t test.

RESULTS: Preeclamptic women had significantly lower plasma levels of VEGF and PlGF than women with normotensive pregnancies. After correcting for placental weight, logistic regression analysis showed an independent association between preeclampsia and both VEGF and PlGF plasma levels.

Table 1: Clinical parameters and growth factor plasma levels in preeclampsia and control groups.

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia (n=21)</th>
<th>Control (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Age (wks)</td>
<td>35.6±3.1</td>
<td>37±3</td>
<td>n/a</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>174±24</td>
<td>158±14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>113±4</td>
<td>81±1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2852±746</td>
<td>3038±869</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Placental weight (g)</td>
<td>472±174</td>
<td>665±247</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PlGF (pg/ml)</td>
<td>186±110</td>
<td>551±339</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VEGF (pg/ml)</td>
<td>1.86±5.12</td>
<td>18.68±1.98</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

CONCLUSION: Patients with severe preeclampsia have decreased maternal levels of both VEGF and PlGF. Decreased levels of these angiogenic substrates may be responsible for the placental dysfunction reported in pregnancies with severe preeclampsia.

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INTERLEUKIN-10 ADMINISTRATION PREVENTS INJECTION MEDIATED PRETERM BIRTH IN A RAT MODEL. DA Terman*, KR Ranchar*, PS Barrilleaux, Jr, JM Martin Jr., JP Granger; WA Bennett* Dept. Ob/Gyn, Univ. Mississippi Medical Center, Jackson, MS.

OBJECTIVE: To determine if interleukin-10 (IL-10) can prevent preterm delivery in rats treated with intrauterine lipopolysaccharide endotoxin (LPS).

STUDY DESIGN: Pregnant Sprague-Dawley rats (n=23) underwent surgical implantation of uterine catheters on day 15 or 16 of a 22 day gestation per a previously described model. Animals were then randomly assigned to receive either infusion of 50 μg of LPS, 50 μg of LPS with 500 ng of IL-10, or saline. All infusions were in a volume of 1 ml infused over a four-hour period.

RESULTS: Pups born to L-NME treated mothers (5.2±0.2g) were significantly (p<0.0001) smaller than controls (6.5±0.1g). The differences persisted even at postnatal day 77 (see graph). SBPs were not different between the LPS-50/IL-10 and saline infused rats compared to LPS-50 infused animals (p>0.05).

CONCLUSIONS: Rats with in-uterine exposure to L-NME exhibited decreased neonatal WT, postnatal growth, fertility, and subsequent delay in delivery. There were no differences between LPS-50/IL-10 alone (p>0.05 for both). The pup birth weights were significantly greater for both the LPS-50 and saline groups as compared using unpaired t-test. p<0.05 was considered significant.

---

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POSTER SESSION I

Thursday, February 3, 2000
10:00 am - Noon

Fontainebleau Ballroom A/B

CATEGORIES
Prematurity
Neonatology
Epidemiology

Poster Numbers
69-189

Judges: Steve N Caritis, MD
        Michael K. Lindsay, MD
        Charles J. Lockwood, MD
GLUTATHIONE SUPPLEMENTATION INCREASES FETAL SURVIVAL AFTER ENDOTOXIN ADMINISTRATION IN A MURINE MODEL.

I. Bukowski and CP Weiner. Dept. of Ob./Gyn., Univ. of Maryland School of Medicine, Baltimore, MD

Objective: To determine if dosing of maternal antenatal betamethasone at 12 versus 24 hour intervals has an effect on the reduction of neonatal outcome, morbidity and mortality.

Study Design: All premature deliveries at our institution between November 1993 and July 1997 that had received a single course of two 12 mg intramuscular injections of antenatal betamethasone for fetal indications were analyzed. The study population was divided into two groups based on the dosing interval: 12 versus 24 hours. Deliveries between 24 & 0/7 and 34 & 6/7 weeks gestational age and occurring within 7 days of the initial steroid administration were included. Neonatal mortality, morbidity, and outcomes were compared. Secondary, the proportion of deliveries in the 12-hour group that occurred after 24 hours was compared to the number in the 24 hour group that delivered in less than 24 hours.

Results: The outcomes of 424 neonates were analyzed; 314 in the 12 hour group and 110 in the 24 hour group. There were 22 neonatal deaths in the 12 hour group and 5 in the 24 hour group, P<0.05. There was a significantly higher number of cases of neonatal sepsis in the 12 hour group, 12% vs. 4%, P<0.009. The incidence of neonatal respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, patent ductus arteriosus, respiratory and seizures was not significantly different between the groups. There was a significant difference between the two groups in the requirement for mechanical ventilation, days on the ventilator, length of stay, and survival.

Conclusion: The proposed combined use of the cervical sonography and fFN testing is a practical diagnostic tool for predicting preterm delivery with higher sensitivity and NPV than any of these methods alone.
**73 ACTIVATION OF APOPTOSIS IN PROM: CASPASE INDEPENDENT?**

Ramkumar Menon, M.S., Salvatore J. Lombardi, M.D., Stephen J. Forunato, M.D. Pernazza Research Center of the Women’s Health Research and Education Foundation, Nashville, TN 37205

**OBJECTIVE:** Our laboratory has recently demonstrated a role for apoptosis in PROM as an inducer of MMP activity. Multiple pathways can trigger apoptosis, the most common one being the caspase cascade. This study examines the mechanism of apoptosis induction in PROM.

**METHODS:** Human fetal membranes were collected from women with PROM, PTM, and after term delivery (n=10). Fragmentation of DNA was studied by LM-PCR (ligase mediated PCR). RNA extracted from fetal membranes was reverse-transcribed and a multiplex PCR (MPCR) strategy was used to study the expression of Caspases 3, 5, 8, 9, Apaf-1 (caspase 3 activator). Quantitative PCR was employed to document the changes in the expression pattern of Bcl-2 and Bax.

**RESULTS:** LM-PCR data showed typical “DNA laddering” in fetal membranes from PROM (8/10) compared to term (3/10) and preterm labor (0/10). Caspase 3 and 9 expression was seen in all samples while Apaf-1 (cytochrome dependent caspase 3 activator), caspase 5 and 8 expression was not detected in any of the samples tested regardless of the condition. A 100 fold increase in Bax expression coincided with a significant drop in Bcl-2 expression in PROM membranes compared to the other two groups (p<0.01). A similar increase in the Bax inducer p53 was also seen in PROM.

**CONCLUSION:** DNA fragmentation was minimal in fetal membranes from PROM and can be detected only by highly sensitive by LM-PCR. Although caspase 3 and 9 genes are expressed, their activator protein genes (caspase 5, 8 and Apaf-1) are not expressed in fetal membranes. DNA fragmentation induced a p53 and Bax increase and a drop in Bcl-2 suggesting p53 mediated apoptosis in PROM membranes (M-PROM).

**74 VEGF RECEPTOR EXPRESSION IS INCREASED AT THE RUPTURE SITE IN PRETERM PREMATURe RUPTURE OF THE MEMBRANES (PROM):**

RB Wolf, CY Cheung, LV Bogics, Dept of Reproductive Medicine, Division of Perinatal Medicine, University of California at San Diego, La Jolla, CA.

**OBJECTIVE:** We hypothesize that localized activation of vascular endothelial growth factor (VEGF) and/or its receptor, Flt-1 (a tyrosine kinase receptor) in amniotic membranes leads to activation of tissue plasminogen activator (TPA) and metalloproteinases (MMPs) which break down collagen resulting in membrane rupture. This localized premature collagenolysis in the extracellular matrix of the fetal membranes could provide a mechanism for PROM in the absence of labor. This study is designed to determine whether regional differences in gene expression of VEGF and Flt-1 occur within the amnion, chorion and decidua in PROM patients.

**STUDY DESIGN:** Full-thickness membranes were obtained from preterm patients delivering vaginally with spontaneous rupture of membranes which occurred either (1) prematurely (i.e., prior to onset of labor) or (2) after the onset of preterm labor. Membranes were sampled from two regions: close to the site of placental attachment and in the region morphologically distinct as the rupture site. Quantitative in situ hybridization was used to determine the expression of VEGF and of the membrane-bound form of Flt-1.

**RESULTS:** Regional differences in VEGF gene expression were not detected. The expression of its receptor, Flt-1, however, was significantly increased in fetal amnion and decidua at the rupture site (p<0.05) compared to the site of placental attachment. Further, increased expression of Flt-1 at the rupture site was detected in PROM patients regardless of labor status.

**CONCLUSION:** These results suggest that localized over expression of the VEGF receptor Flt-1 may cause premature activation of TPA and MMPs in PROM patients.

**75 IN VIVO TESTING OF PURIFIED BOVINE COLLAGEN INJECTION AS A POTENTIAL THERAPY FOR CERVICAL INCAPACITANCE:**


**OBJECTIVE:** Patients with an incompetent cervix have been shown to have a decreased ratio of collagen to muscle when compared to patients with a normally intact cervix. Inappropriate collagen may improve this condition. We hypothesized that the injection of Contigen® into one cervix of New Zealand White (NZW) rabbits would delay delivery or prolong labor in the treated uterine horn as compared to the untreated horn.

**STUDY DESIGN:** Eight NZW rabbits were bred to a gestational age of 15-19 days (term = 29-35 days). Anatomically, rabbits have dideplic biocular uersi with a small vaginal septum. Between days 15-19, each rabbit underwent a midline laparotomy and vaginotomy to expose both cervices. One cervix was injected with a total of 0.3-0.4 ml of Contigen® at the 2.5,7 and 10 o’clock points around the cervix. The opposite cervix was injected with an equal volume of sterile saline at comparable locations. Pregnancy continued for a total of 38 days. Delivery dates for each uterine horn were recorded. The rabbits were euthanized, and the histologic appearance of each cervix was examined.

**RESULTS:** Of 8 rabbits bred for this study, 5 were available for data analysis. Four out of 5 subjects (80%) delivered with either a delayed time between uterine horns of 2-5 days (n=2), or delivered their control horn but failed to deliver the treated horn by gestational day 28 (n=2). Grossly, no migration or breakdown of collagen was noted in the injected specimens. Histologically, there was minimal inflammation surrounding the collagen injection sites compared to the control cervix (5 WBC/hpf). The injected cervical horn demonstrated minimal collagenolysis. Contigen® appears to delay delivery or arrest delivery of the treated uterine horn compared to the control horn. Presently, Contigen® is being safely used for the treatment of urinary and rectal incontinence and may be a potential outpatient therapy for cervical incompetence. Further testing in appropriate animal models with a longer gestation will be necessary.

Contigen® is a trademark of Bard Pharmaceuticals, Inc.

**76 MIDTRIMESTER PREMATURE RUPTURE OF MEMBRANES: NEONATAL AND MATERNAL OUTCOME**

R Elston, S Grisar, R Geisel, M Kaplan, A Samueloff, Dept of OB/GYN, Dept Neonatology, Shari Zedek Medical Center, Jerusalem, Ben Gurion Univ Beer Sheva, Israel

**OBJECTIVE:** To assess factors associated with neonatal survival and maternal complication rate in cases of midtrimester premature rupture of membranes (M-PROM).

**STUDY DESIGN:** The population consisted of women whose pregnancy was complicated by M-PROM (1995-99). Data was obtained by maternal and infant chart review. Statistics was performed by Student t test and Mann Whitney U test.

**RESULTS:** 21 consecutive women presented with M-PROM at 16-26 weeks (mean 25.6). Three opted for termination of pregnancy and one was lost to follow up. Seventeen (80.9%) respected expectant management. They were followed until labor (32.9%) or clinical chorionamnionitis (47%). The overall perinatal survival was 29.4%. Pulmonary hypoplasia accounted for three deaths (25%). Characteristics of the surviving vs non surviving neonates are presented in Table. In particular there was no difference in the rate of antenatal tocolysis, steroids and antibiotics, cesarean section rate and male gender distribution.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Survivors</th>
<th>Non survivors</th>
<th>N=12</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gest age at diag (w), (mean)</td>
<td>24.28</td>
<td>25.33</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Gest age at delivery (w), (mean)</td>
<td>28.51</td>
<td>25.00</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>MPROM/delivery interval (days), (mean)</td>
<td>30.2</td>
<td>15.08</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Anion Index at MPROM, (mean)</td>
<td>14.8</td>
<td>14.44</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Birth Weight, g, (mean)</td>
<td>1263</td>
<td>895.5</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Delivery 28 weeks, N (%)</td>
<td>5(60)</td>
<td>2(16)</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

The maternal course was complicated by postpartum endometritis in 8 cases (47%). The median maternal hospitalization time was 14.5 days (range 3-64), not significantly different between the two groups.

**CONCLUSIONS:** Survival and neonatal perinatal outcome after expectant management of M-PROM are low. However, longer interval until delivery which resulted in birth after 28 weeks and a higher amount of amniotic fluid at diagnosis increased the survival. The long period of M-PROM and high maternal and fetal morbidity should be taken into consideration when counseling women with M-PROM.

OBJECTIVE: Fetal fibronectin testing for the "diagnosis" of preterm labor has a quantifiable false positive and false negative rate. The objective of our study was to assess the impact of these test inaccuracies on both expected maternal complications from tocolysis and fetal morbidities that result from false positive/negative results of testing in comparison to the 2 other possible strategies.

STUDY DESIGN: We used decision analysis to compare 3 strategies for the management of women with symptoms of preterm labor (i.e., the population studied for FN testing): FN testing, tocolyse, for all, and no tocolysis for all. In the FN strategy, if the FN was positive, patients received tocolysis and steroids. If the FN was negative, patients were assumed to have received neither of these. Separate models were created for hypothetical cohorts of women presenting at 26, 28, 30, 32, and 34 weeks gestation. Our primary outcomes were the number of anticipated maternal complications from tocolysis and the number of major fetal morbidity events (RDS, IVH, NEC, sepsis, death) that would be expected. Probability estimates for FN sensitivity/specificity, maternal tocolytic complications, antenatal steroid effectiveness, frequencies of neonatal morbidities, and others were estimated from the literature.

RESULTS: The rate of major maternal complications from tocolysis across gestational ages was 2.5/1000 in the FN group, 10/1000 in the tocolyse cohort, and 0/1000 in the no tocolyse cohort.

CONCLUSION: Tocolyse for all consistently yielded the lowest number of neonatal abnormalities, at the cost of the highest rate of maternal complications. However, given the extremely small differences in expected neonatal morbidity at 20 weeks and beyond and the increased number of maternal complications with tocolyse, consideration of either FN testing or no tocolyse is reasonable.

TOCOLYSIS OF PATIENTS PRESENTING WITH ADVANCED CERVICAL DILATATION FROM PRETERM LABOR (GK Law, TH Strong, JP Elliott Good Samaritan Regional Medical Center Phoenix, AZ.

OBJECTIVE: To determine whether patients who present with advanced cervical dilatation secondary to preterm labor can be effectively tocolyzed.

METHOD: A retrospective case-control study was done of all patients admitted for preterm labor to Good Samaritan Regional Medical Center during 1998. Preterm labor was defined as cervical change in the presence of regular uterine contractions. Case patients had an admitting dilatation > 5 cm (advanced cervical dilatation). Controls were a convenience sample of patients who had an admitting cervical exam <=5cm. All patients were started on intravenous magnesium sulfate (6 gm bolus, with 3 gm/hr basal rate titrated to effect) as the initial tocolytic agent. Terbutaline (SQ or PO), NSAIDs (such as indomethacin) and nifedipine were used as adjunctive tocolytics on an as needed basis. The interval from admission to delivery was recorded. The first clinically relevant endpoint was 48 hr. after administration of the first corticosteroid dose (i.e., the steroid window). Total length of delivery was also recorded.

RESULTS: 142 total preterm labor patients were included for study. 95/142 were admitted with advanced cervical dilatation (range 4-8cm). 47/142 patients were admitted with SVE <=3cm (controls). 75/95 patients (78.9%) in the advanced cervical dilatation group reached their steroid window. The range of delay until delivery was from 2 hours to 43.8 days. The mean delay was 8.36 +/- 9.6766 days. Additionally, 60.9% of patients with SVE > 5cm achieved their steroid window. In comparison, 42/47 patients in the control group (89.4%) attained their steroid window (mean duration 17.900 +/- 16.4566 days). There was no significant difference between study and control patients when either delay of delivery interval or the proportion reaching their steroid window was compared.

CONCLUSION: Women who present with advanced cervical dilatation can have delivery delayed, at least to the point of achieving maximal steroid benefit.

IS BETAMETHASONE EFFECTIVE MORE THAN 7 DAYS AFTER TREATMENT? S Verrillat, D Soper, R. Newman. Dept. of OB/GYN, Medical Univ. of SC, Charleston, SC.

OBJECTIVE: To determine if the incidences of respiratory distress syndrome (RDS) and intraventricular hemorrhage (IVH) are influenced by the time interval between antenatal betamethasone administration and delivery.

STUDY DESIGN: We performed a prospective observational analysis of 216 liveborn singletons delivered between 28 and 34 weeks gestation after a single course (two 12 mg doses over a 24 hour interval) of betamethasone. Patients were subdivided into three groups based on the time interval between betamethasone dosing and delivery: (1) 0-2 days, (2) 3-7 days, and (3) 8-14 days. We excluded patients with ruptured membranes for > 24 hours prior to delivery, delivery prior to the second betamethasone dose, or exposure to > 2 doses of betamethasone. Data were analyzed by the Student’s t-test, chi square test, ANOVA, and Fisher’s exact test with p<0.05 considered significant.

RESULTS: The 216 patients segregated into 97 delivering in 0-2 days, 78 delivering in 3-7 days, and 41 delivering in 8-14 days after completion of a single course of betamethasone. Deliveries occurred at 31.1+5.6 (X ± S.D.), 31.1±1.6, and 31.1±1.7 weeks gestation respectively. The groups were similar with respect to selected demographics, tocolytic exposure, mode of delivery, and birthweight. There were no statistically significant differences in the frequencies of RDS (39.2% vs 41.1% vs 36.6%; p=0.89) or grades 3-4 IVH (1.1% vs 1.3% vs 0%; p=0.92) between the groups. The frequencies of chorioamnionitis, early-onset neonatal sepsis, and postpartum endometritis were also similar between the groups.

CONCLUSIONS: There were no differences in the neonatal outcomes for those infants delivering 8-14 days after maternal exposure to betamethasone compared to those delivering within 7 days of exposure.
PREGNANCY OUTCOMES FOLLOWING RECURRENT PRETERM LABOR IN TWIN GESTATIONS TREATED WITH SUBCUTANEOUS VS. ORAL TOCOLYTICS. F. Law*, N.K. Berger*, E.J. Proteau*, C.J. Stanziano, California Pacific Medical Center, San Francisco, CA, Maria Healthcare, Marbeya, GA

OBJECTIVE: To compare clinical and cost-effectiveness of using continuous subcutaneous terbutaline (CST) vs. oral tocolytics (PO) after recurrent preterm labor (RPTL) in twin gestations (TG).

STUDY DESIGN: A matched cohort design was used. Inclusion criteria applied to a perinatal database: TG, PO after initial PTL at >20 weeks, RPTL with hospitalization at <35 weeks, available outcome data. Data were divided by those with CST for tocolysis after RPTL, and those with continued PO. Patients were matched for gestational age (GA) at RPTL. A standardized cost model was used to compare total antepartum hospital (HOSP), nursery and outpatient charges (OS).

RESULTS: There were 355 women per group. GA at RPTL was 31.3 ± 2.3 weeks GA at delivery was 35.2 ± 2.0 weeks (CST) vs 34.5 ± 2.3 weeks (PO) vs 36.19 ± 4.17 (20 cases). Additional data are summarized in the table:

<table>
<thead>
<tr>
<th></th>
<th>CST n=353</th>
<th>PO n=353</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSP (days)</td>
<td>3.7±5.9</td>
<td>8.1±9.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NICU admission</td>
<td>58.2%</td>
<td>58.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth weight &lt;1500gms</td>
<td>4.1%</td>
<td>8.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nursery stay (days)</td>
<td>9.6±12.2</td>
<td>12.9±15.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Charges/pt. ($)</td>
<td>58,152±50,82</td>
<td>55,147±60,893</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Means, SD, or percentage. 1Wilcoxon Signed Rank, McNemar’s X

CONCLUSION: Women treated with CST had greater GA at delivery than those treated with continued PO. Fewer HSP and nursery days and decreased utilization of the NICU suggests cost-effectiveness of CST. The cost per pregnancy was approximately $17,000 less in the CST group.

PERIODONTITIS AND PRETERM LABOR. R. Dempsey*, G. Ashmead, N. Bassada, S. J. Chapp, S. Anne* Dept. Ob/Gyn MetroHealth Medical Center, Cleveland, OH and Dept Periodontics, Case Western Reserve Dental School, Cleveland, OH

OBJECTIVE: The purpose of this study was to substantiate whether or not periodontitis contributes to preterm labor and/or low birth weight.

STUDY DESIGN: Sixty-five subjects were recruited for this study, thirty-nine subjects were recruited from a high risk obstetric clinic and twenty-six subjects experiencing uncomplicated pregnancies. A periodontal examination was performed on each subject between twenty and twenty-five weeks gestation to assess the level of periodontal health and the degree of clinical gingival inflammation. The estimated gestational age at the time of delivery and the birth weight for each subject were recorded. The data was analyzed by means of Chi-square and paired t-tests. The analysis was performed by first comparing the high and low risk groups and then the full term and preterm groups.

RESULTS: The high risk group was found to have significantly (p < 0.01) more plaque (mean plaque index 1.52 vs 0.79), more gingival inflammation (mean gingival index 1.56 vs 0.62), and more bleeding on examination (mean percentage of sites bleeding 30.7% vs 11.92%) than the low risk group. However, significant differences were not found between these groups with respect to estimated gestational age at the time of delivery or birth weight.

CONCLUSION: Based on an analysis of the findings of this study, the concept that periodontitis is a risk factor for preterm labor was not supported.


BACKGROUND: We (1998) observed higher concentrations of inflammatory cytokines in neonatal blood of 31 mostly-term children with CP than in controls. Yoon et al (1990) reported higher median concentrations of IL-1, IL-6, and TNF-α in an amniotic fluid of 8 children with CP born <36 weeks GA than in controls. Preeclampsia, associated with lower risk of CP in preterm infants, is a potential confounder.

METHODS: Concentrations of interleukins 1 through 18, TNF-α, TGF-β, chemokines, colony stimulating factors, and VEGF were assayed by recycling immunoaffinity chromatography with laser-enhanced fluorescence and chemiluminescence in archived neonatal blood of infants <32 weeks, excluding infants of women with preeclampsia unless there was clinical evidence of infection. There were 65 children with CP and 105 controls.

RESULTS: Mean and median GAs were closely similar in cases and controls. No differences between cases and controls were observed in mean or median concentrations, nor in distributions, for any of the 25 substances tested, including IL-1, IL-6, and TNF-α.

CONCLUSION: Cytokine concentrations in neonatal blood of infants born <32 weeks GA to nonpreeclamptic women did not distinguish children with CP from control children.

IS PHYSICAL EFFORT DURING PREGNANCY A RISK FACTOR FOR PRETERM BIRTH? E. Shear*, S. Gazit-Nissim, J. Shoham-Vardi, M. Hallak, M. Katz, M. Mazor Depts of Ob/Gyn, Wayne State University School of Medicine, Detroit, MI, and Epidemiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negers, Beer-Sheva, Israel.

OBJECTIVE: To examine the relationship between physical activity at home and at work during pregnancy and the occurrence of preterm birth.

STUDY DESIGN: A case-control study, which compared 99 women with preterm birth to 189 patients with term deliveries, was performed. The risk for preterm birth was analyzed in relation to broad working characteristics at home and out of the house. All women were interviewed in the postpartum period during their hospitalization.

RESULTS: The level of education was significantly lower among the study group as compared to the control group (39% had academic education vs 47% in the control group, P=0.001). No other statistically significant differences were observed between the groups in relation to sociodemographic and obstetric factors. Three months prior to delivery, women who delivered preterm devoted less time to household chores (mean of 3.7 hours vs 4.8 hours in the control group, P=0.002). In addition, those women spent less time walking in the house than women in the control group (1.2 vs 1.5 hours, P=0.02). A significantly lower percentage of women who delivered preterm were active in sport as compared to the controls (Odds ratio = 0.22, 95% Confidence interval 0.08-0.65, P=0.002). No differences were found between the groups in relation to physical activity outside the house, nor in the duration of work.

CONCLUSIONS: Women who delivered preterm had a lower level of education than those who delivered at term. This relation may have resulted from a lower compliance rate to doctor’s recommendations. It appears that in a population of women which were generally not exposed to significant physical activity, and had access to adequate prenatal care, physical effort during pregnancy was not related to an increased risk for preterm birth.
65 INDOMETACIN THERAPY FOR PRETERM LABOR PROLONGS GESTATION AND IS NOT ASSOCIATED WITH INCREASED NEONATAL COMPLICATIONS IN INFANTS DELIVERED PRIOR TO 32 WEEKS. Fausett MB, Esplin MS, Osorio BT, Yoder JF, Gordon MC, and Higby K. Univ of Utah Health Sciences Center, SLC UT, and Wilford Hall Medical Center, Lackland AFB, TX.

OBJECTIVE: Indomethacin had been shown to prolong gestation in women with preterm labor but its use remains controversial because of concern for potential adverse fetal and neonatal effects. The purpose of this study was to compare the incidence of adverse effects in neonates with antenatal exposure to indomethacin and controls that were born prior to 32 weeks.

METHODS: Data was collected prospectively on all infants born between 3/90 and 12/98 that were admitted to the neonatal ICU at Wilford Hall Medical Center. There were 455 early (24 0/7 to 31 6/7 weeks EGA) preterm deliveries. Of these, 304 were diagnosed with preterm labor. These 304 patients were divided into a study and two control groups. The study group included all 100 infants exposed to a minimum of 72 hours of antenatal indomethacin (+/- other tocolytics). The control groups consisted of 126 fetuses that were not exposed to any tocolytics and 78 infants who were exposed to other tocolytics (magnesium and/or beta-mimetics).

RESULTS: There were no significant differences with regard to demographic factors including: maternal age, race, and gravidity. The mean time from initiation of therapy to delivery was longer in the indomethacin treated group versus the other tocolytics and the no tocolytic groups (18.2 versus 5.6 and 4.9 days respectively, P < .0001). The comparisons are shown in the table below.

<table>
<thead>
<tr>
<th>Indomethacin</th>
<th>Other Tocol</th>
<th>No Tocol</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGA at admit</td>
<td>25.2 ±3.0</td>
<td>27.7 ±2.9</td>
<td>26.0 ±3.0 0.0001</td>
</tr>
<tr>
<td>EGA at delivery</td>
<td>27.8 ±2.5</td>
<td>28 ±2.5</td>
<td>27.6 ±2.8 0.054</td>
</tr>
<tr>
<td>Any IVH</td>
<td>52/99 (53%)</td>
<td>74/111 (67%)</td>
<td>56/122 (46%) 0.31</td>
</tr>
<tr>
<td>IVH grades 3&amp;4</td>
<td>10/100 (10%)</td>
<td>11/78 (14%)</td>
<td>15/126 (12%) 0.64</td>
</tr>
<tr>
<td>NEC</td>
<td>3/100 (3%)</td>
<td>5/100 (5%)</td>
<td>5/126 (4%) 0.14</td>
</tr>
<tr>
<td>PDA lactation</td>
<td>9/100 (9%)</td>
<td>4/78 (5%)</td>
<td>8/126 (6%) 0.57</td>
</tr>
<tr>
<td>Mortality</td>
<td>17/100 (17%)</td>
<td>11/78 (14%)</td>
<td>32/126 (25%) 0.10</td>
</tr>
</tbody>
</table>

CONCLUSIONS: When given for up to 72 hours, indomethacin tocolytic therapy prolongs gestation, but is not associated with an increase in adverse neonatal outcomes.

66 PRETERM DELIVERY IN WOMEN WITH CHRONIC HYPERTENSION OR PREGESTATIONAL DIABETES VERSUS NORMAL PREGNANCY. BM Sabo for the MFMU, Bethesda, MD

OBJECTIVE: To investigate rates of spontaneous or indicated preterm delivery in women with chronic hypertension (CHTN) or pregestational diabetes (IDDM) as compared to normal women

STUDY DESIGN: Secondary analysis of data from women with singleton gestations without medical complications enrolled in a prospective, blinded, randomized control comparison. A total of 3, 5, 12 and 34 deliveries at <28, <30, <32 and <34 weeks gestation. At 15-20 weeks and 21-24 weeks' gestation CL was more sensitive than other parameters for predicting spontaneous preterm birth. At 15-20 weeks, CL had higher PPV than the other parameters. The use of antenatal steroids is not associated with an increased risk of sepsis in neonates of patients who are later diagnosed with IAI and who deliver before 32 weeks gestation.

RESULTS: The mean ± SD gestational age at delivery was 35.5 ± 3.1 weeks. There were 5, 5, 12, and 34 deliveries at <28, <30, <32, and <34 weeks gestation. Cervical length was equal or better than the other parameters. The table summarizes the best cervical length cutoffs at each testing period and the test of efficacy results:

<table>
<thead>
<tr>
<th>Cervical length ≤2.5 cm @15-20 weeks</th>
<th>Cervical length ≤1.5 cm @21-24 weeks</th>
<th>Cervical length ≤2.0 cm @25-28 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
</tr>
<tr>
<td>Sens (%)</td>
<td>67 60 40 31</td>
<td>67 60 33 33</td>
</tr>
<tr>
<td>Spec (%)</td>
<td>97 98 100 100</td>
<td>87 88 88 89</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>40 60 80 100</td>
<td>12 18 24 41</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>99 98 94 88.5</td>
<td>99 98 92 86</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The use of antenatal steroids is not associated with an increased risk of sepsis in neonates of patients who are later diagnosed with IAI and who deliver before 32 weeks gestation.

67 ANTEnatal STEROID THERAPY IN WOMEN WHO LATER DEVELOp INTRAUTERine INFECTION (IAI) IS NOT ASSOCIATED WITH AN INCREASED RISK OF INFECTION IN PRETERM NEONATES. Fausett MB, Osorio BT, Esplin MS, Yoder JF, Gordon MC, and Higby K. Univ of Utah Health Sciences Center, SLC UT, and Wilford Hall Medical Center, Lackland AFB, TX.

OBJECTIVE: Antenatal steroid therapy may alter both maternal and fetal immune function and increase susceptibility to infection. The purpose of this study was to compare the rate of sepsis in infants delivered of pregnancies complicated by IAI who had or had not previously been exposed to antenatal steroids.

METHODS: Data was collected prospectively on all infants born between 3/90 and 12/98 that were admitted to the neonatal ICU at Wilford Hall Medical Center. There were 185 early (24 0/7 to 31 6/7 weeks EGA) preterm deliveries. Of these, 97 were diagnosed with IAI. IAI was defined according to standard criteria. Fifty-five neonates were exposed to antenatal betamethasone and 42 were not. The neonates were divided into three groups: Culture proven sepsis, clinical sepsis (culture negative) and no sepsis.

RESULTS: There were no significant differences with regard to demographic factors including: maternal age, race, gravidity or incidence of PROM. There were no differences between the three groups with regard to mortality (6/16 and 4/15, p=0.13) or the incidence of sepsis (p=0.792).

| Cx proven Clinical No sepsis |
|------------------|------------------|------------------|
| Betamethasone 9 | 20 | 26 |
| No betamethasone 5 | 15 | 22 |

CONCLUSIONS: The use of antenatal steroids is not associated with an increased risk of sepsis in neonates of patients who are later diagnosed with IAI and who deliver before 32 weeks gestation.

88 A COMPARISON OF SONOGRAPHIC CERVICAL PARAMETERS IN PREDICTING SPONTANEOUS PRETERM BIRTH IN TWIN GESTATIONS. Br Gasson, C Walters1, N Merkouts, W Kinder, R Waldron2, J Nigam3, AM Vinzileus, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVES: To compare various sonographic cervical parameters in their ability to predict spontaneous preterm birth (PTB) in twin gestations.

STUDY DESIGN: 117 twin gestations were longitudinally evaluated between 15 and 28 weeks gestation with transvaginal cervical sonography and transabdominal transvaginal ultrasound. The sonographic cervical parameters obtained were: funnel width and length (FL), cervical length (CL), % funneling ([FL/FL+CL]×100), and cervical index (1/FL+CL). Receiver operating characteristic curve analysis was used to determine the best sonographic cervical parameter at 15-20, 21-24 and 25-28 weeks for predicting spontaneous PTB <28, <30, <32 and <34 weeks gestation. Tests of efficacy were performed using the best cervical parameter in each testing period for predicting PTB.

RESULTS: The mean ± SD gestational age at delivery was 35.5 ± 3.1 weeks. There were 5, 5, 12, and 34 deliveries at <28, <30, <32, and <34 weeks gestation. Cervical length was equal or better than the other parameters. The table summarizes the best cervical length cutoffs at each testing period and the test of efficacy results:

<table>
<thead>
<tr>
<th>Cervical length ≤2.5 cm @15-20 weeks</th>
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</thead>
<tbody>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
<td>&lt;28 &lt;30 &lt;32 &lt;34</td>
</tr>
<tr>
<td>Sens (%)</td>
<td>67 60 40 31</td>
<td>67 60 33 33</td>
</tr>
<tr>
<td>Spec (%)</td>
<td>97 98 100 100</td>
<td>87 88 88 89</td>
</tr>
<tr>
<td>PPV (%)</td>
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<td>12 18 24 41</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>99 98 94 88.5</td>
<td>99 98 92 86</td>
</tr>
</tbody>
</table>

The strongest feature of CL was its negative predictive value (NPV), in all testing periods, for all degrees of PTB. The positive predictive value (PPV) was better at 15-20 weeks gestation in comparison to the other testing periods. A CL of ≤2.5 cm in 15-20 weeks' gestation had 100% PPV for PTB <34 weeks gestation. At 15-20 weeks and 21-24 weeks gestation CL was more sensitive at predicting earlier PTB (<28 and <30 weeks).

CONCLUSIONS: CL was equal to or better than the other sonographic parameters and effective in predicting pregnancy outcome. The specificity at 15 weeks for all degrees of PTB and its NPV for delivery <30 weeks at all testing period were excellent.
## A Comparison of Sonographic Cervical Parameters in Predicting Spontaneous Preterm Birth in Triple Gestations

**Authors:** ER Guzman, C Walters*, NB Metrowitz, W Kindler, K Gipouy*, N Nigara*, AM Vlouzilencia, UMDNJ-Robert Wood Johnson Medical School/Saint Peter’s University Hospital, New Brunswick, NJ.

**OBJECTIVES:** To compare various sonographic cervical parameters in their ability to predict spontaneous preterm birth (PTB) in triplet gestations.

**STUDY DESIGN:** Triplet gestations were longitudinally evaluated between 15 and 28 weeks of gestation with transvaginal cervical sonography and transabdominal ultrasound. The cervical parameters evaluated included: anterior commissure width and length (AC/FL), cervical length (CL), % funneling (FL/CL x 100), and cervical index (1 + FL/CL). Receiver operating characteristic (ROC) curve analysis was used to determine the best sonographic cervical parameter at 15-20, 21-24 and 25-28 weeks for predicting spontaneous PTB.

**RESULTS:** The mean ± SD gestational age at delivery was 31.6 ± 4.2 weeks. There were 9, 13, 20 and 29 deliveries at <28, <30, <32 and <34 weeks gestation. Tests of efficacy were performed using the best cervical parameter in each testing period for predicting spontaneous PTB.

<table>
<thead>
<tr>
<th>Cervical Length ≤2.5 cm</th>
<th>Cervical Length ≤1.5 cm</th>
<th>Cervical Length ≤2.0 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>@ 15-20 weeks</td>
<td>@ 21-24 weeks</td>
<td>@ 25-28 weeks</td>
</tr>
</tbody>
</table>
| Sensitivity (%)         | Specificity (%)         | Positive Predictive Value (%)
| 56 (100)                | 100 (100)               | 92 (100)                |
| 42 (92)                 | 100 (100)               | 92 (92)                 |
| 29 (96)                 | 97 (61)                 | 67 (67)                 |
| 26 (86)                 | 66 (66)                 | 61 (61)                 |
| PPV (%)                 | NPV (%)                 |< 28 <30 <32 <34 <28 <30 <32 <34 <28 <30 <32 <34 |
| 100 (100)               | 100 (100)               | 95 (95)                 |
| 95 (95)                 | 90 (90)                 | 84 (84)                 |
| 84 (84)                 | 71 (71)                 | 72 (72)                 |
| 65 (65)                 | 100 (100)               | 61 (61)                 |

The sensitivity of CL improved with advancing gestational age at time of testing. Within each testing period, CL was better at predicting earlier PTB (<28 vs <30 weeks). Cervical length ≤2.5 cm at 15-20 weeks had excellent predictive positive value (PPV) and positive predictive value (PPV) at 100%. At each testing period, CL had better negative predictive value (NPV) for early preterm birth (<28 vs <30 weeks).

**CONCLUSIONS:** Cervical length was equal to or better than the other sonographic parameters and effective in predicting pregnancy outcome. The PPV at 15-20 weeks for all degrees of PTB was excellent while the NPV at 17-20 weeks for all degrees of PTB was significant.

## Preterm Premature Rupture of Membranes (pPROM) Without Labor is Not Associated with Increased Levels of Matrik Metalloproteinase-9 (MMP-9) Protein

**Authors:** M Kush, W Donahoe*, RP Bechtel, J Janosky, ER Guzman, N Nigara*, AM Vlouzilencia, UMDNJ/Women’s Research Institute and Dept OB/Gyn and Womens Health, Univ of Pittsburgh, Pittsburgh, PA.

**OBJECTIVES:** To determine whether the initial amniotic fluid volume assessment of preterm premature rupture of the membranes (PPROM) or the trend in the amniotic fluid index correlated with latency period or infectious morbidity.

**STUDY DESIGN:** A computer generated search was conducted from July 1, 1996 through June 30, 1998 for patients admitted with a diagnosis of PPROM. All patients received 48 hours of intravenous, broad-spectrum antibiotics intended to prolong the latency period as well as glucocorticoid therapy to induce fetal pulmonary maturity. Only those patients completing the 48-hour protocol and at a gestational age range of 26 to 34 weeks’ gestation were included for analysis. Of the 160 patients with PPROM during the study period, 53 satisfied the inclusion criteria.

**RESULTS:** The latency period and infectious morbidity in these individuals with an initial amniotic fluid index indicating severe oligohydramnios (i.e., ≤2.0 cm) were not significantly different from those individuals with an initial amniotic fluid index ≥2.8 cm (8.0 ± 5.3 days versus 8.0 ± 5.9 days, NS). During the study period, 53 satisfied the inclusion criteria.

**CONCLUSION:** The presence or the subsequent development of severe oligohydramnios did not measurably change the length of the latency period or the subsequent development of infections. Because it, likewise, had not significantly impacted upon perinatal mortality, we currently do not alter conservative management of PPROM if severe oligohydramnios is encountered provided there is no evidence of maternal or fetal compromise.
IMPACT OF INCREASING CONSECUTIVE PRETERM BIRTHS ON SUBSEQUENT BIRTHS. N.P. Yost, S.L. Bloom, D. D. McNamara, K.J. Lefosso, Dept OB/Gyn, Univ. Texas Southwestern Medical Center, Dallas, TX

OBJECTIVE: To test the hypothesis that the risk of preterm birth increases with the number of consecutive antecedent preterm deliveries.

STUDY DESIGN: Using a computerized database, women whose first four consecutive pregnancies delivered at our hospital between January 1, 1988 and December 31, 1998 were identified. This analysis was limited to singleton livebirths without anomalies. To be included all deliveries had to follow spontaneous preterm labor, defined as 24-36 completed weeks of gestation. Chi square was used for statistical analysis.

RESULTS: Shown in the figure is the percentage of recurrent preterm births in women with one, two or three consecutive prior preterm births. The percentage increased incrementally from 27% recurrence to 71%. Of those women with a recurrent preterm birth, 43% delivered within one week of the gestational age of the proximal delivery and 62% delivered within 2 weeks.

CONCLUSIONS: The risk of preterm birth increases in proportion to the number of prior preterm births. The majority of recurrent preterm births occur within 2 weeks of the gestational age of the prior preterm delivery.

MATERIAL STATUS SEVEN DAYS AFTER THE FINDING OF A VERY SHORT CERVIX BEFORE 30 WEEKS. G. Jones, C. Nimrod, Dept MFM, Univ. of Ottawa, Ont., Canada

OBJECTIVE: The use of repeated courses of maternal steroids in women at risk of very preterm birth is controversial. To help rationalize their use, the role of repeat risk assessment 7 days after a diagnosis of a cervical length ≤ 19 mm was investigated.

STUDY DESIGN: An ultrasound database covering a 31 month period was searched to identify women with a cervical length ≤ 19 mm found between 18 and 29 weeks gestation. Exclusion criteria included multiple pregnancy and use of cerclage. All images were reviewed by the lead author using a digital image storage system with on-screen calipers. Only transvaginal images were used.

RESULTS: A total of 101 patients were enrolled: 51 received a single course of therapy, 22 had multiple courses, and 29 served as controls. There were no differences in gestational age, maternal age, race or weight between BTM and control patients. Capillary glucose values from days 3-7, 10-14, 17-21 and 24-28 were pooled and averaged. FBS and 1 hr pp values are shown below.

CONCLUSIONS: Betamethasone resulted in a significant continuous elevation of fasting capillary glucose that correlated with the number of treatment courses. Postnatal values indicated a temporary rise. The clinical significance of these findings is unknown.

EFFECT OF BETAMETHASONE ON GLUCOSE HOMEOSTASIS IN NON-DIABETIC GRAVIDAS. S. Skelton, K. Boggess, T. Smith, W.N.P. Herbert Department of Obstetrics & Gynecology, Duke University Medical Center, Durham, NC

OBJECTIVE: Corticosteroid use is known to increase glucose, but few data are available regarding its effect on glucose homeostasis in non-diabetic pregnant women. We sought to evaluate the effect of betamethasone (BTM) on maternal glucose levels following both single and multiple courses of therapy.

METHODS: A prospective cohort study was performed on pregnant women receiving BTM between 24-34 weeks gestation, excluding those with diabetes, multiple gestations, beta agonist use, or other steroid treatment. Capillary glucose assessments were obtained daily on fasting (FBS) and 1-hour postprandial blood (1 hr pp) samples. Hospitalized patients undelivered seven days after the previous therapy received a repeat course of BTM. A gestational age matched control group of outpatients who had not received BTM underwent weekly FBS and 1-hr pp capillary glucose testing for three consecutive weeks.

RESULTS: A total of 101 patients were enrolled: 51 received a single course of therapy, 22 had multiple courses, and 29 served as controls. There were no differences in gestational age, maternal age, race or weight between BTM and control patients. Capillary glucose values from days 3-7, 10-14, 17-21, and 24-28 were pooled and averaged. FBS and 1 hr pp values are shown below.

CONCLUSIONS: Carefully selected PPROM patients can be successfully managed as outpatients following initial hospitalization.

OUTPATIENT VERSUS INPATIENT MANAGEMENT OF PPROM. J. Stengel, C. Trapp, G. Ingardia, J. Wax Hartford Hospital, Hartford, CT

OBJECTIVE: Compare outcomes in patients with prolonged preterm premature rupture of membranes (PPROM) managed as outpatients to patients requiring inpatient management until delivery.

STUDY DESIGN: The obstetric and neonatal databases were reviewed from 1/1/94-12/31/98 Patients with singleton, PPROM at ≥20 and <37 weeks, and latent phases >72 hours were evaluated. Candidates for outpatient management had uneventful hospital stays of 1 week following ROM, no evidence of infection, AFI >5 cm, reassuring fetal testing, stable psychosocial situation.

RESULTS: 45 patients met study criteria. Two were excluded: one electively terminated at 20/4 weeks and one chart was lost. Of the 43 evaluable patients, 22 were managed as inpatients from identification of PPROM to delivery and 21 as outpatients following initial hospitalization. Reasons for continued hospital stay following PPROM included continued leakage of amniotic fluid, oligohydramnios, placenta previa, active substance abuse. No differences in age, gravidity, parity, or race existed between groups.

CONCLUSIONS: Carefully selected PPROM patients can be successfully managed as outpatients following initial hospitalization.

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CONCLUSIONS: Carefully selected PPROM patients can be successfully managed as outpatients following initial hospitalization.
**DELAY OF DELIVERY BY INHIBITION OF CYCLOOXYGENASE-2 IN THE RAT CERVIX.** R Bukowski1, L McKay2, S. Q. Shi3, M. Naganamani4, G. Saade4, R. Garfield5. Dept. of Ob/Gyn, The Univ. of Texas Med Branch, Galveston, TX.

**OBJECTIVE:** To test the hypothesis that cervical application of nimesulide, a specific cyclooxygenase-2 (COX-2) inhibitor, can delay ripening and thus prolong pregnancy in rats.

**STUDY DESIGN:** Timed pregnant Sprague-Dawley rats were randomly allocated to receive nimesulide 50mg/kg/day (n=18) or its hydroxypropylcellulose vehicle (n=17) applied on the cervix daily from day 14 until term on day 22. In a separate experiment, animals were treated with indomethacin 10mg/kg/day (n=6) or its hydroxypropylcellulose vehicle (n=6) applied on the cervix daily from day 19 to 22. We evaluated the following variables: number of animals delivered on day 22 vs 23, time to delivery of the first pup (midnight on day 22 = 0 hours), birthweight and weight gain of pups. In the nimesulide/vehicle group, plasma concentrations of progesterone were determined on days 17, 19 and 21.

**RESULTS:** Significantly more animals in the nimesulide group delivered on day 23 compared with control (15/18 vs 6/17; p<0.006). In the indomethacin treated group as well as in its control group, 3/6 animals delivered on day 23. Time from midnight on day 22 to delivery of the first pup was significantly longer in the nimesulide group compared to control (43.3 ± 7.9 vs. 21.6 ± 9.8 hours, 95%CI=4-16.9, p<0.001). There was no significant difference in the pups' birthweight, gross appearance, survival, or weight gain within the first week of life between the nimesulide and control groups. Compared with the control group, a significantly higher number of pigs in the indomethacin group died in utero and the surviving pigs had significantly lower birthweight than the control group (p<0.001). There was no difference in the overall course and extent of prostogesterone withdrawal between animals treated with nimesulide and controls.

**CONCLUSIONS:** Cervical application of a COX-2 inhibitor delays delivery by a mean of 10 ± 8 hours, a considerable delay in such a tightly controlled event and pregnancy lasting only 22 days. Unlike indomethacin, a nonspecific COX inhibitor, nimesulide is well tolerated by pregnant animals and fetuses. Prolongation of pregnancy is likely due to inhibition of cervical ripening because (1) the start of treatment coincided with the onset of the cervical ripening process and preceded by several days initiation of uterine contractions, (2) local treatment with nimesulide did not have a lutetonic effect, (3) prior experiments have shown that treatment with nimesulide closer to term does not delay delivery.

**IS HOME MANAGEMENT OF PRETERM PREMATURE RUPTURE OF THE MEMBRANES SAFE?** K. Tobar1, A James1, A. Martina1, T. Smith1, W. Herbert2. Dept. Ob/Gyn.; Duke University Medical Center, Durham, NC

**OBJECTIVE:** At least two studies have addressed home management of patients with preterm premature rupture of the membranes (PPROM), one of which found that in the small proportion of women who met strict inclusion criteria, home management was safe. The purpose of this study was to further evaluate the safety of home management of patients with PPROM.

**STUDY DESIGN:** Participants included patients admitted between September, 1997 and February, 1999 with confirmed spontaneous rupture of membranes less than 34 weeks gestation, without other indication for delivery. Demographic and clinical data were collected and the interval from the time of a sentinel event (defined as an event that signaled impending delivery or need for delivery) to the time of delivery was calculated. The subset of patients who met the previously published strict criteria for home management was then analyzed.

**RESULTS:** Sixty patients presented with PPROM without other indication for delivery. Twenty-eight met criteria for home management. Five of the 28, or 18%, had events that would have been potentially disastrous at home: one had acute fetal distress, one had a precipitous labor and delivery, two had cord prolapse and one patient developed choioamnionitis, and at the time of diagnosis, was found to have a malpresentation.

**CONCLUSION:** We conclude that, even with strict criteria for home management, patients with PPROM are at considerable risk for an untoward outcome.

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**DIFFERENTIAL EFFECTS OF ATP- AND Ca2+-DEPENDENT POTASSIUM CHANNEL OPENERS ON ISOLATED AORTA AND UTERUS FROM PREGNANT RATS.** M. A. Ashrafi, E. Fulep, Y. Vedernikov, G. Saade, R. Garfield. Dept. of Gyn/Ob, The Univ. of Texas Med Branch, Galveston, TX.

**OBJECTIVE:** Potassium channel openers (KCs) are known to relax uterine as well as vascular smooth muscle. Our objective was to test the hypothesis that KCs may have a differential influence on the isolated aorta and uterus from pregnant rats.

**STUDY DESIGN:** Aortic and uterine rings from timed pregnant Sprague-Dawley rats (day 20/21) were mounted for isometric tension recording in organ baths containing Kreb's solution at 37°C, gassed with 5% CO2 (pH 7.4). Subsequent to a stable pre-contraction with 100 nM U46619 (thromboxane A2 opener), pinacidil (KATP opener) and NS1619 (Ca2+ opener) were determined Data were analyzed using Student's t-test or one-way ANOVA (α significance: p < 0.05).

**RESULTS:** The inhibitory effect of pinacidil was significantly greater than minoxidil (KATP opener), pinacidil (KATP opener) and NS1619 (Ca2+ opener) in uterine rings. In addition, the magnitude of the inhibition by pinacidil was significantly greater in uterine than aortic rings (Figs 1 & 2).

**CONCLUSIONS:** Pinacidil is far more effective on uterine than aortic rings. Hence, due to this relative selectivity and the possibility of reduced vascular effects, pinacidil may be potentially useful tocolytic.

**MATERNAL AND UNIMBILICAL SERUM NITRIC OXIDE METABOLITES ARE LOWER IN PRETERM COMPARED TO TERM LABOR.** Ochmpati, R. Bogges, J. Locklear, and W. Herbert. Duke Med Center Dept of Ob/Gyn Durham, NC

**OBJECTIVE:** Synthesis of nitric oxide and its metabolites (NOx) are increased in response to infection, and infection has been associated with preterm delivery. However, NO is also a smooth muscle relaxant believed to be involved in the maintenance of uterine quiescence. We sought to determine the relationship between maternal and umbilical serum NOx levels and preterm labor and delivery.

**STUDY DESIGN:** Maternal serum samples were obtained prospectively from 104 women without chonic chiorioamnionitis seeking care at Duke Univ. Dietary nitrite and nitrate intake was ascertained by the food frequency method. Serum NOx levels were measured using the Greiss reaction. "Preterm" was defined as < 37 weeks and "subclinical infection (SI)" by placental histology. Women were divided into four groups: antepartum (AP), preterm contractions, delivered at term (PTC); preterm labor delivered preterm (PTL); and term labor and delivery (TL). Unimbilical venous sampling was done in PTL and TL groups. Comparison of maternal or umbilical serum NOx levels was done using the Sign Rank or Wilcoxon test, and adjustment for diet and/or SI using multiple regression analysis.

**RESULTS:** Maternal demographics were similar between groups. After adjustment for diet and SI, median maternal and unimbical NOx levels were lower in PTL versus TL groups:

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Unadjusted Maternal NOx</th>
<th>Maternal NOx</th>
<th>Unimblical NOx</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>22</td>
<td>37 (32-47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTC</td>
<td>15</td>
<td>43 (35-106)</td>
<td>32</td>
<td>34</td>
</tr>
<tr>
<td>PTL</td>
<td>26</td>
<td>35 (18-55)</td>
<td>46</td>
<td>32</td>
</tr>
<tr>
<td>TL</td>
<td>41</td>
<td>38 (19-81)</td>
<td>50</td>
<td>47</td>
</tr>
</tbody>
</table>

* 1adjusted for diet, p=0.04, 2adjusted for diet and SI, p=0.06, 3adjusted for SI, p=0.1

**CONCLUSIONS:** After correcting for dietary nitrate and nitrate intake and SI, we found lower maternal and umbilical serum NOx levels in preterm versus term labor, suggesting that the mechanisms for maintenance of uterine quiescence may be abnormal in patients who ultimately deliver prematurely.
101 ASSOCIATION OF SHORTENED CERVICAL LENGTH AT 16-22 WEEKS AND SPONTANEOUS PRETERM DELIVERY. J Hubbard, M Tart*, A Moscad. Dept Ob/Gyn, Univ of Chicago, Chicago, IL.

OBJECTIVE: Shortened cervical length (Cx Lgh) at 24 and 28 wks is highly associated with an increased risk of spontaneous preterm delivery (SPTD). We wanted to determine whether the same holds true when the Cx Lgh is measured by transvaginal ultrasound (TV-US) at an earlier gestational age (GA) 16-22 weeks.

STUDY DESIGN: Prospective observational study in an urban tertiary population. Cx Lgh was measured by TV-US as part of our routine anatomy survey in all consenting OB patients at our center 7/97-7/99. Included were 760 gravidas 16-22 wks who completed delivery during this time period. Excluded were any induced preterm deliveries for maternal or fetal indications, and any patient with a cerclage. Technicians were trained in standardized Cx Lgh techniques by TV-US, with intraobserver variability of less than 10%. The main predictor variable was Cx Lgh while the primary outcome was gestational age at delivery. SPTD was analyzed at <37, <35, and <32 wks, while shortened Cx Lgh was defined by the 10th, 5th, and 2.5th percentile for our population. The Yates corrected Chi-square was used to determine relative risk (RR) and 95% CI, and sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were calculated.

RESULTS: The mean cervical length was 38.5 ± 8.0mm measured at a mean 19.9 ± 1.5 wks and the mean GA at delivery was 38.3 ± 2.8 wks. SPTD occurred in 85 gravidas <37 wks, 51 delivered <35 wks, and 27 at <32 wks. Sensitivity ranged from 29% to 45% and specificity from 90% to 98%, while PPV was 12% to 44% and NPV 91% to 98%.

<table>
<thead>
<tr>
<th>RR (95% CI) for SPTD</th>
<th>Cx Lgh</th>
<th>n</th>
<th>&lt;37 wks</th>
<th>&lt;35 wks</th>
<th>&lt;32 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>10th</td>
<td>≥30</td>
<td>87</td>
<td>3.8 (2.6-5.6)</td>
<td>5.4 (3.5-9.0)</td>
<td>6.3 (3.0-15.0)</td>
</tr>
<tr>
<td>5th</td>
<td>≥27</td>
<td>40</td>
<td>4.5 (2.4-8.9)</td>
<td>7.5 (4.5-12.5)</td>
<td>7.8 (3.6-16.7)</td>
</tr>
<tr>
<td>2.5th</td>
<td>≥22</td>
<td>21</td>
<td>5.2 (3.8-3.5)</td>
<td>9.7 (5.8-16.1)</td>
<td>8.4 (3.5-19.9)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Cx Lgh measured transvaginally at routine US 16-22 wks in asymptomatic gravidas may help identify patients at risk for SPTD.

102 SERIAL MATERNAL SERUM INTERLEUKIN-6 LEVELS IN PATIENTS WITH PRETERM PREMATURE RUPTURE OF MEMBRANES AND CHORIOAMNIONITIS. AP Martha*, TS Smith*, WNP Herbert. Dept of Ob/Gyn, Duke University Medical Center, Durham, NC.

OBJECTIVE: Impending chorioamnionitis remains difficult to diagnose in patients with preterm, premature rupture of membranes (PPROM). We sought to determine if maternal serum interleukin(IL-6) levels rise before the onset of clinical evidence of infection in patients with PPROM.

STUDY DESIGN: All patients admitted with PPROM from 22-34 weeks gestation were offered enrollment. After consent was obtained, maternal blood samples were drawn daily until delivery. The first result obtained (at least 48 hours prior to delivery) was compared to the result of the sample obtained 12-36 hours prior to delivery so as to determine if a change in maternal serum IL-6 concentrations occurred in PPROM patients with and without histologic chorioamnionitis. IL-6 levels were determined by ultra-sensitive ELISA technique. No patient had evidence of clinical chorioamnionitis or labor at the time of sample collections. The mean maternal serum IL-6 levels were log transformed and analyzed using Students T test, with significance defined as Pc. 05.

RESULTS: Sufficient data for analysis were available in 22 patients. There was no difference in maternal age, race, insurance status, or preterm delivery and rupture to delivery interval between PPROM patients with and without histologic chorioamnionitis. Those with histologic chorioamnionitis had significantly higher serum IL-6 levels at 12-36 hours prior to delivery when compared to samples obtained greater than 48 hours prior to delivery (Pc.002). In contrast, PPROM patients lacking histologic chorioamnionitis had no significant change in serum IL-6 levels at those intervals (Pc.17).

CONCLUSION: In patients with PPROM, maternal serum IL-6 concentrations appear to rise prior to the onset of labor or the appearance of clinical evidence of chorioamnionitis. Therefore, maternal serum IL-6 may be a useful marker for impending chorioamnionitis or labor in patients with PPROM. Work supported by a grant MO1-RR-30, National Center for Research Resources, Clinical Research Centers Program, NIH.

103 MATERNAL AND NEONATAL OUTCOMES FOLLOWING SINGLE versus MULTIPLE COURSES OF CORTICOSTEROIDS. K Sirmber, 1 Lange, Dept Ob/Gyn, Univ of California, Foothills Hospital, Calgary, AB.

OBJECTIVE: To compare the effects of single versus multiple doses of corticosteroids on maternal and neonatal outcomes.

STUDY DESIGN: A retrospective cohort study of all patients receiving corticosteroids with subsequent delivery between 24 and 34 weeks gestational age. Only patients with intact membranes were included. The study period was from January 1991 through December 1997 inclusive. Patients receiving one full course of corticosteroids (n=469) were compared to those receiving more than one course (n=169). The rates of respiratory distress syndrome (RDS), grade 3 or 4 intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), chorioamnionitis, post-partum endometritis, sepsis, days on ventilator, days in neonatal intensive care unit (NICU), days in hospital, and birth weights were examined. A subset of the single-course infants with a latency from steroids to delivery of 7-14 days (n=41) was compared to a subset of repeat-course infants with a latency of 1-7 days (n=85). Chi-square analysis was performed as was linear regression analysis comparing number of doses of corticosteroids with birthweight; a p<0.05 was considered significant.

RESULTS: There was a significant improvement in the rate of RDS with repeated courses (22%) versus single course (39%) (p<0.05) for the subsets examined. There was also a significant difference in the number of infants on ventilator for the repeat course subset (4.2 days) versus single course (7.2 days) (p<0.05). There were no differences in the incidences of NEC, BPD, IVH, chorioamnionitis, post-partum endometritis, sepsis, days in NICU or days in hospital. There was a trend towards decreased birthweight and repeat courses of corticosteroids (p=0.07) which showed a significant relationship to number of courses of corticosteroids, even after controlling for gestational age (p<0.05).

CONCLUSIONS: Repeated corticosteroids may be associated with an improvement in the incidence of RDS. There may be a suppressive effect of repeat courses on birthweight.

104 BIOACTIVE ACTIVIN A DOES NOT PREDICT PRETERM DELIVERY. A. Sarris* and E. Wang*. Dept of Ob/Gyn, Northwestern University, Chicago, IL.

OBJECTIVE: Activin A is a dimeric protein related to inhibin, which is synthesized by the fetal membranes, placenta, and endometrium. Inhibin and activin A levels are not more elevated in patients with preterm contractions who deliver preterm than in those who carry to term. Bioactive activin A does not appear to be a marker for preterm delivery.

METHODS: Patients from 24 to 33 6/7 weeks gestation who presented with preterm contractions (>5 an hour) were eligible for enrollment. Exclusion criteria included preterm rupture of membranes, placenta previa, cervical cerclage, and multiple gestation. Blood samples were obtained in all patients prior to initiation of tocolysis. Serum samples were aliquoted, undergoing only one freeze/thaw cycle. A specific monoclonal ELISA measuring free activin A was used. Student’s T, Mann Whitney U, and Wilcoxon Two Sample tests were used when appropriate.

RESULTS: The mean gestational age at the time of presentation was 30.6 weeks. Ninety of 85 patients delivered preterm (mean gestational age 32.5 weeks). The mean activin A levels of those patients delivering preterm was 0.9 +/-0.9 ng/ml, which was not statistically different from the 5.9 +/-15.7 ng/ml for those patients who continued their pregnancies to term. Subgroup analysis found that patients who delivered at less than 32 weeks had a mean activin A level of 1.3 +/-1.3 ng/ml and for those delivering <28 weeks the mean was 0.5 +/-0.4 ng/ml. Neither of these values was significantly different from the mean concentration in the term delivery group. Of the 36 women who received tocolysis, the mean activin concentration in those that delivered preterm (0.9 +/-1.0 ng/ml) was not significantly different from those that delivered at term (0.8 +/-0.5 ng/ml).

CONCLUSION: Data from this prospective descriptive study suggest that free activin A levels are not more elevated in patients with preterm contractions who deliver preterm than in those who carry to term. Bioactive activin A does not appear to be a marker for preterm delivery.

OBJECTIVE: Fetal fibronecin (FFN) testing to predict spontaneous preterm birth (SPB) uses a single cutoff of 50 ng/ml to define populations at high and low risk for preterm SPB. In this study, we determined the relationship between specific quantitative FFN values and subsequent SPB in women presenting with symptoms of preterm labor.

STUDY DESIGN: The FFN assays from 563 women who were enrolled in a prospective multicenter trial designed to determine the predictive value of FFN for subsequent SPB were reviewed. The study population consisted of women who presented to the hospital between 240/7 and 346/7 weeks gestational age with symptoms suggestive of preterm labor, a singleton pregnancy, intact membranes, no prior tocolysis, and cervical dilatation < 3 cm. The managing physicians were blinded to the FFN results. Tocolytics were withheld regardless of result.

RESULTS: The mean gestational age at the time of sampling was 30 weeks (SD = 2.99). The median FFN value was 8.4 ng/ml with a range of 0 ng/ml to 1648 ng/ml. Quantitative FFN values were initially grouped into 10 ng/ml increments for analysis. The rates of delivery within 7, 14, and 21 days following sampling were noted to cluster into three distinct FFN intervals as depicted in the table. As FFN values increased above 100 ng/ml, there was no further increase in the risk of SPB.

<table>
<thead>
<tr>
<th>FFN ng/ml</th>
<th>0-7 Days</th>
<th>0-14 days</th>
<th>0-21 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>486</td>
<td>3.0%</td>
<td>5.9%</td>
</tr>
<tr>
<td>10-100</td>
<td>25</td>
<td>8.9%</td>
<td>16.9%</td>
</tr>
<tr>
<td>&gt;100</td>
<td>40</td>
<td>30.0%</td>
<td>46.5%</td>
</tr>
</tbody>
</table>

CONCLUSION: In women with symptoms of preterm labor, an increase in the quantitative FFN from 40 ng/ml to 100 ng/ml is associated with a progressive increase in the risk of subsequent SPB. The use of a single FFN cutoff of 50 ng/ml for defining a positive test in women with symptomatic preterm labor should therefore be reevaluated.

FETAL FIBRONECTIN AT LESS THAN 20 WEEKS IS ASSOCIATED WITH CHORIOAMNIONITIS IN PRETERM DELIVERIES. M. Vullagan*, R. Goldberg, R. Copper* for The University of Alabama at Birmingham, Birmingham, AL, and the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: An elevated cervical or vaginal fetal fibronecin (VFn)-test at 24 weeks' gestational age (GA) is not only strongly associated with a subsequent spontaneous preterm delivery, but also with histological chorioamnionitis (HCA), both of which occur on average approximately 3 weeks later. The objective of this study was to determine the relationship between IFN testing results performed at 8-22 wks GA and HCA among women who deliver preterm.

STUDY DESIGN: Asymptomatic women being screened for participation in a bacterial vaginos~is-Thrombosis in Vaginal Cervix (TBV) study were also screened prospectively for VFn. A positive IFN test was defined as >250 ng/ml and preterm birth was defined as <37 wks GA. Although not part of the original study, at one participating institution, the medical records of women who had a positive IFN test and who delivered preterm were reviewed to obtain the placental histology reports that were performed as part of routine care. The pathology reports were abstracted for the presence of HCA, invasion and abrasion, without knowledge of the IFN test results.

RESULTS: 80 women who had VFn testing, delivered preterm and had a histological placental examination were identified. These women had a mean GA at VFn screening of 15.5±5.4 wks and a mean GA at delivery of 29.6±5.0 wks. Of the women, 18 (25%) had a positive IFN test, 35 (43%) had HCA, 28 (35%) had evidence of invasion, and 9 (11%) evidence of abrasion. The women without HCA had a mean VFn value of 56±159 ng/ml vs 122±217 ng/ml for those with HCA (p<0.05). Of the women with a positive VFn test, 61% had HCA compared to only 33% whose VFn was negative (RR 1.7, 95% CI 1.1-2.9). A positive VFn test was not associated with placental invasion or abrasion.

CONCLUSION: A positive VFn test from 8-22 wks GA is associated with a 1.7-fold increase in the risk of HCA among women who deliver preterm. Since the value of the testing was performed at a mean GA of 13 wks and delivery occurred at a mean GA of 29 wks, these data suggest that early 2nd trimester VFn testing can predict SPB associated with HCA several months prior to its occurrence. This data provides additional evidence for the chronology of the upper genital tract infection leading to preterm birth.

ENDOMETRIAL MICROBIAL COLONIZATION AND PLASMA CELL ENDOMETRITIS ARE COMMON THREE MONTHS POSTPARTUM. WW Andrews, JC Hauth, S Cliver*, M Conners*, RL Goldberg, Deps of Ob/Gyn & Pathology, Univ of Alabama at Birmingham, AL.

OBJECTIVE: To determine the frequency of upper genital tract microbial colonization and/or histologic inflammation at three months postpartum.

STUDY DESIGN: Postpartum, we prospectively collected vaginal, cervical (swabs) and endometrial specimens (using a Pipelle®) 3 months postpartum in women following spontaneous (Mean 84, range 55-121 days) or indicated preterm (Mean 85, range 57-121 days) or term birth (mean 85, range 57-121 days). Histology was performed for 4 cultures for aerobic, anaerobic, T. vaginalis, N. gonorrhoeae, S. agalactiae & genital mycoplasmas were performed. Endometrial histology for the presence of plasma cells was performed.

RESULTS: The study population (n=546) was 70% black, 31% white, 65% single and 74% had ≤12 years of education. The mean gestational age at delivery in the spontaneous vs indicated group was 26±3.7 vs 24.9±4.6 weeks (p<0.05). Endometrial cultures were positive for one or more microorganisms in 79% of women. The most common endometrial isolates were, G. vaginalis (39%), Lactobacillus spp. (29%), and S. cruenta (13%). In 516 specimens sufficient for histologic examination, plasma cell endometritis was present in 31%. Endometrial cultures were positive in 18% of women who had plasma cell endometritis and plasma cells were present in 13% of women who had positive endometrial cultures. Among women with positive cervical/vaginal cultures for U. urealyticum (55%), M hominis (31%), and S. agalactiae (21%), endometrial colonization rates for these microorganisms were 11%, 23%, and 26%, respectively. Therefore, if 100% of the positive endometrial cultures for these three organisms were considered to be a result of contamination during specimen acquisition, the rate of contamination would be 11 to 25%.

CONCLUSIONS: The frequency of microbial colonization of the endometrium and plasma cell endometritis is common in women three months postpartum. Microbial colonization is frequently present in the absence of plasma cell endometritis.

ENDOMETRIAL MICROBIAL COLONIZATION AND PLASMA CELL ENDOMETRITIS FOLLOWING SPONTANEOUS OR INDICATED PRETERM VS. TERM BIRTH. WW Andrews, JC Hauth, S Cliver*, M Conners*, RL Goldberg, Deps of Ob/Gyn & Pathology, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To determine if endometrial microbial colonization or plasma cell endometritis are increased following spontaneous vs. indicated preterm birth (PTB) or a spontaneous term birth (STB).

STUDY DESIGN: Postpartum, endometrial specimens were obtained in women following a spontaneous (Mean 84, range 55-121 days) or indicated (Mean 85, range 57-121 days) PTB at ≤34 weeks gestation and following a STB (mean 85, range 57-121 days). Cultures for aerobes, anaerobes, T. vaginalis, and genital mycoplasmas were performed. Endometritis was defined as the presence of plasma cells.

RESULTS: The study population (n=546) was 70% black, 30% white, 65% single and 75% had ≥12 years of education. Endometrial cultures were positive for at least one microorganism in 79% of the women. The mean number of microorganisms isolated from the endometrium in the spontaneous vs. indicated PTB group was 1.4±1.4 vs 1.2±1.3 organisms (p=.219) and in the spontaneous vs an indicated PTB (81% vs 70%, p=.059), or a spontaneous PTB vs a STB (81% vs 81%, p=.844). The distribution of the most commonly isolated microorganisms from the endometrium (in descending order: G. vaginalis, Lactobacillus spp., and S. cruenta) was similar among the three groups (p=.05). No significant difference in positive endometrial cultures was observed among women following a spontaneous vs an indicated PTB group (81% vs 70%, p=.099), or a spontaneous PTB vs a STB (81% vs 81%, p=.844). In 516 specimens sufficient for histologic examination, plasma cell endometritis was present in 31% Plasma cell endometritis was also similar in the three groups (spontaneous PTB, 31%, indicated PTB, 38%; STB, 30%; p=.575).

CONCLUSIONS: Microbial colonization of the endometrium and plasma cell endometritis are similar three months after spontaneous or indicated preterm or term births. These results do not explain the increased risk of subsequent PTB following a prior spontaneous PTB ≤34 weeks gestational age.
IS THE ETIOLOGY OF PRETERM BIRTH AMONG ADOLESCENTS THE SAME AS IN ADULTS? H Miles, MD, A Becher, and K Hennegan. Obstetrics Medical Group & Dept Ob/Gyn, Univ of AZ, Tucson, AZ.

OBJECTIVE: To evaluate behavioral characteristics, antenatal risk factors and clinical outcomes that differentiate preterm birth occurring to adolescents versus adults.

STUDY DESIGN: We conducted a retrospective case-control study comparing adolescents (<19) to adults delivering preterm (24/07-36/6/7 weeks), between 1990-97. The neonates were well dated and major anomalies were excluded. The medical records were reviewed for multiple demographic, antenatal and neonatal outcome variables. Data were analyzed using the unequal sample’s t test or Chi-square test with Yates correction as appropriate. Significance was defined as a p value of <0.05.

RESULTS: Of the 28,639 inborn neonates delivered, 419 (34%) preterm births occurred to adolescents and 811 (66%) to adults for a total of 1230. Adolescents comprise 3177 (11.1%) of our obstetrical population resulting in a RR=3.3, 95% CI 3.1 to 3.7, p<0.0001 for preterm birth among adolescents.


OBJECTIVE: PGE2 and the PGE2 receptor subtype EP1 are known to increase in cultures of amnion WHISH cells in response to cytokines. The cytokines are also known to be produced in response to infection and have been associated with the onset of labor. This investigation was designed to provide an experimental linkage between bacterial vaginoses (BV) and PGE2 in amnion WHISH cell cultures.

STUDY DESIGN: Amnion WHISH cells were grown to 80% confluence and incubated with culture fluid containing a 5% solution of vaginal discharge mixed in normal saline taken from pregnant patients diagnosed at term with BV. Cultures were incubated for 24 hours at 37°C and 5% CO2. Control cultures were incubated with discharge from pregnant patients without BV. Changes in EP1 receptor levels were evaluated by Western blot analysis. Culture fluid PGE2 was measured by enzyme-immunoassay.

RESULTS: A 2-3 fold increase in amount of EP1 receptor protein was found after incubation with vaginal secretions from term pregnant patients with BV compared to uninfected term pregnant patient controls (n=5, P<0.05). A two-fold increase in culture fluid PGE2 levels (pg/mg protein) was also observed for cultures incubated with the discharge from BV patients (n=5, P<0.05).

CONCLUSIONS: Vaginal secretions in patients with BV have the capability of both upregulating the PGE2 EP1 receptor as well as increasing the production of PGE2 by amnion WHISH cells in culture. This evidence provides a direct potential link to the association of BV and chorioamnionitis with the initiation of labor.

AMNIOTIC FLUID INTERLEUKIN-6 IS CORRELATED WITH THE LATENCY PERIOD IN PRETERM LABOR WITHOUT INTRAAMNIOTIC INFECTION. CD Hsu, H Harirah, K Aversa, R Bahado-Singh, JA Copel, Dept OB/GYN, Yale Univ School of Medicine, New Haven, CT.

OBJECTIVE: To determine whether amniotic fluid (AF) levels of cytokines [interleukin-6 (IL-6), leukemia inhibitory factor (LIF), chemokine ([interleukin-8 (IL-8), GRO-alpha]), nitric oxide (NOx), and cGMP were correlated with the latency period (interval from amnioncensis to delivery) in preterm labor without intra-amniotic infection (PTL/NAI).

STUDY DESIGN: AF specimens were obtained by amniocentesis from 36 women with preterm labor and intact fetal membranes. NIAI was defined as the absence of a positive AF culture. AF samples from 20 women with PTL, 20 women with PTL/NAI, and 20 post-term controls were collected. The samples were centrifuged at 3,000 g for 10 min and the supernatant was assayed for cytokines and NOx using ELISA. The cytokines were determined using enzyme immunoassay.

RESULTS: The mean gestational age was 29.5 weeks and the latency period was 21.4 days in PTL/NAI. AF IL-6 levels were negatively correlated with the latency period (r = 0.30, p = 0.02). There were no significant correlations between AF glucose, leukocytes, LIF, IL-8, GRO-alpha, NOx, and cGMP and the latency period. After adjustment for gestational age, cervical dilatation, and cervical effacement at amnioncensis using multiple regression analyses, AF IL-6 remained significantly correlated with the latency period (r = 0.40, p = 0.02). With a cutoff value of 11.3 ng/ml, 53% of women pregnant above this value delivered within 2 days. In contrast, 94%, 65%, and 52% of women remained pregnant after 2, 7, and 21 days when AF IL-6 was less than 11.3 ng/ml.

CONCLUSIONS: Among the AF markers, IL-6 is the best predictor of reduced latency period in PTL/NAI. In addition to its value for the rapid diagnosis of IAI, AF IL-6 is of clinical utility for counseling and managing PTL/NAI patients.

DOES ANTENATAL CORTICOSTEROID THERAPY REDUCE NEONATAL MORBIDITY BY SUPPRESSING FETAL INFLAMMATORY CYTOKINES? S. Longo, M.S. Palmgren, J. Ross, M. Alh, R. Holland, Department of OB/GYN, Tulane University School of Medicine, New Orleans, LA.

OBJECTIVE: To demonstrate an association between antenatal corticosteroid therapy, which reduces preterm neonatal morbidity, and the inflammatory cytokines, tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), and interleukin-8 (IL-8).

STUDY DESIGN: Clinical data was collected for 125 maternal-neonatal pairs (6 sets of twins) between 24-34 weeks gestation that included steroid therapy and antibiotic administration. We analyzed by Enzyme Linked Immunosorbent Assay (ELISA) 131 umbilical cord sera for TNF-α, IL-1β, IL-6, and IL-8. Patients were further divided into antibiotic and no antibiotic groups. Cytokine levels were analyzed within each group between patients receiving steroids and those who did not. Analysis of Variance on Ranks determined statistical significance.

RESULTS: Ninety maternal patients received steroids (81 with antibiotics) and 35 did not receive steroids (19 with antibiotics). Of those who received antibiotics, there was no statistical difference between median cytokine levels for steroid versus no steroid. TNF-α: 25.7, 27.0, IL-1β: 10.8, 28.7, IL-6: 253 vs 41.1, IL-8: 1104 vs 9251 (all units in pg/ml). Similar results were observed for the no antibiotic group. TNF-α: 15.3 vs 22.9, IL-1β: 12.4 vs 22.8, IL-6: 46.1 vs 25.5, IL-8: 1544 vs 556 (all units in pg/ml).

CONCLUSION: The cytokine concentrations were not significantly lower in those patients who received corticosteroid therapy with or without antibiotic administration.
113 INFLUENCE OF IL-1β ON OXYTOCIN RECEPTOR SIGNALING IN HUMAN DECIDUAL CELLS. U. Frade-Hoffmann,4 J P. Chao,4 P. N. Rauk, Magee-Womens-Research-Institute, University of Pittsburgh, Pittsburgh, Pennsylvania

OBJECTIVE: Oxytocin (OT) binding to its specific receptor (OTR) leads to uterine contractions, mediated by the second messenger mositol triphosphate (IP3). Furthermore it stimulates arachidonic acid release from the cell membrane with subsequent stimulation of prostaglandin production. During preterm labor, high concentrations of the inflammatory cytokine IL-1β are found in the amniotic fluid. We have previously demonstrated that the OTR is downregulated with prolonged incubation with IL-1β. The purpose of this study was to evaluate the influence of prolonged IL-1β treatment on oxytocin signaling in human decidua.

STUDY DESIGN: Primary cultures of human decidua (n=54) were treated with IL-1β for 24 hours. After incubation with different oxytocin concentrations (0-5000nM), we measured the production of mositol triphosphate (IP3) and the release of arachidonic acid in decidual cells prelabelled either with 3H-lysoarachidonic acid or 3H-arachidonic acid. Prostaglandin E2 (PGE2) and its higher concentrations of PGE2 were produced up to 12.5x higher concentrations of PGE2 compared to untreated cells. No further alteration of prostaglandin production was detected by oxytocin treatment.

RESULTS: The production of IP3 was significantly increased by oxytocin in control treated cells. OT did not have a significant effect on IP3 production in IL-1β treated cells. IL-1β treated cells released less arachidonic acid at all oxytocin concentrations compared to control cells. IL-1β treated cells produced up to 12.5x higher concentrations of PGE2 compared to untreated cells. No further alteration of prostaglandin production was detected by oxytocin treatment.

CONCLUSION: The ability of decidual to produce IP3 and arachidonic acid correlates with the concentration of OT. This study demonstrated up-regulated IP3 production and arachidonic acid release in primary cultures of human decidua under prolonged IL-1β treatment while prostaglandin production is enhanced. From this study, we conclude that OT signaling is negatively influenced by prolonged IL-1β treatment.

This work was supported by the Deutsche Forschungsgemeinschaft (Fr 1402/1-1) and the NIH (HD34373-03).

114 FACTORS ASSOCIATED WITH EARLY AND LATE MIDTRIMESTER PROM. BM Mercer, NL Meyer, JM O'Brein, P Hare, BM Sibai. The Prematurity Center, University of Tennessee, Memphis, TN

Prenatal PROM and early preterm delivery are associated with a high risk of intrapartum infection. Some have suggested that other mechanisms may also play a role in early midtrimester delivery.

OBJECTIVE: To determine if mid trimester PROM (mPROM) occurring at 16-20 weeks is different from mPROM near term (21-26 weeks).

STUDY DESIGN: All 433 pregnancies complicated by mPROM between 1989 and 1998 were evaluated. 13 women choosing elective induction were included. Clinical outcomes were evaluated based on fetal and neonatal outcomes.

RESULTS: The incidence of delivery within 48 hours is presented in the Table. The incidence of delivery within 48 hours is presented in the Table. There were no significant differences between the Early and Late groups regarding maternal age (23.8 ± 4.5 years), weight (167 ± 102 lb), initial hematocrit (32 ± 9%) nulliparity (57 ± 46%), race (86 ± 7%) African American, no prenatal care (2 vs 10%), tobacco use (19 ± 7%), or illicit drug use (8 ± 15%). Also, the groups were similar regarding prior vaginal bleeding (19 vs 14%), prior amnioncentesis (5 vs 2%), and twins/triplets (7 vs 8%). Latency to delivery was similar in the two groups (1.7-2.5 days, p=0.52). For 272 managed conservatively, latency from admission to delivery was also similar (2.3-3.0 days, p=0.69). Of 288 with admission cervical cultures, % were positive for bacterial (85%), and % were positive for E. coli (17%). We conclude that while IL-1β is a critical mediator of gram negative septic shock (confirming prior observations), it is not essential for labor in this model of intrapartum infection.

115 OUTCOMES AFTER MIDTRIMESTER PROM AT THE END OF THE 20TH CENTURY. BM Mercer, JM O'Brien, NL Meyer, LW Livingston, BM Sibai, The Prematurity Center, University of Tennessee, Memphis, TN

Because of its rarity, studies evaluating clinical outcomes after mid trimester PROM (mPROM) include small numbers and group patients over a wide range of gestations where morbidity and mortality could change dramatically.

OBJECTIVE: To evaluate current clinical course and outcomes after conservative management of mPROM.

STUDY DESIGN: 433 pregnancies with mPROM (1989 and 1998) were evaluated by chart review. "Conservatively managed" women were identified by excluding 147 requiring delivery for maternal/fetal indication on admission and 15 choosing elective induction. Perinatal outcomes were evaluated based on gestation at PROM. Infant mortality is reported for surviving infants.

RESULTS: 273 women with mPROM (298 babies) were conservatively managed over 10 years. Relevant pregnancy outcomes are summarized in the Table. Definitions include respiratory distress syndrome (RDS), blood or CSF culture proven sepsis, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD). Four survivors with PROM <20 weeks had prolonged latency (mean 58 days) and thus low morbidity.

CONCLUSION: Survival after mPROM increases with advancing gestation past 21 weeks. However, even at 26 weeks most infants will suffer serious acute complications and are at risk for serious long term sequelae.

116 INTERLEUKIN 1 (IL-1) IS NOT ESSENTIAL FOR INFECTION-INDUCED PRETERM BIRTH: EVIDENCE FROM A MURINE KNOCKOUT MODEL. Rebecca A Mutele, Jacques Peschon, and Emmat Horovitz, Dept of Ob/Gyn, Columbia University, New York, NY and Immunex Corporation, Seattle, WA.

OBJECTIVE: To test whether disruption of IL-1 signaling inhibits labor in a murine model of intrauterine infection.

STUDY DESIGN: In a blinded experiment, mice lacking one or both copies of the Type I IL-1 receptor (IL-1R1) and littermate controls on day 14.5 of a 19.20 day gestation underwent intratracheal inoculation with varying amounts of killed E. coli bacteria.

RESULTS: The incidence of delivery within 48 hours is presented in the Table. There were no significant differences between the Early and Late groups regarding maternal age (23.8 ± 4.5 years), weight (167 ± 102 lb), initial hematocrit (32 ± 9%) nulliparity (57 ± 46%), race (86 ± 7%) African American, no prenatal care (2 vs 10%), tobacco use (19 ± 7%), or illicit drug use (8 ± 15%). Also, the groups were similar regarding prior vaginal bleeding (19 vs 14%), prior amnioncentesis (5 vs 2%), and twins/triplets (7 vs 8%). Latency to delivery was similar in the two groups (1.7-2.5 days, p=0.52). For 272 managed conservatively, latency from admission to delivery was also similar (2.3-3.0 days, p=0.69). Of 288 with admission cervical cultures, % were positive for bacterial (85%), and % were positive for E. coli (17%). We conclude that while IL-1β is a critical mediator of gram negative septic shock (confirming prior observations), it is not essential for labor in this model of intrapartum infection.

Deletion of the IL-1 receptor did not reduce the incidence of preterm delivery. Other observations including delivery in these animal models and associated evacuation of the uterus after delivery were no different among the three groups. With 10% bacteria, 100% of controls (n=4) and 65% of heterozygotes (n=8) died or became moribund and required euthanasia due to a shock-like syndrome, while all IL-1R1 homoyzygous knockouts survived without deficit (n=6) (P<0.005).

CONCLUSION: We conclude that while IL-1 is a critical mediator of gram negative septic shock (confirming prior observations), it is not essential for labor in this model of intrapartum infection.

**Table:**

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<tr>
<td>IL-1R1 heterozygote</td>
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**Inoculum (killed E. coli):**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Inoculum (killed E. coli)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1R1 knockout</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>IL-1R1 heterozygote</td>
<td>1/6 (17%)</td>
</tr>
<tr>
<td>Wild-type</td>
<td>0/4 (0%)</td>
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<tr>
<td>F value</td>
<td>0.49</td>
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</tbody>
</table>

Deletion of the IL-1 receptor did not influence the incidence of preterm delivery. Other observations including delivery in these animal models and associated evacuation of the uterus after delivery were no different among the three groups. With 10% bacteria, 100% of controls (n=4) and 65% of heterozygotes (n=8) died or became moribund and required euthanasia due to a shock-like syndrome, while all IL-1R1 homozygous knockouts survived without deficit (n=6) (P<0.005).

CONCLUSION: We conclude that while IL-1 is a critical mediator of gram negative septic shock (confirming prior observations), it is not essential for labor in this model of intrapartum infection.
PERIOPERATIVE TRANSVAGINAL SONOGRAPHY AS AN ADJUNCT TO CERVICAL CERCLAGE: El-Azem SA, Colombo D, Samuels P, Fullana M, Walker H, Iams JD, Deps of Obstetrics and Gynecology, The Ohio State University, Columbus, and St. Elizabeth Hospital, Youngstown, OH

OBJECTIVE: To relate perioperative changes in cervical length (CL) in women undergoing cerclage to pregnancy outcome.

STUDY DESIGN: Enrolled subjects had cerclage sutures placed because of a typical history with or without ultrasound evidence of incompetence. Total CL and CL above (UCL) and below (LCL) the plane of the suture were measured pre and post cerclage. The CL variables and precerclage funnelling were related to delivery <34 vs ≥34 weeks.

RESULTS: Nine (17.3%) of 52 women studies delivered <34 weeks. Mean postoperative total CL for all 52 subjects was significantly longer than the preoperative total CL (22.7 ± 6.8 vs 34.1 ± 5.3 mm, p<0.0001), but there were no differences in pre- and post-operative Total, UCL, or LCL in women delivered <34 vs ≥34 weeks. Gestational age at delivery was not different in women with or without perioperative funnelling.

CONCLUSIONS: Cervical cerclage results in an immediate increase in total CL, but neither precerclage funnelling, CL nor postcerclage total CL, UCL, or LCL were predictive of delivery <34 weeks.

RESPONSE OF THE THREE COMPONENTS OF A VAGINAL GRAM STAIN SCORE TO METRONIDAZOLE TREATMENT AND IN RELATION TO PRETERM BIRTH: J. Health for the NICHD MFMU Network, Bethesda, MD.

OBJECTIVE: To determine the occurrence and response to metronidazole treatment of each component a vaginal Gram Stain score ( Nugent criteria) and with subsequent preterm birth (PTB).

STUDY DESIGN: In a NICHD MFMU Network at 25 hospitals, randomization to metronidazole did not result in a reduction of PTB or low birthweight compared to a placebo. This is a further analysis of the effect of treatment on each component of the Gram score and in relation to PTB. Score components included large Gram positive (+) rods - Lactobacillus, small Gram variable rods - G. vaginalis/ Bacterodes (GB), and long curved Gram negative (-) or variable rods - Mobiluncus (M).

RESULTS: At randomization in 1934 women, 4(+) Lactobacillus occurred in only 6.6% of women, GB in 86% and M in 45%. No Lactobacillus were identified in 57%, no GB in 39% and/or no M in 48%. Following treatment with metronidazole more women had a reduction in 4(+) GB and M morphotypes (p<0.001) and more had none of these adverse morphotypes identified (p<0.001). Following metronidazole more women developed 4(+) Lactobacillus (p<0.001) and fewer had no Lactobacillus identified (p<0.001). Women assigned to the placebo had similar Gram stain score components at randomization and after treatment. At randomization, 81% of the patients in both treatment groups had a BV score of 7-10. At follow-up, only 24% of the patients in the metronidazole group had a score of 7-10, compared to 69% of the patients in the placebo group (p<0.001). No component of the score or their response to treatment was predictive of subsequent PTB or low birthweight.

CONCLUSION: In women with a vaginal Gram stain score of ≥7, treatment with metronidazole resulted in a significantly lower vaginal Gram stain score, but improvement in each of the three components used to determine the score. These results had no effect on the subsequent occurrence of PTB.
122  SERIAL BETAMETHASONE USE IN A CLINIC PRACTICE: DOES IT AFFECT FETAL GROWTH? DM Estes, J Paus, JFX Egan, St. Francis Hospital & Med Ctr; and Univ of CT, Farmington, CT.

OBJECTIVE: To determine the effect of serial betamethasone (Bmeth) administration on fetal growth in a clinic practice. The null hypothesis is that there is no effect of serial use of betameth on birthweight (BWT) and neonatal head circumference (HC) at 39 weeks.

STUDY DESIGN: Review of all singleton pregnancies delivered of clinic patients between 7/1/94 and 12/31/98 was done from a computerized database and chart review. Gestational age was determined by dates and ultrasound. Exclusion criteria included major congenital anomalies and infections, maternal age less than 16 years, hypertension or diabetes of any etiology, medical disorders known to alter fetal growth and use of other steroids during the pregnancy, cocaine use, or smoking. Bmeth use and number of doses to 34 weeks were determined from department databases, pharmacy logs and chart review. The control group had patients who received no Bmeth. Linear regression and ANOVA were used to analyze the effect of serial Bmeth on BWT and HC at delivery at 39 weeks.

RESULTS: 1791 met the inclusion criteria and of these 488 delivered at 39 weeks. The mean BWT (3857g) of controls vs. that of patients who received >3 doses of Bmeth (3057g) were significantly different (p<0.02). There was no difference in the mean HC between these groups. By linear regression the effect of serial Bmeth use on BWT and HC was significant. (See graph).

CONCLUSION: Serial Bmeth use had a significant effect on BWT and HC in patients delivered at 39 weeks. The mean BWT in the group who received >3 doses was significantly smaller than that in the control group. A Type II error may explain the lack of a significant difference in mean HC in these two groups. Antenatal serial use of Bmeth in patients who ultimately delivered at 39 weeks appeared to have an effect on fetal growth in this practice.

123  COMPARISON OF TRANSABDOMINAL VERSUS TRANSVAGINAL CERCLAGE IN PATIENTS WITH PRIOR FAILED TRANSVAGINAL CERCLAGE. V Berghella, G Davis, M Talucci, RJ Wagner, Div of MFM, Dept of Ob/Gyn, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: To compare preterm delivery (PTD) incidence between transabdominal (TAC) and transvaginal cerclage (TVC) in patients with prior failed TVC.

STUDY DESIGN: Singleton pregnancies who received a prophylactic (11-14 weeks) TAC or TVC after ≥1 prior failed prophylactic TVC were retrospectively reviewed (TAC 1988-99, TVC 1995-98). Prior failed TVC was defined as ≥1 PTD <35 weeks following TVC in the prior pregnancy(ies). Patients with a cervix too short for TVC placement, placenta previa or congenital fetal anomalies were excluded. Primary outcome was PTD <35 weeks.

RESULTS: Thirty-three prophylactic TAC and 14 prophylactic TVC patients met above criteria, including prior failed TVC. These 2 groups were similar for age, race, and payer status. The TAC group had more prior failed cerclages per patient (1.8±1 vs 1.1±0.3, p=0.01) and more prior 14-24 weeks spontaneous abortions per patient (2.6±1.3 vs 1.1±0.005, compared to the TVC group.

<table>
<thead>
<tr>
<th>Cerclage type</th>
<th>PTD &lt;35w % (n)</th>
<th>PTD &lt;35w % (n)</th>
<th>GA at del wks ±SD</th>
<th>Birth weight grams</th>
<th>PPROM % (n)</th>
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<tbody>
<tr>
<td>TAC</td>
<td>15 (5)</td>
<td>6 (2)</td>
<td>36.2±4.2</td>
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<td>6 (2)</td>
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<tr>
<td>TVC</td>
<td>43 (6)</td>
<td>36 (5)</td>
<td>33.9±7.3</td>
<td>2694±1318</td>
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</tr>
<tr>
<td>OR</td>
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<td>95% CI</td>
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<td>0.01-0.57</td>
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</tr>
</tbody>
</table>

CONCLUSION: In patients with prior failed transvaginal cerclage, transabdominal cerclage is associated with a lower incidence of PTD compared to transvaginal cerclage.


OBJECTIVE: To determine in patients with a cervical length (CL) <25mm on transvaginal ultrasound (TVU) at the severity of CL shortening predicts preterm premature rupture of membranes (PPROM).

STUDY DESIGN: Retrospective review of asymptomatic singleton pregnancies at high risk for preterm delivery (PTD) by prior obstetric history and TVU CL <25mm between 14 and 25 6/7 weeks. Cases with PPROM <35 weeks were compared with controls without PPROM (NPPROM) for TVU cervical characteristics.

RESULTS: One hundred and eighty-three women at high risk for PTD were followed with TVU. Of 60 patients identified to have a CL <25mm, 27 (30%) had PPROM, and 42 (61%) did not (NPPROM). Thirty-three prophylactic TAC and 14 prophylactic TVC were performed prior to PPROM. Of 60 patients identified to have a CL <25mm, 27 (30%) had PPROM, and 42 (61%) did not (NPPROM). Thirty-three prophylactic TAC and 14 prophylactic TVC were performed prior to PPROM. The TAC group had more prior failed TVCs (p=0.01), compared to NPPROM. These 2 groups were similar for age, race, and payer status. The TAC group had more prior failed TVCs (p=0.01), compared to NPPROM. These 2 groups were similar for age, race, and payer status. The TAC group had more prior failed TVCs (p=0.01). The TAC group included more prior failed TVCs (p=0.01). The TAC group included more prior failed TVCs (p=0.01). The TAC group included more prior failed TVCs (p=0.01). The TAC group included more prior failed TVCs (p=0.01). The TAC group included more prior failed TVCs (p=0.01).

CONCLUSION: In patients at high risk for PTD because of obstetrical history and TVU CL <25mm, CL <10mm and/or CF >75% were most predictive of PPROM.

SMFM Abstracts S57
**125 WITHDRAWN**


**OBJECTIVE: It has been suggested that magnesium sulfate (MGSO4) is neuroprotective. Other studies have shown that this may be due to an increase in mortality. We investigated the effect of MGSO4 on neonatal mortality and morbidity in a large low birthweight perinatal database.**

**METHODS:** 918 consecutive inborn neonates weighing ≤ 1750 g were divided into two groups on the basis of maternal exposure to MGSO4. Groups were compared for gestational age, RDS, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), upper lesions (grade III, IV IVH, any IVH and PVL or PVL), necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), and sepsis. These groups were further stratified according to indication for MGSO4 usage and the strata were compared for the risk of IVH/PVL and major lesions. Fisher’s exact test and logistic regression was used for the analysis.

**RESULTS: Comparison of the two groups showed no difference in the incidence of death, RDS, PDA, NEC, sepsis, a decrease in major lesions, higher use of steroids and lower incidence of chorioamnionitis. The logistic model for the risk of IVH/PVL and major lesions controlling for gestational age, steroids, race, maternal body mass index (BMI), and parity were compared to cervical length and gestational age at delivery using Student test, Chi-square and Fisher exact test.**

**RESULTS: The mean cervical length at 16-23 weeks was 3.8 ± 0.9 cm (10th percentile = 2.9, 50th percentile = 4.9). The mean gestational age at delivery was 39.2 ± 1.8 weeks, with 6.9% preterm (<37 weeks). The mean cervical length for preterm patients was 3.4 ± 0.8, whereas the mean for term patients was 3.9 ± 0.9 cm (p<0.05).** Fewer multiparas had cervices ≤ 3.0 cm (10th percentile) than did primiparas (5.9% vs. 11.6%, p<0.05), giving a relative risk of preterm delivery for multiparas of 0.65 (95% CI 0.44-0.97). **Low maternal BMI (BMI ≤ 20%) was associated with cervical length < 3.0 cm (RR 2.5, p<0.05) but not with PTB. Cervical length and PTB were not significantly different between ethnic or age groups.**

**CONCLUSIONS:** Second trimester transperineal sonography can identify asymptomatic patients at risk for PTB. Fewer multiparas had shortened cervices (<10% vs. 20%) which correlated with a reduced risk of PTB. Low maternal BMI was associated with shortened cervix but not with PTB in this study. Maternal age and ethnicity showed no association with cervical length or PTB. The addition of transperineal cervical length to routine second trimester sonography may improve detection of patients at risk for PTB.

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**127 SHORTENED SECOND TRIMESTER TRANSPERINEAL CERVICAL LENGTH IN ASYMPTOMATIC PATIENTS IS ASSOCIATED WITH PRETERM BIRTH. B R. Pringle, G. Hongh, P. Richter*, T. R. Moore, Dept. of Perinatal Med, Dept of Repro Med., Univ. of Calif. at San Diego, La Jolla, CA.**

**OBJECTIVE: To correlate routine second trimester transperineal cervical length in asymptomatic patients with preterm birth (PTB).**

**STUDY DESIGN:** 302 patients presenting for routine fetal anatomy scans between 16 and 23 weeks gestation underwent prospective assessment of cervical length using transperineal ultrasound. After delivery, cervical lengths were correlated with gestational age at birth. Demographic data including age, race, maternal body mass index (BMI), and parity were compared to cervical length and gestational age at delivery using Student test, Chi-square and Fisher exact test.

**RESULTS:** The mean cervical length at 16-23 weeks was 3.8 ± 0.9 cm (10th percentile = 3.0, 90th percentile = 5.0). The mean gestational age at delivery was 39.2 ± 1.8 weeks, with 6.9% preterm (<37 weeks). **The mean cervical length for preterm patients was 3.4 ± 0.8, whereas the mean for term patients was 3.9 ± 0.9 cm (p<0.05).** Fewer multiparas had cervices ≤ 3.0 cm (10th percentile) than did primiparas (5.9% vs. 11.6%, p<0.05). **Fisher’s exact test revealed lower preterm delivery rates for women with cervixes ≤ 3.0 cm (95% CI 0.44-0.97). Low maternal BMI (BMI ≤ 20%) was associated with cervical length < 3.0 cm (RR 2.5, p<0.05) but not with PTB. Cervical length and PTB were not significantly different between ethnic or age groups.**

**CONCLUSIONS:** Second trimester transperineal sonography can identify asymptomatic patients at risk for PTB. Fewer multiparas had shortened cervices (<10% vs. 20%) which correlated with a reduced risk of PTB. Low maternal BMI was associated with shortened cervix but not PTB in this study. Maternal age and ethnicity showed no association with cervical length or PTB. The addition of transperineal cervical length to routine second trimester sonography may improve detection of patients at risk for PTB.

OBJECTIVE: To determine the prevalence and population attributable risk of sociodemographic and lifestyle factors for prematurity singleton birth in a defined community

STUDY DESIGN: An immediate postpartum population based survey was conducted using a self-administered questionnaire at the 5 hospitals providing obstetrical care in a defined community over one calendar year. A standardized questionnaire format was utilized. Univariate analyses were first used to identify factors associated with the risk of premature birth. Separate logistic regression models were created for the risk of premature birth among primiparous and multiparous women. The population attributable risk was calculated to examine the contribution of each of individual risk factor controlling for all other selected factors for premature birth.

RESULTS: 8452 women (87%) completed the questionnaire. Participation was limited by language difficulties and early discharge from hospital. At the univariate level, 10 factors were associated with premature birth. Logistic regression produced a model involving seven of the seven primary risk factors, problems prior to premature birth, prior abortion, short maternal stature, smoking and high perceived stress. 84.6% of all preterm births in the population were attributed to these 7 factors. If the modifiable risk factors of serious health problems, perceived stress and smoking were mathematically reduced by 50%, the resultant decrease in premature birth would be 19%.

CONCLUSION: The success of premature birth prevention programs depend on an understanding of modifiable factors to the overall population attributable risk for premature birth.

TIMING OF CERCLAGE REMOVAL AFTER PPROM—MATERNAL AND NEONATAL OUTCOMES. TM. Jenkins, V. Bergballe, C. McIntyre*, M. Follic*., R.J. Wapner, Div. of MFM, Dep of Ob/Gyn, Jefferson Medical College of Thomas Jefferson Univ., Philadelphia, PA, and Div of MFM, Christiana Hospital, Newark, DE.

OBJECTIVE: To evaluate immediate versus delayed removal of cerclage for women with PPROM with respect to maternal and neonatal outcomes

STUDY DESIGN: A retrospective analysis was performed on women who presented between 5/90 and 6/99 with premature rupture of membranes (PPROM) ≤35 weeks, prior cerclage placement, and complete records. Exclusion criteria included chromosomun, active labor, or nonreassuring fetal status upon presentation. Patients with PPROM ≤24 weeks who elected termination were also excluded. Timing of cerclage removal (immediate or delayed) was based upon physician preference. Outcomes of immediate or delayed removal were compared. The primary outcome was the rate of neonatal sepsis (positive blood culture <10 days after delivery) Secondary outcomes included length of latency, birth weight, maternal infection, and neonatal morbidity/mortality. Student's t-test, chi square analysis and logistic regression were performed where appropriate. A p-value of < 0.05 was significant.

RESULTS: Fifty-five women met inclusion criteria: 14 were excluded secondary to the criteria listed above. Forty-one women were available for analysis, 32 in the immediate removal group, 9 in the delayed removal group. These two groups did not differ regarding maternal age, parity, socioeconomic status, risk factors for preterm delivery, rates of salvage or prophylactic cerclage, or gestational age at cerclage placement. Average time to removal was 4.6 ± 151.4 hours, respectively. Rates of antibiotic (74% v 89%) and betamethasone use (60% v 67%) after PPROM were similar for both groups, respectively. Short-term tocolytic use for betamethasone was higher in the delayed removal group (0% v 22%, p < 0.046). Gestational age at rupture was similar for both groups (28.2 ± 5.7 vs 28.6 ± 6.0), respectively. Of note, length of latency was significantly longer for the delayed removal group (54.4 ± 48.4 days, p = 0.015).

CONCLUSION: With the current management scheme of PPROM, cerclage retention significantly increases length of latency without significantly altering maternal or neonatal outcome. Higher rates of infection in both mothers and neonates, may occur with delayed removal.

ANTENATAL MANAGEMENT OF MOTHERS WHO DELIVER AN INFANT <1500 GM: IN-BORN VERSUS OUT-BORN NEONATES. A. Schoppke, P. Shlissman, K. Leef, D. Paul*, Divs. of MFM and Neonatology, Children's Hospital, Newark, DE, USA.

OBJECTIVE: Recent reports have found that neonates who are born in a tertiary care facility have better outcomes than those who are born in a non-tertiary care center and transferred. The reason for the difference in outcomes is unclear. We compared differences in the antenatal management of very low birth weight (VLBW) neonates born in our tertiary care teaching hospital (in-born) versus VLBW neonates who were born in a non-tertiary care facility and transferred to our hospital (out-born).

STUDY DESIGN: We reviewed our neonatal database from July 1993 to July 1998, for infants who weighed <1500 gm. Neonates with congenital malformations were excluded. Mothers who were transferred from a non-tertiary care facility, but delivered infants at our facility, were included in the in-born group. We reviewed each neonate's antenatal care for maternal age, presence of multiple gestation, race, growth restriction (IUGR), maternal diabetes (DM), preeclampsia, chorionamnionitis (CHORIO), maternal drug use, tocolytic use, prophylactic steroid use, premature rupture of the membranes (PROM), premature labor (PTL), gestational age, type of delivery, and birthweight (BW). Student's t-test, chi square analysis and logistic regression were used where appropriate. A p-value of < 0.05 was significant.

RESULTS: A total of 654 neonates were included in the analysis, 590 in-born and 64 out-born. There was no significant difference in the rate of DM, CHORIO, drug use, PROM, or PTL between groups. The in-born group had a higher maternal age (28.0 v 25.1, p = 0.001), a higher number of multiple gestations (26% v 8%, p = 0.006), a higher number of IUOR neonates (14% v 5%, p = 0.04), a higher rate of preeclampsia (19% v 5%, p = 0.005), a higher gestational age at delivery (28.4 ± 2.9 vs. 27.5 ± 2.6 wk, p = 0.02), a higher cesarean delivery rate (58% v 37%, p = 0.002), a greater use of tocolytics (57% v 15%, p = 0.001), and a higher rate of prophylactic steroid use (63% v 14%, p = 0.002) when compared to the out-born group. After adjusting for multiple potential confounding variables, prophylactic steroid use (OR 8.4; 95% CI 3.4 v 20.6) and use of tocolytics (OR 5.7; 95% CI 1.2 v 5.1) remained higher in the in-born group.

CONCLUSIONS: In our population of VLBW neonates, in-born neonates were more likely to receive prophylactic steroids and tocolytic medications than out-born neonates. From these data, we cannot determine whether these differences are secondary to a discrepancy in obstetrical practices or due to differing clinical situations.


OBJECTIVE: To evaluate whether serial amnioinfusions for persistent oligohydramnios can affect the perinatal and long-term neurologic outcome in extremely preterm premature rupture of membranes (PROM).

STUDY DESIGN: All singleton pregnancies with PROM ≤26 weeks and lasting ≥4 days between 1/91 and 6/98 were included. Amniotic fluid (AF) volume was assessed sonographically twice weekly. Consenting women with persistent (≥4 days) oligohydramnios (maximum cord-free pocket of AF ≤5 cm) received serial transluminal amnioinfusions to maintain AF volume >2 cm. The pregnancy outcome of those with successful amnioinfusion (n=11) was compared with that of women with PROM and persistent oligohydramnios (n=25) using Wilcoxon Rank-sum test and Fisher's exact test. Neurological outcome was assessed at 1 year of age using the Milani-Compari and Giodoni scale.

RESULTS: Oligohydramnios Amnioinfusion P value
G.A. at PROM (wks) 19.5 (14.0-25.2) 16.5 (14.0-21.0) <0.05
G.A. at delivery (wks) 24.4 (17.0-29.0) 25.4 (12.0-25.3) <0.001
Days PROM at delivery 22 (9-105) 39 (48-135) 0.02
Chorionamnionitis 8/25 0/11 0.08
Pulmonary hypoplasia 13/21 1/11 <0.01
Neonatal survival 6/25 (24%) 8/11 (73%) <0.01
Neurologic outcome 2/6 1/8 0.5

CONCLUSIONS: Despite lower gestational age at PROM, pregnancies with oligohydramnios managed successfully with serial amnioinfusions have a better outcome than those with persistent oligohydramnios.
LAMELLAR BODY COUNTS ARE PREFERABLE TO TRADITIONAL PHOSPHOLIPID ANALYSIS AS A PRIMARY ASSAY FOR FETAL LUNG MATURITY. MC Norgaard, EL Hauy, RK Silver, JC Dolman, ER Ashwood, and IS Lee. Evanston Northwestern Healthcare, Northwestern University Medical School, Evanston, IL, University of Utah, Salt Lake City, UT, University of Ulsan College of Medicine, Asan Medical Center, Seoul, S. Korea.

OBJECTIVE: To compare the predictive value of lamellar body nuclear density (LBND) to the L/S ratio and to phosphatidylglycerol (PG) in assessing the likelihood of fetal lung maturity.

INTRODUCTION: Lamellar bodies are packages of phospholipids produced by type II alveolar cells that can be easily quantified by a standardized platelet counter. In contrast, L/S ratios require thin-layer chromatography and are relatively labor intensive. LBND testing costs less than half the charge of an L/S ratio and results are typically available in one third of the time.

STUDY DESIGN: LBND values, L/S ratios, and PG assays were obtained between 1992 and 1999 on 1660 amniotic fluid specimens from pregnancies at risk for preterm delivery. Cases in which delivery occurred within 72 hours of amniocentesis (n=603) were analyzed. Specific breakpoints for predicting the likelihood of RDSs for both the LBND and L/S ratio were derived from receiver-operator curves using unrelated samples, while PG was reported as present or absent. Standard clinical and radiographic criteria were used to diagnose RDS, which was confirmed by review of newborn records.

RESULTS: A total of 80 infans developed RDS (12%). Focusing on the ability of LBND, L/S, and PG to predict the absence of disease (n=603), the following frequencies were observed:

<table>
<thead>
<tr>
<th>RDS-NO</th>
<th>RDS-YES</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mature LBND</td>
<td>451</td>
<td>15</td>
</tr>
<tr>
<td>Mature L/S Ratio</td>
<td>320</td>
<td>8</td>
</tr>
<tr>
<td>PG Present</td>
<td>203</td>
<td>6</td>
</tr>
</tbody>
</table>

CONCLUSIONS: 1) The LBND predicts the absence of RDS (within 72 hours of delivery) as well as a mature L/S ratio or the presence of PG; 2) Reliance on LBND as the primary screening tool for RDS will provide equivalent predictive value, while reducing the cost of fetal lung maturity assessment, and improving the timeliness of results.

CAN A CYCLO-OXYGENASE TYPE-2 SELECTIVE TOCOLYTIC AGENT AVOID THE FETAL SIDE EFFECTS OF INDOMETHACIN? P Bellini, A Locatelli, P Verzani, V Kiro, V Dorais, and A Ghidini. Dept Obst Gyn, IBSM S Gerardo, and Georgetown University Medical Center, Monza, Italy, and Evanston Northwestern Healthcare, Northwestern University Medical School, Evanston, IL, University of Utah, Salt Lake City, UT, University of Ulsan College of Medicine, Seoul, Korea.

OBJECTIVE: To examine the role of a COX-2 selective tocolytic agent (Nimesulide) in the management of preterm delivery due to preterm labor.

RESULTS: Eighteen cases were included in the study. Nine cases were managed with intravenous Nimesulide (50 mg) every 4 hours until delivery. Median study duration was 102 hours (range 0.9-19230) pg/ml, median 22.5 [0.9-511.6] pg/ml (p<0.05). Median plasma IL-6 was 29.1 pg/ml (range: 0.9-511 pg/ml) (p<0.05).

CONCLUSION: Nimesulide, a 100-fold more powerful COX-2 than COX-1 inhibitor, has been proposed in a case report as a tocolytic agent with minimal fetal effects (Sawdy et al. Lancet 1997;350:256). We have evaluated the effects of Nimesulide on the efficacy of oral Nimesulide 100 mg twice daily. The amniotic fluid (AF) volume was monitored sonographically every 48 hours. Ohgohydramios was noted in 2 cases, suggesting that the COX-2 selectivity of Nimesulide observed in vivo may not be lost in vivo.

THE CLINICAL SIGNIFICANCE OF UMBILICAL ARTERITIS AS A MARKER OF A FETAL INFLAMMATORY RESPONSE. C.J. Kins, B.H. Yoon, R. Romero, J. S. Park, J. G. Chi. Departments of Pathology, and Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea.

OBJECTIVE: Umbilical cord arteritis is an indicator of a more advanced stage of the fetal inflammatory response syndrome than inflammation limited to the umbilical vein. Moreover, umbilical arteritis is a prognostic factor for adverse perinatal outcome.

STUDY DESIGN: This cohort study included 108 cases of preterm delivery (<36 weeks) with inflammation of the umbilical cord. Umbilical cord blood was collected at the time of delivery. Pathologic examination was aimed at characterizing the extent of umbilical cord inflammation, involvement of the vein (phlebitis), one or both arteries (arteritis) and extending into the Wharton’s jelly. This study was conducted to examine if the pattern of inflammation of the umbilical cord correlates with a biochemical marker of systemic fetal inflammation—umbilical cord plasma interleukin-6 (IL-6)—and adverse neonatal outcome.

RESULTS: 1) Neonates with umbilical arteritis had a significantly higher median plasma IL-6 than those without umbilical arteritis (cord plasma IL-6 median 111 pg/ml [range 0.1-19230] pg/ml vs median 22.5 [0.9-511.6] pg/ml [p<0.05]); 2) Severe neonatal morbidity was more frequent in infants with arteritis than in those without arteritis (74% vs 50%; p<0.05); 3) The most severe form of inflammation involving both arteries, vein and Wharton’s jelly was associated with the highest median concentration of plasma IL-6 observed in this study (median: 183 pg/ml [range: 0.1-7,400] pg/ml) while inflammation limited to the vein (phlebitis) was associated with a lower cord plasma IL-6 (median: 29.1 pg/ml [range: 0.9-511] pg/ml) (p<0.05).

CONCLUSION: Umbilical arteritis is an indicator of a more advanced stage of the “fetal inflammatory response syndrome” than inflammation limited to the umbilical vein. Moreover, umbilical arteritis is a prognostic factor for adverse perinatal outcome.


OBJECTIVE: The fetal inflammatory response syndrome (FIRS), a clinical condition characterized by utero multi-organ involvement, is a risk factor for perinatal morbidity/mortality. The diagnosis of FIRS, thus far, has relied upon the detection of elevated cytokine levels in fetal cord blood. A non-invasive alternative is required for the diagnosis of this condition with important clinical, biological and medicolegal implications. The objective of the study was to determine if funisitis inflammation of the umbilical cord at histologic examination of the placenta, could serve this purpose. We examined the relationship between the presence of funisitis and the level of umbilical cord plasma interleukin-6 (IL-6) and neonatal complications in preterm gestation.

STUDY DESIGN: A cross-sectional cohort study was conducted in 315 singleton pregnancies delivered between 20 and 35 weeks of gestation. Histologic examination of the placenta for the diagnosis of funisitis and umbilical cord plasma determinations of IL-6 was performed. Neonatal outcome and infant follow-up to the age of 3 (for diagnosis of cerebral palsy) was obtained. Univariate and multivariate analysis was conducted.

RESULTS: 1) Funisitis was present in 27% of cases; 2) Patients with funisitis had significantly higher median plasma IL-6 cord-median 52.4 [range 0.9-19230] pg/ml vs median 4 [range 0.18-10] pg/ml; gestational age: median 31.1 [range 21.0-35.0] weeks vs median 32.9 [range 21.4-38.5] weeks; p<0.0001 for each); 3) Cord plasma IL-6 of >17.5 pg/ml had a sensitivity of 70% and a specificity of 85% in the identification of funisitis; 4) Clinical chorionamnionitis was more common in patients with funisitis than in those without funisitis (18% vs 4%; p<0.001); 5) Neonates with funisitis had a significantly higher perinatal morbidity than those without funisitis, including congenital proen born, suspected sepsis, bronchopulmonary dysplasia, brain white matter lesions and cerebral palsy (p=0.05 for each); 6) Multivariate analysis demonstrated that funisitis was an independent risk factor for the development of neonatal sepsis and cerebral palsy after adjustment for the gestational age at birth (p<0.05 for each).

CONCLUSIONS: 1) The presence of funisitis is associated with elevated umbilical cord plasma concentrations of IL-6, the hallmark of FIRS; 2) Funisitis is an independent risk factor for short- and long-term neonatal/infant morbidity; 3) Funisitis can serve as a histologic counterpart to FIRS.

OBJECTIVE: To determine whether broad spectrum antibiotic prophylaxis with Ampicillin plus Sulbactam (Unasyn) compared to Ampicillin alone results in prolonged latency in pregnancies complicated by preterm premature rupture of the membranes (PPROM).

STUDY DESIGN: Between May 1997 and October 1998, 51 singleton pregnancies complicated by PPROM between 24-34 weeks gestation were randomized to 72 hours of Ampicillin plus Sulbactam or Ampicillin alone within 24 hours of membrane rupture. The primary outcome was length of latency, defined as time from rupture of membranes to delivery, and was available for 47 pregnancies. Multiple neonatal outcomes also were evaluated. Chi squared and student's t-test were used for univariate comparisons between groups.

RESULTS: Baseline variables between treatment groups were comparable with the exception of gravidity (monogamous vs multigravid) and race (white vs other). In order to adjust for the imbalance between groups, a multivariate linear regression model was used. After adjustment for these differences, the effect of drug on latency remains non-significant (p=0.46). In terms of neonatal outcomes, the only significant difference between treatment groups was a higher rate of clinical sepsis (p=0.04) in the Ampicillin plus Sulbactam group.

CONCLUSION: Identification of the ideal antibiotic, or combination of antibiotics, to prolong latency and/or improve neonatal outcome in pregnancies complicated by PPROM has yet to be determined. Treatment trends have moved from narrow spectrum antibiotics to prevent Group B Streptococcal sepsis to broad spectrum antibiotics to prolong latency. Concern that broader spectrum coverage may lead to untreatable superinfection, and the role such infection may play in the development of cerebral palsy, necrotizing enterocolitis, and other long term neonatal sequelae, is more theoretical. The significant increase in clinical sepsis rates found in the Ampicillin plus Sulbactam group in this study underscores this concern. Optimal neonatal outcome, and not simply prolongation of latency, should be the goal of antibiotic therapy in pregnancies complicated by PPROM.


OBJECTIVE: To systematically describe the presence and clinical significance of cervical dynamics (cervical shortening observed during routine ultrasound examination) in patients with threatened preterm labor (TTL).

STUDY DESIGN: Forty-four patients between 24-34 weeks gestation (EGA) with and without preterm labor (22 in each group) underwent real-time transvaginal ultrasound cervical length measurements over a 15-30 minute observation period. Exclusion criteria included ruptured membranes or cervical dilation > 2 cm. The sonographer was blinded to the contraction monitor during the exam, as well as the number of previous measurements displayed on the ultrasound screen. The ultrasound measurement was the last measurement included in the analysis. The Box test for equality of variance patterns as well as robust MANOVA testing were used to compare differences in cervical length change over time between the two groups. Spearman correlation was used to assess the relationship between the initial measurement, minimum length (nadir), maximum length (peak), and maximum change in comparison to EGA at delivery. Receiver operating characteristic (ROC) curve analysis was then used to assess the informative value of each of these variables in predicting preterm delivery (defined as delivery < 35 weeks EGA).

RESULTS: Comparison of the two groups showed no significant difference in age, gravidity, parity or EGA at time of ultrasound and 29.1 weeks. Mean EGA at delivery was approximately 4 weeks earlier in the TTL group versus the asymptomatic group (35.7 ± 4.7 versus 37.5 ± 2.5, p=0.005). There was greater variation in cervical length in the TTL group (Box test, p<0.005). Mean cervical length over 10 minute intervals was significantly shorter in the TTL group compared to asymptomatic patients (2.0 cm versus 2.9 cm, p=0.008). In symptomatic patients with observable 'dynamism', further analysis revealed that the shortest cervical length was most predictive of preterm delivery during a measurable contraction. EGA at delivery was significantly correlated with initial measurement (r=0.39, p<0.05), peak (r=0.304, p<0.05), nadir, with nadir length being most highly correlated (r=0.446, p<0.01). Surprisingly, maximum change in length was not correlated with EGA at delivery, thus, it was not clinically useful to determine a quantified definition of dynamism. ROC analysis indicated that the minimum observed cervical length was the most informative in predicting preterm delivery (area under curve = 0.75, p<0.01). This finding is superior in predicting early delivery compared to initial cervical length (area under curve = 0.65).

CONCLUSIONS: Observable cervical dynamism (change in length during real-time ultrasound) is more apparent in patients with preterm labor compared to asymptomatic patients, and in most cases occurs in association with a measurable contraction. Minimum sonographic cervical length over time is superior in predicting early delivery compared to initial cervical length or maximum change in length. While the degree of dynamism itself may not appear to be predictive of EGA at delivery, this pilot study suggests that in symptomatic patients, a period of sonographic observation of the cervix to determine the nadir in length (particularly during a contraction) may optimize information for predicting preterm delivery which would be lost if a standard, brief measurement were taken.
141 IMPROVING OUTCOMES IN TWIN PREGNANCIES: NEONATAL OUTCOMES M. Hullemann, B. Luke, University of Michigan Medical School, Ann Arbor, MI.

OBJECTIVE: To evaluate the effect of an intensive prenatal nutrition and educational intervention program on neonatal outcomes in twins.

STUDY DESIGN: Birthweight, gestational age, neonatal morbidity, medical interventions required, and length of birth hospitalization were studied among twins born at the University of Michigan Medical Center from 5/96-5/99. The 140 twin infants of mothers participating in an intensive intervention program were compared with 252 non-program twins, taking into account potentially confounding factors including maternal age, race, insurance status, infertility treatment, and infant sex through logistic and multiple linear regression modeling.

RESULTS: Twins of program participants had significantly higher average birthweight (2488 ± 42 g vs 2051 ± 45 g, p<0.001), longer gestation (33.9 ± 0.2 wks vs 34.0 ± 0.2 wks, p<0.001), and shorter birth hospitalization (9.5 ± 1.1 days vs 16.7 ± 1.4 days, p<0.001) than other twins. Regression analyses confirmed the state of preterm deliveries complicated by chorioamnionitis were independent risk factors. In both groups 30 (94%) were free of major neurological handicap at the time of the mode of delivery was given [H2SO4] (70 mg/kg) by mouth and urine sample were obtained every 8-12 hours until discharge. The amount of [H2SO4] in urine was measured by gas-liquid ratio of water. TOBER, estimates of body composition were performed within 72 hours of birth. Percent body fat (%F) was estimated using TBW with an HC of 80.6%. The purpose of this study was 2-fold: 1) to assess neonatal body composition in healthy infants using stable isotopes of water [H2SO4] with an HC of 80.6%. The %F derived from this new HC was 13.7 ± 5.1% and did not improve the correlation with TOBEC. A new HC was derived using both TBW and TOBEC. A new HC was derived using both TBW and TOBEC.

RESULTS: Of the 73 newborns, 54 (74%) survived the neonatal period (17 (23.5%) died and 22 (3%) had incomplete records). Forty (57%) were delivered vaginally and 30 (43%) by cesarean. The obstetrical and neonatal outcomes of infants born at <37 weeks of gestation between 1990-99 from pregnancies antenatally diagnosed as suspected of preterm chorioamnionitis (PC) and/or PVL and/or seizures. Comparison between the VD group and the NICU group was evaluated by Fisher's exact test. The results were presented as unadjusted OR with 95% CI. The mean gestational age at delivery, birth weight, Apgar score at 1 and 5 minutes, and APGE rate of cases were similar between the VD and NICU groups. The unadjusted OR of NICU admission was 1.5 [0.4, 6.5] * in the VD group compared with the NICU group. In the NICU group, 40 (57%) were free of major neurological handicap at the time of the mode of delivery was given [H2SO4] (70 mg/kg) by mouth and urine sample were obtained every 8-12 hours until discharge. The amount of [H2SO4] in urine was measured by gas-liquid ratio of water. TOBER, estimates of body composition were performed within 72 hours of birth. Percent body fat (%F) was estimated using TBW with an HC of 80.6% (%F-TBW) and correlated with TOBEC. A new HC was derived using both TBW and TOBEC. A new HC was derived using both TBW and TOBEC.

RESULTS: We evaluated 48 healthy term newborns. Each newborn was given [H2SO4] (70 mg/kg) by mouth and urine sample were obtained every 8-12 hours until discharge. The amount of [H2SO4] in urine was measured by gas-liquid ratio of water. TOBER, estimates of body composition were performed within 72 hours of birth. Percent body fat (%F) was estimated using TBW with an HC of 80.6% (%F-TBW) and correlated with TOBEC. A new HC was derived using both TBW and TOBEC. A new HC was derived using both TBW and TOBEC.

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CONCLUSION: Our results suggest that the mode of delivery of infants born at <37 weeks of gestation may influence body composition in healthy term newborns. The %F derived from this new HC was 13.7 ± 5.1% and did not improve the correlation with TOBEC. The %F derived from this new HC was 13.7 ± 5.1% and did not improve the correlation with TOBEC. We speculate that because of the wide variation in TBW, this may not be the optimal method to assess body composition in newborns.
145 GLIAL CELL LINE- DERIVED NEUROTROPHIC FACTOR (GDNF) PROTECTS AGAINST ISCHEMIA/HYPOXIC BRAIN DAMAGE IN NEONATAL RATS. T. Beda, Y. Xia, A. Min, B. Horvath, Drp Ob/Gyn, Myazaki Medical College, Myazaki, Japan.

OBJECTIVE: Hypoxic-ischemic encephalopathy is an important disorder entailing neurological sequelae in fetus and neonate. No effective means of treatment are as yet available. GDNF is a potent peptide neurotrophic factor that has been purified and cloned based on its ability to protect and rescue dopaminergic neurons. GDNF has also been shown to provide protection for non-dopaminergic systems. The purpose of the study is to examine effects of GDNF in ischemia/hypoxia-induced brain injury in neonatal rats.

STUDY DESIGN: GDNF was applied intra-parenchymally in the cortex of 7-day-old rat after hypoxic-ischemic stress. Two or 4 μg of GDNF was administrated into the left cortex after 2 hours of hypoxia (80 % O2, 99 % N2) combined with the common carotid artery ligation.

RESULTS: Vehicle-treatment showed 11/14 (79 %)-13/14 (93 %) of incidence of damage in each brain part at 7 days after insult. Significant reduction of damage was observed in the two GDNF treatment groups: 5/14 (35 %)-10/14 (65 %) and 1/14 (7 %)-4/14 (29 %) of incidence in 2 and 4 μg of GDNF, respectively. The induction of immunoreactive 70 kDa heat shock protein was markedly reduced in cases with 4 μg GDNF treatment at 24 hours of recovery.

CONCLUSION: Although the mechanisms responsible for the neuroprotective effects of GDNF remain unknown, the results of our study strongly suggest that GDNF may be an effective and potent protective agent against perinatal hypoxic/ischemic encephalopathy.

146 PREDISPOSING FACTORS FOR NEONATAL THROMBOCYTOPENIA IN PRETERM INFANTS. ME Benex, MJ Simchen, A Ben-Chen, SMashachi, E Schill, Deps Ob/Gyn and Clinical Epidemiology, Sheba Medical Center and Tel Aviv University, Israel.

OBJECTIVE: To identify predisposing factors for neonatal thrombocytopenia among preterm infants.

STUDY DESIGN: During a 4-year study period between January 1, 1994 and December 31, 1997, a total of 26983 women were delivered at Ichshom, singleton infants in our medical center. Infants delivered between 27-35 weeks were included in this study. Infants with congenital anomalies and infants of diabetic mothers were excluded. Thrombocytopenia on admission to the neonatal ward was defined as ≤ 150,000/ml, and marked thrombocytopenia as ≤ 100,000/ml. The following variables were examined for association with thrombocytopenia using a multivariate analysis: maternal age, mode of delivery, evidence of preclampsia, HELLP syndrome or placental abruption, prolonged PROM, maternal GBS colonization, prenatal steroid exposure, gestational age at delivery, gender, birth weight lower than 10th percentile (SGA), 5 minute Apgar score < 7, evidence of neonatal sepsis or intraventricular hemorrhage (IVH).

RESULTS: Ninety-three thrombocytopenic infants were included in the study group and 212 in the control group. Thrombocytopenic infants suffered from a higher rate of IVH (p<0.04). SGA (OR 3.73, 95% CI 1.98-7.05), low gestational age (OR 1.19, 95% CI 1.07-1.32), low Apgar score (OR 6.14, 95% CI 1.51-25.0) and cesarean delivery (OR 1.99, 95% CI 1.07-3.7) were associated with a higher incidence of neonatal thrombocytopenia. Prolonged PROM (OR 14.2, 95% CI 6.02-9.94) was associated with a lower risk for neonatal thrombocytopenia. No correlation was found between maternal pre eclampsic disease or HELLP syndrome and neonatal thrombocytopenia. When analyzing separately the group of infants with marked thrombocytopenia, growth restriction, lower gestational age and cesarean delivery were found to be significantly independent predisposing factors.

CONCLUSION: Growth restriction and lower gestational age at delivery are significantly associated with neonatal thrombocytopenia, which may lead to IVH and its sequelae. This risk is added to other adverse neonatal outcomes affecting this high-risk group of neonates.

147 SUDDEN INFANT DEATH SYNDROME: IS IT RELATED TO INTRAUTERINE INFECTION? AC Ranzini, S Shen-Schwarz, B Ostfeld, JC Smulian, AM Vintzileos, UMDNJ-Robert Wood Johnson Medical School/Saint Peter’s University Hospital, New Brunswick, NJ.

OBJECTIVE: Sudden infant death syndrome (SIDS) likely results from a defect in infant respiratory or cardiac function, potentially influenced by intrauterine processes. Since placental histology may provide unique information about intrauterine events, we undertook this study to determine whether there were important pathologic changes in SIDS placentas.

STUDY DESIGN: 14 cases of SIDS reported to the statewide SIDS Center who were delivered at Saint Peter’s University Hospital between 1988-1995 were included. During those years, placental pathologic evaluation was routine after all deliveries. Cases were matched with the next two eligible controls delivered for maternal age, parity, gestational age at delivery and puerperal status (clinic/private). All placental histology slides were reviewed by a single perinatal pathologist, who was blinded to group assignment. Fourteen categories of placental abnormalities including: chorioamnionitis, funisitis, villitis, fetal thrombosis, placental infarction, villous histologic abnormalities, maternal vascular abnormalities, abruptio, intervillous thrombosis, abnormal membrane histology, decidua vascular abnormalities, deciduitis, perivillous fibrin deposition and nucleated red blood cells were evaluated. Statistical analysis was accomplished by performing a ≥ test and odds ratios with 95% confidence intervals were computed.

RESULTS: 14 cases and 25 matched controls were evaluated. Maternal age of cases and controls was 24.4 ± 23.1 years, mean gestational age 36.7 ± 35.9 weeks, mean birthweight 2772 ± 728 gm, and mean placental weight 464 ± 454 gm, respectively. There were no differences in median parity or puerperal status. No single pathologic lesion category listed above had a χ2 P-value < 0.05 or an odds ratio which did not cross 1. However, more than twice as many SIDS placentas as control placentas had chorioamnionitis, funisitis or villitis.

<table>
<thead>
<tr>
<th>SIDS</th>
<th>Controls</th>
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<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>Funisitis</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Villitis</td>
<td>5 (36%)</td>
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</table>

Assuming a significance level of 0.05 and power of 80%, the incidences of chorioamnionitis, funisitis and villitis, a post-hoc sample size analysis indicated we would need a total sample size of 192 subjects to confirm our findings.

CONCLUSION: 1.) A trend toward increased frequency of chorioamnionitis, funisitis and villitis among cases compared to controls. A Type II error may explain the absence of statistical significance for this trend. 2.) A large study of SIDS cases and controls is needed in order to conclude that no differences in placental histology exist between groups.

148 FETAL INTRACRANIAL HEMORRHAGE IS ASSOCIATED WITH THROMBOPHILIA. JB Akouzathy, D Skajaki, J Bussel, H Lapkind, PA Chervenak. The New York Hospital-Cornell Medical Center, New York Hospital Medical Center of Queens, New York, NY.

OBJECTIVE: A lack of postnatal hemorrhagic events in neonates with fetal intracranial hemorrhage (ICH) led us to explore thrombophilia as a cause of fetal ICH.

STUDY DESIGN: Retrospective review of ultrasound database for all cases of fetal intracranial hemorrhage from 1/1994 to 6/1999. Medical records were obtained from physicians and phone questionnaires from patients were completed for personal and family histories. Serologic and genetic tests for thrombophilia were obtained from patients, including mothers and children. This hypercoagulability work-up typically included lupus anticoagulant, anticoagulant antibodies, protein S and protein C levels, activated protein C resistance and Factor V Leiden mutation analysis.

RESULTS: 25 fetuses with ICH were discovered. Gestational age range was 17-38 weeks. 5/7 (71 %) mothers tested showed results likely or suggestive for thrombophilia. 5/3 children tested showed results likely or suggestive of thrombophilia or coagulopathy. Suggestive maternal diagnoses included Protein S and Protein C deficiencies, lupus anticoagulant and heterozygote for hyperhomocysteinemia. Likely maternal diagnoses were antiphospholipid antibody syndrome and Factor V Leiden mutation. 3/5 (60%) mothers tested revealed more than one diagnosis (Protein S and Protein C deficiency, Protein S deficiency with heterozygote for hyperhomocysteinemia, and Factor V Leiden mutation with activated protein C resistance and heterozygote for hyperhomocysteinemia). The S children’s results showed activated Protein S resistance, low plasminogen activator inhibitor (PAI-1), and a clinical coagulopathy with elevated partial thromboplastin time.

CONCLUSION: The association of fetal ICH and thrombophilia. A workup for thrombophilia for mother and neonate seems to be indicated.
149  

OBJECTIVE: Epidural use has been associated with a higher rate of neonatal sepsis evaluations. Increased rates of fever in women with epidural analgesia explain some of the increase, but excess neonatal sepsis evaluations in afebrile women are unexplained.

STUDY DESIGN: We analyzed 1295 women with singleton term pregnancies with cephalic presentation who presented in spontaneous labor with a temperature of <38.5°C. Women who were febrile during labor (T>100.4°F) were excluded for a final population of 1109 afebrile women. Neonatal sepsis evaluation was performed based on the presence of one or major or two minor criteria. Apart from fever >100.4°F, major criteria included rupture of membranes for >24 hours or a sustained fetal heart rate of >160. Minor criteria included a maternal temperature of 99-100.4°F, rupture of membranes 12-24 hours, maternal admission white blood cell count of >15 thousands cells/mL, or an Apgar score of <7 at five minutes.

RESULTS: 55.3% of women received epidural analgesia. Infants of afebrile women with epidural analgesia were more than twice as likely to be evaluated for sepsis than those of women without epidural (26.4% vs. 8.9%). An increased risk of sepsis evaluation persisted in regression analysis (OR 2.1, 95% CI 1.2; 4.5) after controlling for confounders and was not explained by longer labors with epidural. No case of neonatal sepsis confirmed by blood culture occurred. Overall, afebrile women met either one major or two minor criteria for neonatal sepsis evaluation in 22.4% of those with epidural analgesia but only 8.1% of those without. Women with epidural were significantly more likely to have fetal tachycardia (4.4% vs. 0.4%), rupture of membranes >24 hours (6.2% vs. 3.4%), low-grade temperature <99-100.4°F (24.5% vs. 5.2%) and rupture of membranes 12-24 hours (27.6% vs. 17.3%) than women without epidural. No differences were seen in 5-minute Apgar scores.

CONCLUSION: Epidural analgesia is associated with increased rates of major and minor criteria for neonatal sepsis evaluations in afebrile women. This information may be used to more accurately counsel women and may be useful in reassessment of neonatal criteria for sepsis evaluation in women with epidural. Despite these findings, epidural analgesia remains the most effective means of pain relief during labor and should be available to women.

150  

OBJECTIVE: Cerebral palsy (CP) is the most common chronic motor disability of childhood. Accumulating evidence supports a link between coagulation disorders and CP. A missense mutation in the factor V gene, the Leiden mutation, is the most prevalent genetic predisposition to thrombosis. Our objective was to evaluate the frequency of this mutation in children with and without CP compared to a control group without CP.

STUDY DESIGN: Children with CP attending a multidisciplinary CP clinic were recruited for enrollment. DNA was extracted from buccal swabs. Allele-specific amplification was used to amplify exon 10 of the Factor V gene. Results were analyzed with a 2x1 contingency table.

RESULTS: Six of 28 (21%) children with CP carried the factor V Leiden mutation compared to 14 of 407 (3%) for the control population $\chi^2 = 19.28, p = 0.00001$. One of the six with CP was homozygous mutant for the factor V Leiden mutation.

CONCLUSION: Fetuses who carry the factor V Leiden mutation may be predisposed to CP. Studies are underway to determine whether this is a direct fetal effect or whether this reflects placental/maternal thrombosis.

151  
ASSOCIATION BETWEEN FUNISITIS AND DECREASED BAYLEY MOTOR SCORES. R. Mittenstorf, V. Saldan, L. Bentz*, M. Berg, N. Rokzon, University of Chicago, Chicago and Wayne State University, Detroit.

OBJECTIVE: In children without congenital cerebral palsy (CP), to learn whether the Bayley Psychomotor Developmental Index (PDI) scores are decreased among those who had funisitis at delivery, as compared to those who did not have evidence of fetal inflammation.

STUDY DESIGN: During the MAGnet Trial, a study of the prevention and causation of congenital cerebral palsy, we submitted from the participating children placenta for histopathologic review at 18-months of age, physical and mental examinations were done for the children by a developmental pediatrician (NR) who was blinded to the prior histopathology.

RESULTS: Examinations were done for 122 children. Six children had CP; of these 6, 5 had precedent funisitis. Of 116 children who did not have CP, histopathology was done for 88% (101/116) of them. Among these children, precedent funisitis occurred in 15% (17/116). Of interest, the median PDI score in the group without CP, but who had precedent funisitis, was 95, whereas the median score in the group without CP and without funisitis was 100 (Mann-Whitney test, p = 0.07). Furthermore, when dichotomizing the data set on the population-based mean PDI score of 100, we find that only 18% (3/17) of children who had precedent funisitis had scores <=100, whereas 51% (45/85) of those without funisitis had scores >100 (two-sided Fisher’s exact test, p = 0.01). When evaluating these data by multiple logistic regression in which we controlled for confounding by birth weight or gestational age, presence or absence of intraventricular hemorrhage, cocaine exposure, exposure to ventilators in the neonatal intensive care unit, and a host of other variables which could be related to decreased scores, the association between funisitis and lower PDI scores remains highly statistically significant (p<0.01).

CONCLUSION: Funisitis is an independent and highly significant predictor of decreased PDI scores, even among children without CP Thus, we believe our data suggest that inflammation in the fetus may have wider influences on brain functioning than reported previously.

152  
OUTCOME AFTER SUCCESSFUL RESUSCITATION OF BABIES BORN WITH APGAR SCORES OF 0 AT BOTH ONE AND FIVE MINUTES. B. Haddad*, B. M Bercer, M. Leung, A. Talait*, B. M. Sibai, Dept Ob/Gyn, University of TN, Memphis, TN.

OBJECTIVE: To evaluate the outcome of infants who underwent successful resuscitation after initial Apgar score of 0 at both 1 and 5 minutes born between January 1986 and February 1999. Outcomes were survival, neurological complications, and long-term development.

RESULTS: 53 of 81,603 infants (0.4/1,000) met study criteria. Obstetrical complications were mainly bradycardia (61%) and abruptio placenta (36%). Deliveries occurred between 23.5 and 42.1 weeks and birth weights ranged from 490 to 4678 grams. The pH ranged from 6.53 to 7.37. Baseline deficit ranged from -35 to -0 mEq/L. Apgar scores at 10 minutes were available for 32 babies, 50% scored 0 and 50% scored <=3. 22 (67%) died during hospitalization and 11 survived. Follow-up was available for only 7 of the 11 survivors, 4 had significant morbidity cerebral palsy (n=1), severe mental retardation (n=1), hypotonia (n=1), and chronic care requirement (n=2). Two infants had normal neurological exams at followup.

<table>
<thead>
<tr>
<th>Death (n=22)</th>
<th>Survivor (n=11)</th>
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</thead>
<tbody>
<tr>
<td>Gestational age (wks)</td>
<td>30.6±6.3</td>
</tr>
<tr>
<td>Birthweight (grams)</td>
<td>1678±1312</td>
</tr>
<tr>
<td>10' Apgar &gt;0 (%)</td>
<td>95*</td>
</tr>
<tr>
<td>Bradycardia (%)</td>
<td>64</td>
</tr>
<tr>
<td>Abruptio placenta (%)</td>
<td>41</td>
</tr>
<tr>
<td>pHa &lt;7.00 (%)</td>
<td>79</td>
</tr>
<tr>
<td>Base deficit &lt;20 mEq/L (%)</td>
<td>65</td>
</tr>
</tbody>
</table>

*of 21 babies

CONCLUSION: Survival in babies born with 1 and 5-minute Apgar score of 0 is predicted by birth weight, gestational age and 10-minute Apgar score. Long term sequelae are common but not assured.
153


OBJECTIVE: To determine if adverse neonatal outcomes and umbilical cord plasma interleukin-6 (IL-6) are higher following spontaneous vs. indicated delivery prior to 32 weeks gestation (GA).

STUDY DESIGN: Outcomes were assessed in 371 consecutively delivered neonates born between 24+7/7 and 31+6/7 weeks' GA due to preterm labor or PROM (Spontaneous, 63%) or maternal medical/obstetrical indications (Indicated, 37%). Neonatal SIRS was defined as the presence of negative cultures (CSF/blood) plus clinically suspected sepsis and/or a band/total WBC ratio > 0.15. IL-6 was determined by ELISA and values above the 75th percentile (54.2 pg/ml) were considered elevated.

RESULTS: Differences in spontaneous (Spon) vs indicated (Ind) groups were observed for delivery GA (27.9±2.3 vs 28.6±2.1 weeks', p=.003), cesarean delivery (40.1 vs 65.9%, p<.001), and chorioamnionitis (21.9 vs 0.7%, p<.001). Race, parity, and infant gender were similar in the two groups (p≥.05). Elevated cord plasma IL-6 was 18x more common (see table) and the median cord GA (27.7±5.3 pg/ml, p=.001) following Spon vs Ind delivery.

The table lists unadjusted risk ratios for selected outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Spon (%)</th>
<th>Ind (%)</th>
<th>P</th>
<th>R.R.</th>
<th>95% C.I</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 (75th percentile)</td>
<td>38.8</td>
<td>3.9</td>
<td>&lt;.001</td>
<td>9.98</td>
<td>3.74-26.59</td>
</tr>
<tr>
<td>IVH (grade 3+)</td>
<td>11.7</td>
<td>2.9</td>
<td>0.030</td>
<td>4.14-11.38</td>
<td></td>
</tr>
<tr>
<td>SIRS</td>
<td>42.0</td>
<td>15.9</td>
<td>&lt;.001</td>
<td>2.63</td>
<td>1.74-3.98</td>
</tr>
<tr>
<td>BPD</td>
<td>21.3</td>
<td>13.7</td>
<td>0.170</td>
<td>1.80</td>
<td>0.80-3.90</td>
</tr>
<tr>
<td>Mech vent use</td>
<td>51.7</td>
<td>50.0</td>
<td>0.750</td>
<td>1.03</td>
<td>0.84-1.27</td>
</tr>
<tr>
<td>Death</td>
<td>10.8</td>
<td>9.4</td>
<td>0.680</td>
<td>0.99</td>
<td>0.91-1.96</td>
</tr>
<tr>
<td>RDS</td>
<td>56.2</td>
<td>75.4</td>
<td>0.040</td>
<td>0.87</td>
<td>0.76-0.99</td>
</tr>
<tr>
<td>PVL</td>
<td>3.9</td>
<td>5.1</td>
<td>0.580</td>
<td>0.76</td>
<td>0.29-2.90</td>
</tr>
</tbody>
</table>

After adjusting for delivery GA, delivery mode, race, gender, antenatal steroid, and surfactant use, IL-6 >75th (OR 13.7, 95%CI 6.4-21.1), IVH (OR 4.6, 95%CI 2.1-10.5), and SIRS (OR 4.1, 95%CI 2.5-6.7) were more common in the Spontaneous vs the indicated group.

CONCLUSIONS: Neonates born <32 weeks' following spontaneous vs indicated delivery have increased complications following SIRS and IVH. This association is observed with elevated cord plasma IL-6.

155

NEITHER NEONATAL POLYMORPHISMS IN THE TUMOR NECROSIS FACTOR ALPHA GENE NOR PLASMA TUMOR NECROSIS FACTOR ALpha LEVELS ARE ASSOCIATED WITH COMPLICATIONS OF PREMATURITY. J.C. Livingston, B. Haddad*, D. Crusoe, V. Park*, M. Cassie*, K. Brown*, M. Quasem* and B. M. Sibai, University of TN-Memphis, TN.

OBJECTIVE: High levels of tumor necrosis factor alpha (TNFa), an inflammatory cytokine, are cytotoxic. Patients with genetic polymorphisms surrounding the TNFa site are variants in TNFa mutations and plasma TNFa levels are related to complications of prematurity.

STUDY DESIGN: We obtained umbilical cord blood at the time of delivery from 52 neonates delivered at <37 weeks' gestation. TNFa mutations were assessed using PCR products were digested with the appropriate restriction enzyme, and genotyped by gel electrophoresis.

RESULTS: Plasma levels of TNFa do not predict neonatal complications. In addition, the genetic polymorphisms at the -308 and +251 sites did not correlate with neonatal complications.

CONCLUSIONS: Plasma levels of TNFa are not predictive of neonatal complications. In addition, the genetic polymorphisms at the -308 and +251 sites did not correlate with neonatal complications.

154


OBJECTIVE: A marker for fetal hypoxic-ischemic injury would be useful to time the "window of opportunity" for effective use of neuroprotective agents. Neuron specific enolase (NSE), a marker of neuronal injury, is elevated in amniotic fluid in neonates who develop intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). We investigated the relationship between maternal serum NSE (MSNSE) and the development of these lesions.

STUDY DESIGN: Maternal bloods within 7 days of delivery in patients who delivered at 24-34 wks with biweekly 750x gestational age were analyzed for NSE by a double antibody immunassay (Sensitivity 5 pg/L). NSE standards in the kits were calibrated against NSE purified by the method of Pahman et al. All neonates had cranial neurosonography on days 3 and 7 of life for evidence of IVH or PVL. Neonates were divided into 2 groups based on the presence of positive neurosonography. The groups were compared for MSNSE levels using Student's T test. The sensitivity, specificity, +/- predictive values for MSNSE were determined using a critical level of 27 pg/L.

RESULTS: Of a total of 51 patients, 10 had positive and 41 had negative neurosonography.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean ± SD (μg/L)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVH/PVL</td>
<td>10</td>
<td>28 ±17.8</td>
</tr>
</tbody>
</table>

Using a critical value of 27 μg/L MSNSE had a sensitivity of 60%, a specificity of 90%, a +/- predictive value of 60% and 90% respectively.

CONCLUSION: MSNSE levels were predictive of neonatal IVH and PVL with a specificity of 90%.

156

ELEVATED UMBILICAL CORD PLASMA interleukin-6 (IL-6) AFTER PRETERM BIRTH (PTB) IS ASSOCIATED WITH ADVERSE NEONATAL OUTCOMES INCLUDING SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS). W. Andrew, W. Carlo*, J. Caselli, S. Cheroe*, R. Goldberg, Depts of Ob/Gyn & Pediatrics, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To determine if adverse neonatal outcomes are associated with elevated umbilical cord plasma IL-6 levels in infants born prior to 32 weeks' gestational age (GA).

STUDY DESIGN: Outcomes were assessed in 263 neonates born between 24+7 and 31+6 weeks' GA. Neonatal SIRS was defined as the presence of positive cultures (CSF/blood) plus clinically suspected sepsis and/or a band/bandh cell ratio > 0.15. IL-6 was determined by ELISA and values above the 75th percentile (54.2 pg/ml) were considered elevated.

RESULTS: The overall delivery GA was 28.2±2.5 weeks. Data in the table reflect unadjusted risk ratios for selected outcomes in infants with (1) and without (0) elevated IL-6 (>54.2 pg/ml).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IL-6(+)</th>
<th>IL-6(-)</th>
<th>P</th>
<th>R.R.</th>
<th>95% C.I</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVL</td>
<td>10.8</td>
<td>1.0</td>
<td>&lt;.001</td>
<td>10.4</td>
<td>2.4-49.1</td>
</tr>
<tr>
<td>SIRS</td>
<td>54.6</td>
<td>20.4</td>
<td>&lt;.001</td>
<td>2.7</td>
<td>1.0-8.8</td>
</tr>
<tr>
<td>NEC</td>
<td>24.2</td>
<td>13.2</td>
<td>0.048</td>
<td>1.6</td>
<td>1.1-6.3</td>
</tr>
<tr>
<td>IVH (grade 3+)</td>
<td>9.2</td>
<td>3.6</td>
<td>0.088</td>
<td>2.5</td>
<td>0.9-7.5</td>
</tr>
<tr>
<td>BPD</td>
<td>12.1</td>
<td>9.5</td>
<td>0.014</td>
<td>1.8</td>
<td>0.9-3.7</td>
</tr>
<tr>
<td>Mech vent use</td>
<td>50.8</td>
<td>42.6</td>
<td>0.253</td>
<td>1.2</td>
<td>0.4-4.1</td>
</tr>
<tr>
<td>Death</td>
<td>9.1</td>
<td>8.1</td>
<td>0.806</td>
<td>1.1</td>
<td>0.5-2.7</td>
</tr>
<tr>
<td>RDS</td>
<td>61.6</td>
<td>64.5</td>
<td>0.903</td>
<td>0.9</td>
<td>0.1-8.1</td>
</tr>
</tbody>
</table>

PVL = periventricular leukomalacia, IVH = intraventricular hemorrhage, NEC = necrotizing enterocolitis, BPD = bronchopulmonary dysplasia, RDS = respiratory distress syndrome. After controlling for delivery GA, mode of delivery, race, antenatal steroid, and surfactant use, (OR 19.6, 95%CI 3.2-120.7) and SIRS (OR 3.9, 95%CI 2.7-5.5) were more common among women with cord plasma IL-6 >75th percentile.

CONCLUSIONS: Umbilical cord plasma IL-6 >75th percentile is predictive of adverse outcomes including SIRS and PVL among neonates born prior to 32 weeks' GA.
158  MICROTUBULAR INVASION OF THE CHORIOAMNION AND HISTOLOGIC CHORIOAMNIONITIS ARE ASSOCIATED WITH SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN PRETERM NEONATES. WW Andinus, W Carbona, JG Hauth, SC Cliver, RL Goldenberg, O Faye-Petersen. Deps of Obst. Gen, Pediatrics & Pathology, University of Alabama at Birmingham, AL.

OBJECTIVE: to determine the association between: microtubular invasion and histologic choriamnionitis with neonatal outcome in infants born prior to 32 weeks' gestational age (GA).

STUDY DESIGN: Outcomes were assessed in neonates born between 240/7 and 316/7 weeks' GA. Placental histology was evaluated at four sites in 302 women and placental cultures (for streptococci, staphylococci, gram-negative mycoplasmas, T. vaginalis, and N. gonorrhoeae) were available for 357 women. Neonatal systemic inflammatory response syndrome (SIRS) was defined as the presence of negative cultures (CSF/blood) plus clinically suspected sepsis and/or a band/band+polym rate >0.15.

RESULTS: The overall delivery GA was 28.2±2.3 weeks. Placental cultures were positive for at least one microorganism in 52% of women and histologic choriamnionitis was identified in 50% of women. Data in the table represents frequencies of selected outcomes in infants with and without positive choriamnion cultures or histologic choriamnionitis.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cultures (%)</th>
<th>Chorioamnionitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS</td>
<td>37.8</td>
<td>26.2</td>
</tr>
<tr>
<td>PVL</td>
<td>17.8</td>
<td>16.9</td>
</tr>
<tr>
<td>NEC</td>
<td>17.7</td>
<td>15.9</td>
</tr>
<tr>
<td>IVH (grade 3-4)</td>
<td>9.1</td>
<td>7.6</td>
</tr>
<tr>
<td>RDS</td>
<td>67.9</td>
<td>71.5</td>
</tr>
<tr>
<td>Mech vein use</td>
<td>54.0</td>
<td>48.0</td>
</tr>
<tr>
<td>BPD</td>
<td>1.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Death</td>
<td>9.7</td>
<td>11.6</td>
</tr>
</tbody>
</table>

PVL = periventricular leucomalacia, IVH = intraventricular hemorrhage, NEC = necrotizing enterocolitis, BPD = bronchopulmonary dysplasia, RDS = respiratory distress syndrome

CONCLUSIONS: Neonatal systemic inflammatory response syndrome is more common among infants born prior to 32 weeks' gestation with a positive choriamnion culture or histologic choriamnionitis.earned.

159  NEONATAL EFFECTS AFTER ANTENATAL TREATMENT WITH INDOMETHACIN VS. SULINDAC. A Scarfone, K Lee, P Bakird, D Paul, D. Pabst, D. Paul. Divisions of Maternal-Fetal Medicine and Neonatology, Christiana Hospital, Newark, Delaware, USA.

OBJECTIVE: Non-steroidal anti-inflammatory drugs (NSAID) are commonly employed for tocolysis. Indomethacin (INDO) was one of first agents described for this use, but has recently been associated with serious adverse neonatal outcomes. Another NSAID, sulindac (SLD), has been shown to prevent recurrent preterm labor and to be as effective as INDO in patients with refractory preterm labor. Early reports showed SLD may not have the same fetal effects as INDO, but recently this has been challenged. We compare the neonatal effects of these two agents when used for tocolysis.

STUDY DESIGN: In this retrospective case-cohort study, we reviewed our neonatal database from July 1994 to July 1999, for neonates who were exposed to antenatal INDO or SLD and had a birthweight <1,500 gm. Neonates exposed to both drugs or with congenital abnormalities were excluded. Our primary outcome variables were: intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEG), bronchopulmonary dysplasia (BPD), patent ductus arteriosus (PDA), serum creatinine > 1.4 mg/dl, and mortality.

| Student's t-test | p value | CONCLUSIONS: Overall, SLD and INDO appear to be associated with similar adverse neonatal effects. However, in our population, exposure to INDO is associated with an increased risk for BPD when compared to exposure of SLD.


OBJECTIVE: To evaluate whether serial amnioinfusions for persistent oligohydramnios can affect the perinatal and long-term neurologic outcome in extreme preterm premature rupture of membranes (PROM).

STUDY DESIGN: All singleton pregnancies with PROM at ≤26 weeks and lasting ≥4 days between 1/91 and 6/98 were included. Amniotic fluid (AF) volume was assessed sonographically (twice weekly) consenting women with persistent (≥4 days) oligohydramnios (maximum cord-free pocket of AF <2 cm) received serial transtubal amnioinfusions to maintain AF volume >2 cm. The pregnancy outcome of those with successful amnioinfusion (n=11) was compared with that of women with PROM not requiring amnioinfusion because residual pocket of AF was ≥2 cm (n=13) using Wilcoxon Rank-sum test and Fisher's exact test. Neurological outcome was assessed at 1 year of age using the Milani Comparato & Gelain score.

RESULTS:

<table>
<thead>
<tr>
<th>Amnioinfusion</th>
<th>Chorioamnionitis</th>
<th>Intraventricular hemorrhage (IVH)</th>
<th>Bronchopulmonary dysplasia (BPD)</th>
<th>Patent ductus arteriosus (PDA)</th>
<th>Serum creatinine &gt; 1.4 mg/dl</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not necessary</td>
<td>0.002</td>
<td>0.8</td>
<td>0.4</td>
<td>0.2</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Successful</td>
<td>0.002</td>
<td>0.8</td>
<td>0.4</td>
<td>0.2</td>
<td>0.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Despite lower gestational age at PROM, pregnancies with oligohydramnios managed successfully with serial amnioinfusions had similar outcomes as those without oligohydramnios.
161 PERINATAL MORTALITY AND LONG TERM NEUROLOGIC MORBIDITY IS RELATED TO DEGREE OF VENTRICULOMEGALY. A Dahl1*, E. Graham1, M. Allen2, G. Hanna3, F. Witter1, 1. Division of Maternal-Fetal Medicine; 2. Division of Neonatology; Johns Hopkins University School of Medicine, Baltimore, MD

OBJECTIVE: Our hypothesis is that cerebral ventriculomegaly identified on prenatal ultrasound is related to aneuploidy, perinatal mortality and long term neurologic morbidity.

STUDY DESIGN: Nineteen cases of ventriculomegaly identified from 6/1/94 to 7/1/99 were examined for prenatal, intrapartum and neonatal complications. Pediatric follow-up was reviewed for infants with ventriculomegaly from birth up to as long as 4 years. Minor neurologic morbidity was defined as a score of 70-80 on the CLAMS/CAT developmental scale and included mild motor/language delay. Major morbidity included a score <70, evidence of cerebral palsies, or seizure disorder. The incidence of neurologic complications and aneuploidy were compared based on the degree of ventriculomegaly using Chi Square and Fisher's exact test with Group 1 being 1.0-1.5 cm and Group 2 >1.5 cm.

RESULTS: 27 cases (15 neonatal tube defects and 9 with holoprosencephaly) were excluded. Among 64 patients, 39 had a ventricular diameter of 1.0-1.5 cm comprising Group 1. Five elected termination, all with other ultrasound anomalies, and 5/5 (60%) had aneuploidy. Of the 34 remaining patients 2 were chromosomally abnormal, and pediactric followup was available on 25. Seventeen of these 25 (68%) were normal at pediatric follow-up. 3 (12%) had minor neurologic morbidity and required ventriculoperitoneal (VP) shunts, 1 (4%) had major neurologic morbidity, and 4 (16%) were perinatal deaths. Two cases were associated with cytomegaly (CMV) infection, one with major neurologic morbidity at 5 months and one resulting in a perinatal death. In Group 2 eight cases, all associated with other ultrasound anomalies elected termination, and 3/8 (37.5%) had aneuploidy. Of the 17 continuing pregnancies one was karyotypically abnormal and pediactric followup was available on 15: 2/15 (13%) were normal, 5/33 (37%) had minor neurologic morbidity with 3 requiring a VP shunt and 4 (26.0%) had major neurologic morbidity with 2 requiring a VP shunt and 1 having CMV infection, and 4 (26.7%) were perinatal deaths. The incidence of aneuploidy was 14% in Group 1 and 7% in Group 2. There was an increase in all neurologic morbidity in group 2 (p=0.04).

CONCLUSION: There is an increase in neurologic morbidity with ventriculomegaly >1.5 cm. The incidence of aneuploidy, minor and major neurologic problems, and perinatal death identified in this study may be helpful in counseling parents with ventriculomegaly on prenatal ultrasound.

163 REPORTED VERSUS EXPECTED INCIDENCE OF DOWN SYNDROME IN THE U. S. FROM 1990 TO 1996. JX Egan, DB Essers, DM Feldman2, PV Lung3, MJ Barssoom3, AF Borgida. St Francis Hospital and Medical Center, Hartford, CT and Univ of CT Health Center, Farmington, CT

OBJECTIVE: To compare the reported birth prevalence (REP) incidence of Down syndrome (DS) in the U. S. with the expected incidence from 1990 to 1996.

STUDY DESIGN: Serum screening and the genetic sonogram have improved the prenatal detection of DS in the 1990s. At the same time the mean age of the reproductive population in the U. S. has increased DS births are traditionally underreported on birth certificates in the U. S. (Heather, CA, 1991; Pol Health, 1983). We reviewed data from the 1990 to 1996 to determine if there was any evidence for the increased detection of DS from birth certificate data. Natality statistics from the National Center for Health Statistics Monthly Vital Statistics Reports were used for both the total number of live births and the reported number of DS livebirths. Age specific maternal birthrates were multiplied by the age specific DS risk (Bray, et al, Pren Diag, 1968) to determine expected rates per year of maternal age for DS from 1990 to 1996.

RESULTS: As shown below there has been a steady decline in the reported birth certificate incidence of DS despite an increase in the EST number of liveborn DS cases. This may be due to either an increased rate of pregnancy termination from prenatal serum and ultrasound screening for DS, or decreased reporting.

<table>
<thead>
<tr>
<th>Year</th>
<th>Deliveries</th>
<th>DS Reported</th>
<th>DS Estimated</th>
<th>REP/EST</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>3,785,585</td>
<td>1,977</td>
<td>3,582</td>
<td>56.6 (42, 71)</td>
</tr>
<tr>
<td>1991</td>
<td>3,707,747</td>
<td>1,788</td>
<td>3,619</td>
<td>48.8 (35, 64)</td>
</tr>
<tr>
<td>1992</td>
<td>3,749,205</td>
<td>1,811</td>
<td>3,618</td>
<td>49.7 (36, 64)</td>
</tr>
<tr>
<td>1993</td>
<td>3,689,996</td>
<td>1,050</td>
<td>3,619</td>
<td>29.7 (21, 40)</td>
</tr>
<tr>
<td>1994</td>
<td>3,707,492</td>
<td>1,089</td>
<td>3,582</td>
<td>29.7 (21, 40)</td>
</tr>
<tr>
<td>1995</td>
<td>3,674,220</td>
<td>1,058</td>
<td>3,635</td>
<td>27.7 (19, 38)</td>
</tr>
<tr>
<td>1996</td>
<td>3,807,842</td>
<td>1,676</td>
<td>4,499</td>
<td>42.8 (30, 56)</td>
</tr>
</tbody>
</table>

CONCLUSION: There has been a steady decline in the number of birth certificate reported liveborn cases of DS in the U.S. from 1990 to 1996. This is most likely due to improved prenatal diagnostic with subsequent pregnancy termination.

164 TIMING OF INFANT DEATH BY GESTATIONAL AGE AT DELIVERY IN PREGNANCIES COMPlicated BY ABRUPTION: A POPULATION-BASED STUDY. CV Ananth, JC Smulian, AM Vintzileos, RA Knuppel, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: 1) To determine the timing of infant death in the first year of life based on gestational age (GA) at delivery from pregnancies complicated only by placental abruption. 2) To determine if abruption infants have different mortality patterns than infants of uncomplicated pregnancies.

STUDY DESIGN: The data for this study were derived from the United States national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics. Analysis was restricted to singleton pregnancies at specified infant ages using relative risks (RR) and 95% confidence intervals. The death rate for infants delivered to both abruption and uncomplicated pregnancies was calculated for GA categories (24-27, 28-32, 33-36, 37+ weeks) identified. Death rates for infants delivered to both abruptlon and uncomplicated pregnancies were calculated for GA categories (24-27, 28-32, 33-36, 37+ weeks) during the first year of life. The death rate for infants from abruption pregnancies was compared with the corresponding infant death rate for UCP pregnancies at specified infant ages using relative risks (RR) and 95% confidence intervals (CI) at each GA category.

RESULTS: There were 3.7% (1,420/40,417) infant deaths in the abruption group and 2.2% (910/41,287) in the UCP group. All abruption-related infant death rates for specific postnatal time periods (<7, 7-27, 28-180 and >180 days) are reported below along with the RR (CI) using UCP pregnancies as the referent.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>&lt;7 days</th>
<th>7-27 days</th>
<th>28-180 days</th>
<th>&gt;180 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=256</td>
<td>8.8%</td>
<td>4.7%</td>
<td>4.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.5%</td>
<td>1.4%</td>
<td>1.2%</td>
<td>1.0%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.3%</td>
<td>1.2%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>n=256</td>
<td>2.2%</td>
<td>2.1%</td>
<td>1.1%</td>
<td>1.8%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.8%</td>
<td>1.2%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.6%</td>
<td>1.2%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.0%</td>
<td>1.0%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>n=256</td>
<td>1.0%</td>
<td>1.0%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>
TIMING OF INFANT DEATH BY GESTATIONAL AGE AT DELIVERY AFTER AN UNCOMPLICATED PREGNANCY: A POPULATION-BASED STUDY IN THE UNITED STATES.

OBJECTIVE: To determine the probability and timing of infant death within the first year of life based on gestational age (GA) at delivery after an uncomplicated pregnancy.

STUDY DESIGN: The data for this study were derived from the United States national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics. Analysis was restricted to live births occurring after 23 completed weeks of gestation and excluding pregnancies complicated by hypertensive diseases, diabetes, bleeding, placental abruption or previa, IUGR (<10th percentile), multiple births, congenital malformations, chromosome abnormalities, missing data on GA or birth weight <500 gms were excluded. Death rates were calculated for GA categories (24-27, 28-32, 33-36, and 37+ weeks) for the first year of life. The relative risk (RR) and 95% confidence interval (CI) for infant death at specified infant ages is reported for each GA category.

RESULTS: The analysis included 6,214,985 singleton live births with GA (n=738,283) and 10,025/738,283 (1.4%) infant deaths in the IUGR group and 22,261/6,214,985 (0.4%) in the UCP group. The actual IUGR infant death rate for infants delivered to both IUGR and UCP pregnancies was 10% and 4% respectively (NS). Frequency of cesarean section in vertex presenting twin-sets was significantly lower in IVF twin-sets. Additionally, the frequency of cesarean section in vertex presenting twin-sets existed 33.5 years (IVF) versus 29.4 (SC) (p<0.05). Frequency of PTB of gestational age (EGA) at time of delivery, mode of delivery, birth weight (BW), and mode of conception (spontaneous conception (SC) vs. in-vitro fertilization (IVF)). Eighteen twin sets were excluded because the mode of conception was not clearly documented in the records. Discordance was defined as >15% or >20% in the SC(n=16) and IVF(n=7) groups was 12% and 14% respectively (p<0.05). Frequency of discordance (>_15%) in the SC(n=29) and IVF(n=19) groups was 10% and 4% respectively (NS). Frequency of cesarean section in vertex presenting twin-sets was significantly lower in IVF twin-sets.

CONCLUSIONS: This is the largest reported series of triplet neonates managed by a single physician group. These results confirm that delivery after 27 weeks is associated with 100% survival, with only rare cases of significant chromosomal anomalies.
EVALUATION OF PRETERM PREMATURE RUPTURE OF MEMBRANES (PROM) IN THE UNITED STATES: IS LABOR A RISK FACTOR FOR ADVERSE NEONATAL OUTCOMES? NB Mentres, CV Ananth, JC Smulian, AM Vintzileos, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: Labor has been implicated as a contributor to adverse neonatal outcomes in the preterm infant. The objective was to determine whether the presence of labor has any impact on neonatal outcomes in women with preterm PROM.

STUDY DESIGN: Data was derived from the national linked birth/infant death data sets assembled by the National Center for Health Statistics and comprised 7,982,795 births during 1995 and 1996. The analysis included women with preterm PROM >12 hours who delivered singleton live infants between 23 and 32 completed weeks of gestation. Labor was considered present if the birth record contained any of the following: tocolysis, cephalopelvic disproportion, labor induction or stimulation, precipitous, prolonged, or dysfunctional labor, VBAC, vacuum, forceps or vaginal delivery, fetal death, congenital anomalies, chromosomal abnormalities, and cases with unclassifiable gestational ages were excluded. Outcome variables contained in the database were: infant death <1 year of age, respiratory distress syndrome (RDS), assisted ventilation, and neonatal seizures. The analysis controlled for maternal obstetrical complications, birthweight, gestational age, fetal distress and mode of delivery. Multivariable logistic regression models were fit to derive adjusted relative risks after controlling for these confounders. Fetal malpresentations were examined separately.

RESULTS: Of all the women with preterm PROM who delivered between 23 and 32 weeks, 73.4% (16,911/23,040) labored and 20.0% (4,608/23,040) had fetal malpresentations. The incidences of infant death, RDS, assisted ventilation, and neonatal seizures were 11.6%, 15.1%, 25.9%, and 0.2% respectively. The table presents adjusted relative risks for labored as compared with non-labored women.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All fetal presentations</th>
<th>Malpresentations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant death &lt;1 year</td>
<td>0.97 (0.88-1.07)</td>
<td>0.91 (0.69-0.97)</td>
</tr>
<tr>
<td>RDS</td>
<td>0.95 (0.88-1.02)</td>
<td>0.89 (0.76-1.04)</td>
</tr>
<tr>
<td>Assisted ventilation</td>
<td>0.97 (0.91-1.02)</td>
<td>0.90 (0.79-1.00)</td>
</tr>
<tr>
<td>Neonatal seizures</td>
<td>1.39 (1.05-2.60)</td>
<td>1.04 (0.51-2.31)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: When controlled for mode of delivery, labor is not a risk factor for infant death, RDS, assisted ventilation or neonatal seizures in infants delivered in the setting of preterm PROM.

WITHDRAWN

DO MATERNAL-FETAL MEDICINE PRACTICE CHARACTERISTICS INFLUENCE HIGH RISK REFERRAL DECISIONS BY GENERAL OBSTETRICIAN-GYNECOLOGISTS? AM Vintzileos, CV Ananth, JC Smulian, RA Knuppel, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: To determine whether the decision of the general obstetrician-gynecologist (OB/GYN) to refer high risk (HR) obstetrical patients depends on the type of practice of the maternal-fetal medicine (MFM) specialist.

STUDY DESIGN: A questionnaire was sent to 1000 randomly selected general OB/GYN's all of whom were ACOG Fellows. The questionnaire included questions regarding accessibility to an MFM specialist, number of years in practicing obstetrics (OB) and practice setting (private practice, university hospital-based, community hospital-based or other). The general OB/GYN's were asked if any of the following MFM practice characteristics influence their decision to refer their HR OB patients to MFM specialists (for consultation, co-management, or total patient care): 1) the MFM specialist practices MFM and HR OB only; 2) the MFM specialist also practices general OB; 3) the MFM specialist also practices general OB/GYN; 4) the MFM specialist is university-salaried; 5) the MFM specialist is community hospital-salaried; 6) the MFM specialist is in private practice. Answer categories included: "more likely to refer," "less likely to refer" or "it does not matter" for each of the six MFM practice characteristics.

RESULTS: One hundred and forty (14%) general OB/GYN's responded; of these, 30 were excluded from the analysis because they had stopped practicing OB. The responses of the remaining 110 are shown below:

<table>
<thead>
<tr>
<th>Answer Category</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>More likely to refer</td>
<td>85 (77%)</td>
</tr>
<tr>
<td>Less likely to refer</td>
<td>24 (22%)</td>
</tr>
<tr>
<td>It does not matter</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

CONCLUSION: General OB/GYN's are more likely to refer high-risk obstetrical patients if the MFM specialists practice only MFM and HR OB. More than 70% are "less likely to refer" when the MFM specialist practices general OB/GYN. The job setting of the MFM specialist (university-salaried, community hospital-salaried or private practice) does not influence the decision of the general OB/GYN to refer HR obstetrical patients.

RISK FACTORS FOR PLACENTAL ABRUPTION IN SINGLETON AND TWIN GESTATIONS IN THE UNITED STATES. CV Ananth, JC Smulian, KD Demissie*, AM Vintzileos, RA Knuppel, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: To identify and contrast risk factors for placental abruption in twins and singleton pregnancies in the United States population.

STUDY DESIGN: We used data from the national linked birth/infant death data files for the United States for 1995 and 1996. Risk of abruption in relation to sociodemographic factors, obstetric history and medical complications of pregnancy were examined in a cohort of 193,266 twins and 7,465,868 singleton pregnancies. Risks and adjusted relative risks for abruption were derived, separately for twins and singleton pregnancies in the United States population.

RESULTS: Placental abruption was recorded in 2,358 (1.2%) twin and 44,032 (0.6%) singleton pregnancies. Significant risk factors for abruption in twins and singleton pregnancies included maternal anemia (adjusted relative risks [RR], 2.3 versus 2.2), intrapartum fever (> 100°F) (1.8 versus 1.2), hydramnios (1.7 versus 2.0), renal disorders (2.5 versus 1.5), preeclampsia/eclampsia (1.7 versus 1.2) and previous preterm infant (2.3 versus 2.8). Chronic hypertension (RR 2.3) and pregnancy-induced hypertension (RR 2.3) were strong risk factors for abruption in singleton but not in twin pregnancies. The risk of abruption was greatest among women who were both older (over 35 years) and multigravid (gravida 3+) (1.3 versus 1.8), compared with primigravid women aged 25-29 years. Number of cigarettes smoked during pregnancy demonstrated a dose-response trend for the risk of abruption in twins and singles up to about 5 cigarettes smoked/day. Therefore, the RR for twins plateaued at 1.6, while the risk in singles continued to increase. Abruption in twins was more likely to occur among women who smoked in the presence of chronic hypertension (2.9 versus 1.4) and eclampsia (5.3 versus 6.2), indicating that the risk for abruption in relation to hypertensive disorders and smoking were far greater than their independent effects.

CONCLUSIONS: Abruption is twice as likely to occur in twins compared with singleton pregnancies. Risk factor profiles for abruption in twin and singleton pregnancies are different, suggesting that abruption in twin pregnancies may result from different underlying processes compared with singleton pregnancies.
173 A COMPARISON STUDY OF PERIPARTUM COMPLICATIONS BETWEEN SPONTANEOUS AND INDUCED LABOR OF TERM AND PRETERM GESTATIONS. R. Hershkoets, O Erez, I. Shoham-Vardi, B. Furman, A. Bashiri, E. Sheiner, M. Mazor Dept. OB/GYN and Epidemiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

OBJECTIVE: To compare maternal outcome among spontaneous and induced labor of preterm and term small for gestational age (SGA) neonates

STUDY DESIGN: The study population consisted of 3921 consecutive SGA singleton births that occurred between 1990-1997. Out of 3921 SGA neonates 367 (9.4%) were born prematurely and 3554 (90.6%) were born at term. A cross-sectional study was designed and four groups were identified according to the mode of delivery and gestational age: 1. Preterm SGA neonates born after induction of labor (n=65). 2. Preterm SGA neonates born after spontaneous onset of labor (n=302). 3. Term SGA neonates born after induction of labor (n=478). 4. Term SGA neonates born after spontaneous onset of labor (n=5076). SGA was decoded as birth weight below the 10th percentile. (SrJ Med Sci 1993, 29:198-203). Patients with antepartum death and congenital anomalies were excluded from this study

RESULTS: The prevalence of the induction of labor in preterm SGA neonates was higher 17.7% (65/367) than among term SGA neonates 13.5% (478/3554).

<table>
<thead>
<tr>
<th></th>
<th>Induced labor</th>
<th>Spontaneous labor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preterm</td>
<td>Term</td>
</tr>
<tr>
<td></td>
<td>n=65 (%)</td>
<td>n=478 (%)</td>
</tr>
<tr>
<td>Hypertensive disorders</td>
<td>36 (55.0)</td>
<td>91 (19.0)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>26 (40.0)</td>
<td>99 (20.7)</td>
</tr>
<tr>
<td>Placental</td>
<td>7 (10.8)</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Abruption</td>
<td>16 (25.4)</td>
<td>188 (42.9)</td>
</tr>
<tr>
<td>Olivepseudomembranes</td>
<td>5 (7.7)</td>
<td>85 (17.9)</td>
</tr>
<tr>
<td>Meconium</td>
<td>2 (3.0)</td>
<td>5 (1.2)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>2 (3.0)</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>

No significant differences were found among the groups in maternal age, gravidity, parity, and in the rate of previous cesarean section

CONCLUSIONS: Hypertensive disorders of pregnancy were significantly higher in women who delivered preterm SGA infants than in those who delivered term SGA neonates. No significant differences were found among the groups in maternal age, gravidity, parity, and in the rate of previous cesarean section

175 IMPROVING OBSTETRIC OUTCOMES (NICU DAYS/1000) UTILIZING A MANAGED CARE MATERNITY MANAGEMENT PROGRAM A. W. Cohen, R. Bondi, A. Bombard, J. Armstrong, Aetna U.S. Healthcare, Blue Bell, PA

OBJECTIVE: To evaluate the effectiveness of a coordinated comprehensive maternity management program adopted by a managed care company to improve the outcomes of pregnancy.

STUDY DESIGN: The outcome of pregnancy, defined as NICU days/1000 deliveries within a population, was assessed before and after the initiation of a coordinated comprehensive maternity management program developed and implemented by a large national managed care company.

RESULTS: The frequency of NICU deliveries to 412 NICU days/1000 deliveries.

CONCLUSION: A coordinate comprehensive maternity management program with trained OB nurse managers, as well as ABOG certified medical directors using a proactive case management approach is effective in reducing neonatal morbidity. The success is related to coordination and utilization of prenatal resources and results in improved neonatal outcomes as judged by NICU days/1000 deliveries.
ANTHROPOMETRIC FACTORS AND THE RISK OF PREECLAMPSIA IN ADOLESCENT PREGNANCY

OBJECTIVE: To determine the effect of prepregnancy body-mass index (BMI) on the subsequent risk of preeclampsia (PE) during adolescent pregnancy

STUDY DESIGN: We performed a retrospective cohort study of 435 pregnant adolescent women, age 12-18 years, over the past three years. These women were categorized into four groups according to BMI: underweight (<20), normal (20-24.9), overweight (25-29.9), and obese (≥30) BMI. The incidence of PE was compared between those with a normal BMI and those with BMI ≥30. The incidence of PE was compared between those with a normal BMI and those with BMI ≥30.

RESULTS: Fifty-six out of 435 pregnant adolescent women (12.9%) developed PE. The incidence of PE in women categorized as underweight, normal weight, overweight, and obese were 9.2%, 11.1%, 19.0%, and 35.7%, respectively. After adjustment for significant factors of weight gain and gynecologic age (years between menarche and conception), the risk of developing PE with a BMI ≥30 remained significant (adjusted OR = 4.3, 95% CI: 1.8-10.9, p=0.001).

CONCLUSIONS: The incidence of PE is higher in pregnant adolescent women than in the general population pregnant women. Obesity prior to pregnancy is a strong risk factor for the development of PE in adolescent pregnancy. To develop a strategy to reduce the frequency of PE in adolescent pregnancy by normalizing BMI before pregnancy warrants further investigation.

PARENTAL AGE DIFFERENCE AND PREGNANCY OUTCOMES IN THE UNITED STATES

OBJECTIVE: Previous studies have suggested that adolescent mothers with adult male partners are more likely to engage in problem behaviors than those with similar age partners. This study was undertaken to determine the risks of adverse pregnancy outcomes based on varying parental age differences.

STUDY DESIGN: Data was derived from the national linked birth/infant death data sets assembled by the National Center for Health Statistics for 1996 and consisted of 3,179,570 singleton pregnancies. Outcome variables analyzed included perinatal mortality, preterm delivery <37 weeks, preterm premature rupture of membranes <57 weeks (PPROM) and abruptio placenta. Multiple gestations, chromosomal or congenital anomalies, infant death >27 days, gestational age <20 weeks and birth weight <500 grams were excluded. Age difference was obtained by subtracting maternal age from paternal age. The relationship between age difference and the outcome variables was evaluated by treating age difference as a continuous variable using non-parametric cubic splines.

RESULTS: Maternal age ranged from 12-49 years and paternal age from 12-69 years. Age difference ranged from -15 to +30 years. There were 392,281 patients assigned to one of six risk category groups: primiparous, multiparous and history of prior C/S. The distribution of patients in the high-risk categories (multiple gestation, malpresentation, <36 weeks and not for trial of labor) were significantly different between hospitals (A: 7.4%, B: 6.5% and U: 16.3%, p=0.001). When eliminating these groups, the recalculated C/S rates were not statistically different (A=11.1%, B=6.3% and U=9.5%, p=0.075). The university low-risk case mix was used as the standard population in the direct standardization analyses. The direct standardization analyses were calculated as follows: A=11.8%, B=6.3% and U=9.6%, p=0.011.

CONCLUSION: We have demonstrated that case mix has an impact on C/S rates. This statistical model could help physicians and medical administrators compare C/S rates between community and university hospitals.

EFFECTS OF TIMING AND DOSE OF IN UTERO ALCOHOL EXPOSURE ON INTELLECTUAL FUNCTION AND BEHAVIOR OF SCHOOLAGED CHILDREN

OBJECTIVE: The study tests whether dose and timing of exposure to alcohol are better indicators of fetal risk than average maternal alcohol intake during pregnancy.

STUDY DESIGN: 244 pregnant women were interviewed regarding drinking around the time of conception, average drinking across pregnancy, and drinking patterns throughout pregnancy. Their children were tested at 7.5 years for intellectual function and behavior.

RESULTS: 16 child outcomes were associated with drinking across pregnancy compared with only 6 with drinking at conception. 3rd trimester drinking predicted 14 child outcomes, whereas 2nd trimester drinking did not predict any. Adverse effects of binge drinking (5 or more drinks at one time) were evident only among the parents who binge infrequently may not expose the fetus during a vulnerable stage of gestation.

CONCLUSION: These data suggest that later pregnancy is a sensitive period for effects of maternal drinking on attention and behavior. The lack of adverse effects from infrequent binge drinking may be due to the rarity of that drinking pattern or because those who binge infrequently may not expose the fetus during a vulnerable stage of gestation.
181 DOES SPECIALIZED HUMAN IMMUNODEFICIENCY VIRUS CARE REDUCE PERINATAL TRANSMISSION?: AN OUTCOMES ANALYSIS.

**Objective:** To determine if an intensive Human Immunodeficiency Virus (HIV) in pregnancy program decreases perinatal transmission.

**Study Design:** The specialized HIV in pregnancy program at our institution includes care through referral to a small group of dedicated HIV/Maternal-Fetal Medicine specialists and peer counselors with access to a full range of social services, substance abuse treatment, and home visits as needed. Emphasis is given to development of appropriate medical regimens for perinatal prophylaxis and maternal treatment; counseling about adherence to medications; counseling and assistance with disclosure; and education about decreasing perinatal transmission and maternal morbidity. Patients receiving non-specialized care at our institution belong to a health maintenance organization and receive routine prenatal care, antiretroviral medications, and perinatal consultations only on request. Transmission data for the two groups of patients were compared.

**Results:** There were 46 (71%) vaginal deliveries and 19 (29%) cesarean (CS) deliveries in the non-specialized care group, compared to 48 (78%) vaginal deliveries and 11 (17%) cesarean deliveries in the specialized care group. The specialized care group had 1 fetal demise to a woman with Pneumocystis carinii pneumonia and 1 neonatal death to a woman with H1V in pregnancy. The specialized care group had 1 patient with fetal demise, and the non-specialized care group had 2 patients with fetal demise. There were 2 (4%) scheduled CS deliveries in the non-specialized care group and 1 (2%) scheduled CS delivery in the specialized care group. The specialized care group had 1 maternal death due to pneumocystis carinii pneumonia and 1 maternal death due to a woman who had an unexplained severe bradycardia on admission. Two (1 CS in labor; 1 vaginal delivery) babies ultimately tested negative for HIV infection; both mothers had received non-specialized care (2/16-12.5%). None of the women who received care through the intensive program had perinatal transmission, p<0.05.

**Conclusion:** Specialized prenatatal care for HIV-infected women resulted in a significantly lower perinatal transmission rate compared to that for women who had standard, non-specialized prenatal care. Despite specialized care, the perinatal mortality remained high in this group of high-risk patients. Nevertheless, our data support an intensified and specialized care program to prevent perinatal transmission and maternal morbidity. Patients receiving non-specialized care had a higher rate of perinatal transmission, p<0.05.

**Conclusion:** Preterm birth was defined as delivery between 22-36 weeks of gestation. Neonatal morbidity includes RDS, IVH (grade III-IV), NEC, PVL, BPD, neonatal pneumonia and sepsis. Perinatal mortality was considered as stillbirth or neonatal death within 28 days from delivery. Information was obtained using our computerized perinatal and neonatal databases using detailed obstetrical and neonatal records simultaneously.

**Results:** The prevalence of neonatal morbidity of the preterm deliveries during the study period was 11% (231/2095). The prevalence of the neonatal morbidity of deliveries associated with PROM was 14.9% (49/327). Adjusted odds ratios of factors associated with PROM for neonatal morbidity are presented as results of a multiple logistic regression analysis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROM</td>
<td>0.99</td>
<td>1.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>&lt;1500 gr</td>
<td>&lt;0.001</td>
<td>0.11-1.0</td>
<td></td>
</tr>
<tr>
<td>1500-1999</td>
<td>0.0001</td>
<td>1.00-1.5</td>
<td></td>
</tr>
<tr>
<td>2000-2499</td>
<td>0.0001</td>
<td>0.00-1.5</td>
<td></td>
</tr>
<tr>
<td>22-24 weeks</td>
<td>&lt;0.001</td>
<td>0.00-1.0</td>
<td></td>
</tr>
<tr>
<td>25-29 weeks</td>
<td>&lt;0.001</td>
<td>0.00-1.0</td>
<td></td>
</tr>
<tr>
<td>29-32 weeks</td>
<td>&lt;0.001</td>
<td>0.00-1.0</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Preterm PROM was not an additional risk factor for neonatal morbidity in preterm births.

182 THE RECURRENCE RISK OF PREECLAMPSIA. D Dobler, A Rashuri, O Erez, B Furman, RJ Lehman, A Porat, M Mazor, Dept. of OB/GYN and Epidemiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

**Objective:** To determine the recurrence risk of preeclampsia and to define the maternal risk factors of recurrence in subsequent pregnancies.

**Study Design:** A retrospective cohort study was designed. Two groups of patients were identified: the study group consisted of 580 primiparous women with preeclampsia, and the control group consisted of 380 primiparous women without preeclampsia. Multiple logistic regression was used for analysis.

**Results:** The recurrence rate of preeclampsia was significantly higher in the study group than in the control group (25% vs 19%, p<0.0001). The following figure demonstrates the recurrence rate of preeclampsia in subsequent gestations. Gestational diabetes mellitus was strongly associated with the recurrence of preeclampsia in subsequent pregnancy after adjusting for confounding variables (OR=5.71, 95% CI 1.15-5.55, p<0.001).

**Conclusion:** Primiparous women with preeclampsia have a 25% recurrence risk in subsequent pregnancies. Gestational diabetes mellitus is an independent risk factor for the recurrence of preeclampsia in the second pregnancy.

183 PRETERM PREMATURE RUPTURE OF MEMBRANES IS NOT AN INDEPENDENT RISK FACTOR FOR NEONATAL MORBIDITY. B Furman, LS Shoham-Vardi, A Bashiri, O Erez, M Mazor, Dept. OB/GYN and Epidemiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

**Objective:** To evaluate the risk factors for the development of neonatal morbidity in cases of preterm premature rupture of membranes (PPROM) in a non-selected parturient population.

**Study Design:** The study population consisted of 2396 singleton preterm births occurring between 1994-1997 at the Soroka University Medical Center. A cross-sectional study was designed. The study group consisted of patients with PPROM (n=376), and the comparison group consisted of patients without PPROM (n=1950). Preterm birth was defined as delivery between 22-36 weeks of gestation. Neonatal morbidity includes RDS, IVH (grade III-IV), NEC, PVL, BPD, neonatal pneumonia and sepsis. Perinatal mortality was considered as stillbirth or neonatal death within 28 days from delivery. Information was obtained using our computerized perinatal and neonatal databases using detailed obstetrical and neonatal records simultaneously.

**Results:** The prevalence of neonatal morbidity of the preterm deliveries during the study period was 11% (231/2095). The prevalence of the neonatal morbidity of deliveries associated with PPROM was 14.9% (49/327). Adjusted odds ratios of factors associated with PPROM for neonatal morbidity are presented as results of a multiple logistic regression analysis.

**Results:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPROM</td>
<td>0.99</td>
<td>1.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>&lt;1500 gr</td>
<td>&lt;0.001</td>
<td>4.18</td>
<td>22.64-76.7</td>
</tr>
<tr>
<td>1500-1999</td>
<td>&lt;0.001</td>
<td>11.0</td>
<td>5.81-20.90</td>
</tr>
<tr>
<td>2000-2499</td>
<td>&lt;0.001</td>
<td>3.61</td>
<td>1.86-6.88</td>
</tr>
<tr>
<td>22-24 weeks</td>
<td>&lt;0.001</td>
<td>12.8</td>
<td>4.90-33.11</td>
</tr>
<tr>
<td>25-29 weeks</td>
<td>&lt;0.001</td>
<td>27.1</td>
<td>17.81-40.85</td>
</tr>
<tr>
<td>29-32 weeks</td>
<td>&lt;0.001</td>
<td>11.1</td>
<td>7.76-15.79</td>
</tr>
</tbody>
</table>

**Conclusion:** Preterm PROM was not an additional risk factor for neonatal morbidity in preterm births.

184 ATTENTION DEFICIT DISORDER: RELATIONSHIP TO FETAL BIOPHYSICAL PROFILE. P.A. Mansung, C.R. Harman, S. Menticoglou, A. David, J. Xie, Dept. Ob/Gyn, Albert Einstein College of Medicine, Bronx, NY, University of Maryland, University of Manitoba, March of Dimes.

**Objective:** To determine the prevalence of attention deficit disorder (ADD) in children age 7-12 years we noted a 6 fold reduction among fetuses subjected to serial antepartum testing by fetal biophysical profile score (BPP). (4.71 vs. 28.1 per 1000 tested/non-tested respectively). The object of this study was to determine the relationship, if any, between last BPP result and subsequent ADD.

**Study Design:** A comparative study of the prevalence of attention deficit disorder (ADD) in children age 7-12 years who had a last BPP of 0 to 8/10 to 13/10 at the study hospital and office records of index cases. The study interval was from 1987-1992 inclusive.

**Results:** In a five year interval study 59 cases of ADD were identified among 19663 tested patients (prevalence 1.99 per 1000). A highly significant inverse exponential relationship between last BPP and prevalence of ADD was observed (R^2 0.781, p<0.001). The prevalence of ADD ranged from 0.8 per 1000 with a last BPP of 0 to 8/10 to 13 per 1000 with a last BPP of 9/10 to 10. The object of this study was to determine the relationship, if any, between last BPP result and subsequent ADD.

**Conclusion:** In a comparative study of the prevalence of attention deficit disorder (ADD) in children age 7-12 years we noted a 6 fold reduction among fetuses subjected to serial antepartum testing by fetal biophysical profile score (BPP). (4.71 vs. 28.1 per 1000 tested/non-tested respectively). The object of this study was to determine the relationship, if any, between last BPP result and subsequent ADD.

**Conclusion:** In a comparative study of the prevalence of attention deficit disorder (ADD) in children age 7-12 years we noted a 6 fold reduction among fetuses subjected to serial antepartum testing by fetal biophysical profile score (BPP). (4.71 vs. 28.1 per 1000 tested/non-tested respectively). The object of this study was to determine the relationship, if any, between last BPP result and subsequent ADD.
Racial Variation in Cervical Length and Preterm Delivery.

**Objective:** To assess cervical length and presence of funneling among Hispanic, Asian, Caucasian, and Black women by transvaginal sonography and evaluate its association with preterm birth.

**Methods:** A prospective cohort of women seeking prenatal care between 1996 to 1998 were recruited for serial transvaginal cervical sonography between 20-26 weeks, 28-32 weeks, and 28-33 weeks gestation. Data from previous pregnancies and outcome of index pregnancy were abstracted. Preterm delivery was defined as delivery ≤37 weeks. Data were analyzed by Chi-square tests, paired t-tests, and ANOVA.

**Results:** 700 pregnancies were included in the study, 65.3% Hispanic, 12.9% Asian, 6.4% Caucasian, and 13.9% Black. Preterm delivery rates did not differ by race (p=0.18). All pregnancies had progressive cervical shortening except Asians. Black women had shorter cervices across all 5 EGA intervals (ANOVA, p=0.05), even after controlling for preterm delivery. Incidental funneling was detected more often in Blacks (37.4% vs 20.5%). Black delivered preterm had even shorter cervices (p=0.017). Poor preterm delivery was associated with recurring preterm delivery in only the Black patients (p=0.00924).

**Conclusions:** When using transvaginal sonography lengths to assess risk for preterm labor and delivery, the cervical length screening criteria may need to be adjusted for Black patients.

Substances of Abuse: A Major Risk for Preterm Delivery.

**Objective:** To assess the risk of preterm delivery associated with substance use.

**Methods:** Substance use histories were collected prospectively by trained observers. For hierarchical logistic regression analysis, the outcome variable was preterm birth, defined as <37 weeks gestation. The independent variables were the proportion drinking day-to-day, dichotomized at the 95th percentile, proportion of prenatal visits on which cocaine use was reported and the 95th percentile, proportion of prenatal visits on which alcohol use was reported and the 95th percentile, proportion of prenatal visits on which tobacco use was reported and the 95th percentile, proportion of prenatal visits on which marijuana use was reported and the 95th percentile, proportion of prenatal visits on which substance use was reported and the 95th percentile.

**Results:** Increased rates of Bwt<10%, HC<10%, Bwt/length<10%, ponderal index <10% were evaluated. Adverse outcomes assessed included 5 minute Apgar <4, Apgar score at 10-20 minutes of <4, severe asphyxia, and abnormal neurologic evaluation at age 7 years.

**Conclusion:** In growth restricted infants, elevated PW/BW ratio is associated with increased rates of perinatal depression, neonatal demise, and abnormal neurologic status at age 7 years. PW/BW may represent an important epidemiologic tool for evaluation of neonatal nutritional status.

Nuchal Cords and Cord Knots Predispose to Altered Fetal Growth.

**Objective:** To assess the risk of preterm delivery associated with nuchal cords and cord knots.

**Methods:** Singleton Collaborative Perinatal Project infants delivered after 36 weeks were evaluated. Population norms for gender and gestational age were used to determine z score adjusted birthweight (Bwt), length, head circumference (HC), Bwt/length ratio, ponderal index, and Bwt/HC ratio. Values ≥10th centile were considered low Placenta/Bwt ratio greater than 1.8 was considered elevated, and was identified in 11% of infants. Infants born with either BW or Ponderal Index <10% were evaluated. Adverse outcomes assessed included 5 minute Apgar <4, Apgar score at 10-20 minutes of <4, severe asphyxia, and abnormal neurologic evaluation at age 7 years.

**Conclusion:** Both tight nuchal cords and tight cord knots were associated with increased rates of perinatal depression, neonatal demise, and abnormal neurologic status at age 7 years. Nuchal cords and cord knots may represent an important epidemiologic tool for evaluation of maternal nutritional status.
PRENATAL COCAINE AND CIGARETTES ASSOCIATED WITH POOR LANGUAGE DEVELOPMENT AT AGE 6-YEARS V. Delaney-Black, C. Covington, T. Temple, T. Kershaw, J. Ager, B. Nordstrom-Klee, N. Clark, A. Surendran, S. Matter and R. J. Sokol, Wayne State University, School of Medicine and College of Nursing, Detroit, MI

OBJECTIVE: Prenatal cocaine exposure (Coc Exp) has been linked to delayed language development, but large, controlled studies are not available. The study aim was to assess language development of 6-year-olds in relation to Coc Exp.

STUDY DESIGN: Coc, cigarette (Cig) and alcohol (ETOH) Exp were defined by prospective pregnancy history. Coc Exp was positive if either history or lab was positive. Child and parent were tested 6 years later. Language was assessed using the Arizona Articulation Proficiency Scale (AAPS) and a language sample.

RESULTS: Language samples were available for 458 children (204 Coc Exp). Mothers of Coc Exp children were older and had more prenatal exposures to Cig, ETOH, and other drugs. No significant univariate differences by Coc Exp were observed for any speech or language variable. Factor analysis performed on the nine speech and language variables yielded a three-factor solution ($R^2 = 68\%$). Linear discriminant function analysis (LDF) and classification and regression tree modeling (CART) were used to explore non-linear composites with Coc Exp as the dependent and the speech and language variables as the independent variables. No significant LDF was identified. CART identified meaningful cut points for predicting Coc Exp. The sample was randomly divided into two sub-samples: a training (N=214) and a validation sample (N=244). The prediction rule developed in the training sample showed good fit in the validation sample. Children with a type to token ratio of less than 42 and with fewer than 97 word types were classified into a low-language group (LOW). Children falling into this LOW category were more likely to be Coc Exp. Of 57 children in the LOW group, 36 (63.16\%) were Coc Exp. Logistic regression confirmed that Coc (p=0.009) and Cig Exp (p=0.054), and lower maternal IQ (p=0.072) were related to low language skills. Prenatal ETOH was not. Holding the covariates constant at their mean value, Coc Exp children were 2.4 times more likely to be in the low ability group compared to controls.

CONCLUSION: In this large, controlled and blinded study supported by the March of Dimes and NIDA, prenatal cocaine and smoking were associated with low language development. Confirmation of these findings will be important in determining services needed for affected children.
POSTER SESSION II

Thursday, February 3, 2000
3:30 pm - 5:30 pm

Fontainebleau Ballroom A/B

CATEGORIES
Diabetes
Hypertension
Infectious Diseases
Computers

Poster Numbers
190-309

Judges: Jorge D. Blanco, MD
Joshua A. Copel, MD
Howard L. Minkoff, MD
John T. Repke, MD
DO GESTATIONAL AND PREGESTATIONAL DIABETES INDEPENDENTLY INCREASE THE RISK OF BRACHIAL PLEXUS INJURY, SHOULDER DYSTOICA, AND BIRTH-RELATED FRACTURES. C J Saphare, RH Lapanski, CA Goodstein, Dept Obst/Gyn and Reproductive Sciences, Mount Sinai School of Medicine, New York, NY 10029

OBJECTIVE: To determine if diet-controlled gestational (A1 DM), insulin-requiring gestational (A2 DM), and pregestational diabetes (B-T DM) are independent risk factors for brachial plexus injury, shoulder dystocia, and birth-related fractures.

STUDY DESIGN: We performed a retrospective cohort study of all women delivering at a single institution over a 12-year period. Women underwent universal diabetes screening. Logistic regression calculated the odds ratios for each class of diabetes compared to controls without diabetes, adjusting for delivery mode and birth weight.

RESULTS: This study included 47,577 controls, 2,127 with A1 DM, 526 with A2 DM, and 186 with B-T DM. As summarized below, A1 DM, A2 DM, and B-T DM increased the risk of brachial plexus injury, although the risk for A2 DM did not reach statistical significance. While A1 DM did not significantly increase the risks of shoulder dystocia or birth-related fractures, A2 DM and B-T DM did.

CONCLUSIONS: Each class of diabetes independently increases the risk of brachial plexus injury, although A1 DM does not have as high a risk of shoulder dystocia and birth-related fractures as A2 DM and B-T DM. We believe these data support uniform counseling regarding the risk of brachial plexus injury occurring with both gestational and pregestational diabetes.


OBJECTIVE: We have previously shown (SPO 1998) that regional comprehensive perinatologists managed gestational diabetes (GDM) resulted in an improved pregnancy outcome compared to individual physician management. The purpose of this study was to evaluate the differences in hospital charges between the two groups.

STUDY DESIGN: Women with GDM who delivered in a two-year period were identified using ICD-9 codes from maternal and neonatal discharge summaries. Patients were stratified into two groups based on whether their GDM was managed by a perinatologist through the Diabetes and Pregnancy Sweeta Success Program (SS group) or by their individual obstetrician or a consulting endocrinologist (Non-SS group). SS treatment consisted of diabetic mode and birth weight.

RESULTS: Total maternal hospital charges per patient were $5,379±248 for the SS patients and $6,136±320 for the Non-SS patients (p<0.01). The corresponding infant charges were significantly greater for the Non-SS patients, $3,566±944 versus $1,556±240 (p<0.01). At delivery, 1.9% of SS infants and 12.5% of Non-SS infants were admitted to the NICU; the NICU charges per case admitted were $12,981 and $18,213 respectively. The breakdown of specific infant charges is shown in the table below.

<table>
<thead>
<tr>
<th>Infant Charges</th>
<th>SS (n=51)</th>
<th>Non-SS (n=72)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed/Room Stay</td>
<td>$1,110±215</td>
<td>$2,129±419</td>
<td>0.08</td>
</tr>
<tr>
<td>Procedures</td>
<td>$243±52</td>
<td>$129±230</td>
<td>0.05</td>
</tr>
<tr>
<td>Laboratory</td>
<td>$189±27</td>
<td>$161±103</td>
<td>0.01</td>
</tr>
<tr>
<td>Medications</td>
<td>$15±11</td>
<td>$15±71</td>
<td>0.06</td>
</tr>
</tbody>
</table>

CONCLUSION: The considerable savings in both maternal and neonatal hospital charges among GDM patients enrolled in a comprehensive perinatologist based treatment program justifies managed care authorization for referral of these patients to such a specialized program.

192 TRANS-PLACENTAL PASSAGE OF ANTI HUMAN INSULIN ANTIBODIES AND ITS EFFECT ON THE FETUS IN DIABETIC PREGNANCIES. Z Nachum, Y Shavit, Y Rakover, S Tal, B Shimoni, Z Weiner, E Weinryc, E Shales, Dept. Obst/Gyn, And Pediatric Endocrine Unit, Hadassah Med. Ctr., Afula, and Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

OBJECTIVE: To assess transplacental passage of anti human insulin antibodies (AHIA) to the fetus, and its effect on neonatal insulin levels and outcome.

STUDY DESIGN: Prospective cohort study in 74 pregnant diabetic women treated with human insulin and 39 pregnant controls.

RESULTS: Thirteen patients had gestational diabetes mellitus (GDM) and 35 pre-gestational (PGDM). AHIA were tested in the patients and controls prior to delivery and in the respective cord blood (semi quantitative RIA, CIS). Fifteen GDM (43%) and 29 PGDM (80%; P<0.001) patients were found to have AHIA, defined as > 3SD of the controls' mean. Comparisons were made between the patients found negative and positive for AHIA in the PGDM and GDM groups. No differences were found between the respective subgroups in background characteristics. No differences were found between the subgroups in mean blood glucose, HbA1c, fructosamine and the daily dose of insulin, injected before delivery. There were no differences in cord levels of insulin, C-peptide and fructosamine between the subgroups. No differences were found in the rate of neonatal complications and macrosomia. Maternal and cord levels of AHIA were highly correlated (r=0.74, P=0.001). Six neonates, positive for AHIA, were followed monthly for six month to measure AHIA levels disappearance. Serum half-life of these antibodies was 6.8±1.5 weeks. No antibodies to pancreatic islet were found in any of the patients. All controls were negative for AHIA, as well 6 women with GDM AHIA.

CONCLUSIONS: AHIA is a common occurrence in DM in pregnancy treated with insulin and readily pass the placenta. However, their presence is not associated with any alteration in glycemic control, cord insulin levels and neonatal outcome.

193 AGE IN WOMEN WITH TYPE I DIABETES IS NOT A RISK FACTOR FOR ADVERSE PREGNANCY OUTCOME. S. M. Eden, M. M. Modinov, A. Buchliander, J G. Krouwer, B M. Rosencranz, TA Siddiqui, Div. MFM, Dept. Obst/Gyn, Univ. of Cincinnati, Cincinnati, OH.

OBJECTIVE: Limited historical data suggests that age is a risk factor for adverse pregnancy outcome in women with Type I diabetes (DM). Therefore, we tested the hypothesis that adverse pregnancy outcome is associated with advanced maternal age in women with Type I DM.

STUDY DESIGN: Three hundred and eighty women with Type I DM enrolled in a prospective interdisciplinary study of diabetes in pregnancy and were divided into 3 age groups: Group I, ages >24 (n=154); Group II, ages 25-30 (n=156); and Group III, ages ≥31 (n=76). Teenagers ≤18 years old were excluded from the analysis. Maternal and neonatal outcomes were analyzed using X2, analysis of variance, and regression analysis.

RESULTS: OR (95% CI) and P values for each class of diabetes compared to controls without diabetes, independent risk factors for brachial plexus injury, shoulder dystocia, and birth-related fractures are shown in the following table:

<table>
<thead>
<tr>
<th>Event</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preconception Enrolment</td>
<td>9 (6)</td>
<td>29 (19)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>Stillbirth/Neonatal Death</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Chronic Hypertension</td>
<td>14 (12)</td>
<td>20 (16)</td>
<td>16 (20)</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>17 (15)</td>
<td>20 (16)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Microvascular Complications</td>
<td>38 (25)</td>
<td>43 (28)</td>
<td>20 (33)</td>
</tr>
<tr>
<td>PTD &lt;37 weeks</td>
<td>35 (30)</td>
<td>46 (37)</td>
<td>25 (35)</td>
</tr>
<tr>
<td>PTD ≥34 weeks</td>
<td>14 (17)</td>
<td>17 (14)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Macrosomia ≥4500g</td>
<td>19 (17)</td>
<td>24 (19)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Adverse Pregancy Outcome*</td>
<td>60 (39)</td>
<td>88 (44)</td>
<td>34 (45)</td>
</tr>
</tbody>
</table>

Data expressed as n (%).

*Adverse pregnancy outcome (composite outcome) = spontaneous abortion or malformation or neonatal death/stillbirth or NICU stay over 7 days or delivery before 32 weeks.

OLDER women were more likely to enroll preconceptionally, have chronic hypertension and PTD ≥34 weeks. However, neonatal outcome was not significantly different between groups.

CONCLUSIONS: Contrary to the belief that advanced age is associated with increased risk of adverse pregnancy outcome in women with Type I diabetes, from our data, age is not a risk factor for adverse maternal or neonatal outcomes. This information should be useful in counseling women with Type I diabetes.
194 PROGRESSION OF DIABETIC RETINOPATHY: ASSOCIATION WITH PREGNANCY AND REDUCED FETAL WEIGHT. S. Melby,* S. Demarin,* M. Miodownik, J. Khouery,* B. Rosenau, G. Kranias,* R. Tsang, Div. MFM, Dept. Obst/Gyn, Univ. of Conn., Cincinnati, OH.

**OBJECTIVE:** Since retinopathy is an indicator for diabetic microvascular disease, we tested the hypothesis that increased neonatal morbidity is expected with progression of diabetic retinopathy in pregnancy.

**STUDY DESIGN:** Women with IDDM (n=253) were enrolled in a prospective interdisciplinary study of diabetes in pregnancy and managed with intensive insulin therapy throughout pregnancy. Patients had ophthalmologic evaluation by ophthalmologists, graded according to a predefined scale in the first and third trimesters and postpartum. Subjects were divided into two groups based on whether diabetic retinopathy progressed (n=62) or remained stable (n=191). Analysis was performed using X², student t-test and logistic regression.

**RESULTS:** Progression of retinopathy occurred in 62/253 (24%) women, and was associated with advanced White classification; 11% in Class B, 23% in C, 36% in D, 50% in E. Neonatal outcomes found to be significantly associated with progression of retinopathy are depicted in the table:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Progression (n=62)</th>
<th>No Progression (n=191)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td>3074 ± 760</td>
<td>3406 ± 731</td>
<td>0.002</td>
</tr>
<tr>
<td>LGA</td>
<td>15 (24)</td>
<td>78 (41)</td>
<td>0.02</td>
</tr>
<tr>
<td>SGA</td>
<td>6 (10)</td>
<td>6 (3)</td>
<td>0.04</td>
</tr>
<tr>
<td>LBW&lt;2500 g</td>
<td>15 (24)</td>
<td>20 (10)</td>
<td>0.07</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>18 (32)</td>
<td>18 (9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Length of stay (d)</td>
<td>5 (4.8)</td>
<td>5 (4.7)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Data expressed as n (%) mean ± SD, median and interquartile range.

There was no significant association between progression of retinopathy and gestational age at delivery, macrosomia (>4000 g), preterm delivery (<37 wks), RDS, Apgars >7 @ 5 min, neonatal hypoglycemia, hyperbilirubinemia or neonatal death. Using multiple logistic regression including gestational age at delivery, chronic hypertension (CHT), preeclampsia, diabetic nephropathy and progression of retinopathy demonstrated that only CHTN (odds ratio [OR] 25; 95% CI 11, 54) and progression of retinopathy (OR 39; 95% CI 26, 90) were associated with reduced fetal growth.

**CONCLUSIONS:** Progression of diabetic retinopathy during pregnancy occurs in one quarter of intensively managed patients and is associated with reduced fetal growth.

195 RISK FACTORS FOR SPONTANEOUS PRETERM BIRTHS IN DIABETIC AND NON-DIABETIC OBSTETRICAL POPULATIONS. B Furman,* A.Witnitzer, L.Shoham-Vardi,* M.Mazor,* Dept. OB/GYN* and Epidemiology,b, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

**OBJECTIVE:** To evaluate the hypothesis that risk factors for preterm births in diabetic patients are different from those of the non-diabetic parturients.

**STUDY DESIGN:** The study population consisted of consecutive singleton deliveries at the Soroka University Medical Center between 1990-1997. The study population included: 1) pregestational DM (PGDM) (n=884); 2) gestational DM (GDM) (n=941); 3) non-diabetic women (NDW) (n=66253). The prevalence of spontaneous preterm delivery was determined in all three groups.

**RESULTS:** Results of multivariate analysis for preterm delivery in diabetic population according to diabetes type and non-diabetic parturients are presented:

<table>
<thead>
<tr>
<th>Variables</th>
<th>PGDM (n=884)</th>
<th>GDM (n=941)</th>
<th>NDW (n=66253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous preterm death</td>
<td>OR 1.85</td>
<td>1.93</td>
<td>1.74</td>
</tr>
<tr>
<td>IUGR</td>
<td>3.34</td>
<td>3.01</td>
<td>2.58</td>
</tr>
<tr>
<td>Severe PPH</td>
<td>3.98</td>
<td>1.30</td>
<td>2.71</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>1.88</td>
<td>1.03</td>
<td>1.10</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>0.40</td>
<td>1.00</td>
<td>1.23</td>
</tr>
<tr>
<td>Preterm PPM</td>
<td>2.79</td>
<td>1.24</td>
<td>1.40</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>3.02</td>
<td>1.50</td>
<td>1.23</td>
</tr>
<tr>
<td>Maternal age &lt;19 yr</td>
<td>0.85</td>
<td>0.97</td>
<td>1.19</td>
</tr>
<tr>
<td>Maturity age &gt;35 yr</td>
<td>0.89</td>
<td>0.97</td>
<td>1.19</td>
</tr>
<tr>
<td>Grand multipara (&gt;5)</td>
<td>0.72</td>
<td>0.83</td>
<td>0.85</td>
</tr>
</tbody>
</table>

**PREGESTATIONAL AND GESTATIONAL DIABETES MELLITUS ARE INDEPENDENT RISK FACTORS FOR PRETERM DELIVERY.** A. Witznitzer, B Furman, A.Bigelman, L Shoham-Vardi, M.Mazor, Dept. OB/GYN* and Epidemiology,b, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

**OBJECTIVE:** To determine whether diabetic mellitus (DM) (gestational and pregestational) is an independent risk factor for preterm delivery.

**STUDY DESIGN:** The study population consisted of consecutive singleton deliveries. Three groups of women were identified: pregestational DM (PGDM) (n=884); gestational DM (GDM) (n=941); non-diabetic women (NDW) (n=66253). The prevalence of the total preterm deliveries was determined in all three groups.

**RESULTS:** The prevalence of spontaneous preterm delivery was 25.5% in pregestational DM, 10% in gestational DM, and 7% in the non-diabetic patients. Results of multivariate analysis for preterm delivery according to diabetes type are presented:

<table>
<thead>
<tr>
<th>Variables</th>
<th>PGDM (n=884)</th>
<th>GDM (n=941)</th>
<th>NDW (n=66253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous preterm death</td>
<td>OR 1.85</td>
<td>1.93</td>
<td>1.74</td>
</tr>
<tr>
<td>IUGR</td>
<td>3.34</td>
<td>3.01</td>
<td>2.58</td>
</tr>
<tr>
<td>Severe PPH</td>
<td>3.98</td>
<td>1.30</td>
<td>2.71</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>1.88</td>
<td>1.03</td>
<td>1.10</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>0.40</td>
<td>1.00</td>
<td>1.23</td>
</tr>
<tr>
<td>Preterm PPM</td>
<td>2.79</td>
<td>1.24</td>
<td>1.40</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>3.02</td>
<td>1.50</td>
<td>1.23</td>
</tr>
<tr>
<td>Maternal age &lt;19 yr</td>
<td>0.85</td>
<td>0.97</td>
<td>1.19</td>
</tr>
<tr>
<td>Maturity age &gt;35 yr</td>
<td>0.89</td>
<td>0.97</td>
<td>1.19</td>
</tr>
<tr>
<td>Grand multipara (&gt;5)</td>
<td>0.72</td>
<td>0.83</td>
<td>0.85</td>
</tr>
</tbody>
</table>

When adjusted by a multivariate model for other risk factors of preterm delivery, the presence of diabetes still remained an independent risk factor for spontaneous preterm delivery: Pregestational DM – OR= 3.95; 95% CI 2.65-5.36; Gestational DM – OR= 1.98; 95% CI 1.1-3.48.

**CONCLUSIONS:** Diabetes mellitus (gestational and pregestational) is an independent risk factor for spontaneous preterm delivery.
198

PREGESTATIONAL DIABETES MELLITUS IN WOMEN OVER FORTY. A. Weizman, B. Farman, A. Smolin, G. Holberg, M. Mazor. Department of OB/GYN, Soroka University Medical Center; Faculty of Health Sciences; Ben-Gurion University of the Negev, Beersheba, Israel.

OBJECTIVE: To evaluate the maternal and neonatal outcomes in women over forty years old with pregestational diabetes mellitus.

STUDY DESIGN: The study population consisted of 173 consecutive singleton pregnancies enrolled between 1997-1999 as a diabetic daily care unit. A cross-sectional study was designed according to maternal age. The study group consisted of patients over 40 (n=18), and the comparison group included patients under 40 (n=155). Maternal and neonatal outcomes were collected prospectively from computerized database.

RESULTS: Maternal and neonatal outcomes are presented.

<table>
<thead>
<tr>
<th></th>
<th>Women &gt; 40 yrs</th>
<th>Women &lt; 40 yrs</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (yrs)</td>
<td>41.8±2.7</td>
<td>35.2±3.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Parity</td>
<td>7.5±3.7</td>
<td>2.9±1.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Type I (IDDM)</td>
<td>8/18 (44.4%)</td>
<td>17/155 (11.0%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Type II (NIDDM)</td>
<td>13/18 (72.2%)</td>
<td>108/155 (69.7%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Prenatal visits</td>
<td>18/2.1±11.0</td>
<td>16/9±8.8</td>
<td>0.63</td>
</tr>
<tr>
<td>HbA1c I trimester (%)</td>
<td>7.3±2.3</td>
<td>7.1±1.1</td>
<td>0.83</td>
</tr>
<tr>
<td>HbA1c II trimester (%)</td>
<td>6.3±1.2</td>
<td>5.9±1.2</td>
<td>0.92</td>
</tr>
<tr>
<td>Gestational age</td>
<td>37.9±2.7</td>
<td>39±2.4</td>
<td>0.56</td>
</tr>
<tr>
<td>Birth weight (gr)</td>
<td>3318±720.9</td>
<td>3152±635.7</td>
<td>0.77</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>15/18 (72.2%)</td>
<td>67/155 (43.2%)</td>
<td>0.018</td>
</tr>
<tr>
<td>LGA</td>
<td>4/18 (22.2%)</td>
<td>17/155 (11.0%)</td>
<td>0.23</td>
</tr>
<tr>
<td>RDS</td>
<td>3/18 (16.6%)</td>
<td>9/155 (5.8%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>3/18 (16.6%)</td>
<td>21/155 (13.5%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Polyhydramnosa</td>
<td>0</td>
<td>15/155 (9.8%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>3/18 (16.6%)</td>
<td>25/155 (15.9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>IUFD</td>
<td>0</td>
<td>3/155 (1.9%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Cardiomegalic</td>
<td>3/18 (16.6%)</td>
<td>5/155 (3.2%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Cerebral natal</td>
<td>0</td>
<td>2/155 (1.3%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Skeletal natal</td>
<td>0</td>
<td>2/155 (1.3%)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Even after controlling for parity, prenatal visits and the type of diabetes using forward stepwise regression analysis, maternal age did not have a significant influence on pregnancy outcome.

CONCLUSION: In women > 40 years old with pregestational diabetes maternal and fetal outcomes were generally favorable. This information may be helpful for counseling women over 40 years old with pregestational diabetes who are considering pregnancy.

199

THE EFFECT OF GESTATIONAL AGE AT Diagnosis ON PREGNANCY OUTCOME IN GESTATIONAL DIABETES. N T Field, M J. Plessas,* N M. Boe, E M. Ebiswillet,* W M. Gilbert, Mercy Healthcare Sacramento and Denver, OB/GYN, University of California, Davis, CA.

OBJECTIVE: To determine whether the gestational age at the time of diagnosis of gestational diabetes (GDM) affects maternal and neonatal outcome.

STUDY DESIGN: In an ongoing study, women with GDM who were enrolled in a California Sweet Success Diabetes and Pregnancy Program during a 2 year period were identified using ICD-9 codes from maternal discharge summaries. Patients were stratified into two groups based on whether their GDM was diagnosed prior to 20 weeks gestation because of indications for early glucose screening (Early GDM) or after 24 weeks gestation (Late GDM). All patients were managed in an identical manner by a single perinatologist. Sweet Success treatment consisted of medical nutrition therapy, daily self-monitoring of blood glucose values, weekly review of glucose data, and insulin therapy with dose adjustments when indicated. Maternal and neonatal outcomes were evaluated in the two groups.

RESULTS: Women with Early GDM were older, of higher parity, and significantly more obese (BMI 32 ± 5.5 vs. p=0.01) than patients with Late GDM. A significantly greater number of Early GDM patterns, 62.5% ± 19.2%, required insulin to achieve good glycemic control (p=0.01) and their mean insulin dose at delivery was over twice as high as that of the Late GDM patients. The incidences of operative vaginal delivery and non-elective cesarean section were equal in both groups and over 55% of all patients had normal spontaneous vaginal deliveries. Among those women who underwent glucose testing 6-8 weeks postpartum, 50% of the Early GDM group had evidence of either impaired glucose tolerance or overt diabetes as compared to only 12.5% of the Late GDM group (p=0.04). Gestational age at delivery, mean birthweight, and percentage of LGA infants were not significantly different between the two groups. Although more neonates in the Early GDM group developed hypoglycemia (18.3% ± 9% vs. p=0.02), NICU admissions, length of hospital stay, and overall neonatal outcome were similar.

CONCLUSION: Early gestational age at the time of GDM diagnosis does not seem to adversely affect neonatal outcome. However, the majority of these women required insulin to achieve good glycemic control and half of them had evidence of abnormal glucose metabolism postpartum. This persistent glucose intolerance is suspicious for a diagnosis of diabetes prior to their recently completed pregnancy.

200

RELATIONSHIP BETWEEN AMNIOTIC FLUID INSULIN LEVELS AND FETAL ABDOMINAL CIRCUMFERENCE RELATIONSHIP BETWEEN AMNIOTIC FLUID INSULIN LEVELS AND FETAL ABDOMINAL CIRCUMFERENCE AT TIME OF AMNIOCENTESIS IN PREGNANCIES WITH DIABETES. U M Schaufer-Graf3, A Engel1,2, W Henrich2x, K Bühling2x, B L Kjos3, TA Buchanan, T Heuener2x, JW Dudenhausen2x, K Vetter,1* Department of Perinatal Medicine, Neukölln Hospital, 2 Department of Obstetrics, Humboldt University, Berlin, Germany, 3 Department of Fetal-Maternal-Medicine, University Southern California, Los Angeles, CA.

OBJECTIVE: In recent studies we showed that measurements of the fetal abdominal circumference (AC) can be used as additional criteria to guide therapy in pregnancies with gestational diabetes. We used the 70th or 75th percentile of the AC as threshold for the need of insulin therapy. In pregnancies with diabetes excessive growth is related to fetal hyperinsulinism which can be diagnosed by determination of amniotic fluid insulin (AFI). The aim of this study was: 1.) To test the correlation between AFI and fetal AC. 2.) To determine if the threshold we used for insulin therapy meets the threshold of an increased risk of fetal hyperinsulinism.

STUDY DESIGN: In 121 pregnant women with diabetes (32 type I, 89 GDM) AFI was determined. Women with vascular diseases were excluded. In prior studies an AFI level >7 µU/ml was defined as 90th percentile. AC measurements which were obtained at time of amniocentesis were transformed into continuous percentiles using the Hadlock formula. AFI levels and the fraction of AFI >7 µU/ml were correlated with the AC percentiles.

RESULTS: There was a significant positive correlation between the level of AFI and the AC percentiles (r=0.3, p<0.0001). When fetal AC percentiles were divided into 10 percentile groups, visual inspection suggested a step increase in the fraction of infants with AFI >7 µU/ml at the 80th percentile AC. This step was confirmed by ROC analysis. 48% of infants with an AC >28th percentile had an AFI >7 µU/ml compared to only 22% newborns with an AC <20th percentile (p=0.005).

CONCLUSION: In pregnancies with diabetes measurements of the fetal abdominal circumference can identify a fetus at risk of hyperinsulinism. There is an increased risk with nearly 50% hyperinsulinism when the fetal abdominal circumference exceeds the 80th percentile.


OBJECTIVE: Examine the hypothesis that leptin levels are related to indices of adiposity and differ in the 9 year old (y) /o mother-child dyads of large for gestational age (LGA) and appropriate for gestational age (AGA) diabetic (GDM) vs control (C) gestations.

STUDY DESIGN: Mother-child dyads were enrolled from the Diabetes in Pregnancy Program at Women & Infants Hospital Mothers have been followed since the index pregnancy; offspring since 4 y/o. We evaluated 71 9y/o children (16 AGA-C; 17 LGA-C, 23 AGA-DM; 14 LGA-DM) mothers. Pregnancy data were available, and height, weight, skin-fold measurement and systolic and diastolic blood pressure (SBP, DBP) of the mother-child dyads were recorded at the 9 y/o visit. Fasting glucose, insulin and leptin levels were determined. ANOVA and Pearson correlations were performed.

RESULTS: For both mothers and children, there were no significant differences in fasting serum leptin in the four groups examined; adult levels were 35fold greater than child levels, and female exceeded male values. Adult leptin significantly correlated with prepregnancy weight, pregnancy weight gain, pre- and postpregnancy body mass index (BMI). Child leptin levels correlated significantly with weight, BMI, sum of four skinfolds, SBP, DBP, MAP, and fasting insulin. The majority of these correlations were maintained in the AGA-C, LGA-C, AGA-DM child subgroups. Only indices of adiposity were correlated with leptin in the LGA-DM group. Maternal leptin correlated with offspring leptin for GDM, but not Control.

CONCLUSION: Hyperleptinemia in neonatal offspring of diabetes, and in adult diabetes reflecting insulin resistance. At nine years from the index pregnancy, leptin is a marker for adiposity in mother-child dyads irrespective of GDM history. Leptin is not an indicator of presumpptive insulin resistance in this population.
202 IS "INCIDENT NEPHROPATHY" ASSOCIATED WITH AN INCREASED RATE OF PREECLAMPSIA IN WOMEN WITH PREGNATAL DIABETES? H. How for the NICHD Maternal-Fetal Medicine Units (MFMU) Network, Bethesda, MD

OBJECTIVE: To confirm previous reports (Obstet Gynecol 1999, Lancet 1999) that the rate of preeclampsia in women with gestational diabetes with "incident nephropathy" (defined as proteinuria of 30-500 mg protein/24h) when compared to those without proteinuria (<30 mg protein/24h) was then determined.

STUDY DESIGN: Relevant data from 466 insulin requiring pregnant women with type I and type II diabetes (White's class R/F/R) previously enrolled in a multicenter trial of low dose aspirin for prevention of preeclampsia, were secondarily analyzed. The women were assigned to one of the 4 groups, based on the level of proteinuria at enrollment (15-26 weeks gestation): group 1 comprised women with <30 mg protein/24h (n=278), group 2, those with 30-189 mg protein/24h (n=82), group 3, those with 190-599 mg protein/24h (n=55); group 4, those with 8900mg protein/24h (n=65). The rate of preeclampsia, using strict predefined criteria according to the degree of baseline hypertension and/or proteinuria, was then determined.

RESULTS: Ninety-two women (20%) developed preeclampsia. The table below summarizes the rate of preeclampsia for the four groups. Using receiver-operating characteristic curve we did not find a proteinuria threshold that best predicted preeclampsia in women with gestational diabetes with "incident nephropathy" when compared to women with gestational diabetes without proteinuria.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urine Protein (mg/24h)</th>
<th>N</th>
<th>Preeclampsia (n%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;30</td>
<td>278</td>
<td>52 (18.7)</td>
</tr>
<tr>
<td>2</td>
<td>30-189</td>
<td>82</td>
<td>12 (14.6)</td>
</tr>
<tr>
<td>3</td>
<td>190-499</td>
<td>55</td>
<td>7 (20)</td>
</tr>
<tr>
<td>4</td>
<td>500+</td>
<td>65</td>
<td>21 (32.3)</td>
</tr>
</tbody>
</table>

CONCLUSION: Contrary to previous reports, we did not find an increased rate of preeclampsia in women with gestational diabetes with "incident nephropathy" when compared to women with gestational diabetes without proteinuria.

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204 OBESITY INCREASES CESAREAN RATES IN GESTATIONAL DIABETES. S. Brickman. MG Newman, BD Raynor Department of Gynecology and Obstetrics, Emory, Atlanta, Georgia.

OBJECTIVE: To determine if obesity is an independent risk factor for cesarean delivery in gestational diabetes (GDM).

STUDY DESIGN: The medical records of all GDM delivered between January 1, 1992 to December 31, 1996 were reviewed. Obesity was defined as prepregnancy body mass index ≥ 30 kg/m². Demographic and perinatal outcome data were compared by univariate analysis. Ninety-five percent CI excluding 1 was considered significant.

RESULTS: Three hundred sixty-one (40%) of 950 GDM met criteria for obesity. Obese patients were more likely to have had a previous term delivery, be African-American and have chronic hypertension. Obese women were more likely to need insulin (OR: 2.95, CI: 1.43-5.77); develop macrosomia (OR: 2.29, CI: 1.43-3.71); need labor induction (OR: 1.81, CI: 1.22-2.75). Fifty-four (231%) of nonobese GDM required cesarean compared to 148 (411%) of obese patients (OR: 2.32, CI: 1.57-3.29). A logistic regression model was constructed with cesarean as the dependent variable and obesity, labor induction, insulin use, IUGR, macrosomia, non-vertex presentation, nulliparity, and previous cesarean as independent variables. The model confirmed obesity as an independent factor for cesarean delivery (OR 1.85, CI 1.41-2.39).

CONCLUSION: Obesity is an independent risk factor for cesarean delivery in gestational diabetes.

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205 PREDICTION OF LARGE FOR GESTATIONAL AGE INFANTS IN GESTATIONAL DIABETES WITH MODERATE FASTING HYPERGLYCEMIA. S. Eoy, A. Buley, E. Schaffer, A. Vinerx, T. Buchananx, Dept. OB/GYN, Univ. Southern Calif., Los Angeles,CA

OBJECTIVE: To determine predictors large for gestational age (LGA) infants in women with gestational diabetes (GDM).

STUDY DESIGN: Possible predictive variables for LGA infant growth were assessed in 98 women with gestational diabetes (GDM) whose initial diagnostic fasting plasma glucose (FPG) was 105-120 mg/dl. Subjects were followed in a randomized trial to assess ultrasound-guided therapy. Logistic regression methods were used to evaluate possible factors associated with increased infant birth weight. The model was calculated for GA and birth weight. The model was calculated for GA and birth weight in women with GDM with moderate fasting hyperglycemia whose pregnancy was complicated by diabetes.

RESULTS: The model identified several maternal weight variables (pre-pregnancy and predelivery weight or BMI, pregnancy weight change per week) and an initial AC > 70th percentile for GA shortly after diagnosis of GDM in women was strongly associated with greater anthropometric newborn growth despite good glycemic control and insulin therapy.

CONCLUSIONS: In GDMs with moderate fasting hyperglycemia, who achieved subsequent euglycemia, having a LGA infant was independently associated with an initial fetal AC > 70th percentile for GA and pregnancy weight. An initial fetal AC > 70th percentile for GA shortly after diagnosis of GDM in women was strongly associated with greater anthropometric newborn growth despite good glycemic control and insulin therapy.
PREDICTION OF COMPLICATED GESTATIONAL DIABETES MELLITUS AT THE TIME OF DIAGNOSIS. D. E. Caliendo, M.T. Harelbaker, S. Hassricx, M.B. Landon. The Ohio State University College of Medicine, Columbus, Ohio.

OBJECTIVE: To assess whether maternal risk factors and/or indices of glucose intolerance obtained at the initial diagnosis of gestational diabetes mellitus (GDM) can predict a need for insulin therapy, fetal macrosomia, and cesarean section.

METHODS: Information was obtained from a database of women with GDM receiving care in the Ohio State University Diabetes and Pregnancy Clinic. Variables traditionally thought to be risk factors (i.e. age, race, percentage above ideal body weight, gravidity, parity, and family history) and glucose tolerance test values were selected and compared to outcomes.

RESULTS: 150 women with the diagnosis of GDM were collected over a 2-year period. Women with an elevated fasting glucose were over twice as likely to require insulin treatment in pregnancy (RR=2.14). The relationship between elevated fasting glucose and subsequent cesarean section was also significant (X2=4.32, p=0.04). There was a strong association between insulin requirement and the number of abnormal values in 3-hour glucose tolerance testing (X2=17.29, p=0.0017) However, logistic regression modeling revealed that fasting glucose was the only significant independent predictor of the likelihood for insulin requirement (X2=11.36, p=0.0008) and the risk of cesarean section (X2=4.19, p=0.041). Both X2 and logistic regression exhibited unacceptably predictive percentages, 65% and 61% respectively, suggesting that additional information is required to adequately predict the need for insulin treatment based upon initial diagnostic testing. None of the criteria evaluated were able to predict the risk of fetal macrosomia.

CONCLUSIONS: Risk factors are not useful to predict the need for insulin treatment, risk of a macrosomic infant, or cesarean section in women with GDM.

SECOND STAGE OF LABOR AND RELATED EXPULSIVE EFFORTS: ASSOCIATION WITH PROGRESSION OF DIABETIC RETINOPATHY. S.S. McElyey, M. Moscovitz, B. Rosenz, A. Buchbinder, J.C. Elroy, G. Krizman, D. Fishman, Dept. Obst/Gyn, Ohio State University College of Medicine, Columbus, OH.

OBJECTIVE: Maternal expulsive efforts during the second stage of labor abruptly increase blood pressure and may cause retinal lamennorrhage in women with Type I diabetes. Whereas some obstetricians elect to deliver these women by cesarean section, others believe that the post-artenorial retinal vascular changes are unlikely to be affected by yasaka efforts associated with vaginal delivery. There is no data to support either of these approaches. Therefore, we tested the hypothesis that the second stage of labor and related expulsive efforts are associated with development and/or progression of diabetic retinopathy in women with Type I diabetes.

STUDY DESIGN: Women with Type I diabetes (n=192) White class B-RF were enrolled in a prospective interdisciplinary study of diabetes in pregnancy and managed with intensive insulin therapy throughout pregnancy. Women had ophtalmologic evaluation at enrollment, before 20 weeks gestation, in the third trimester, and postpartum. Ophthalmologic examination was performed by one of two ophthalmologist and graded according to a predefined scale. Data on duration of stages of labor and mode of delivery were collected. Subjects were divided into 3 groups: Group I (n=60), women who had elective cesarean section without labor, Group II (n=69), women who labored but were delivered by cesarean section before the second stage; and Group III (n=63), women who delivered vaginally. Data was analyzed using X2 analysis of variance and logistic regression.

RESULTS: The following table depicts changes in development and/or progression of retinopathy throughout gestation and postpartum.

<table>
<thead>
<tr>
<th>Group</th>
<th>No Labor</th>
<th>No 2nd Stage</th>
<th>Vag Deliv</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 Wks to 3rd Trimester</td>
<td>9 (15)</td>
<td>14 (20)</td>
<td>14 (22)</td>
<td>0.58</td>
</tr>
<tr>
<td>&gt;20 Wks to Postpartum</td>
<td>9 (15)</td>
<td>16 (23)</td>
<td>12 (19)</td>
<td>0.50</td>
</tr>
<tr>
<td>3rd Trimester to Postpartum</td>
<td>5 (8)</td>
<td>8 (12)</td>
<td>5 (8)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Data expressed as n (%). Development and/or progression of retinopathy was measured using the following criteria: severe nonproliferative diabetic retinopathy, mild proliferative diabetic retinopathy, severe proliferative diabetic retinopathy. Each group was compared to the others using the Student's t-test. No significant difference was noted. Data was analyzed by the Statistical Analysis System using the X2 test.
210 ONE OR TWO HOUR POSTPRANDIAL GLUCOSE MEASUREMENTS: ARE THEY THE SAME? B. Weiss1*, E. Homko2, E. Schiff1, M. Dulinz3, S. Mashiach2, E. Reece1, E. Sivan1, C. Shaffer1, C. E. Schaff1, D. Ob/Gyn, Sheba Medical Center, Tel Hashomer, Israel1; Dept. Of Ob/Gyn, Temple Univ. Phila., PA2

OBJECTIVE: To compare the rate of abnormal glucose levels measured one hour (>140 mg/dl) versus two hours (>120 mg/dl) post-prandially in women with diet-controlled gestational diabetes.

STUDY DESIGN: 78 women were included in this study. All had gestational diabetes (GDM) based on the criteria of Carpenter-Coustan. Women with fasting glucose levels ≥109 mg/dl were excluded. All women were starting on a diet according to ADA recommendations. The women measured daily capillary blood glucose levels at fasting, one hour and two hours post-prandially for one week. Glucose levels were obtained by memory-based glucometers. All women were followed in a special gestational diabetes clinic throughout the pregnancy. Epidemiological and perinatal data was collected from medical charts.

RESULTS: The average age of the women was 32 ± 6.4 years. 35% were primipara. The mean gestational age at diagnosis was 27 ± 5.4 weeks. Glucose measurements included 618 readings during fasting, and 2730 either one or two-hours post-prandial. Rates of abnormal glucose (>140 mg/dl) one hour or >120 mg/dl two hours after each meal per-person were: Post-breakfast - 21.5% abnormal levels after one hour versus 8% after two hours (p<0.05); Post-Lunch - 16.3% abnormal levels after one hour and 17.8% after two hours (NS); Post-Dinner - 15.4% abnormal levels after one vs. 28.2% after two hours (p<0.05).

CONCLUSION: The rate of abnormal values was 2.5 fold greater one hour after breakfast versus two hours, in contrast to an opposite ratio of a 2.0 fold increase in the rate of abnormal values two hours post dinner versus one hour. Therefore, differential measurement (one hour after breakfast and two hours after dinner) might improve stricter criteria for controlling blood glucose levels. Further clinical research should explore whether differential measurements might reduce the rate of diabetes associated complications.

211 THE IMPACT OF FETAL REDUCTION ON THE INCIDENCE OF GESTATIONAL DIABETES. E. Maman1*, E. Sivan1, S. Liptau1, M. Duzitki1, C. Homko1, E. Reece1, E. Sivan1, C. Shaffer1, D. Ob/Gyn, Sheba Medical Center, Tel Hashomer, Israel1; Dept. Ob/Gyn, Temple Univ., Philadelphia, PA2

OBJECTIVES: To establish the rate of gestational diabetes (GDM) in triplet pregnancies and to assess the impact of fetal reduction on the incidence of this complication.

METHODS: One hundred and three consecutive triplet pregnancies delivered at the Sheba Medical Center between 1994-1998 were compared to 85 triplet gestations that underwent induced fetal reduction during the same time period. The incidence of GDM (based on the criteria of Carpenter and Coustan) and other outcome variables were compared between the two groups. For statistical analysis chi square and student T tests were used as appropriate.

RESULTS: The age of the women was 29.3±4.2 and 29.2±4.8 in the triplet and reduction groups respectively. Similar median parity (1.0) was found in both groups. The rate of GDM was significantly higher in triplets when compared to the reduction group (22.3% vs. 5.5%, respectively; p<0.05). A lower birth weight and an earlier gestational age at delivery were observed in the triplets vs. the reductions group (1765±430 g vs. 2208±558 g; p<0.001 and 33±2.8 vs. 36±2.8 weeks; p<0.001, respectively).

CONCLUSIONS: The number of fetuses in multi-fetal pregnancies influences the incidence of GDM. These findings support the hypothesis that an increase in placental mass and thus an increase in diabeticogenic hormones play a role in the etiology of GDM.

212 IS THERE AN ASSOCIATION BETWEEN DECREASED INSULIN REQUIREMENTS AND PERINATAL OUTCOME IN LATE PREGNANCY? Retina1, A. Villareal1, D. Conroy1, O. Langer1, Dept. of Ob/Gyn, UTHSCSA, San Antonio, TX

OBJECTIVE: To investigate if decreased insulin requirements negatively affect pregnancy outcome.

METHODS: In a prospective cohort study during 1997-99, all consecutive pre-existing and gestational diabetes subjects were assessed from the 33rd week gestation for insulin requirements and fetal outcome. All patients were treated with the intensified management approach. Patients with decreased insulin requirements (DIR) were compared to a matched control by gestational age and diabetic type in the ratio of 1:1.

RESULTS: The rate of DIR for pre-existing diabetes was 10/206 and 12/976 in GDM women. In the 10 DIR GDM patients, a decrease of 19±12% was found. In contrast, an increase of 18±5% was found in the matched control subjects. For the 12 DIR GDM subjects, a decrease of 17±5% was found compared to an increase of 8±3% in the control group (p<0.01). No association was found between DIR and duration of diabetes, maternal age, BMI, and weight gain in pregnancy. The table below summarizes neonatal outcome

| DIR GDM | Control GDM | DIR GDM | Control
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>PGDM</td>
<td>n=12</td>
<td>n=36</td>
<td>n=10</td>
</tr>
<tr>
<td>Micro</td>
<td>0%</td>
<td>25%</td>
<td>40%</td>
</tr>
<tr>
<td>Macros</td>
<td>3%</td>
<td>80%</td>
<td>30%</td>
</tr>
<tr>
<td>Polyc</td>
<td>0%</td>
<td>36%</td>
<td>0%</td>
</tr>
<tr>
<td>Hyperl</td>
<td>11%</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td>Hypo</td>
<td>0%</td>
<td>19%</td>
<td>20%</td>
</tr>
<tr>
<td>Respir</td>
<td>0%</td>
<td>3%</td>
<td>10%</td>
</tr>
<tr>
<td>NICE</td>
<td>8%</td>
<td>3%</td>
<td>14%</td>
</tr>
<tr>
<td>Stillb</td>
<td>0%</td>
<td>0%</td>
<td>0.03%</td>
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</table>

CONCLUSION: Continuous decreased insulin requirements after the 35th wk gestation is a rare event for GDM and PGDM women. The decrease does not enhance the risk for complications in infants of GDM mothers. A trend for higher risk complications was identified in infants of PGDM patients.

213 FASTING BUT NOT POSTPRANDIAL BLOOD GLUCOSE VALUES PREDICT BIRTHWEIGHT IN GESTATIONAL AND TYPE II DIABETES. A. An2, A. D. Hall1, T. Moore, Dept of Perinatal Medicine, Med of Reproductive Medicine, Univ of California, San Diego, CA.

OBJECTIVE: Correlation of fasting (F) and 1 hour postprandial (PP) capillary glucose (CG) levels with birthweight (BW) to determine which strategy minimizes macrosomia in gestational (GDM) and Type II (DMII) diabetes.

STUDY DESIGN: Retrospective review of 77 diabetics (21 DMII, 56 GDM) who recieving 29±10% of F and PP four times daily in the 29±6 weeks prior to term. Mean F and PP CG were stratified and compared to birthweight and gestation-corrected birthweight percentile (BW%).

RESULTS: The infants’ mean ± SD BW was 3470±852 g, delivered at 38.9±1.3 weeks, with a mean BW of 54±65 g. Mean FCG was 87±12 and PPCG was 113±15 mg/dl. ANOVA demonstrated a significant correlation between BW, BW% and FCG (p<0.01, 0.02) but no correlation with PPCG (p=0.04, 0.06). See Figures. Intergroup comparisons showed significantly lower BW when mean FCG was kept below 88 mg/dl (p<0.05).

CONCLUSIONS: This analysis of meticulously recorded CG values at 36-38 weeks indicates that strict control of FCG is superior to PPCG in preventing macrosomia with GDM and DMII. These findings contrast with prior studies, but are based on a more complete profile on metabolic control.

<table>
<thead>
<tr>
<th>Birthweight Percentile vs FCG</th>
<th>Birthweight Percentile vs PPCG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean FCG (mg/dl)</td>
<td>Mean PPCG (mg/dl)</td>
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<table>
<thead>
<tr>
<th>10</th>
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<th>20</th>
<th>25</th>
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<td>0</td>
<td>20</td>
<td>40</td>
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<td>80</td>
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</table>
**214 PREDICTORS OF NEONATAL HYPOGLYCEMIA IN PREGNANCIES COMPLICATED BY GESTATIONAL DIABETES.** DL Conway, SM Gulmson, O Langer. Dept of Ob/Gyn, UTHSCSA, San Antonio, TX.

**OBJECTIVE:** Neonatal hypoglycemia occurs in 15-30% of infants born to women with pre-existing diabetes mellitus. Acute adverse effects include seizures, apnea and cyanosis while longer-term problems include cerebral palsy and mental retardation. The purpose of this study was to determine what antepartum and intrapartum factors are associated with hypoglycemia in infants born to women with gestational diabetes (GDM).

**STUDY DESIGN:** Inclusion criteria: women with GDM who delivered over a six-month period. Exclusion criteria: labor <2 hrs. in duration, fetal demise or elective cesarean delivery. Intrapartum management of patients with GDM consisted of fingerstick capillary glucose levels every four hours (A1) or every two hours (A2). The IV fluid type and use of insulin were per physician discretion. Neonates were evaluated for hypoglycemia at 30, 60, 90, 120, and 180 minutes of life, with feedings at 30 minutes and 3 hours after birth. Neonatal hypoglycemia was defined as any glucose value <40 mg/dl in the first four hours of life. Subjects were stratified as to whether the neonate developed hypoglycemia (cases) or not (controls). Predictive variables examined included maternal demographics and maternal glycemic profiles (antepartum and intrapartum).

**RESULTS:** 120 women met inclusion/exclusion criteria. The overall neonatal hypoglycemia rate was 13.7%. Women delivering hypoglycemic infants did not differ from controls in terms of GDM class (A1 vs A2), BMI (<25 vs ≥25), or GA at delivery. Furthermore, no difference was found in terms of type of intrapartum IV fluid, mean intrapartum glucose, any glucose value >100 mg/dl during labor, or time (in hours) between last glucose >100 mg/dl and delivery. However, the mean birthweight %I was significantly different between the groups (54% vs 70%, p=0.01), showing a tendency for larger neonates in the hypoglycemic group. Logistic regression analysis showed that birthweight %I (p=0.02) and any glucose >100 mg/dl in labor (p=0.02) were associated with neonatal hypoglycemia.

**CONCLUSION:** Our findings suggest that in women with GDM, neonatal hypoglycemia may have its origins in excessive fetal growth, rather than intrapartum diabetic management. However, the rate of neonatal hypoglycemia in GDM is similar to that reported in pre-existing diabetics.


**OBJECTIVE:** Due to paucity of information on lipid profile in pregnant PGDM patients, we sought to investigate this relationship.

**STUDY DESIGN** There were 271 PGDM patients (n=168 class B, n=71 class C, n=13 class D, n=10 class F, n=5 class RF, n=4 class R) enrolled who used self-monitored blood glucose technique during pregnancy. Lipid profile (cholesterol, HDL, LDL, and triglycerides) was obtained at first visit and then during each trimester.

**RESULTS:** Chart displays difference in lipid components during pregnancy

<table>
<thead>
<tr>
<th>Component</th>
<th>Entry</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chol</td>
<td>0</td>
<td>250</td>
<td>200</td>
<td>150</td>
</tr>
<tr>
<td>HDL</td>
<td>150</td>
<td>100</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>LDL</td>
<td>0</td>
<td>50</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>TG</td>
<td>150</td>
<td>100</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

(1) all lipid components increased significantly at each determination throughout pregnancy; (2) cholesterol levels showed a significant positive correlation with fasting plasma glucose (r=0.46, p<0.001) and an inverse relation to weight gain during pregnancy (r=-0.13, p<0.05); (3) a significant association was found between maternal size and blood pressure (r=26, p=006); (4) prepregnancy weight was significantly associated with all lipid profile components (approximately r=26, p<0.001); (5) no significant association found for total insulin dose, lipid profile components, and fasting plasma glucose.

**CONCLUSION:** Our data suggest that hyperlipidemia plays a role in the pathogenesis of PGDM, although it does not influence the insulin requirements in patient treatment.

**216 DIABETES AT TERM: DO LUNG Maturity TEST RESULTS PREDICT NEONATAL RESPIRATORY MorBIDITY?** MF Piper, EM Xenakis, O Langer. Dept. Ob/Gyn, UTHSCSA, San Antonio, TX.

**OBJECTIVE:** Standard of care requires amniotic fluid assessment for fetal lung maturity (AF-FLM) prior to elective delivery of diabetic women, even at term gestations. We sought to evaluate the role of AF-FLM testing to predict neonatal lung disease in term diabetic women who underwent testing within 3 days of delivery.

**STUDY DESIGN:** Consecutive diabetic women who delivered ≥27 weeks gestation within 3 days of AF-FLM were analyzed for neonatal respiratory morbidity (transient tachypnea, wet lung, or hyaline membrane disease). Diabetic pregnancies were stratified by maternal glucose control (Good <100 mg/dl, Poor >100 mg/dl) and gestational age (best obstetric estimate) for comparison of neonatal respiratory morbidity by AF-FLM. Potential confounding factors were also examined (maternal demographics, delivery characteristics, diabetes class, other maternal complications).

**RESULTS:** 335 diabetic women delivered at ≥27 weeks with AF-FLM within 3 days of delivery. Rates of neonatal respiratory morbidities were displayed below for good and poor control

<table>
<thead>
<tr>
<th>Gestation</th>
<th>Good</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>37 wks</td>
<td>0% (0/32)</td>
<td>1% (1/100)</td>
</tr>
<tr>
<td>38 wks</td>
<td>0% (0/56)</td>
<td>0% (0/54)</td>
</tr>
<tr>
<td>≥39 wks</td>
<td>0% (0/41)</td>
<td>1.9% (2/187)</td>
</tr>
</tbody>
</table>

AF-FLM results were PG negative in 12% at 37 weeks, 9% at 38 weeks, and 0% at or beyond 39 weeks. There were no cases of hyaline membrane disease in this cohort. All 3 cases of neonatal respiratory morbidity occurred in infants delivered by cesarean section and 4/5 cases were PG+. (Other was L/S 2/1).

**CONCLUSION:** Neonatal respiratory morbidity was rare at or beyond 38 weeks gestation in this cohort of intensely managed diabetic pregnancies. AF-FLM testing did not predict neonatal respiratory morbidity. Reliance on AF-FLM testing in well-dated term diabetic pregnancies could potentially increase perinatal mortality and morbidity by unnecessarily delaying delivery.

**217 LONGITUDINAL STUDY OF THE MIDDLE CEREBRAL ARTERY (MCA) BLOOD FLOW VELOCITY (BFV) IN INFANTS OF DIABETIC MOTHERS (IDM).** HMertzo, NSmith, D Zaccaro, CTegeler, JCVeille, Depts of Ob/Gyn, Neurology and *Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC.

**INTRODUCTION:** IDM have been shown to have significant metabolic alteration and cardiovascular changes.

**PURPOSE:** To study longitudinally the BFV of the MCA throughout gestation and immediately after birth in a cohort of IDM.

**MATERIALS & METHODS:** Ten IDM were studied at 16-18 weeks of gestation and every month throughout gestation (average 4.6 studies) and once in the immediate postnatal period. Pulsed Doppler (PD) studies were obtained using color ultrasound Waveforms were recorded, videotaped and subsequently traced using a tablet digitizer in order to obtain the acceleration/ejection time (AC/ET) and the time velocity integral (TVI-cml). Statistical analysis was done using PROC-MIXED model (SAS) to compare IDM with a cohort of normal fetuses/neonates.

**RESULTS:** 1) TVI of the MCA appears similar in both groups (Figure 1). 2) AC/ET is significantly lower in IDM when compared to normals (Figure 2). 3) This difference is present even early in gestation.

**CONCLUSIONS:** 1) IDM do not exhibit any significant difference in MCA TVI 2) AC/ET is significantly decreased in IDM. This may reflect decreased distal cerebral artery resistance due to differences in cerebral metabolism or autoregulation. Whether this is unique to this vascular bed remains to be elucidated (Supported by NIH grant no RO1-HL 58296)
1 Longitudinal Study of the Fetal Right (RV) / Left (LV) Ventricular Function (VF) in Infants of Diabetic Mothers (IDM) Using Pulsed Doppler (PD). JC Voile, N Smith, D Zaccarelli, Deps Obst/Gyn & Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC.

Introduction: IDM have been shown to have adverse effect on VF. This longitudinal study evaluates fetal VF in IDM from the 16th week of gestation to the neonatal period. (1 IDM was followed to year 1).

Material and Methods: To date, 10 IDM had fetal echocardiograms using PD from the 16th weeks of gestation and every month until the neonatal period. RV PD and LV PD were recorded and subsequently traced using a tablet digitizer in order to obtain the time velocity integral (TVI-cm), the Early (E-Peak) and Atrial (A-Peak), and the deceleration time to determine ventricular stiffness. Statistics were done using PROC-MIXED models Data are means ± SEM.

Results: 1) RV and LV TVI were significantly higher in the IDM (p < 0.05 & 0.05 respectively), 2) Both the RV and LV E/A ratios were lower in IDM but this was not statistically significant this time, 3) RV ventricular stiffness only was significantly higher (p < 0.02) in the IDM.

Conclusions: 1) IDM exhibit significant changes in ventricular function and this difference appears to be present early in gestation, 2) the etiology and the ramification of such findings need further longitudinal studies [Supported by NIH Grant # RO1-HL58296]

2 Cesarean Sectionis Unaffected by Insurance Status in Diabetic Women. WL Holcomb, Jr, DJ Mostello, GF Leguizamon, Divisions of Maternal-Fetal Medicine, St. Louis University and Washington University, St. Louis, MO.

Objective: Private insurance has been associated with an increased Cesarean section (CS) rate in some studies. We tested the hypothesis that insurance status affected CS rate among women in a program for diabetes.

Study Design: Factors potentially affecting CS risk were evaluated among 199 women with type 1 and 2 diabetes. Fisher's exact test and logistic regression were used.

Results: Ninety-six patients had private insurance (PR) and 103 had Medicaid insurance (MC). The overall CS rate was 53.8% for PR and 54.4% with MC (NS). Correcting for hemoglobin A1c, education, Whiteconst, obesity, type 1 or 2 diabetes, age, parity, maternal status, gestational age at onset of care, and large for gestational age birth weight, there was no evidence of an effect of PR on CS. The odds ratio (OR) for PR was 0.92 (0.45 - 1.85, p=0.81). The only factors significantly associated with CS were White class D or more (OR 4.9; p=0.01) and large for gestational age birth weight (OR 2.5; p=0.02). Findings were similar if scheduled repeat CS cases were excluded. The power of this study to detect a 20% difference in CS rate was 0.78.

Conclusions: Private versus Medicaid insurance did not affect the occurrence of Cesarean section in this group of high-risk women with preexisting diabetes.

3 Parity and Maternal Age Affect Excess Fetal Growth Contrariwise in Diabetes. WL Holcomb, Jr, DJ Mostello, GF Leguizamon, Divisions of Maternal-Fetal Medicine, St. Louis University and Washington University, St. Louis, MO.

Objective: Demographic factors affecting fetal growth have been studied extensively, but women with diabetes are a special case. We assessed the effect of maternal age (AGE) and parous state (PAR) on the occurrence of large for gestational age birth weight (LGA) in women with type 1 and 2 diabetes.

Study Design: A GE, PAR (versus nulliparous), race, marital status, insurance status, White class (D or more), education, gestational age at onset of care, type 1 versus 2 diabetes, and obesity (BMI>29) were evaluated by univariate and multivariate analysis as predictors of LGA.

Results: LGA occurred in 59 of 199 (25.6%) women with preexisting diabetes. Only PAR (p=0.003) and White class (p=0.001) were significantly related to LGA by univariate analysis. Multivariate logistic regression indicated PAR (odds ratio 4.6, p=0.001),AGE (odds ratio 0.91 per year; p=0.002), and White class (odds ratio 0.18; p=0.002) as significant predictors of LGA. Late pregnancy hemoglobin A1c was positively associated with LGA; addition of this variable to the logistic regression model did not change the relationships among AGE, PAR, and LGA.

Conclusions: Being parous markedly increases, and increasing maternal age decreases, the risk for LGA in women with preexisting diabetes.

4 Worse Glycemic Control Persists in African-American Women during Pregnancy. DJ Mostello, WL Holcomb, GF Leguizamon. Div. Maternal-Fetal Medicine, Dept. OB/GYN, St. Louis University and Washington University, St. Louis, MO.

Objective: To examine the effect of African-American ethnicity (AA) on glucose control in pregnancy.

Study Design: We have previously shown that AA is a risk factor for poor glycemic control at presentation for care in diabetic pregnancy. 197 women with pregestational diabetes had hemoglobin A1c level (HbA1c) measured at presentation for prenatal care and periodically throughout pregnancy. We tested associations of HbA1c and AA throughout gestation, correcting for demographic and socioeconomic variables, using logistic regression, Fisher's and Mann-Whitney tests as appropriate.

Results: When controlled for insurance status, education, severity of diabetes, obesity, diabetes type, age, parity, gestational age at entry and marital status, women of AA (n=96) were significantly more likely to have a high HbA1c (>8%) at entry into care (median 8.9 vs 7.6, p=0.01, odds ratio 3.8, p<0.01). When the last HbA1c during pregnancy was assessed, this disparity persisted (6.7 vs 6.1, p<0.01). The fall in HbA1c over the course of pregnancy in women of AA was greater (2.0 vs 1.5, p<0.01). Women of AA were more likely to be obese (p<0.01), unmarried (p<0.01), not privately insured (p<0.01), to have entered care later (p<0.04), and to have type 2 diabetes (p<0.01). These factors did not explain the effect of AA on HbA1c. Gestion rate, birth weights and gestational age at delivery were not different for women of AA.

Conclusions: Self-identified AA is a risk factor for poor glycemic control at presentation for care in diabetic pregnancy. The presence of worse glycemic control persists during pregnancy, though women of AA show greater improvement in response to medical attention.
ELEVATED PLATELET ACTIVATING FACTOR CONCENTRATIONS IN PREECLAMPSIA. B Rowland*, S Vermeiren*, W. Roudebush*. Dept. of OB/GYN, Medical Univ of SC, Charleston, SC

OBJECTIVE: To determine if an association exists between preeclampsia and circulating platelet activating factor (PAF) levels

STUDY DESIGN: We performed a cross-sectional observational study of circulating PAF concentrations that were obtained from nonpregnant males (gender controls), nonpregnant females (pregnancy controls), normotensive pregnant women in third trimester (preeclampsia controls), and third trimester preeclamptic women. PAF concentrations were measured by commercially available PAF-specific radioimmunoassay (Dupont-NEN; Boston, Mass.). The primary outcome was the difference in mean PAF concentrations between the four groups. Preeclampsia was defined by ACOG criteria. Data were analyzed by the Student's t-test, Chi-square test, ANOVA, and the Tukey test for pairwise multiple comparisons with significance established at p<0.05.

RESULTS: The mean PAF concentration (X±SE) ng/ml was significantly higher (p<0.05) in the preeclamptic group when compared to both the normotensive group and the nonpregnant female group. The two pregnant groups were similar with respect to selected demographic characteristics and gestational age at the time of collection. There was no significant difference in the mean PAF concentrations between the preeclampsic and nonpregnant male groups or between the normotensive pregnant and nonpregnant female groups. Mean PAF concentrations of the groups are listed.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Mean PAF (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsic Pregnancies</td>
<td>11</td>
<td>358±1-29.8</td>
</tr>
<tr>
<td>Normotensive Males</td>
<td>11</td>
<td>245±2-88.5</td>
</tr>
<tr>
<td>Nonpregnant Females</td>
<td>12</td>
<td>237±9-20.9</td>
</tr>
<tr>
<td>Normotensive Pregnancies</td>
<td>11</td>
<td>217±9-25.9</td>
</tr>
</tbody>
</table>

CONCLUSIONS: PAF concentrations are increased in pregnancies affected with preeclampsia. PAF may serve as a marker for the increased platelet aggregation and thromboxane production that occurs in preeclampsia.

SHOULD THE DEFINITION OF PREECLAMPSIA INCLUDE A RISE IN DIASTOLIC BLOOD PRESSURE ≥15 MM Hg? RF Levine, for the CPEP Study Group, NICHD, Bethesda, MD

OBJECTIVE: To compare baseline characteristics and perinatal outcomes in normotensive women who did or did not develop a ≥15 mm rise in diastolic pressure with proteinuria (normotensive preeclampsia, NPE).

STUDY DESIGN: We studied 4592 women from the Calcium for Preeclampsia Prevention (CPEP) trial who delivered ≥20 wks. Pregnancy-associated hypertension (PAH) was a diastolic >15 mm rise twice 4-168 hr apart. Proteinuria was defined as + or + + or protein/creatinine ≥20.35. NPE was proteinuria within 5 days of a diastolic rise over baseline ≥15 mm Hg twice 4-168 hr apart in a woman without PAH. Baseline blood pressure was the mean of measurements at 2 clinic visits before 22 wks. Normal women were those who did not develop PAH or NPE. Perinatal morbid/mortal was RDS, requiring ventilatory support, seizures, IVH grade 3-4, necrotizing enterocolitis, and/or death.

RESULTS: Except for greater body mass index (p<0.001), baseline characteristics of women who developed NPE were similar to normal women. Unlike women who developed PAH or preeclampsia, they did not have higher systolic and diastolic pressures, greater % non-white race, and lower % smoking. Women with NPE had no fatal or NICU deaths and only one (1.5%) vs. 20 (0.6%) normal women had a placental abruption. Although women with NPE had larger babies and a doubled rate of delivery by section, there was little evidence of adverse perinatal outcomes.

<table>
<thead>
<tr>
<th>N</th>
<th>Normal 3149</th>
<th>NPE 80</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induced labor (%)</td>
<td>11.3</td>
<td>10.0</td>
<td>NS</td>
</tr>
<tr>
<td>Delivery by section (%)</td>
<td>13.0</td>
<td>27.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Delivery &lt;34 wks (%)</td>
<td>4.2</td>
<td>2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>3201</td>
<td>3867</td>
<td>0.01</td>
</tr>
<tr>
<td>Birthweight &lt;2500 g (%)</td>
<td>8.3</td>
<td>6.3</td>
<td>NS</td>
</tr>
<tr>
<td>Birthweight &gt;4000 g (%)</td>
<td>6.1</td>
<td>12.5</td>
<td>0.05</td>
</tr>
<tr>
<td>SGA (&lt;10th, %) race-adjusted</td>
<td>8.3</td>
<td>13.8</td>
<td>NS</td>
</tr>
<tr>
<td>Perinatal morbid/mortal (%)</td>
<td>5.7</td>
<td>8.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

CONCLUSION: During normotensive pregnancy a ≥15 mm rise in diastolic pressure with proteinuria appears to be benign and is not a useful clinical construct.
VALIDITY OF COMMONLY USED DEFINITIONS OF HYPERTENSION IN PREGNANCY. J. Zhang, M. Klebanoff, J. M. Roberts, NICHD, NIH, Bethesda, MD; Magee Womans Research Institute, Pittsburgh, PA.

OBJECTIVE: Definitions of hypertension in pregnancy have never been carefully validated. This study is to examine quantitatively the ability of commonly used definitions of this syndrome to identify adverse outcomes.

STUDY DESIGN: We included 9,133 singleton, nulliparous pregnancies with early prenatal care in a large prospective cohort study. Severe maternal and perinatal morbidity and mortality were used as the outcome measurements (e.g., perinatal death, very premature birth, severe SGA, abruptio placentae, low Apgar score, cesarean delivery and convulsion). Sensitivity, specificity and positive predictive value for the outcomes were compared among various definitions.

RESULTS: Hypertension in pregnancy, preeclampsia in particular, is a significant risk factor for severe adverse maternal and perinatal outcomes. However, most of the commonly used definitions have poor sensitivity and specificity. The predictivity of the poor outcomes by blood pressure alone is no better than guessing. Isolated mild systolic hypertension and mild hypertension occurring for the first time in labor (intrapartum hypertension) were not associated with the adverse outcomes.

CONCLUSION: Neither blood pressure nor proteinuria and proteinuria is an accurate predictor for severe adverse maternal and perinatal outcomes. Isolated systolic hypertension and intrapartum hypertension are not at all predictive of adverse outcome.

ALTERATIONS IN LEVELS OF SERUM IGF-I AND IGFBP-1 IN THE SECOND TRIMESTER OF PREGNANCY IN WOMEN WHO ULTIMATELY DEVELOP PREECLAMPSIA. W.A. Grodman1, W.R. Kaiser1, Dept. of Ob/Gyn, Northwestern University Medical School, Chicago, IL.

OBJECTIVE: To determine whether second-trimester serum levels of insulin-like growth factor-I (IGF-I), and insulin-like growth factor-binding protein-1 (IGFBP-1) differ between women who become preeclampsia and women who are normotensive throughout their pregnancy.

STUDY DESIGN: 205 women with no history of hypertension, diabetes mellitus, or renal disease donated serum samples during either the early (16-20 weeks) or late (24-28 weeks) second trimester of pregnancy. Twelve women eventually developed preeclampsia (PE), none of whom had abnormal glucose tolerance. These cases were matched with 24 controls who remained normotensive throughout their pregnancy. Three groups based on the presence or absence of pulmonary edema were 1) PE, 2) Controls with pulmonary edema, and 3) Controls without pulmonary edema.

RESULTS: There were no significant differences between the study and control groups with respect to multiple demographic factors. As demonstrated by analysis of variance, there were also no significant differences between the groups with respect to serum levels of IGF-I and IGF-BP-1.

CONCLUSIONS: Serum levels of IGF-I and IGFBP-1 are not altered in the second trimester of pregnancy in women who are destined to have preeclampsia. Alterations of these proteins once clinical signs of preeclampsia are evident may not be reflective of trophoblastic dysfunction but instead may reflect reduced clearance resulting from the physiologic abnormalities of preeclampsia.

PREECLAMPSIA WITH AND WITHOUT PULMONARY EDEMA: AN ECHOCARDIOGRAPHIC ANALYSIS. S. Verma1, J. Scard02, J. Ellings2, S. Clauhan2, Dept. of OB/GYN, *Medical Univ. of SC, Charleston, SC, and 2Spartanburg Regional Medical Center, Spartanburg, SC.

OBJECTIVE: To compare the echocardiographic measurements of periparturients with preeclampsia and pulmonary edema to those with preeclampsia alone.

STUDY DESIGN: We performed a prospective observational analysis of echocardiographic measurements obtained from peripartum preeclampsia patients divided into two groups based on the presence or absence of pulmonary edema. Preeclampsia was defined as hypertension (> 140/90 mmHg) combined with proteinuria (> 300 mg/24 hrs or ≥1+ on urine dip 6 hrs apart). Pulmonary edema was defined by the presence of both radiographic criteria and an arterial blood gas of PO2 < 60 mmHg. Echocardiographic measurements including chamber dimensions and ejection fractions were determined by 3D M-mode. Demographic, laboratory, and mean arterial blood pressure (MAP) data were also collected for analysis. Data were analyzed by the Student’s t-test, chi square test and Fischer’s exact test with significance established at p<0.05.

RESULTS: Thirty preeclampsia patients were equally divided into two groups based on the presence or absence of pulmonary edema. Both groups were similar with respect to selected demographics, gestational age at delivery, number of antepartum patients, and number with preexisting chronic hypertension. Patients with pulmonary edema had a significantly greater mean MAP (mmHg) (128±14 vs 112±14; p=0.01) (X±SD), mean left ventricular diastolic diameter (cm) (5.9±0.7 vs 5.1±0.5; p=0.001), and mean left ventricular systolic diameter (cm) (4.9±0.8 vs 3.2±0.7; p=0.001) than the patients with preeclampsia alone. Patients with pulmonary edema demonstrated a significantly lower mean cardiac ejection fraction (%) (58±5 vs 66±1; p=0.02) and mean serum albumin level (g/dl) (2.1±0.4 vs 2.8±0.5; p=0.005) compared to those patients without pulmonary edema.

CONCLUSIONS: Preeclampsia with pulmonary edema is associated with altered hemodynamic function and decreased serum albumin concentrations compared to preeclampsia without pulmonary edema.
230 PLACENTAL EXPRESSION OF BAX AND BCL-2 IN PRE-ECLAMPSIA.

A.D. Allen*, S.R. Wells, B.A. Lessay*, Dept. Ob/Gyn, Univ. of NC, Chapel Hill, NC.

OBJECTIVE: To determine if the mediators of apoptosis, Bcl-2 and Bax, are differentially expressed in placentas from pre-eclamptic pregnancies compared to controls.

STUDY DESIGN: Placental samples from 31 pre-eclamptic and 31 gestational age-matched controls were frozen in liquid nitrogen immediately after delivery. Six micrometer cryosections were then analyzed using immunohistochemistry Rabbit polyclonal antibody Bcl-2 and Bax antibodies were used followed by avidin-biotin immunoperoxidase staining to evaluate expression in the placent al villus trophoblast, stroma, and endothelial cells.

Results: Intensity of staining was quantified by calculating an H-score (a continuous rank test). Observers were blinded to the study group of each subject during analysis. A p value of <0.05 was considered significant using the Wilcoxon sign-rank test.

RESULTS: There was no statistically significant difference in the expression of Bcl-2 or Bax in the villus trophoblast, stroma, or endothelium.

Median H-scores are presented in the following table:

<table>
<thead>
<tr>
<th>Study (n=31)</th>
<th>Control (n=31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bax</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trophoblast</td>
<td>1.10 (0.60, 1.80)</td>
<td>1.60 (0.60, 2.00)</td>
</tr>
<tr>
<td>Stroma</td>
<td>1.80 (1.40, 2.30)</td>
<td>1.60 (1.20, 2.30)</td>
</tr>
<tr>
<td>Endothelium</td>
<td>1.40 (1.10, 1.80)</td>
<td>1.60 (1.20, 1.85)</td>
</tr>
<tr>
<td>Bcl-2</td>
<td>3.55 (2.80, 5.70)</td>
<td>3.30 (2.80, 3.60)</td>
</tr>
<tr>
<td>Stroma</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
</tr>
<tr>
<td>Endothelium</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
</tr>
</tbody>
</table>

Data is presented as median (inter-quartile range). NS - not significant.

CONCLUSION: Altered expression of Bcl-2 and Bax is not seen in placentas from pre-eclamptic women compared to controls.

232 HYPERTENSIVE DISORDERS IN TWIN VERSUS SINGLETON PREGNANCIES.

BM Sibai, MD for the MFMUN, Bethesda, MD.

OBJECTIVE: To compare the perinatal effects of gestational hypertension (GHTP) and preeclampsia when these complications develop in twin and in singleton pregnancy.

STUDY DESIGN: Secondary analysis of prospective data from women with twin (n=684) and singleton (n=2,946) gestation enrolled in 2 separate multicenter trials of low-dose aspirin for prevention of preeclampsia. Endpoints were rates of GHTP, preeclampsia, and perinatal outcomes in women with hypertensive disorders. In twins, we also compared outcome in the hypertensive to normotensive group.

RESULTS: Compared to singleton pregnancies, women with twins had higher rates of GHTP (RR=2.0, 95% CI, 1.6-2.6) and preeclampsia (RR=2.6, 95% CI, 2.0-3.4). Compared to singleton pregnancies, women with GHTP in twins had higher rates of delivery at ≤37 wks (51.1% v 5.9%, p≤0.0001) and ≤35 wks (18.2% v 7.0%, p≤0.04) in addition, when outcomes associated with preeclampsia were compared, women with twins had higher rates of delivery at both ≤37 wks (66.7% v 19.6%, p≤0.0001) and ≤35 wks (35.4% v 6.3%, p≤0.0001), and more abruptio placentae (4.7% v 0.7%, P<0.007). Interestingly, among women with twins, those who remained normotensive had significantly more adverse perinatal outcome than those who developed hypertensive complications.

CONCLUSIONS: Compared to women with singleton gestation, women with twins had higher rates of hypertensive complications and higher rates of adverse neonatal outcome when hypertensive complications developed. On the other hand, among women with twins, adverse perinatal outcomes were significantly higher in those who remained normotensive.

231 CORTICOSTEROID DOSING AND LABORATORY CHANGES IN PATIENTS WITH HEMOLYSIS, ELEVATED LIVER ENZYMES AND LOW PLATELET COUNT (HELLP SYNDROME). JM O'Brien, JR Barton, DA Milligan, Perinatal Diagnostic Center, Central Baptist Hospital, Lexington, KY.

OBJECTIVE: The purpose of this study was to determine if corticosteroid administration in patients with antepartum HELLP syndrome altered laboratory values diagnostic for the disease.

STUDY DESIGN: Pregnancies with antepartum HELLP syndrome (defined by Sibai (platelet count <100,000 per mm³, AST ≥20 U/L, and LDH >600 U/L) managed between March 1995 and July 1999 were reviewed. Patients were classified on the basis of their exposure to steroid and dose.

RESULTS: Thirty-seven patients were identified with antepartum HELLP syndrome. Eleven patients did not receive corticosteroid, 15 were given a standard dose, and 11 underwent high dose therapy. The observed changes in laboratory values are shown in the Table. For each laboratory assessed, the groups differed significantly, all p ≤ 0.002. A significant improvement in platelet count was noted in the high dose vs standard groups, p≤0.04.

CONCLUSIONS: Antepartum administration of corticosteroids in patients with HELLP syndrome improves platelet count and reduces liver enzyme abnormalities. This effect is dose dependent. Any trial evaluating the efficacy of corticosteroids in patients with HELLP syndrome should consider a higher dose than standard regimens for fetal lung maturity enhancement.

233 THE PARADOXICAL PROTECTIVE EFFECT OF SMOKING AND PREECLAMPSIA: IS CARBON MONOXIDE THE MISSING LINK?


BACKGROUND: It has been speculated that smokers have a reduced incidence of preeclampsia (PET) due to lower expansion of their plasma volume, inhibition by nicotine of the production of thromboxane, the hypotensive effect of thioctanylate (Am J Obstet Gynecol 1997; 177:166-64) and down-regulation of endothelial sensitivity by chronic endothelial injury (Placenta 1999;20:273-9). Smokers are exposed to high concentrations of Carbon Monoxide (CO) that lice Nitric Oxide produce arterial relaxation and prevent platelet aggregation.

OBJECTIVE: To compare the End Tidal CO (ETCO2) breath levels in women with or without pregnancy induced hypertension (PIH) and PET.

STUDY DESIGN: We prospectively performed ETCO2 measurements corrected for ambient CO (ETCO2c), using a CO-StarTM End Tidal Breath Analyzer (Natus Medical Inc., CA). The study group included 22 women in late gestation (≥31 Wk) with hypertension or symptoms of PET. The control group included 20 normotensive women. In addition, ETCO2c was determined during the first post-partum day in 20 non-smoking in others, 31 mothers exposed to the other, among women with twins, adverse perinatal outcomes were significantly higher in those who remained normotensive.

RESULTS: The mean ± SD ETCO2c measurements were significantly lower (p≤0.001) in the hypertensive compared to the control group, 1.17±0.35 vs 1.70±0.54 ppm, median (range) 1.10 (0.70-4.90) vs 1.65 (0.70-3.20). The study women had a significantly higher number of low (<1.2 ppm) ETCO2c measurements, 13 (59.1%) vs 1 (5.0%), p=0.001. The ETCO2c levels remained significantly lower compared to the control group when the study group was divided into women with PIH (n=11) or with PET (n=11). 1.10±0.37 and 1.15±0.41 ppm, respectively. The post partum maternal ETCO2c levels were significantly higher (p<0.001) in active smokers 3.8±5.65 ppm compared with both non smokers 1.3±0.84 and passive smokers 1.0±0.88 ppm.

CONCLUSIONS: Our findings suggest that CO formation may be significantly lower in women with PIH and PET. Hence, CO could be a contributory role in the apparent paradox of the seemingly “protective” effect of smoking to decrease the risk of preeclampsia.

S86 SMFM Abstracts

January 2000
Am J Obstet Gynecol
MATERNAL HEMODYNAMICS, CYTOKINES AND ENDOTHELIAL ACTIVATION IN WOMEN AT RISK FOR PREECLAMPSIA. Diarrhoea, A Farrand,a, G McDonald,b, DA Brateng,c, TR Easterling, Dept of Ob/Gyn, Univ of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA.

OBJECTIVE: To evaluate the differences in cardiac output (CO), tumor necrosis factor-α (TNF-α), TNF receptors (TNFR-I and TNFR-II), and vascular cell adhesion molecule-1 (VCAM-1) between women with risk factors for preeclampsia and women without risk factors.

STUDY DESIGN: An ongoing prospective study of two groups: 1) Low Risk (LR) women without risk factors for preeclampsia, and 2) High Risk (HR) women with a prior history of preeclampsia, chronic hypertension, elevated second trimester blood pressures, or obesity. Cardiac output, TNF-α, TNFR-I, TNFR-II, and VCAM-1 are measured in the second trimester. TNF-α has a short half-life; therefore, TNFR-I and TNFR-II, which have longer half-lives, reflect TNF-α activity, are also measured.

RESULTS: Thirty-two women are in the HR and nine are in the LR group. Maternal age, parity, and gestational age do not differ significantly between the groups. Weight (105.1±25.7 vs 70.1±18.8 kg) and MAP (97.0±10.7 vs 79.5±7.8 mmHg) do differ significantly between HR and LR groups (p<0.01). The data are compared by the two-tailed t test and listed as mean±sd.

<table>
<thead>
<tr>
<th>High Risk (n=32)</th>
<th>Low Risk (n=9)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO (L/min)</td>
<td>9.7±1.8</td>
<td>7.7±1.9</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>194.3±70.1</td>
<td>6.4±12.5</td>
</tr>
<tr>
<td>TNFR-I (pg/mL)</td>
<td>532 ±110.9</td>
<td>441.5±89.3</td>
</tr>
<tr>
<td>TNFR-II (pg/mL)</td>
<td>14.4±20.2</td>
<td>8.1±7.9</td>
</tr>
<tr>
<td>VCAM-1 (ng/mL)</td>
<td>510.9±145.0</td>
<td>440 ±112.9</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Women with risk factors for preeclampsia as compared to women without risk factors have: 1) elevated cardiac output, and 2) increased activation of maternal inflammatory response. An exaggerated maternal inflammatory response in pregnancy is believed to be involved in the pathogenesis of preeclampsia. Preeclampsia prevention strategies should be aimed at this population since aberrant hemodynamics and differences in cytokine activation are detectable early in pregnancy in these women.
239 ANGIOTENSIN I CONVERTING ENZYME AND ANGIOTENSINOGEN GENE INTERACTION ASSOCIATED WITH PREECLAMPSIA. J. Knaulons", L. Nelson", K. Ward, Deps. of Ob/Gyn and Human Genetics, Univ of Utah School of Medicine, Salt Lake City, UT

OBJECTIVE: We tested the hypothesis that the angiotensin I converting enzyme Insertion / Deletion (ACE I/D) polymorphism was associated with preeclampsia. We also investigated whether there was a gene interaction between the ACE I/D variant and the angiotensinogen (AGT) T235M, a variant known to be associated with preeclampsia.

STUDY DESIGN: The genotype frequencies of the ACE I/D and the AGT T235M polymorphisms were examined in Caucasian obstetrical patients who developed preeclampsia, (n=268) in comparison to Caucasian obstetrical patients without hypertension delivering an AGA term infant, (n=202) as control group. Genotypes were obtained using the polymerase chain reaction (PCR) to amplify the region of the MTHFR gene around nucleotide 677. The PCR products were digested with the restriction enzyme Hinf I. The digested PCR products were size fractionated on agarose gels and visualized with ethidium bromide.

RESULTS: The T allele frequency was lower in preeclampsia patients compared to controls. The allelic frequency of the T235M polymorphism was not different between the study and control groups. The genotype frequencies of the ACE I/D and the AGT T235M genotype were also similar between the two groups.

CONCLUSION: There is no correlation between the MTHFR C677T polymorphism and preeclampsia with or without HELLP syndrome in our population.

240 VASCULAR REACTIVITY IN PREGNANT MICE LACKING A FUNCTIONAL INDUCIBLE NITRIC OXIDE SYNTHASE. GA Sade, R. Garfield*, Deps. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX

OBJECTIVE: To examine the role of inducible nitric oxide synthase (iNOS) in regulation of vascular tone during pregnancy using transgenic mice lacking a functional iNOS (KO) mice.

STUDY DESIGN: Two millimeter segments of aorta were obtained from normotensive, midpregnant (day 14) and term (day 18) female iNOS KO mice (iNOS2 -/-) from Jackson Laboratory and their corresponding wild-type control (iNOS2 +/+). The rings were mounted in a small vessel myograph and responses to pressor and relaxant agents were studied. ANOVA and Student's t-tests were used for statistical analysis and a P<0.05 denoted statistical significance.

RESULTS: Contractions to depolarizing solution were not significantly different between the groups. Phenylephrine-induced (10^4 to 10^5 M) contraction, in the absence (Figure) or presence of the NOS inhibitor N^6-nitro-L-arginine methyl ester (L-NNAME, 10^5 M), was significantly attenuated in nonpregnant KO but increased at mid (Figure) and term gestation as compared to their corresponding wild-type control (Figure). Endothelial cell-dependent relaxation by acetylcholine (10^6 to 10^5 M) was greater in nonpregnant KO compared to control. As compared to nonpregnant mouse, acetylcholine response in pregnancy was not altered in the KO mice, whereas it was greater at mid-gestation but not at term in the wild-type control animals. Relaxations by both NO donor sodium nitroprusside (10^5 to 10^4 M) were not significantly different between the various groups.

CONCLUSIONS: Lack of a functional iNOS changes the direct and endothelium-mediated vascular responses. The physiological and pathological implications in pregnancy are significant and differ from those in the nonpregnant state.
242 ARE TYROSINE HYDROXYLASE SHORT TANDEM REPEATS ASSOCIATED WITH PREECLAMPSIA? JR Jato, K Hashiguchi, L Nelson, K Ward, Dept of Ob/Gyn, School of Medicine Univ of Utah, Salt Lake City, UT.

OBJECTIVE: Tyrosine hydroxylase (TH) is the rate-limiting enzyme in catecholamine synthesis. Catecholamine turnover is possibly associated with a TH short tandem repeat (STR), which is located in the first intron of the human TH gene. Recently, it was reported that TH activity was enhanced in preeclampsia (PE) and TH-STR was implicated in the development of essential hypertension (HT). We tested whether the TH-STR is associated with PE.

STUDY DESIGN: Blood samples were collected from 124 normotensive controls and from 174 Caucasian pregnant women who had a hypertension disorder in pregnancy. Genomic DNA was prepared and the TH-STR was amplified using PCR. PCR products were run on an ABI 373A sequencer. TH-STR alleles were assigned using Genescan software. Five typical alleles were identified and designated A, B, C, D, and E.

RESULTS: No significant difference was found in allele frequencies between the hypertensive group and control group. Allele frequencies were as follows:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>242</td>
<td>149</td>
<td>.125</td>
<td>143</td>
<td>.339</td>
</tr>
<tr>
<td>All patients</td>
<td>250</td>
<td>144</td>
<td>.126</td>
<td>141</td>
<td>.339</td>
</tr>
<tr>
<td>chronic HT</td>
<td>292</td>
<td>119</td>
<td>119</td>
<td>143</td>
<td>.357</td>
</tr>
<tr>
<td>mild PE</td>
<td>257</td>
<td>147</td>
<td>.154</td>
<td>132</td>
<td>.309</td>
</tr>
<tr>
<td>severe PE</td>
<td>250</td>
<td>150</td>
<td>.107</td>
<td>143</td>
<td>.350</td>
</tr>
<tr>
<td>HELLP</td>
<td>200</td>
<td>133</td>
<td>.100</td>
<td>167</td>
<td>.409</td>
</tr>
</tbody>
</table>

CONCLUSION: Our results suggest that this polymorphism of TH-STR is not associated with the development of PE.

244 TUMOR NECROSIS FACTOR ALPHA POLYMORPHISMS, PLASMA LEVELS, AND SEVERE PREECLAMPSIA. JC Livingston, V Park, JR Barton, B Haddad, D Crouse, S Eltering, M Quasney, B Mahe, BM Shai, University of Tennessee-Memphis, Memphis, TN and Central Baptist Hospital, Lexington, KY.

OBJECTIVES: Overproduction of tumor necrosis factor alpha (TNFα), an inflammatory cytokine, can be harmful to endothelial cells. Patients with a homozygous mutation in the TNFα gene secrete higher levels of TNFα both in vivo and in vitro. Elevated maternal (M) levels of TNFα have been reported in pregnancies complicated by pre eclampsia (PRE). The study purpose was to determine whether maternal or fetal (F) polymorphisms at the G−251/A and G−308/A sites are associated with severe pre eclampsia.

STUDY DESIGN: We performed a prospective cross-sectional study to compare the M and F phenotype frequencies. Patients with severe pre eclampsia (n=114) were matched for gestational age to normotensive pregnancies (n=94). Cord blood was obtained on 88 control pregnancies and 89 pre eclamptic patients. DNA was extracted from leukocytes and PCR was performed. PCR products were digested with the appropriate restriction enzymes and fractionated by gel electrophoresis. Maternal plasma TNFα levels were assayed by dual monoclonal antibody sandwich ELISA technique. Severe pre eclampsia (n=76), control (n=51). Chi-square test and Student’s t-test were performed to determine statistical significance.

RESULTS: Differences in phenotype frequencies were not statistically significant. (Table) Moreover, mean maternal TNFα plasma levels in severe pre eclampsia patients were not significantly different from controls (32.6 pg/ml vs 33.3 pg/ml, p=0.92).

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>G-251</th>
<th>Normal</th>
<th>High secretor</th>
<th>G-308</th>
<th>Normal</th>
<th>High secretor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (M)</td>
<td>0.600</td>
<td>0.340</td>
<td>0.989</td>
<td>0.011</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (PRE (M)</td>
<td>0.715</td>
<td>0.287</td>
<td>0.974</td>
<td>0.029</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (F)</td>
<td>0.705</td>
<td>0.297</td>
<td>0.951</td>
<td>0.069</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (PRE (F)</td>
<td>0.672</td>
<td>0.328</td>
<td>0.970</td>
<td>0.030</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSION: Maternal and fetal TNFα polymorphisms are not associated with severe preeclampsia. In addition, plasma levels of TNFα are not elevated in severe preeclampsia.

243 MYELOPEROXIDASE IN MATERNAL AND CORD PLASMA IN PREECLAMPSIA. S Bruckman, BD Raynor, KT Jiang, N Santanam, S Parthasarathy, Emory University, Department of Gynecology and Obstetrics, Atlanta, Georgia.

OBJECTIVE: Neutrophil activation has been demonstrated in preeclampsia. Myeloperoxidase (MPO) is a product of neutrophil activation which is also a potent stimulus of lipid peroxidation, another pathogenic process involved in preeclampsia.

STUDY DESIGN: Plasma was collected from women admitted for delivery at 35 weeks or diagnosed with preeclampsia. Immediately after delivery, plasma was collected from umbilical cord. Plasma was stored at −80°C. MPO concentration was determined with ELISA (R&D Systems, Minneapolis). Statistical analysis used unpaired t test.

RESULTS: A total of 20 mother-baby pairs from normal and 18 from preeclamptic pregnancies were analyzed. Mean (SD) maternal MPO levels were not different between preeclampsia (5.5±9.1 ng/ml) and normals (3.5±9.1 ng/ml). Cord MPO levels were also not different (9.9±17.5 ng/ml preeclampsia; 19.2±30.8 ng/ml normal). The variance in both maternal and cord samples was large. 4 mothers and 5 fetuses of 18 preeclamptics had no detectable MPO as did 6 mothers and 4 fetuses of 20 normals.

CONCLUSIONS: MPO may not be a reliable marker of neutrophil activation in preeclampsia. Other factors may effect MPO production in this setting.

245 APOLIPOPROTEIN E E3/E4 HETEROZYGOSITY IS MORE PREVALENT IN PATIENTS WITH PREECLAMPSIA. H Bakran, J Nelson, K Ward, Dept of Human Genetics, Dept OB/GYN, University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: The Apolipoprotein E (Apo E) is a glycoprotein involved in lipid metabolism. Various Apo E alleles have been associated with cardiovascular and other diseases. Our objective was to test for an association between Apo E and pregnancy-induced hypertension (PIH) and preeclampsia (PE) in our study population.

STUDY DESIGN: DNA samples were obtained from patients presenting with pregnancy-induced-hypertension and mild, moderate and severe preeclampsia (n=156) and normotensive controls (n=105). Apo E genotypes were determined using a published PCR assay, revealing six common genotypes.

RESULTS: Preliminary data from 135 PE patients with 21 PIH patients shows a significant increase of the E3/E4 genotype.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>PE only</th>
<th>PE &amp; PIH Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>E2/E2 (0)</td>
<td>90%</td>
<td>(2) 1.9%</td>
</tr>
<tr>
<td>E2/E3 (12)</td>
<td>8.5%</td>
<td>(15) 9.6%</td>
</tr>
<tr>
<td>E3/E3 (74)</td>
<td>54.8%</td>
<td>(96) 55.1%</td>
</tr>
<tr>
<td>E3/E4 (41)</td>
<td>30.4%</td>
<td>(45) 28.9%</td>
</tr>
<tr>
<td>E4/E4 (6)</td>
<td>4.4%</td>
<td>(6) 3.3%</td>
</tr>
<tr>
<td>E2/E4 (2)</td>
<td>1.5%</td>
<td>(4) 2.6%</td>
</tr>
</tbody>
</table>

CONCLUSION: Our results indicate that the Apo E genotype E3/E4 may be associated with a risk for development of PE and PIH.

OBJECTIVE: Elevated plasma homocysteine (Hcy) is a risk factor for occlusive vascular disease in non-pregnant adults and during pregnancy is associated with PE, placental abruption and infarction. We sought to determine whether mid-trimester Hcy levels are elevated in women who develop PE, PIH or IUGR

STUDY DESIGN: Five hundred eighty women with plasma zinc levels below the median at 19 wks were randomized to receive either zinc (n=294) or placebo (n=286) until delivery. Hcy levels were measured by HPLC-fluorescence detection method in all available specimens (zinc n=231, placebo n=206) at 25 and 37 wks. Of these, 16 women developed either PIH (n=12) or PE (n=4) and 22 pregnancies were complicated by IUGR (birthweight less than 10th percentile for GA by Breastn standards).

RESULTS: Maternal demographics including age, parity, GA and zinc supplementation were similar between the groups. In women that developed either PIH or PE, mean Hcy levels were similar at 26 (5.2 ± 1.3 μM vs. 4.7 ± 1.9 μM, p=.26), while at 37 wks gestation, mean Hcy levels were significantly higher in women with PIH/PE (6.6 ± 2.1 μM vs. 5.3 ± 1.9 μM, p<.006). Hcy levels in IUGR pregnancies were similar to controls at both 26 (4.9 ± 1.8 μM vs. 4.7 ± 1.9 μM, p=.61) and 37 (5.7 ± 1.9 μM vs. 5.3 ± 1.9 μM, p=.43) wks gestation.

CONCLUSION: Plasma Hcy levels elevated at 37 wks in women with PIH/PE, but not at 26 wks. There were no differences in Hcy at either 26 or 37 wks in women who subsequently delivered an IUGR infant.

247 BAROREFLEX FUNCTION IN MILD PREECLAMPSIA. L Leduc, D Birnsteín, Dept Obstetrics & Gynecology, Ste-Justine Hospital, U de Montréal, Montreal, Quebec, Canada.

PURPOSE: To document the baroreflex function (BR) in mild preeclampsia in using the valsalva maneuver (vals).

STUDY DESIGN: The vals tests the afferent, central and efferent parasympathetic and sympathetic baroreflex pathways. Ambulatory blood pressure monitoring, heart rate (HR) and continuous R-R intervals (msec) (Holter/ambulatory blood pressure, AMP model AM 5600) were measured in 8 pregnant women (28.6±4.2 y.o.) between 39-52 weeks (31.0±0.9) (P), in 11 mild preeclampsia (PE) (29.0±7.2 y.o.; 31.7±3.5 weeks) and in 16 normotensive non pregnant (NP) women (29.6±5.3 y.o.). Women were at rest in supine position for 5 minutes before recording R-R intervals. A sampling of 2 minutes was analyzed. The vals was carried out with a p<0.05. Resting (HR) was used as a covariate to analyze the data.

RESULTS: 1) There was no difference in baseline of R-R with or without nicotine administration; 2) 3 out of 6 rabbits showed decreased FML after nicotine administration during ischemia (P<0.05); 3) 4 of 6 rabbits showed increased FML at 60 minute reperfusion after nicotine administration (P<0.05).

CONCLUSION: Nicotine appears to decrease leukocyte adhesion to vascular endothelial cells in the ischemia condition in vivo.

SPECULATION: Leukocyte activation and increased leukocyte-endothelial adhesion have been observed in preeclampsia. The effects of nicotine in decreasing leukocyte-endothelial adhesion might be significant in the epidemiology of preeclampsia since smoking is associated with a reduced risk for this pregnancy disorder.

248 EFFECTS OF NICOTINE ON LEUKOCYTE ADHESION TO UTERINE VASCULAR ENDOTHELIUM IN PREGNANT RABBITS AS ASSESSED BY IN VIVO INTRAVITAL MICROSCOPY. Paul Speer, C. David Atair, Yuping Wang, Dept. of OB/GYN, LSU Medical Center, Shreveport, LA.

OBJECTIVE: To study the effects of nicotine on leukocyte adhesion to vascular under ischemia/reperfusion conditions during pregnancy.

STUDY DESIGN: Effects of nicotine on leukocyte adhesion to uterine vasculature were assessed by in vivo intravital microscopy. Leukocyte adhesion was determined by fluorescent marked leukocytes (FML) on vascular endothelium. Briefly, pregnant New Zealand rabbits (n=6) underwent laparotomy with general anesthesia. Intravenous and intra-arterial catheters were placed in the rabbit ears. EKG was monitored during the entire procedure. Fluorescent dye was injected to mark leukocytes. Images were continuously recorded on videotape and the images of a baseline level of epifluorescence before ischemia, during ischemia (occluding uterine artery), and 60 minutes after reperfusion with or without administration of nicotine were chosen for the evaluation of leukocyte adhesion as measured by FML. Each rabbit used its own baseline level as control.

RESULTS: 1) There was no difference in baseline of FML with or without nicotine administration; 2) 3 out of 6 rabbits showed decreased FML after nicotine administration during ischemia (P<0.05); 3) 4 of 6 rabbits showed increased FML at 60 minute reperfusion after nicotine administration (P<0.05).

CONCLUSION: Nicotine appears to decrease leukocyte adhesion to vascular endothelial cells in the ischemia condition in vivo.

SPECULATION: Leukocyte activation and increased leukocyte-endothelial adhesion have been observed in preeclampsia. The effects of nicotine in decreasing leukocyte-endothelial adhesion might be significant in the epidemiology of preeclampsia since smoking is associated with a reduced risk for this pregnancy disorder.


OBJECTIVE: Paraoxonase (PON) is an HDL-associated enzyme implicated in atherosclerosis. We hypothesized that PON may also have a role in preeclampsia (PE), since PE has pathophysiological similarities to atherosclerosis. We examined whether a functional PON gene variant is a risk factor for PE.

STUDY DESIGN: Blood samples were collected and DNA was extracted from 160 normotensive pregnant controls and 276 women with PE. All controls and cases are Caucasian. The polymerase chain reaction was used to amplify the region of the PON gene that includes position 192 Gln → Arg mutation followed by allele-specific restriction digestion with AlwI for mutation detection. The DNA variant without a restriction site is referred to as A for A, and the variant containing the restriction site as B A and B alleles frequencies were analyzed in PE cases and normotensive pregnant controls and then did an expiratory strain with the mouth closed. The standard

RESULTS: *ref. Serrato and Marian **p<0.001

CONCLUSION: Results indicate that PON gene variant does not play a role in the pathophysiology of PE. Although PE share many clinical features of atherosclerosis, these and other data highlight differences in risk factors and susceptible populations.
250  SERUM LEVELS OF ADHESION MOLECULES IN WOMEN WITH PREECLAMPSIA. H. Zeiser, J. C. Livingston, C. Schatten*, C. Tempfer*, M. Knöller*, BM Sibai, P. Husslein*, Dept. of Ob/Gyn, University Hospital of Vienna, Vienna Austria and Dept of Ob/Gyn, University of Tennessee- Memphis, TN.

OBJECTIVES: Preeclampsia is a disease of endothelial cell damage. Adhesion molecules anchor immune competent cells to endothelial cells which can result in endothelial cell damage. The purpose of this study was to investigate whether intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) platelet endothelial cell adhesion molecule-1 (PECAM-1), and P-selectin serum levels are associated with the need for delivery due to worsening preeclampsia.

STUDY DESIGN: In a matched pair study, ICAM-1, VCAM-1, PECAM-1 and P-selectin serum levels were measured in women with preeclampsia (n=40) and normotensive pregnant controls (n=40). Serum levels were determined using a sandwich enzyme-linked immunosorbent assay. Multivariate logistic regression models were used to analyze serum levels of adhesion molecules in relation to preeclampsia and the necessity for delivery due to preeclampsia.

RESULTS: Calculating a multivariate logistic regression with forward selection, ICAM-1, VCAM-1, systolic blood pressure (SBP) and gestational age (GA) revealed a significant difference in preeclampsia versus normotensive women. (WAld-statistic, P=0.005, P=0.005, P=0.0001, and P=0.004, respectively). VCAM-1 and P-selectin were not associated with preeclampsia. VCAM-1, SBP and GA revealed a statistically significant influence on the need for delivery due to worsening preeclampsia (WAld-statistic, P=0.002, P=0.004, and P=0.04, respectively).

CONCLUSIONS: Our data indicate that the expression of ICAM-1 and PECAM-1 is upregulated in preeclamptic patients. Moreover, the elevation of serum PECAM levels was associated with worsening preeclampsia requiring delivery.

251  PLASMA, URINARY, AND SALIVARY 8-ISO-PROSTAGLANDIN F2α LEVELS IN NORMOTENSIVE AND PREECLAMPSIC PREGNANCIES. E T McKinney, R Shouri*, RS Hunt*, RA Ahokas, and BM Sibai, Dept Ob/Gyn, University of Tennessee, Memphis, TN.

OBJECTIVE: 8-iso-PGF2α (8-isoP) is an accurate marker of oxidative stress in vivo. The purpose of our study was to measure and compare concentrations of 8-isoP in preeclamptic, normotensive pregnant and normotensive non-pregnant women.

STUDY DESIGN: Concentrations of plasma free and total, urinary and salivary 8-isoP were measured by enzyme immunoassay (EIA) after partial purification by solid phase (G6S cartridge) extraction. Urine samples were further purified by thin-layer chromatography prior to EIA analysis. Analysis was by ANOVA and Fisher's PLSD.

RESULTS: Neither free nor total 8-isoP were increased in pregnancy compared to the nonpregnant state. Concentrations of free and total plasma 8-isoP were similar in normotensive pregnancies and preeclampsia. Patients with severe preeclampsia had lower levels of urinary 8-isoP compared to normotensive patients, but the differences were not significant (p=0.10). Salivary 8-isoP levels were increased significantly in normotensive gravidas compared to nonpregnant women (p=0.01), and were significantly lower (p=0.04) in patients with severe preeclampsia compared to normotensive patients.

CONCLUSIONS: Plasma free and total 8-isoP were not increased in women with preeclampsia. In severe preeclampsia, there was a trend (p=0.1) toward reduced urinary excretion, and a significant reduction in salivary levels (p=0.04). Salivary 8-isoP concentrations may prove useful in the diagnosis of severe preeclampsia.


OBJECTIVES: To determine the frequency of fetal deterioration with expectant management of severe preterm preeclampsia and to identify biophysical markers of fetal status that may predict which pregnancies would not benefit from attempted expectant management.

STUDY DESIGN: This was an observational study of all patients with singleton gestations at <34 weeks (wk) admitted between 6/96 and 6/99 with the diagnosis of severe pre eclampsia (per ACOG criteria) and planned delivery. Subjects ultimately developing preeclampsia in comparison to those not developing preeclampsia in a population of patients being evaluated for delivery due to worsening preeclampsia.

RESULTS: Serum activin A and inhibin A levels were measured by ELISA from residual sera of patients having blood sampled for possible developing preeclampsia. Subjects ultimately developing preeclampsia (n=25) were matched to subjects developing gestational hypertension (n=25) and subjects not developing hypertensive disorders (n=25) by gestational age (GA) revealed a significant difference in preeclampsia versus normotensive women. (Wald-statistic, P=0.005, P=0.005, P=0.0001, and P=0.004, respectively). VCAM-1 and P-selectin were not associated with preeclampsia. VCAM-1, SBP and GA revealed a statistically significant influence on the need for delivery due to worsening preeclampsia (Wald-statistic, P=0.002, P=0.004, and P=0.04, respectively).

CONCLUSIONS: Our data indicate that the expression of ICAM-1 and PECAM-1 is upregulated in preeclamptic patients. Moreover, the elevation of serum PECAM levels was associated with worsening preeclampsia requiring delivery.

253  MATERNAL SERUM ACTIVIN A AND INHIBIN A LEVELS FOR PREDICTION OF PREECLAMPSIA IN PATIENTS EVALUATED FOR "R/O PREECLAMPSIA" H. Shobot, G. Messerli*, J. Canick*, Deps Ob/Gyn and Pathology,Women & Infants’ Hospital of RI, Brown University, Providence, RI.

OBJECTIVE: To demonstrate that activin A and inhibin A levels are increased in patients ultimately developing preeclampsia in comparison to those not developing preeclampsia in a population of patients being evaluated for delivery due to worsening preeclampsia.

STUDY DESIGN: Serum activin A and inhibin A levels were measured by ELISA from residual sera of patients having blood sampled for possible developing preeclampsia. Subjects ultimately developing preeclampsia (n=25) were matched to subjects developing gestational hypertension (n=25) and subjects not developing hypertensive disorders (n=25) by gestational age (GA) within one week. Clinical variables were compared by Students t-test with Bonferroni correction. Activin A and inhibin A levels were compared using Kruskal-Wallis test, multiple linear regression, and ANCOVA. The Bonferroni correction was used for pairwise comparisons. Receiver operating curve (ROC) analysis compared preeclampsia to normotensive pregnancies.

RESULTS: Mean maternal activin A levels were significantly increased in ultimately preeclamptic pregnancies (26.4 ± 20.7 ng/ml, 2.0 MOM) in comparison to those not developing hypertensive disorders (13.4 ± 8.1 ng/ml, 1.0 MOM), P = 0.006. There was no significant difference in inhibin A levels between groups nor activin A levels between those undergoing delivery due to worsening preeclampsia and the other groups. ROC analysis of this limited preliminary data suggests a level of 20 ng/ml as a good discriminator with a sensitivity of 60% and a specificity of 90%. This level detected all eight cases ultimately developing severe preeclampsia, within a range of 1.57 days prior to diagnosis of preeclampsia.

CONCLUSIONS: Maternal serum activin A levels are significantly increased in pregnancies evaluated for incomplete stigmata of preeclampsia who subsequently develop preeclampsia and may prove to be a useful clinical test.
THE IMPACT OF COMBINATION ANTIRETROViral THERAPy ON MATERNAL HEALTH AND PREGNANCY. KP Beckman, MT Shannon, Department of Obstetrics, Gynecology & Reproductive Sciences University of California, San Francisco; UCSF Positive Health Program.

OBJECTIVE: We sought to test the hypothesis that suppression of maternal HIV-1 viral replication during pregnancy results in improved maternal health and pregnancy outcome.

STUDY DESIGN: A retrospective chart review was performed of all 99 known HIV-1 infected mothers and exposed infants delivered at UCSF/SFGH hospitals from January 1994 through July 1999.

RESULTS: CD4 T-cell counts at baseline and delivery were retrieved for 71 mothers. Baseline and delivery viral viral burden (V) measurements were available for 41 mothers. In 1994-6, prior to availability of combination anti-retroviral therapy (ART), the mean CD4 count for the population fell from 39 cells/mm³ from baseline to delivery. By 1997-9, 46 of 52 mothers elected to take 2, 3, or 4 drug combinations, resulting in a reduction of maternal V to undetectable in 26 and by an average of 1.5 log10 copies/ml in the remaining 20. Among treated mothers, a mean gain of -1.02 CD4 cells/mm³ (P<0.03) was observed. There were no differences in mean birth weight or gestational age between the two groups. The cesarean section rate was 15%. Six infants were infected: 3 in 1994-5 were born to mothers who received either no therapy (1) or azidothymidine alone (2) and 3 to mothers who received either no prenatal care and were not identified in labor (2) or 1 prenatal visit who was delivered by cesarean section (1).

CONCLUSIONS: Our early experience suggests that combination ART during pregnancy effectively suppresses maternal HIV-1 disease activity and halts or reverses maternal immune system destruction. Mean infant birth weight and gestational age were not significantly different between treated and untreated mothers. Vertical transmission events appear to be confined to mothers receiving no ART or azidothymidine alone (1994-6), or no/limited prenatal care (1997-9).

VEGF LEVELS THROUGHOUT GESTATION IN NORMAL PREGNANCY AND PREECLAMPSIA. EF Funai, S Borkowsky, K Kwan, TJ Rosen, TH Finlay, M Papazias, A Rebarber. NYU School of Medicine, Dept. of OB/GYN.

OBJECTIVES: We sought to describe VEGF levels throughout gestation in both normal pregnancies and preeclampsia in order to ascertain both the timing of maximal angiogenic activity (as represented by VEGF) and to determine if angiogenic activity is perturbed in preeclampsia.

STUDY DESIGN: Plasma specimens were obtained in each trimester in 15 normal pregnant, and 5 patients who eventually developed preeclampsia. A commercial VEGF ELISA was utilized. Data analysis was by Mann-Whitney Rank Sum Test for unpaired samples and Wilcoxon Signed Rank Test for paired samples.

RESULTS: We found statistically significant differences in the VEGF levels by trimester for the 15 patients involved.

CONCLUSIONS: These results lend validity to our hypothesis that angiogenic activity, which can be represented by VEGF levels in the plasma, is highest during the second trimester when placental invasion is maximal. These experiments warrant further investigation in a broad-based case-control fashion, across various gestational ages.

THE CHANGE IN GLUTATHIONE PEROXIDASE LEVELS IN NORMAL AND PREECLAMPTIC PREGNANCIES APPEARS SIMILAR TO CHANGES IN VEGF AND ANGIOSTATIN. EF Funai, D Ziegler, TJ Rosen, TH Finlay, MP Papazias, A Rebarber. NYU School of Medicine, Dept of OB/GYN.

OBJECTIVES: We have previously found that VEGF and angiotensin levels peak in the second trimester, when trophoblast invasion is maximal. Glutathione peroxidase has recently been shown to be involved in nitric oxide (NO) transport. We sought to determine if glutathione peroxidase (GPx) levels followed similar trends as VEGF and angiotensin in normal and preeclamptic pregnancies.

STUDY DESIGN: GPx levels were determined in the serum of normal pregnant women (i.e. not preeclamptic, n=10) and pregnant women who developed preeclampsia (PE, n=3). GPx levels were determined serially during pregnancy with an enzyme-linked immunosorbent assay (ELISA) kit (Ox International, Inc., obtained through R&D Systems). The presence of GPx is detected by means of a biotinylated-polyclonal antibody to extracellular GPxs.

RESULTS: In normal pregnant women, serum GPx levels are highest in the 2nd trimester, which is similar to our finding for VEGF and angiotensin. When compared in the second trimester, GPx levels appear to be lower in preeclamptic patients than normals. Because GPx may be involved in NO transport from hemoglobin to peripheral tissues, this finding may be indicative of a disturbance in NO transport in preeclampsia.
258 PREECLAMPSIA IS ASSOCIATED WITH DECREASED THROMBIN ACTIVITY IN THE SECOND TRIMESTER. MJ Pandus, Y Arkel, A Rebarbar, W Ku, H Roque, E Kuczynski, E Funas, T Rosen, R Wem, L O'Neill, S Khan, CJ Lockwood, Dept of Ob/Gyn, NYU School of Medicine, New York, NY.

OBJECTIVE: We hypothesize that deficient remodeling of the uteroplacental vasculature in PE would be associated with decreased, not increased, thrombin activity. Thus, we determined if PE is associated with decreased levels of Thrombin Precursor Protein (Tpp), American Biogenetic Sciences, Inc, Copagle, NY), a novel, exquisitely sensitive indicator of thrombin activity.

STUDY DESIGN: In this prospective nested case control study, we measured Tpp in 42 healthy women in each trimester (tr) and in 29 asymptomatic pregnant women who subsequently developed PE according to ACOG criteria (Technical Bulletin, #219, 1996). Women were matched for parity, gestational age at blood draw (GA), maternal age and race. Plasma was collected with sodium citrate and stored at -70°C. Tpp was measured by immunoassay (reference range 0.3-83 pg/ml) Data were analyzed by Wilcoxon Rank Sum and Student's t test, p<0.05.

RESULTS: There were no differences between PE and non-PE patients in gestational age at blood draw, race, or maternal age. In normal pregnancy, Tpp increases with gestational age. However, in patients with PE, Tpp levels are lower (median, range, pg/ml)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preecclampsic</th>
<th>Control</th>
<th>pval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Tr (&lt;14wks)</td>
<td>Tpp</td>
<td>0.9 (0.1-5)</td>
<td>1.9 (0.4-9.3)</td>
</tr>
<tr>
<td>2nd Tr (14-25wks)</td>
<td>Tpp</td>
<td>2.05 (0.6-30)</td>
<td>3.3 (0.3-30)</td>
</tr>
</tbody>
</table>

CONCLUSION: The second trimester of pregnancy is associated with increased thrombin activity. Paradoxically, preeclampsia is associated with lower levels of Tpp, consistent with impaired uteroplacental vascular remodeling Tpp may be a novel marker for preeclampsia.

259 OXIDANT STRESS IN SEVERE PREECLAMPSIA: NO EVIDENCE OF INCREASED LIPID PEROXIDATION IN VITRO. CL Regey and GA FitzGerald, for the CPEE Study Group, Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA and NICHD, Bethesda, MD.

OBJECTIVE: Data on lipid peroxidation in preeclampsia is conflicting, due to cross-sectional design of studies and utilization of suboptimal markers of oxidative stress in vivo. In this longitudinal study we evaluated the role of lipid peroxidation in the pathogenesis and evolution of severe preeclampsia using a novel marker.

STUDY DESIGN: A nested case control study design was employed, using outcome data and urine specimens from women in the trial of Calcium for Preeclampsia Prevention (CPEP). Cases were women with severe preeclampsia (PE), defined according to CPEP. Controls were women without hypertension or proteinuria, matched to cases by medical center and gestational age at urine collection. Urinary levels of the isoprostane 8,12-iso-PF2a-V1, a marker of lipid peroxidation in vivo, were determined by gas chromatography - mass spectrometry 10-20 weeks prior to diagnosis of PE, 3-9 weeks prior to diagnosis, and at time of diagnosis (1 day prior to delivery). The relationship between isoprostane levels over time and development of PE was explored using conditional logistic regression.

RESULTS: 29 cases and 29 controls were studied. No significant difference in urinary 8,12-iso-PF2a-V1 was seen either preceding or following development of severe PE. Mean isoprostane levels were not associated with the development of PE, the time point of the specimen, or the interaction of these factors. Subgroup analysis revealed no differences.

CONCLUSION: This longitudinal study of lipid peroxidation in severe preeclampsia does not support a role for oxidative stress in the pathogenesis of the disease.


OBJECTIVE: In 19 children with isolated LCHAD deficiency, a point mutation G to C 1528 has been implicated. The LCHAD enzyme is located in the alpha subunit of the mitochondrial trifunctional protein. The G to C 1528 mutation causes a substitution of glutamate for a glutamic acid at position 474 of the maternal protein. In the mothers of these children, 79% experience either acute fatty liver of pregnancy (ALFP) or hemolysis, elevated liver enzymes, and low platelet counts (HELLP). We investigated whether women suffering from severe preeclampsia (PE) or HELLP carry this point mutation and whether this mutation may be a predictor of these disorders.

STUDY DESIGN: DNA was extracted from 70 mothers affected with HELLP syndrome, 51 of their infants, and 121 mothers affected with severe PE. The samples were screened for the G to C mutation at position 1528 of the LCHAD gene. The area surrounding position 1528 was amplified using the polymerase chain reaction, presence of the mutation was identified after enzymatic digestion with Fak followed by gel electrophoresis and visualization with ethidium bromide and UV light.

RESULTS: None of the women or children tested carried the G to C 1528 mutation. A natural Pol I site ensured sensitivity of their reaction.

CONCLUSION: G to C 1528 mutation in the LCHAD gene appears to have no association with the development of HELLP or severe PE in our population. It appears that the mothers of children with LCHAD deficiency develop HELLP or APEL as a result of the fetal disease and not a direct correlation with carrier status of this particular mutation.

ELEVATED SERUM SOLUBLE FAS IN HELLP SYNDROME. H Harrah, J Copel, H Basheera, CD Hsu, Dept of Ob/Gyn, Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Fas/Fas ligand, a programmed death factor system, has been shown to be involved in hepatic disorders. The purpose of this study was to determine whether serum levels of soluble Fas (sFas) and soluble FasL (sFasL) were altered in HELLP syndrome.

STUDY DESIGN: Twenty pregnant women with HELLP syndrome were matched with 20 normotensive healthy women with singleton pregnancies. Subjects were matched for maternal age, gestational age, parity and race. HELLP syndrome was defined by ACOG criteria. Serum levels of sFas and sFasL were determined by enzyme immunosassays. Mann-Whitney and Spearman's rank correlation tests were used for statistical analyses. Data are presented as medians with ranges.

RESULTS: sFas and sFasL were detected in the sera of normotensive healthy women with singleton pregnancies. Subjects were matched for maternal age, gestational age, parity and race. HELLP syndrome was defined by ACOG criteria. Serum levels of sFas and sFasL were determined by enzyme immunosassays. Mann-Whitney and Spearman's rank correlation tests were used for statistical analyses. Data are presented as medians with ranges.

RESULTS: sFas and sFasL were detected in the sera of normotensive healthy women with singleton pregnancies. Subjects were matched for maternal age, gestational age, parity and race. HELLP syndrome was defined by ACOG criteria. Serum levels of sFas and sFasL were determined by enzyme immunosassays. Mann-Whitney and Spearman's rank correlation tests were used for statistical analyses. Data are presented as medians with ranges.

CONCLUSIONS: (1) Presence and correlation of circulating sFas and sFasL levels may indicate a physiologic role of apoptosis in normal pregnancy (2) Elevated serum sFas in HELLP syndrome may be secondary to hepatic and endothelial cell damage and shedding in maternal circulation.
262

CHOOSING A PREVENTIVE STRATEGY FOR EARLY-ONSET GROUP B STREPTOCOCCAL DISEASE IN A LOW PREVALENCE SETTING. C. Steen\textsuperscript{a}, M. Boulvais\textsuperscript{b}, P. Boxer\textsuperscript{a}, R. Auckenthaler\textsuperscript{c}, O. Irim\textsuperscript{d}. Dept. Ob/Gyn, University Hospital, Geneva, Switzerland.

**OBJECTIVE:** Preventive strategies for neonatal early-onset group B streptococcal disease (EOGBS) are based either on antenatal screening or on the presence of risk factors. Our objective was to determine the most appropriate strategy to prevent EOGBS in a low risk population.

**STUDY DESIGN:** We estimated the prevalence of colonization by group B streptococci at delivery, performing rectovaginal cultures on Todd-Hewitt medium in a cohort of 255 pregnant women. Of these, 293 had also a previous culture at 35-39 weeks. A decision analysis and an economic evaluation, using local epidemiological estimates and costs data from the literature, were performed to compare 3 strategies (watchful waiting, screening, risk factors).

**RESULTS:** The prevalence of maternal colonization during labor was 8% (95% confidence interval: 5-11). The sensitivity of the antenatal screening was 35%, for a specificity of 95%. Risk factors were present in 18% of pregnancies. The strategy based on screening would prevent death from EOGBS in 10.5/1,000,000 infants, while the strategy based on risk factors would prevent 8.4 deaths/1,000,000. The marginal cost per life-saved would be $490,000 for risk factors and $284,000/000 for screening. The cost-effectiveness ratio would be $69,641 for QALY for risk factors, and $14,890/QALY for screening. Sensitivity analysis did not affect the ranking of the strategies.

**CONCLUSIONS:** A strategy based on screening is more effective in preventing EOGBS. However, the additional cost of screening may be prohibitive, as the marginal benefit is low and the cost is high, as compared to the risk factors strategy. In our epidemiological context, because of the low prevalence and low sensitivity of the antenatal culture, a risk factor approach appears to be preferable.

263

CHANGING PATTERNS OF CARE AND PREGNANCY OUTCOMES AMONG HIV INFECTED PREGNANT WOMEN Julie D. Lamb\textsuperscript{a}, B. S and Pattna M. Gencu, M.D., M.P.H Dept. of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, Ill.

**OBJECTIVE:** To describe the changing patterns of care and pregnancy outcomes for HIV infected pregnant women since the introduction of combination antiretroviral therapy (c-ART).

**STUDY DESIGN:** A review was conducted of 112 consecutive patients with 121 pregnancies referred to a specialized perinatal HIV clinic from January 1992 to June 1999. Infant HIV infection status was obtained for all live births.

**RESULTS:** The Northwestern Perinatal HIV Cohort is similar to the US population of HIV infected women; 75% are women of color, 79% are medically indigent and heterosexual transmission is the predominant mode of acquisition (70%). The outcomes were 83 (69%) live births, 31 (27%) elective terminations, 3 (2.5%) spontaneous abortions (sAb) and 3 total deaths (2.5%). The outcomes were as follows: III (52%), Ia (25%), V (9%), II (6%), and Ib (4%). Serotype frequencies of invasive GBS is important to ensure the effectiveness of prophylactic and pregnancy and to guide vaccine development.

264

ASSOCIATION BETWEEN PROPHYLACTIC ERYTHROMYCIN AND PROLONGED LATENCY AFTER RUPTURE OF MEMBRANES. R. Mittendorf, C. Harris, N. Sukkar, R. Scudiero\textsuperscript{a}, M. Borg\textsuperscript{b}, L. Benz\textsuperscript{c} and M. Ismail, University of Chicago, Chicago, and Wayne State University, Detroit.

**OBJECTIVE:** To learn which common prophylactic antibiotics extend latency from preterm premature rupture of membranes (PPROM) to delivery

**STUDY DESIGN:** In the Magnesium and Neurologic Endpoints (MAGNET) Trial, we studied a number of relationships, including the possible influence of prophylactic antibiotics on latency and cerebral palsy. During data analysis, we computed the length of the latency period (PPROM to delivery) and matched this period to the prophylactic antibiotics used in our hospital.

**RESULTS:** During the study, 76 of 78 (97%) undelivered mothers with PPROM were placed on one or more prophylactic antibiotics. The exposure days for the four most common ones were: ampicillin, 298, erythromycin, 206; clindamycin, 160; and amoxicillin 240. Of these mothers with PPROM, most got ampicillin (n=62), erythromycin (n=62), or both (n=58). Median latency following PPROM was five days. The table below shows univariate analyses for the 4 most commonly-used antibiotics (ABX) and their latencies.

<table>
<thead>
<tr>
<th>Latency: ABX p-value:</th>
<th>&gt;2 days</th>
<th>&gt;5 days</th>
<th>&gt;7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>0.32</td>
<td>0.47</td>
<td>0.21</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>0.11</td>
<td>0.54</td>
<td>0.68</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.61</td>
<td>0.74</td>
<td>0.08</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Erythromycin + Ampicillin</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
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</tbody>
</table>

Erythromycin is the only prophylactic found to be statistically significantly associated with prolonged latency of >2, and >5 days. Using multiple logistic regression which permits simultaneous control for other variables of interest, such as exposure to other antibiotics and gestational age, erythromycin remains an independent predictor of prolonged latency.

**CONCLUSION:** In regards to prolonged latency, in these data, we find that erythromycin is the essential and independent predictor
266 INTRAUTERINE INFECTION AND CEREBRAL PALSY IN PRETERM CHILDREN. J.K. Grether1, K.B. Nelson2 Birth Defects Monitoring Program, Emeryville, CA and NINDS, Bethesda, MD

OBJECTIVE: To examine the association of cerebral palsy (CP) with clinical markers of intrauterine infection in children born <32 weeks gestational age (GA) in a new cohort.

BACKGROUND: We have reported from a previous cohort that intrauterine infection is a risk factor for CP in children of normal birthweight but not in very low birthweight children. Some but not all investigators have found an association of infection with CP in preterm infants. Prechlamia, associated with lower risk of CP in preterm infants, is a potential confounder.

METHODS: In singleton infants <32 weeks GA born 1988-1994, clinical and histologic findings in children with CP were compared with observations in controls. Infants of preeclamptic women were excluded.

RESULTS: There were no significant differences, cases vs. controls, on univariate analysis or after adjustment for gestational age.

CONCLUSIONS: In contrast with infants of normal birthweight, in whom we previously found indicators of maternal infection to be associated with increased risk of CP, but in agreement with our earlier findings in very low birthweight children, in these infants born before 32 weeks GA to nonpreeclamptic women, clinical and histologic markers of intrauterine infection were observed with similar frequency in children with CP and in control infants.

267 FETAL SONOGRAPHIC ABNORMALITIES AND INTRAUTERINE VIRAL INFECTION Batschat A A1,2, Harman C.R.3, Townsh J A2,3, Werner C.P.1, 1Dept. Ob/Gyn, Reproductive Sciences, Univ Maryland, Baltimore MD, and 2Dept of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX.

OBJECTIVE: To evaluate the frequency and identity of fetal viral infection in normal and abnormal pregnancies

STUDY DESIGN: Amniotic fluid, fetal blood, or pleural fluid were analyzed with the polymerase chain reaction (PCR) using primers for cytomegalovirus (CMV), herpes simplex virus (HSV), parvovirus B19, adenovirus, enterovirus, Epstein-Barr virus (EBV), and respiratory syncytial virus (RSV). The frequency of viral genome positive samples in 240 routine mid trimester genetic amnioncentesis (GA) was compared to 138 procedures performed for fetal complication (FC), including fetal anomalies, intrauterine growth restriction and proven maternal infection.

RESULTS: Viral genome was detected in 47/478 (12.4%) of samples. Adenovirus was detected in 39 (10.3%), Enterovirus in 5 (1.3%), CMV in 3 (0.8%) patients and RSV, EBV and Parvovirus in 1 patient respectively (0.3%). Three patients had infection with more than one virus. S.Pauls showed viral genome in only 20/2,400 (0.9%) samples whereas FC samples were positive in 27/138 (19.6%; p<0.005). Adenovirus was more commonly isolated from abnormal pregnancies (16/240 vs. 23/138, p<0.005). Central nervous system malformations (n=7), intrauterine growth restriction and multiple malformations (n=4) were the most commonly observed abnormalities in the presence of viral infection.

CONCLUSION: Viral infection is more common in pregnancies with sonographic abnormalities of the fetus. Adenovirus infection is most frequent in this setting, although no correlation with specific abnormalities is recognized.

268 HIV RAPID SCREENING IN AN OBSTETRIC POPULATION R. Mansfield, B. Jones1, D. Fritiofa, Dept. Ob/Gyn, Louisiana State Univ., and Charity Hospital, New Orleans, LA.

OBJECTIVE: To evaluate the performance of HIV rapid testing methods in a high seroprevalence obstetric population.

STUDY DESIGN: Obstetric patients presenting to labor and delivery without documentation of prior antepartum HIV screening were offered voluntary HIV screening with informed consent. Patients consenting for screening were tested concurrently with a conventional ELISA (Abbott Lab. HIV-1/HIV-2 assay) and the Murex Single-Use Diagnostic System (SUDS) rapid ELISA assay. A confirmatory Western blot documented true positive screens. Patients were informed of the results of the SUDS test and those with positive SUDS tests were offered the option of initiating antiretroviral therapy for the reduction of vertical transmission of HIV infection.

RESULTS: In the first six months of the screening program 230 patients underwent rapid HIV screening using the SUDS assay. Thirteen positive SUDS tests were documented of which 12 were confirmed by Western blot. A single false positive SUDS test was documented as discordant with conventional HIV testing. The SUDS test performance in the study population as compared with conventional ELISA demonstrated a sensitivity of 96%, specificity of 99.5%, positive predictive value of 92% and negative predictive value of 100%. During the study period rapid screening was responsible for identifying 20% of delivered HIV seropositive mothers. Among delivering women with positive SUDS tests, 63% received intrapartum Zidovudine (ZDV) therapy and 100% of their newborns were initiated on ZDV prophylaxis prior to hospital discharge.

CONCLUSIONS: The performance of the SUDS HIV rapid test assay in a high seroprevalence obstetric population is comparable to previously reported experiences in non-obstetric populations. Rapid HIV screening improves the ability to administer peripartum antiretroviral therapy for vertical transmission reduction in seropositive women presenting for delivery without prior diagnosis or treatment.

269 INTRAUTERINE INFECTION DOES NOT AFFECT LONG-TERM COGNITIVE OR PSYCHOMOTOR DEVELOPMENT IN LOW BIRTH WEIGHT INFANTS. MB. Fausett, MS. Espin, B. Stier1, S. Smith2, B1. Osburo, FT. Porter and MW. Gerner. Univ of Utah, SLC, UT.

OBJECTIVE: To compare the cognitive and psychomotor development of infants born with a birth weight <1,500 grams whose antenatal course was complicated by intraamniotic infection (IAI) with those who had no evidence of infection at the time of delivery.

METHODS: Infants born between 1993 and 1998 with a birth weight <1,500 grams whose antenatal course was complicated by intraamniotic infection (IAI) with those who had no evidence of infection at the time of delivery.

RESULTS: There were 375 infants included in the study (IAI group=80, control group=295). The mean gestational age at delivery was lower in the IAI group (20 3.22 weeks) and in the control group (20 5.25 weeks) (p=0.0001) but there was no significant difference in mean birth weight when controlled for gestational age (p=0.57).

CONCLUSION: Among surviving, very low birth weight infants enrolled in a regional follow-up program, the antenatal diagnosis of IAI is not associated with an increased risk of long-term cognitive or psychomotor delay when compared with non-infected controls Likewise, there was no detectable association between IAI and cerebral palsy in this population.
ASSOCIATION BETWEEN LATENCY > 7 DAYS IN LENGTH AND CEREBRAL PALSY. R. Mitteda, R. Scudiero, M. Borg, L. Bentz, and N. Sokker. University of Chicago, and Wayne State University, Detroit.

OBJECTIVE: To learn whether there is an association between increasing latency (period of time between preterm premature rupture of the membranes (PPROM) and delivery) and cerebral palsy (CP).

STUDY DESIGN: In the MAGNET Trial, we studied a number of relationships between congenital cerebral palsy and its possible predictors, including the use of prophylactic antibiotics following PPROM, the genera and species of bacteria cultured aseptically from the chorionicamnion space at delivery, and the possible association of increased latency and cerebral palsy. In this part of our study, data on the latency period for mothers with PPROM was linked to the developmental findings on our children at age 18 months. We report on bacterial associations, as well as prophylactic antibiotics elsewhere.

RESULTS: During the study, 78 undelivered mothers were admitted for PPROM. Of the 3 children with CP whose mothers had PPROM, and for whom we have culture results, median latency was 15 days, of those 75 without CP, and for whom culture results were available, the median latency was 4 days. This difference (15 days vs 4 days) is statistically significant (Mann-Whitney test, p = 0.025). To control for possible confounding by gestational age, the most important predictor of CP, we developed a bivariate logistic model evaluating several different latency ("Gesleng") periods with the gestational length ("Lateng") dichotomized on 28-completed weeks of pregnancy. Refer to the table below.

<table>
<thead>
<tr>
<th>Latency:</th>
<th>&lt;3 days:</th>
<th>&lt;6 days:</th>
<th>&gt;7 days:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP p-values for the latency periods</td>
<td>p = 0.48</td>
<td>p = 0.14</td>
<td>p = 0.048</td>
</tr>
</tbody>
</table>

CONCLUSION: When controlling for gestational age, as latency increases, the association between it and cerebral palsy becomes more significant. Given our current interest in prolonged latency, we need to be aware of this finding.

CAN POSTPARTUM INFECTIOUS MORBIDITY BE DECREASED BY VAGINAL PREPARATION WITH POVIDONE IODINE PRIOR TO CESAREAN DELIVERY? G. C. Redd, Katherine E. Hartmann, Michael J. McMahon, Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, NC.

OBJECTIVE: Our purpose was to determine whether vaginal preparation with povidone iodine prior to cesarean delivery decreases the incidence of postpartum infections morbidity.

STUDY DESIGN: 501 women were randomized to sterile vaginal preparation with povidone iodine (n=250) or no sterile vaginal preparation (n=251) from May 1996 to August 1998. Postpartum infectious morbidity included: 1) febrile morbidity, defined as any fever ≥ 38°C after the day of surgery; 2) endometritis, defined as febrile morbidity with documentation of abdominal or uterine tenderness and the utilization of intravenous antibiotics; and 3) wound infection, with documented disruption in the abdominal incision that required wound care. Overall rates of postpartum infectious morbidity, in addition to relative risks (RR) and 95% confidence intervals (95% CI) for the effect of vaginal preparation between the two groups, were calculated.

RESULTS: There was no difference between the two groups with respect to maternal age, parity, race, education, prior cesarean delivery, type of anesthesia, labor before current cesarean delivery, vaginal examinations in labor, internal fetal monitoring, gestational age at delivery, or payment status. The rate of febrile morbidity in the study population was 21.2%, endometritis 8.1%, and wound infection 7.0%. Vaginal preparation with povidone iodine prior to cesarean delivery had no effect on the risk for febrile morbidity (RR 1.14, 95% CI 0.79 - 1.64), endometritis (RR 1.16, 95% CI 0.62 - 2.20), or wound infection (RR 0.63, 95% CI 0.32 - 1.32).

CONCLUSION: Our rates of febrile morbidity, endometritis, and wound infection are similar to those reported in the literature. Vaginal preparation with povidone iodine prior to cesarean delivery had no effect on the incidence of febrile morbidity, endometritis, or wound infection.

NORMAL SALINE PELVIC AND INTRAUTERINE IRRIGATION IN THE HIGH-RISK CESAREAN SECTION (CS) PATIENT AS A SAFE AND COST EFFECTIVE METHOD OF INFECTION PROPHYLAXIS. S. H. Copel, R. M. Hampson, Dept. of Ob/Gyn, Texas Tech University Health Sciences Center, Amarillo, TX.

OBJECTIVE: Prophylactic IV antibiotics at cord-clamp can significantly decrease the incidence of infectious morbidity in the CS patient and may contribute to the selection of resistant organisms. Patients with rupture of membranes or labor for greater than 6 hours, emergency CS, and the indigent population are at high risk for endometritis (as high as 90%). Cephalosporin antibiotic irrigation has been demonstrated to be as effective as IV antibiotic prophylaxis; however, the systemic absorption may present a problem. The objective of this study is to determine the impact of copious antibiotic irrigation, versus normal saline (NS) irrigation, on the incidence of postcesarean wound infections.

STUDY DESIGN: Patients at high risk for infection at the time of CS were randomly placed in two groups. One group received antibiotic irrigation (n=290) with ceftazolin using 2 grams in 1000 cc NS. The other group (n=290) received irrigation with NS alone. 700 cc of solution was used as intrauterine irrigation, then 100 cc in each gutter, and 100 cc sc. The patients were then followed for the remainder of their hospital stay, and 6-8 weeks post-op, for endometritis, wound or urinary tract infections.

RESULTS: Only 2 of 40 high risk patients who received prophylactic irrigation developed endometritis. Both received ceftazolin irrigation. One of these 2 patients went on to develop a wound infection. One patient who received NS irrigation developed a wound infection. None of the patients who received irrigation developed endometritis. All of the patients with infection had rupture of membranes greater than 6 hours. No patients in the study developed UTIs.

CONCLUSION: These preliminary results indicate that copious intrauterine and pelvic irrigation may result in a significant decrease in the rate of postcesarean infections in the high-risk patient population. The use of NS irrigation alone may eliminate the risk of allergic drug reactions and the emergence of drug-resistant bacteria.

MAST CELL DEGRANULATION MODULATES CERVICAL CONTRACTILITY IN GUINEA PIG. E. Bytaster, V. Vederinkov, G. Saade, R. Romero, R. Garfield, Dept of Ob/Gyn, The Univ of Texas Med Branch, Galveston, TX.

OBJECTIVE: To study the effect of endogenous mast cell (MC) degranulation and histamine on contractility of cervical strips from nonpregnant and pregnant guinea pigs.

STUDY DESIGN: Longitudinal strips (1cm x 2.5mm) from nonpregnant and pregnant (day 16 and 40) guinea pigs were mounted in organ chambers (Krebs' buffer, 5% CO2 as an air, 37°C, pH 7.4) for isometric tension recording. After equilibration, a reference contraction to KCl (60 mM) was obtained. The strips were then washed, rested for 1 hr, then incubated for 30 min with solvent (control), histamine (10^-5 M, inhibitor of MC degranulation), and histamine on contractility of cervical strips from pregnant (day 40) guinea pigs.

RESULTS: Compound 48/80 and histamine significantly increased contractility of cervical strips in all 3 groups of animals. Cromolyn and H1 antagonists significantly reduced responses to compound 48/80 and histamine, respectively, in all 3 groups. H2 receptor antagonists significantly inhibited responses to compound 48/80 in nonpregnant and day 40 pregnant guinea pigs. H2 receptor antagonists did not alter responses to compound 48/80 or histamine.

CONCLUSIONS: Degranulation of MC releases histamine and other mediators that stimulate cervical contractility through H2 receptors. Cervical infiltration and modulation of contractility by MC may play an important physiological and/or pathological role in control of cervical function during pregnancy.
CONGENITAL VARICELLA SYNDROME IS RARE IN A PROSPECTIVE COHORT OF 347 PREGNANT WOMEN. J.M. Ernst for the NICHD Maternal-Fetal Medicine Unit Network, Bethesda, MD.

OBJECTIVE: To determine the frequency of congenital varicella syndrome (CVZV) in neonates born to women developing varicella-zoster virus (VZV) infections during pregnancy.

STUDY DESIGN: Pregnant women with clinically-defined VZV infection during pregnancy were enrolled at 10 centers. Maternal and fetal IgG and IgM serology by fluorescent antibody confirmed 68% of cases. Specimens were examined at 04 to 06 months, 5-17 months and 18-30 months after delivery to detect abnormalities of their eyes, hearing and physical and developmental features (Bayley or Denver scales). A hierarchical set of criteria was used to define CVZV. A panel of 4 investigators decided the classification of all findings.

RESULTS: In 302 women enrolled from 1999-06, 15 had herpes zoster and 347 had primary VZV infection. VZV infected 141 women (39.0%) in first trimester, 122 (33.7%) in second and 99 (27.3%) in third trimester. Five twins were included. Incomplete follow-up caused exclusion of 125 infants, and 11 were lost to follow-up before delivery. Only one case (1/251=0.43%) of definite CVZV was found. A 3860 gram female having a left retinal macular lesion with typical skin scars after maternal VZV at 24 weeks. The maternal blood sample at birth was negative for IgG antibodies to toxoplamosis and cytomegalovirus. We classified 29 cases of "possible" CVZV, 24 of 26 of them had maternal IgG and IgM results. None or unknown ART or VL. These correlates suggest lack of adherence to ART andVL. The results are consistent with vertical transmission occurring 1) in each of the categories ART received; 2) at all levels of VL, including non-measurable. More precise estimates of the risk of vertical transmission according to maternal ART and VL will be possible once larger numbers of mother-infant pairs are accrued.

CONCLUSIONS: VTR were highest among HIV-infected women with none or unknown ART or VL. These correlate suggest lack of adherence to ART andVL. The results are consistent with vertical transmission occurring 1) in each of the categories ART received; 2) at all levels of VL, including non-measurable. More precise estimates of the risk of vertical transmission according to maternal ART and VL will be possible once larger numbers of mother-infant pairs are accrued.

STUDY DESIGN: Medical record abstraction of data on 347 mother-child pairs enrolled in the Pediatric AIDS Clinical Trials Group (PACTG).

RESULTS: HIV infection status was known for 347 infants born to women recruited at study sites. Twelve of these infants were identified with HIV (overall VTR=3.5% [95% CI: 1.8% to 6.0%]. VTR according to receipt of ART during the third trimester were: no ART or unknown if ART received: 5/18 [27.6%] (CI: 9.6% to 48.8%); mono-therapy: 7/91 [7.5%] (5.1%, 15.2%); ZDV/3TC: 0/112 [0.0%] (0.0%, 3.3%), multi-agent therapy without a protease inhibitor: 0/14 [0.0%] (0.0%, 4.8%); multi-agent therapy with a PI: 2/112 [1.8%] (0.2%, 6.3%]. VTR according to maternal HIV RNA concentration determined closest to delivery were: unknown or none recorded: 5/43 [11.5%] (3.9%, 21.5%); non-measurable: 1/109 [0.9%] (0.0%, 6.0%); <10,000 copies/ml: 5/131 [3.8%] (2.5%, 5.6%); >10,000 copies/ml: 21/904 [2.3%] (1.0%, 4.1%)

CONCLUSIONS: The uninnzinated status of mother and infant at birth is associated with the outcome of ART andVL. We evaluated the role of ART andVL in the association of vertical transmission occurrence. The results are consistent with vertical transmission occurring 1) in each of the categories ART received; 2) at all levels of VL, including non-measurable. More precise estimates of the risk of vertical transmission according to maternal ART andVL will be possible once larger numbers of mother-infant pairs are accrued.
278  MATERNAL AND TRANSPLACENTAL PHARMACOKINETICS OF

OBJECTIVE: To evaluate and characterize the maternal and fetal pharmacokinetics of azithromycin during pregnancy.

STUDY DESIGN: Twenty women scheduled for elective cesarean delivery were prospectively enrolled and received 1 g of azithromycin at either 6, 12, 24, 72, or 168 hours preoperatively. All women in this investigation received spinal anesthesia at which time a sample of cerebrospinal fluid (CSF) was obtained for analysis. Maternal serum and urine were obtained just prior to the surgery. Intraoperatively, samples of amniotic fluid, umbilical cord blood, and placenta were obtained. Azithromycin was quantitatively determined using a high-pressure liquid chromatography (HPLC)-atmospheric pressure chemical ionization mass spectrometry assay. Data on placental and amniotic fluid levels of azithromycin were pending at the time of this submission but will be presented.

RESULTS: Maternal serum and urine levels of azithromycin (ng/mL) peaked by 6 hours and declined to a plateau 24-72 hours post-dose administration. In contrast, umbilical cord serum levels (UCS) peaked later at 12.5 hrs with lower levels than observed in the maternal serum. Undetectable levels of azithromycin were noted in the maternal CSF.

CONCLUSION: Azithromycin penetrates the fetal compartment, peaking later and with lower levels than in the maternal compartment. Azithromycin has a broad antimicrobial spectrum, is reported to have deep tissue penetration in adults (10-100x higher tissue to serum levels) and may have potential use for the treatment of perinatal infections.

SITE  6 hr (n=2)  12 hr (n=7)  24 hr (n=5)  72 hr (n=5)  168 hr (n=1)
Serum  311±170  144±79  63±57  69±51  <10
Urine  42230±8846  52620±2072  10733±5968  5861±3335  <1000
CSF  <16  <16  <16  <16  <16
UCS  19±6  26±16  27±13  19±7  <10


OBJECTIVE: Mycoplasma genitalia has recently been identified as a potential pathogenic organism associated with STDs in non-pregnant women. However, unlike other pathogenic agents such as Ureaplasma urealyticum and Mycoplasma hominis, the relationship of M. genitalium to adverse pregnancy outcomes is unknown. We sought to determine the prevalence of M. genitalium in midtrimester in a group of women with a subsequent spontaneous preterm birth (SPB) <37 weeks.

STUDY DESIGN: Among women in an ongoing prospective study on lower genital tract infections and pregnancy outcomes, we identified 127 women who subsequently had a SBP. Participants in this study had vaginal samples obtained between 21-25 weeks for pH, bacterial vaginosis (BV) gram stain, and cultures for G. vaginalis, M. genitalium, and T. vaginalis. Aliquots of stored samples were chased, then analyzed for M. genitalium utilizing previously validated PCR primers. The PCR results were compared with clinical and laboratory outcomes.

RESULTS: Of the 124 women with a SBP and sufficient samples for analysis, only five women (3.9%) had a positive PCR for M. genitalium. The mean delivery gestational age was similar between women with a positive PCR (34.6 ± 2.2 weeks) and a negative PCR (34.0 ± 2.7 weeks) (p=0.62). None of the women with a positive PCR tested positive for any other STD compared to 36% of women with a negative PCR. One woman (20%) with a positive PCR had BV, while 22 women (18%) with a negative PCR had BV. Of the five women with M. genitalium, a vaginal pH ≥5.3 was only noted in the woman who had BV, while the other four women had a pH ≤4.4.

CONCLUSIONS: The occurrence of midtrimester vaginal M. genitalium is infrequent in women with a SBP and is unlikely to be a contributing factor or a significant marker for a subsequent SPB.

280  CHORIOAMNIONITIS IS ASSOCIATED WITH INCREASED RATES OF FETAL GROWTH RESTRICTION IN TERM AND PRE-TERM INFANTS. M.C. Williams, W.F. O'Brien, R Nelson*, Deps. Of Pediatrics and OB/GYN, Univ. of South Florida, Tampa, FL.

OBJECTIVE: The association between chorioamnionitis and fetal growth restriction is poorly understood. Although commonly understood to be an acute process, some reports indicate that chorioamnionitis may be associated with increased rates of fetal growth restriction. We evaluated fetal growth parameters in pregnancies complicated by chorioamnionitis.

STUDY METHODS: Collaborative Perinatal Project infants with recorded placental pathology determinations were studied. Population norms were used to determine birthweight (BW), length, head circumference (HC), BW/length ratio, and BW/HC<0.95 for gestational age and gender, and to perform z score analyses of these characteristics. Moderate or marked infiltrates of chorio, amnion, or umbilical cord were considered evidence of chorioamnionitis. Associations between markers of fetal growth restriction and chorioamnionitis were evaluated.

RESULTS: Chorioamnionitis was found in 13.8% or infants at 28-32 weeks, 8.3% of infants at 33-36 weeks, and 5.1% of infants at >37-40 weeks.

CONCLUSIONS: Chorioamnionitis is significantly associated with various types of fetal growth restriction in pre-term and term infants, with stronger associations noted in pre-term infants.
THE ROLE OF AMNIOTIC FLUID NUCLEOSOMES AND CYTOKINES IN PRETERM INTRAAMNIONIC INFECTION. CD Han, K Aversa, H Harirah, H Basheera, LC Lu, R Samelson, J McNama, SMFM Abstracts 1999;208:284.

Antenatal therapy and viral load in 464 HIV-infected women in 1998-1999 (PACTG 367). R Tuomeni, D Shapiro, S Burchett, G Gapka, J McNamara, H Pollack, J Reid, Brigham & Women's Hosp, Harvard Med Sch, Boston MA; Harvard Sch Pub Hlth, Boston MA; Albany Med Ctr; Albany NY; BC Children's Hosp, Boston MA; Frontier Science, Buffalo NY, NIAID, Bethesda MD; NY Ums Med Gr, NY, NY; and NICHD, Bethesda MD. The objective of this study was to determine antiretroviral therapy (ART) and maternal plasma HIV RNA viral load (VL) during pregnancy in HIV-infected women.

STUDY DESIGN: Retrospective abstraction of prenatal records of HIV-infected women delivering between January 1998 and May 1999 at one of 32 sites participating in the Pediatric AIDS Clinical Trials Group (PACTG). Outcomes considered were ART during pregnancy, the majority had detectable VL prior to delivery. The majority of women had detectable VL at delivery, and 20% of women had detectable VL at delivery. The majority of women had detectable VL at delivery. The majority of women had detectable VL at delivery.

OBJECTIVE: Human Immunodeficiency Virus (HIV) infection leads to higher rates of prematurity.

STUDY DESIGN: The specialized HIV in pregnancy program includes both HIV/Maternal Fetal Medicine specialists and specialized social services at our institution. We reviewed the medical records of all HIV-infected women who had care through our specialized HIV in pregnancy program from 1/97-8/99. Information was abstracted pertaining to gestational age at the time of delivery, maternal comorbidities, and antiretroviral therapy. They were then compared to the rates obtained from the women without HIV infection who delivered at our hospital within the same time period. The data results were evaluated by X^2 analysis.

RESULTS: The institutional rate of prematurity was 1021/5671 (18%) among uninfected women for the study period. HIV-infected women in the specialized care program had a rate of 15/50 (30%), p<NS. Premature births to HIV-infected mothers included 1 set of twins and 3 sets of triplets. Within the subgroups of HIV-infected women, those who took antiretroviral therapy with a protease inhibitor had a rate of premature delivery of 7/27 (26%) compared to 6/26 (23%) in those who did not take protease inhibitors, p<NS. Factors associated with premature delivery included preterm premature rupture of membranes (PPROM), preterm labor, substance abuse, chromosome anomalies, and placenta previa.

CONCLUSION: The rate of prematurity in HIV-infected women does not appear to be altered by the infection itself, but rather the maternal comorbidities. Additionally, the rate of prematurity was not altered by the use of protease inhibitors. The women who took a protease inhibitor during pregnancy and delivered prematurely did not have a statistically different rate of prematurity compared to HIV-infected women who did not take a protease inhibitor during pregnancy. The incidence for premature delivery in the case of PPROM in the HIV-infected women may have been increased by our protocol of immediate delivery compared to our protocol for expectant management in the case of PPROM in women who are not HIV-infected. While women infected with HIV may have a higher rate of premature births, this rate is not related to medication patterns.

287 PATIENTS PRESENTING WITH CERVICAL FUNNELING IN THE MIDTRIMESTER AND WHO SUBSEQUENTLY DELIVERED A PRETERM NEONATE <34 WEEKS HAVE EVIDENCE OF INCREASED EXTRACELLULAR MATRIX DEGRADATION AND SUBCLINICAL INTERUTERINE INFLAMMATION. O. Rubi MD, R. Adams MD, J. Baldiuc MD, J. Defilvo DO, R. Romo MD.

OBJECTIVE: To determine if intraamniotic and/or genital tract inflammation or other process (thrombophilic state) are associated with cervical funneling diagnosed sonographically during the 2nd trimester of pregnancy in patients who subsequently delivered preterm.

STUDY DESIGN: A prospective study was conducted to identify patients with cervical funneling by transvaginal ultrasound between May 98-Aug 99. Patients meeting criteria underwent an amniocentesis to diagnose microvascular invasion of the amniotic cavity, urine culture and genital tract chlamydia, GBS, NG, Mycoplasmas and bacterial vaginosits. Vaginal secretions were evaluated for the presence of fetal fibronectin (FFN). The amniotic fluid white blood cell count, glucose and interleukin-6 were determined. A thrombophilic workup was also conducted.

RESULTS: 62 patients were included in the study; the prevalence of preterm delivery <34 weeks was 39% (24/62). Results of different parameters are displayed in the table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preterm Group</th>
<th>Near Term Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFN</td>
<td>57.9%</td>
<td>26.5%</td>
<td>0.05</td>
</tr>
<tr>
<td>AFI-6/5mg/ml</td>
<td>25.0%</td>
<td>5.5%</td>
<td>0.06</td>
</tr>
<tr>
<td>Bact Vaginosis</td>
<td>23.8%</td>
<td>29.4%</td>
<td>0.09</td>
</tr>
<tr>
<td>Ureaplasma</td>
<td>30.0%</td>
<td>36.4%</td>
<td>0.8</td>
</tr>
<tr>
<td>GBS</td>
<td>25.0%</td>
<td>10.4%</td>
<td>0.3</td>
</tr>
<tr>
<td>Urine Culture</td>
<td>4.3%</td>
<td>2.7%</td>
<td>0.7</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>4.0%</td>
<td>20.6%</td>
<td>0.2</td>
</tr>
</tbody>
</table>

All amniotic fluid cultures were negative for microorganisms. No other genital pathogen demonstrated significance.

CONCLUSION: Patients with cervical funneling who subsequently delivered a preterm neonate <34 weeks had a higher rate of positive FFN and Trend towards an elevated amniotic fluid IL-6 compared to patients who delivered at term. These observations suggest the potential of an underlying pathologic process in patients with cervical funneling.

288 DOES A FETAL NEURAL TUBE OR CONGENITAL HEART DEFECT INDICATE INCREASED RISK OF MATERNAL HYPERTENSION? KD Weinstock and M DuBard, Dept OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: In separate studies, the 677 C–T mutation of methylene tetrahydrofolate reductase (MTHFR) has been associated with fetal neural tube defects (NTDs), fetal congenital heart defects (CHD), and hypertension (HTN). We sought to determine if mothers of NTD or CHD offspring are at increased risk for any form of HTN.

STUDY DESIGN: We included all pregnancies evaluated from 1998 to 1999 and carried to ≥24 weeks. Cases had a fetus with either isolated NTD (n=219) or CHD (n=85); controls were all clinic patients with nonanomalous fetuses (n=333,489). If the patient had multiple pregnancies, the last was evaluated. The incidence of all HTN in cases and controls were compared.

RESULTS: Cases and controls were similar with respect to maternal age (25.3±4.6 vs 24.9±5.9 years) and gestational age at delivery (36.6±5.5 vs 38.3±5.6 weeks).

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>HTN</th>
<th>PIH</th>
<th>Pre E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>62</td>
<td>25.0%</td>
<td>20.6%</td>
<td>10.4%</td>
</tr>
<tr>
<td>NTD Case</td>
<td>25</td>
<td>30.4%</td>
<td>17.8%</td>
<td>11.6%</td>
</tr>
<tr>
<td>CHD Case</td>
<td>48</td>
<td>19.6%</td>
<td>11.4%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Pre E</td>
<td>20</td>
<td>30.0%</td>
<td>15.0%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Pre E</td>
<td>40</td>
<td>19.5%</td>
<td>11.6%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Pre E</td>
<td>68</td>
<td>22.1%</td>
<td>12.7%</td>
<td>13.2%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Black women with NTD or CHD fetuses were not at increased risk for HTN, probably because the incidence of NTDs is low and HTN has many etiologies in this group. However, white women with CHD fetuses are at significant increased risk to have chronic HTN. Since HTN itself is not believed to cause CHDs, it is possible that both HTN and CHD are associated with the same enzyme defect.

289 HIGHLY ACTIVE ANTIRETROVIRAL THERAPY FOR THE PREVENTION OF PERINATAL HIV. A.W. Helgason, N. Eriksson, S. Lewis, M. Doyle, D. Pearson, C. Budrick, Ob/Gyn, Univ. of Florida and Univ. of West Florida, Pensacola, Florida and the Univ. of Texas-Houston, Texas.

OBJECTIVE: To examine the impact of highly active antiretroviral therapy (HAART) on the perinatal transmission of HIV.

STUDY DESIGN: The records of 52 pregnant women were reviewed to determine the impact of HAART on the prevention of perinatal transmission of HIV. Type of therapy, method of delivery, immunologic function, and HIV viral loads were among the data reviewed. Data analysis was performed with the SAS statistical package.

RESULTS: The majority of the women were African American (81%) and 16/52 (31%) had AIDS. The women were treated predominantly with Combid and a protease inhibitor [nelfinavir (31), indinavir (16), and combinations (5)]. The majority received AZT in labor (96%). The mean±SD duration of therapy was 16.0±9.0 weeks. Patients experienced significant increases in CD4 counts from 370±257/mm³ at baseline to 416±267/mm³ at 3 months follow up (p<0.01). They also experienced a significant drop in the HIV PCR from 4.280±0.7 log copies/ml to 2.97±0.8 log copies/ml (p<0.001), at 3 months follow up 28 women (54%) achieved undetectable viral loads. The average EGA at delivery was 38.8±1.0 weeks. The transmission rate of HIV was 2/52 (3.1%). The mean±SD duration of therapy was 16.0±9.0 weeks. Patients experienced significant increases in CD4 counts from 370±257/mm³ at baseline to 416±267/mm³ at 3 months follow up (p<0.01). They also experienced a significant drop in the HIV PCR from 4.280±0.7 log copies/ml to 2.97±0.8 log copies/ml (p<0.001), at 3 months follow up 28 women (54%) achieved undetectable viral loads. The average EGA at delivery was 38.8±1.0 weeks. The transmission rate of HIV was 2/52 (3.1%). The mean±SD duration of therapy was 16.0±9.0 weeks. Patients experienced significant increases in CD4 counts from 370±257/mm³ at baseline to 416±267/mm³ at 3 months follow up (p<0.01). They also experienced a significant drop in the HIV PCR from 4.280±0.7 log copies/ml to 2.97±0.8 log copies/ml (p<0.001), at 3 months follow up 28 women (54%) achieved undetectable viral loads. The average EGA at delivery was 38.8±1.0 weeks. The transmission rate of HIV was 2/52 (3.1%).

CONCLUSION: HAART in pregnancy had a significant role in improving immune status and decreasing viral loads. In cases where women were adherent and had a good response, it was effective in preventing perinatal transmission. Women not taking the medications with high viral loads were at risk for transmitting the virus to their babies.

OBJECTIVE: On January 1, 1995 we introduced an intrapartum maternal and infant treatment protocol for the prevention of Group B Streptococcus (GBS). We sought to measure the impact of the introduction of this protocol on neonatal GBS sepsis at Parkland Hospital.

MATERIALS: We assessed the incidence of GBS neonatal sepsis over an 11-year period (1988 to 1998) using a before-after study design. Prophylactic penicillin G in the delivery room; preterm infants received 25,000 units with all antibiotics for GBS prevention were not used between 1988 and 1 January 1995. Thereafter, all women with preterm labor (< 36 weeks) and prolonged ruptured membranes (> 18 hours) at term received intrapartum ampicillin until delivery. In addition, all term infants received 50,000 units of aqueous penicillin G in the delivery room; preterm infants received 25,000 units within 1 hour of birth. In all 11 study years, chorioamnionitis was treated with ampicillin and gentamicin. Infants with sepsis were defined by positive blood cultures within the first 5 days of life. We compared rates by 2x2 analysis and OR calculation.

RESULTS: There were 102,913 livebirths before the GBS protocol and 54,207 since the introduction of combined prophylaxis. The rate of early-onset GBS sepsis was 2.94 per 1000 births from 1988 - 1994 and 0.55 per 1000 births from 1995 - 1998 (P < 0.001; OR 0.27, 95% CI 0.18 – 0.48).

CONCLUSION: We observed a sustained four-fold decrease in GBS sepsis contemporary with introduction of a combined GBS prevention protocol.

BACTERIAL PRESENCE IN AMNIOTIC FLUID AT TIME OF GENETIC AMNIOCENTESIS. G.R. Marken*, D. Grooms, M. Slapak, J. Baskett, R. Mifflin, A. Bashiri, I. Shoham-Vardi, S. Patel, S. Saudino, J. Haas, B. Marciniak, O. Erez, A. Bashiri, O. Erez, M. Mazor. Dept OB/GYN and Epidemiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beersheva, Israel.

OBJECTIVE: To evaluate maternal infectious morbidity outcome in cases of preterm premature rupture of membranes (PPROM) in a non-selected parturient population.

STUDY DESIGN: The study population consisted of 5660 singleton preterm births (24-36 weeks' gestation). A cross-sectional study of maternal infectious morbidity adjusted for gestational age at delivery was designed. The study group consisted of patients with PPROM without and of non-PPROM group included patients without PPROM (n=4692). The data were analyzed by SPSS package.

RESULTS: The rates of clinical chorioamnionitis were significantly higher in the PPROM group compared with the group without PPROM at 26-28 wk, 29-31 wk, and ≥ 32 wk of gestational age at delivery: 43.5% vs. 12.4%; 35.7% vs. 6.8%, 11.5% vs. 1.5%, (P<0.001), respectively. The rates of bacteremia were higher in PPROM patients in the same gestational age groups. 12.7% vs. 5.9%, (P=0.06); 16.7% vs. 8.3%, (P=0.02); 8.3% vs. 4.7%, (P<0.001) when compared with the patients without PPROM. Genitourinary tract infections were higher in women with PPROM only in the gestation group ≥ 32 wk, 4.4% vs. 3.1%, (P=0.06). The rates of postpartum endometritis were significantly higher in the PPROM group than those with intact membranes who delivered after 32 wk of gestation, 2.2% vs. 1.5%, (P=0.04). Multiple logistic regression was used to assess the contribution of different risk factors to maternal infectious morbidity.

CONCLUSIONS: 1) PPROM is an independent risk factor for the development of maternal infectious morbidity in preterm births. 2) A prolonged latency period of an admission-to-delivery interval of more than 48 hours is an additional risk factor for increased maternal infectious morbidity.


OBJECTIVE: The development of effective monotherapy is desirable in treatment of human postpartum endometritis. In the controlled setting of the rabbit model, we compared parental clindamycin-gentamicin (CL/GM) to trovafloxacin (TROVA), a new quinolone with activity suitable for genital infections.

STUDY DESIGN: Rabbits do at 90-95% gestation were endoscopically inoculated intracervically with 10^8 cfu each of GBS, E. coli and Prevotella bivia. All animals were susceptible to Kirby Bauer testing. Labor was induced if the gestation was undelivered after inoculation. At death or after 7 days, does were sacrificed, and blood, peritoneal and uterine cultures were performed. When the does became ill postpartum, maternal blood cultures were performed and antibiotics were initiated. Does were randomized to receive TROVA 20 mg/kg/day divided q12h or CL 35 mg/kg/day plus GM 4.5 mg/kg/day divided q8h. Our primary outcome was clinical cure, and secondary outcomes were microbiologic cure and abscess development. With an equivalence trial, the sample size would be large, so a pilot trial of 15 animals per arm was chosen.

RESULTS: No significant differences in clinical cure, microbiologic cure or abscess formation were noted. However, there were significant differences in persistence of GBS in the uterus of the TROVA animals and E. coli in the CL/GM animals. GM levels were therapeutic (5-6 µg/mL).

OUTCOME TROVA CL/GM P-value

Clinical cure 14/15 (93.3%) 14/15 (93.3%) NS
Microbiologic cure 4/15 (26.7%) 8/15 (53.3%) NS
Pos uterine culture@ necropsy 11/15 (73.3%) 7/15 (46.6%) NS
Persistant GBS 13/15 (86.7%) 4/15 (26.7%) 0.007
Persistant E. Coli 1/15 (6.7%) 7/15 (46.6%) 0.005
Pos blood culture@ necropsy 0/14 NS
Abscess formation 6/15 (40%) 4/15 (26.7%) NS

CONCLUSIONS: Clinical cure rates were excellent in both groups. Despite in vitro susceptibility, there was substantial persistence of positive cultures in both groups, and abscess formation was also high. We speculate this is due to factors influencing in vivo antibiotic efficacy locally. Supported by Pfizer grant: 2532819.

BACTERIAL PRESENCE IN AMNIOTIC FLUID AT TIME OF GENETIC AMNIOCENTESIS. G.R. Marken*, S. Patel, J.P.O. Grady, L.A. Bayer-Zwirello, Baystate Medical Center, Dept. of MFM. Tufts University School of Medicine, Springfield MA.

OBJECTIVE: The purpose of this study is to determine whether an association exists between interleukin-6 (IL-6) and bacteria in amniotic fluid (AF) at the time of genetic amniocentesis. Outcomes such as low birth weight or preterm delivery were specifically targeted.

STUDY DESIGN: AF from asymptomatic patients presenting for genetic amniocentesis between 15-21 weeks gestation were analyzed. Bacteria were tested by PCR with consensus eubacterial primers to 16S rRNA and IL-6 concentration was tested by ELISA. Newborn weights and gestational age at delivery were compared.

RESULTS: 61 samples were available for analysis. 17% were PCR-positive for bacteria and 21.3% had elevated levels of IL-6. There was no correlation between IL-6 levels and bacterial presence as IL-6 levels in the PCR positive and negative groups were identical. However increased levels of IL-6 alone, were strongly associated with low birthweight, and bacterial colonization had no impact on birthweight.

CONCLUSION: The presence of bacteria in AF from asymptomatic pregnancies does not appear to correlate with an inflammatory response or have an impact pregnancy outcome. Although a preliminary report this supports that early bacterial colonization is not necessarily a pregnancy complication.
**294** MIDTRIMESTER AMNIOTIC FLUID MACROPHAGE INFLAMMATORY PROTEIN-1α: NOT A PREDICTOR OF POOR PREGNANCY OUTCOME.

J Anaíz, E Moonan, M Varner, DP Brennerman, CY Song, SDMP, NICHD, NIH, and Departments of Ob/Gyn, University of Utah and Georgetown University Medical Center, Bethesda, MD, Salt Lake City, UT and Washington, DC.

OBJECTIVE: Macrophage inflammatory protein-1α (MIP-1α) is an inflammatory chemokine produced by maternal decidual cells and associated with preterm labor. Previous work has demonstrated that in asymptomatic women in the midtrimester, abnormal cytokine levels are associated with poor pregnancy outcome. Thus this study was designed to evaluate whether the chemokine MIP-1α is a marker of poor pregnancy outcome in asymptomatic midtrimester women.

STUDY DESIGN: Patients with non-anomalous singleton gestations who underwent midtrimester genetic amniocentesis (15-29 wks) with no conditions associated with poor pregnancy outcome and available outcome information were included. Poor pregnancy outcome included development of eclampsia, fetal demise or preterm delivery (<37 wks). Patients were matched (1:2 ratio) with controls based on year of amniocentesis, maternal age and parity.

RESULTS: 56 women met inclusion criteria for poor pregnancy outcome (50 controls). Protein concentration was not different between study [5.47 (2.1 - 5.7) mg/ml] and control [3.2 (1.1 - 11.6) mg/ml, P=05]. MIP-1α levels were also not different between study [5.6 (0.21 -4.14 pg/ml)] and control [5.9 (0.36 -8.2) pg/ml]. Subgroup analysis also revealed no difference in MIP-1α levels.

CONCLUSIONS: In the uncomplicated midtrimester patient, amniotic fluid MIP-1α levels are not predictive of poor pregnancy outcome. Since MIP-1α is strongly associated with infection, underlying asymptomatic midtrimester infections may not comprise a significant component of poor pregnancy outcome.

**296** INFLAMMATION AND INCREASED APOPTOSIS IS NOT FOUND IN THE FETAL BRAIN FOLLOWING SHORT COURSE INTRA-AMNIOTIC INFEC-

TION (IAI) IN THE RABBIT.

J Davé, CD Spong, SDMP, NICHD, NIH, and Departments of Ob/Gyn, Yale University School of Medicine, New Haven, CT.

OBJECTIVE: IAI has been associated with cerebral palsy (CP), possibly due to elevated levels of cytokines. Yoon et al. (AJOG, 1998) found increased evidence of apoptosis in the fetal brain following chronic infection in the rabbit model, and have associated this with lesions in the periventricular area—the lesions found in CP. Some apoptosis may occur in rapidly developing fetal cases. We investigated the fetal brain histologically, with particular attention to inflammation and apoptosis.

STUDY DESIGN: As part of a study of cytokines in IAI (Leslie, SGI, 1999), rabbit does at 70% gestation were endoscopically inoculated intra-amnionically with 10^6 cfu of E. coli. At 6, 4, 8, 16, 24, and 30 hrs following inoculation, doies were sacrificed. At necropsy, maternal, fetal, peritoneal fluid, amniotic fluid, and uterus were cultured. Fetal tissues including brain were collected and examined with HE staining. Forty high-powered fields (HPF) were examined for inflammation and apoptotic bodies (AB). TUNEL staining is planned.

RESULTS: Only animals with positive uterine and/or amniotic fluid cultures were included. Statistical analysis compared the mean number of AB found at each time point using ANOVA.

<table>
<thead>
<tr>
<th>Time Post Inoc. (hrs)</th>
<th># Pups</th>
<th>Inflammation (MeanzSEM/40HPF)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3</td>
<td>33±7.6</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>37±16.9</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>31±5.7</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>8</td>
<td>17±8.0</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>3</td>
<td>17±14.3</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>3</td>
<td>48±23.5</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: Neither inflammation nor a significant increase in AB was noted in the fetal brain by 30 hrs after inoculation. Some apoptosis is seen at tome 6, suggesting this is a normal finding in rapidly dividing tissue. We speculate that a critical length of time for bacterial replication and production of cytokines is necessary in the fetal compartment to effect inflammation and increased apoptosis in the fetal brain, possibly contributing to CP. We speculate that this time is longer than 30 hrs from cervical inoculation. Support MOD#2532823 and NIH MD31641.

**295** HISTOLOGIC INFLAMMATION OCCURS IN THE MATERNAL BUT NOT THE FETAL COMPARTMENT EARLY IN INTRA-AMNIOTIC INFEC-

TION (IAI) IN A RABBIT MODEL.

J Davé, R Shikes, S Lee, S Woodcock, R McDuflie, R Gibbs, Dept. Ob/Gyn & Path, UCHSC, Denver, CO.

OBJECTIVE: IAI has been associated with cerebral palsy and respiratory distress syndrome. Studies of IAI and histologic inflammation (HI) have been primarily limited to the placenta and membranes. In IAI, microbes can enter the fetal compartment by hematogenous spread from the placenta or by ingestion of infected fluid into the lung/gut. We sought to evaluate HI in maternal and fetal tissues in the rabbit after IAI.

STUDY DESIGN: 40 pregnant rabbits at 70% gestation were inoculated intra-amniotically with 10^6 cfu of E. coli. Doies were sacrificed at 4, 8, 16, 24 and 30 hours following inoculation. At necropsy, blood, peritoneal fluid, amniotic fluid, and uterus were cultured. Fetal lung, heart, gut, and kidney were collected for HE staining. Tissue Gram stain was performed on placenta and fetal lung to identify microorganisms. Animals were excluded if no cultures were positive. Necrosis, infiltration, congestion, and edema were each assessed semiquantitatively on a scale of 0-4. Mean composite HI scores were compared with ANOVA.

RESULTS: A significant increase in HI score was seen in the uterus, but not fetal tissues. The placenta showed a nonsignificant trend toward increasing score. Tissue Gram stain showed no organisms until 24 hrs. *P<0.016

**297** IN VITRO EFFECT OF LIPOPOLYSACCHARIDE ON FAS LIGAND EXPRES-

S HAN FETAL MEMBRANES.

H Hanrahan, CD Hsu, Dept. of Ob/Gyn, Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Increased apoptosis of human fetal membranes has been reported to be associated with intramnionic infection (IAI). We also found that lipopolysaccharide (AF) soluble Fas ligand (sFasL) was elevated in IAI. This study was to investigate the effect of lipopolysaccharide (LPS) on FasL expression in human fetal membranes in vitro.

STUDY DESIGN: Fetal membranes (n=5) were collected from elective cesarean sections at term without labor. Membranes were cut into pieces of 1 cm in diameter and placed in 6-well tissue culture plates. The culture medium consisted of Dulbecco's modified Eagle's medium (DMEM) with Ham's 12 (1:1), pemcillin/streptomycin, 2 mM glutamine and 15% fetal bovine serum.

Tissues were incubated for additional 24 hr. Tissue viability was confirmed by trypan blue exclusion. FasL expression in human fetal membranes in vitro. This suggests that human fetal membranes may not contribute to the elevation of sFasL in IAI. The physiologic role of FasL in human fetal membranes remains to be determined.

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298 LACTOFERRIN: A NATURAL ANTIMICROBIAL AGENT IN THE HOST DEFENSE AGAINST INTRATERINE INFECTION. P Paone¹, E Maymon¹, M.T. Gerbas², K Bianco³, S.E. Edwin³, B.H Yoon⁴, R Romero Perinatology Research Branch, NICHD, Bethesda, MD and Dept. Obst/Gyn, Wayne State University, Detroit, MI

OBJECTIVE: A central question in modern obstetrics is why some pregnant women develop an ascending intrauterine infection while most do not. Lactoferrin is a natural antimicrobial agent with amphipathic properties, although the specific factors responsible for these activities have not been determined. Lactoferrin and defensins, potent anti-microbial proteins/peptides, are present in cervical mucus and AF and have been implicated in the mechanisms of host defense against ascending intrauterine infection. This study was conducted to determine if AF lactoferrin concentrations change with intra-amniotic infection (IAI) in preterm and term gestations.

STUDY DESIGN: A cross-sectional study was conducted in 248 women in the following categories: 1) term with and without IAI; 2) preterm labor (PTL) with and without IAI; 3) preterm premature rupture of the membranes (PROM) with and without IAI; and 4) midtrimester. Lactoferrin concentrations in AF were determined using sensitive and specific immunosassays sensitivity 0.124 ng/ml.

RESULTS: 1) Lactoferrin was detectable in 92.3% (229/248) of all samples collected and absent in all midtrimester samples (23/23); 2) The concentration of lactoferrin increased with advancing gestational age: p<0.0001, p<0.001; 3) IAI was associated with a significant increase in AF lactoferrin concentrations in patients with preterm (Group 4 vs. Group 5: p<0.001) and term gestation with intact membranes (Group 3 vs. Groups 1 and 2, p<0.01) as well as preterm PROM (Group 7 vs. Group 6, p<0.005). 4) Lactoferrin Median (Range) 349 3 (<1.24-836) ng/ml vs term delivery median: 36.5 ng/ml; range: 24.8-224.9 ng/ml; p=0.0740; PTL: (preterm delivery, median: 36 2 ng/ml, range: 0.57-189.5 ng/ml vs term delivery, median: 36.5 ng/ml, range: 0.57-183.8 ng/ml; p<0.0001, 3) IAI was associated with a significant increase in AF lactoferrin concentrations in patients with preterm (Group 4 vs. Group 5: p<0.001) and term gestation with intact membranes (Group 3 vs. Groups 1 and 2, p<0.01) as well as preterm PROM (Group 7 vs. Group 6, p<0.005).

CONCLUSIONS: 1) IAI is associated with a dramatic increase in lactoferrin concentrations in AF; 2) The increased concentrations of lactoferrin with advancing gestational age may explain the greater antimicrobial activity of AF in term than preterm gestations; 3) We propose that lactoferrin is part of the repertoire of host defense mechanisms against intrauterine infection.

299 THE RISK OF PREECLAMPSIA IN A HUMAN IMMUNODEFICIENCY VIRUS INFECTED POPULATION H B Bernstein, G. V. Hanna¹, E. D. Garewitsch¹, J. R. Anderson¹, Department of Gynecology & Obstetrics, The Johns Hopkins Univ Sch of Med, Baltimore, MD

OBJECTIVE: Current theories on the mechanism of preeclampsia include activation of peripheral blood leukocytes (PBLs) associated with maternal endothelial cell activation. This is dependent on the presence of a placenta and ultimately leads to endothelial cell dysfunction and the clinical manifestations associated with preeclampsia. Assuming that activation of PBLs are integral to the development of preeclampsia, we hypothesized that gravida with a defective immune response, human immunodeficiency virus (HIV) infected women, have a lower incidence of preeclampsia.

STUDY DESIGN: The rate of preeclampsia in HIV infected and uninfected women were compared in a retrospective cohort analysis of all women delivered at our institution from 1996-1999 and all women entered into our obstetrical database from 1988-1995. Patients were considered to have preeclampsia if they met the criteria described by the American College of Obstetricians & Gynecologists of BP:140/90, with proteinuria or edema or without a positive AF culture for microorganisms. MMP-1 concentrations in AF were determined using sensitive and specific immunoassays as a positive AF culture for microorganisms.

RESULTS: 1) MMP-1 was detectable in 92% of AF samples (210/229) and absent in all midtrimester samples (23/23); 2) The MMP-1 concentrations in 229 women in the following categories: 1) term not in labor (n=23), 2) term in labor (n=23), 3) preterm labor (PTL) who delivered at term (n=21); 4) PTL who delivered at term (n=22), 5) PTL who delivered preterm with IAI (n=20), 6) preterm premature rupture of membranes (PROM) without IAI (n=22) and with IAI (n=29) IAI median: 15.3 ng/ml, range: 0.57-151.0 ng/ml vs PROM without IAI (n=22) and with IAI (n=29) IAI median: 29.0 ng/ml, range: 1.57-79.7 ng/ml.

CONCLUSIONS: 1) IAI is associated with a decrease in AF MMP-1 concentration; 2) Term in labor and prepartum IAI were not associated with a decrease in AF MMP-1 concentration; 3) Term in labor and prepartum PROM were not associated with a decrease in AF MMP-1 concentration; 4) MMP-1 concentrations in AF decreased with advancing gestational age (r=0.7, p<0.001); 5) MedP1 in PROM decreased with advancing gestational age (r=0.7, p<0.0001); 6) MMP-1 concentrations in PROM decreased with advancing gestational age (r=0.7, p<0.0001); 7) MMP-1 concentrations in PROM decreased with advancing gestational age (r=0.7, p<0.0001).

300 CLINICAL CHORIOAMNIONITIS IS ASSOCIATED WITH A DECREASED MATERNAL-FETAL CONCENTRATION GRADIENT OF IONIZED MAGNESIUM IN PATIENTS RECEIVING MAGNESIUM SULFATE: A RANDOMIZED STUDY. S.C. Blackwell¹, M Hallak¹, S.S. Hassan², G. Norman², J. R. Anderson¹, Department of Gynecology & Obstetrics, Wayne State University, Detroit, MI

OBJECTIVE: Chorioamnionitis is strongly associated with the development of adverse neonatal outcomes. Magnesium sulfate (MgSO4) may have neuroprotective effects. Our objective was to investigate the effects of clinical chorioamnionitis on the maternal: fetal concentration gradient of ionized magnesium (Mg++) in patients receiving intrapartum MgSO4 or placebo (lactated ringer solution) in labor.

STUDY DESIGN: Inclusion criteria were: gestational age (GA) >32 weeks on admission, no clinical indications for MgSO4 therapy (preterm labor or tocolysis), and either clinical chorioamnionitis or prolonged rupture of membranes. Patients were randomized in a double-blinded fashion for either MgSO4 (6gm load then 2gm/hr) or lactated ringer solution (LR) solution. Maternal serum and umbilical venous Mg++ levels were compared between patients with and without chorioamnionitis. Chorioamnionitis was defined as maternal temperature >38°C, temperature >39°C in fetal scalp, fetal heart rate >150 or <100, fetal tachycardia, maternal tachycardia, or foul smelling discharge. Mg++ concentration gradient was expressed as the umbilical venous Mg++/maternal median level x 100. Statistical analysis included Two-way ANOVA and Student's t-test P < 0.05 was considered significant.

RESULTS: Clinical chorioamnionitis was associated with a decreased maternal: fetal Mg++ concentration gradient in patients receiving MgSO4, but not in those receiving LR (see table).

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>No chorioamnionitis</th>
<th>Chorioamnionitis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobr</td>
<td>119+9%</td>
<td>125+9%</td>
<td>0.5909</td>
</tr>
<tr>
<td>MgSO4 (n=7)</td>
<td>131+36%</td>
<td>95±13%</td>
<td>0.035</td>
</tr>
</tbody>
</table>

CONCLUSION: We speculate that chorioamnionitis decreases the placental transfer of MgSO4 and in the presence of intrauterine infection increased doses may be required to achieve fetal levels necessary for neuroprotection.

301 A STUDY OF THE RELATIONSHIP BETWEEN MMP-1 (COLLAGENASE-1) AND PARTURITION, RUPTURE OF MEMBRANES AND INTRATERINE INFECTION. E. Maymon¹, P. Paone¹, K Bianco³, S.E. Edwin³, B.H Yoon⁴, R Romero Perinatology Research Branch, NICHD, Bethesda, MD and Dept Obst/Gyn, Wayne State University, Detroit, MI

OBJECTIVE: Parturition involves degradation of the extracellular matrix in fetal membranes and increased activity of matrix degrading enzymes or matrix metalloproteases (MMPs). Rupture of membranes (ROM) is thought to result from the effect of physical forces in localized areas of the membranes weakened by degradation of structural collagenases-1, or MMP-1, has been implicated in parturition. The objective of this study was to determine the relationship between human parturition, spontaneous ROM and intraterine infection (IAI) and MMP-1 in term gestations.

STUDY DESIGN: A cross-sectional study was conducted to determine MMP-1 concentrations in 292 women in the following categories: 1) term in labor with intact membranes (n=22), 2) term in labor (n=23), 3) preterm labor (PTL) who delivered at term (n=21); 4) PTL who delivered preterm with IAI (n=20), 6) preterm premature rupture of membranes (PROM) without IAI (n=22) and with IAI (n=29) IAI median: 36.1 ng/ml, range: 7.0-350.9 ng/ml vs in labor, median: 36.5 ng/ml, range: 7.1-241.7 ng/ml, p<0.005 (n=11) vs without IAI, median: 36.1 ng/ml, range: 7.0-350.9 ng/ml vs with IAI, median: 36.5 ng/ml, range: 7.1-241.7 ng/ml, p<0.005).

CONCLUSIONS: 1) Collagenase-1, or MMP-1, is a physiologic constituent of AF. 2) ROM and parturition in these women are associated with a decrease in the AF MMP-1 concentrations; 3) Preterm parturition, IAI and PROM were not associated with changes in AF concentrations of MMP-1. These observations provide evidence of a complex mechanism regulation of MMPs, as MMP-9, but not MMP-1, concentrations are increased with infection, ROM and parturition (Am J Obstet Gynecol 1998, 179 1248S-53).
302


OBJECTIVE: Intrauterine infection is a cause of membrane rupture. Two distinct matrix metalloproteinases (MMPs), MMP-9 (inducible form) and MMP-2 (constitutive form), have been implicated in the degradation of fetal membranes. This study was conducted to determine its intraamniotic infection (IAI) is associated with an increased activity of MMP9 and MMP2 in vitro.

STUDY DESIGN: A cross-sectional study was conducted with 139 women in the following categories: 1) preterm labor (PTL) who delivered preterm (n=39); 2) PTL with IAI (n=59); 3) preterm premature rupture of the membranes (PPROM) without IAI (n=39); and 4) PPROM with IAI (n=52). Active forms of MMP-2 and MMP-9 were measured by a novel assay that uses a substrate developed by protein engineering.

RESULTS: 1) IAI in patients with PTL was associated with a significant increase in the median concentration of the MMP-9 active form but not of MMP-2 (Groups 5 vs 4 median 0.74 vs 0.59, p<0.02); 2) IAI in women with PPROM was also associated with a significant increase in the concentration of active MMP-9 and decrease in MMP-2 (Groups 3 vs 4; p<0.03 and p<0.05, respectively).

CONCLUSIONS: The in vitro activity of the inducible gelatinease MMP-9 is dramatically increased in the presence of infection. We propose that proinflammatory cytokines released during intrauterine infection induce the production of MMP-9 and contribute to membrane rupture.

303


OBJECTIVE: Interleukin-18 (IL-18) is a proinflammatory cytokine with pleiotropic biological effects implicated in the host defense against infection. Recent evidence indicates that IL-18 plays a significant role in the pathogenesis of sepsis, as IL-18 deficient animals are highly susceptible to endotoxin shock. Il-18 was detectable in all AF, maternal and umbilical cord blood samples. IL-18 concentration decreased with advancing gestational age (r=0.5, p<0.05). IAI in preterm and term labor was associated with a significant increase in IL-18 AF concentrations. PTL (n=40) median 0.59 (range 0.19-3.75) vs IAI (n=40) median 0.74 (range 0.19-6.57), p<0.05; 2) PTL with IAI (n=40) median 0.59 (range 0.19-3.75) vs IAI (n=40) median 0.74 (range 0.19-6.57), p<0.05; 3) PPROM without IAI median 0.78 (range 0.19-4.82) vs IAI (n=40) median 0.74 (range 0.19-6.57), p<0.05; 4) PPROM with IAI median 0.78 (range 0.19-4.82) vs IAI (n=40) median 0.74 (range 0.19-6.57), p<0.05; 5) PROM in labo* (n=19); and 4) PPROM with IAI (n=40).

CONCLUSIONS: The in vitro activity of the inducible gelatinease MMP-9 is dramatically increased in the presence of infection. We propose that proinflammatory cytokines released during intrauterine infection induce the production of MMP-9 and contribute to membrane rupture.

304


OBJECTIVE: To compare the rates of cesarean section and operative vaginal delivery between women who are receiving oxytocin for labor induction or augmentation or are in spontaneous labor, with and without intraamniotic infection (IAI).

STUDY DESIGN: This ongoing analysis, singleton pregnant women undergoing induction of labor or receiving oxytocin augmentation of labor were compared to the next matched control in spontaneous labor. Patients with recent antibiotic use, pre-eclampsia, malpresentation, fetal demise and gestational age < 35 weeks were excluded. Cesarean section and operative vaginal delivery rates were compared between women receiving oxytocin and those in spontaneous labor, further stratified by the presence or absence of intraamniotic infection.

RESULTS: To date, 335 women have been analyzed. IAI rates were significantly higher in women receiving oxytocin (17%) vs. those in spontaneous labor (5%, p<0.05).

<table>
<thead>
<tr>
<th>Oxytocin</th>
<th>Spontaneous Labor</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAI</td>
<td>No IAI</td>
</tr>
<tr>
<td>Op Vag Del (%)</td>
<td>10.3 (10.3) vs 9.78 (1.89-5.77, p&lt;0.001)</td>
</tr>
<tr>
<td>C/S (%)</td>
<td>51.7 (10.6) vs 40 (&lt;0.53-3.95, p&lt;0.001)</td>
</tr>
</tbody>
</table>

1P < 0.001 vs no IAI

Overall, women with IAI had a five-fold higher risk of cesarean section than those without IAI (OR 5.05 [1.75-15.81]).

CONCLUSION: Women in labor who develop IAI are more likely to require cesarean delivery. This is particularly true for women who are receiving oxytocin for induction or augmentation of labor.

305

THE DEVELOPMENT OF A NEURAL NETWORK TO PREDICT DELIVERY IN 7 DAYS AMONG WOMEN WITH PRETERM LABOR, G. Macouy, S. E Edwin, J. Pipet, M. McFarland. Department of Ob/Gyn, University of PA Health System, Philadelphia PA.

OBJECTIVE: To develop a sensitive and specific neural network to predict the likelihood of delivery within 7 days among women with preterm labor. We performed a case-control study at our institution and we measured MgSO4 for tocolysis with minimal degrees of cervical dilation on admission <2 cm. A case was defined as a patient who received tocolysis and delivered within 7 days (n=50) while a control was defined as a patient who received MgSO4 and did not deliver within 7 days of admission (n=195). The medical and prenatal records of cases and controls were reviewed and information on over 60 clinical and historical variables was abstracted. Using these data, a multivariate model was developed, trained, and tested. The network was tuned on numerous parameters, including error tolerance, density of hidden layers and connections, and learning rate to obtain the maximum sensitivity and specificity. We then sought to compare the test characteristics of the neural network to those obtained with multivariable modeling. For the development of the multivariate model, cases and controls were first compared with standard multivariate statistics. A multivariate predictive index was then developed using these data, and the sensitivity and specificity recorded.

RESULTS: The final multivariable model included 2 variables—bleeding on admission and substance abuse. Using regression modeling, we were able to achieve a sensitivity of 59% and a specificity of 74% for delivery within 7 days of admission. Using multiple combinations of variables in the neural network, we were able to achieve a slight improvement in specificity (82%) with a slight decrement of sensitivity (58%). The areas under the ROC curves for the multivariable model and neural network were similar.

CONCLUSIONS: In this case, the neural network performed similarly to standard multivariable modeling. While the specificity obtained with the neural network is comparable to other clinical/biochemical predictors in this setting, the sensitivity is substantially lower.
PREDICTING CESAREAN DELIVERY: DECISION TREE MODELS


OBJECTIVE: The purpose of the study was to determine whether decision tree-based methods can be used to predict cesarean delivery

STUDY DESIGN: The design is an historical cohort study of women delivered at Magee-Womens Hospital from January 1, 1995 through December 31, 1997. 22,157 unique women delivered a liveborn neonate. The frequency of cesarean delivery was 17%. There were 69 variables used for analysis. Predictive factors were chosen if they were present in 0.6% of deliveries to ensure adequately fit models. The statistical model using decision tree rule-based methods was applied to 50% of the sample to develop the predictive training model

RESULTS: Decision tree ROC Area was nulliparous 85, parous 93. Examples of computer generated predictive rules are demonstrated in Figs. 1 and 2, nulliparous and multiparous, respectively


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OBJECTIVE: To test the technical feasibility of Internet-based upload of fetal ultrasound and relatively inexpensive tools.

STUDY DESIGN: Fetal images were pushed from ATL HDI 5000 machines located in Los Angeles, Rochester and Detroit via a TCP/IP-DICOM connectivity package into an image server (Detsot). The server consisted of a Dell® 4200 computer, a 16 GB SCI RAIID 5 hard drive, and Microsoft® Windows® NT 4.0 with Microsoft SQL Server™ 6.5. 3Dex® Digital Jacket® software was used as a storage server class provider and Adobe® Photoshop® 5/6 DicAcc DicomAccess® software was used for image review. The protocol of sending images from each site included 10 gray scale images of fetal heads and 10 color images of 3-chamber fetal hearts. The images were sent once in 30-second intervals and then as a set of 20 images at once. For tuning purposes, the clocks on the remote ultrasound scanner and the image server were synchronized prior to the transmission

RESULTS: A set of 49 images was received from each institution. None of the images was lost or corrupted. The individual images arrived into the remote server within 60 seconds from the initiation of the transmission (mean 27 seconds for gray and 44 seconds for color). These times were not related to the physical distance between the server and the remote location. When images were sent as a group, it took 2 minutes for gray (5MB) and 8 minutes for color (9MB) to be stored on image archive. The subjective evaluation of the images showed no noticeable degradation in image quality

CONCLUSION: Given adequate safeguards for patient confidentiality, the Internet in conjunction with commercially available and relatively inexpensive software can be used to gather ultrasound images from various remote sites into a centralized image archive. This may provide cost effective image archiving solutions for perinatal ultrasound. Implementation of image databases which would gather and share via Internet pathological and educational images from sites around the globe is now a real possibility.
POSTER SESSION III

Friday, February 4, 2000
10:00 am – Noon

Fontainebleau Ballroom A/B

CATEGORIES
Fetal Assessment
Ultrasound
Dopple
Labor

Poster Numbers
310-430

Judges: Gary A. Dildy, MD
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310 PREDICTING THE OUTCOME OF LABOR BY ANALYSIS OF FETAL HEART RATE RECORDS, OBTAINED WITHIN 7 DAYS OF DELIVERY, USING CLASSIFICATION AND REGRESSION TREES. T. Thurlé*, O. Skansoni*, Department of Obstetrics and Gynecology, Rambam Medical Center, Technion, Faculty of Medicine and Computer Sciences, Haifa, Israel.

OBJECTIVE: To identify antepartum FHR features that would best predict the outcome of labor and help differentiate between low-risk and high-risk fetuses using classification and regression trees (CART) analysis.

STUDY DESIGN: A prospective study was performed in 1057 pregnant women at term. Thirty minutes recordings of fetal heart rate were obtained within 7 days of delivery. Each recording was sampled into a computer. A baseline was fitted to the FHR using a two-way digital filter and a set of programs performed numerical analysis of the FHR. Only the most recent record was used in the analysis. Outcome variables included fetal distress leading to operative delivery, birth weight, umbilical arterial blood gas values, Apgar scores and admission to the neonatal intensive care unit. The groups with normal and bad outcome were compared using Student t test, Wilcoxon Rank-Sum test, Chi-squared analysis and Fisher’s exact test. CART classification analysis was performed, based on all calculated FHR variables.

RESULTS: Forty women had a bad outcome and 1047 had a normal one. The mean number of FHR accelerations in fetuses with good outcome of labor was significantly greater compared to those with bad outcome (9.0±4.17 and 6.0±4.17 respectively, p<0.0001). In particular, medium and long-term accelerations were significantly more frequent in fetuses with normal outcome. The mean duration of FHR decelerations was significantly higher in the bad outcome group (28.2±16.1 sec vs. 22.9±8.0 sec, p<0.005). Both medium- and short-term heart rate variation were significantly lower in fetuses with bad outcome compared to those with good outcome (mean minute range 17.8±3.26 bpm vs. 21.6±4.39 bpm, p<0.0002; bandwidth variation 0.51±3.06 bpm vs. 0.78±3.06 bpm, p=0.02, respectively). CART classification analysis generated a tree with a root node split by accelerations < or > than 21 bpm and a mean deceleration area (or > or > 52% beats). The tree had a specificity of 86.2% and a sensitivity of 71.4%.

CONCLUSION: Within a week of delivery, fetuses with an abnormal outcome of labor have significantly different FHR patterns compared to those with a normal one. CART classification analysis yields an unprecedented sensitivity and thus can be served as a form of intrapartum risk assessment.


OBJECTIVE: To examine the effect of steroids on the biophysical profile score (BPS) of healthy fetuses, and the timing of onset and duration of their effect.

STUDY DESIGN: The study group consisted of 25 singleton pregnancies between the gestational ages of 26 and 34 weeks, mean (±SD) 32 weeks (±1.22) who were at increased risk of preterm labor. After initial fetal BPS of 8 or more was documented, two doses of 12mg betamethasone 24h apart were administered to accelerate pulmonary maturity. BPS were performed at 6 (preterm), 24h (before the second dose), 48, 72, 96 and 120 hours. BPS were computed with Friedman’s test, and individual parameters of the BPS were compared with Cochran’s Q test. Statistical significance was defined as p<0.05.

RESULTS: Mean delivery time was 36.2 (±24.1). 5 Min Apgars were 9.5 (±1.5) (range 8 to 10) to neonatal death or neonatal infection was documented. 25 fetuses of the original 29 received all six biophysical profile assessments. There was a statistically significant difference in the frequency of the following findings in pre- compared to post steroid measurements: absent body movements (48 hours, p<0.05), non-reactive fetal heart rate tracings (24, 48 and 72 hours, p<0.05 ) and absent breathing movements (24, 48 and 72 hours, p<0.05 ). Neither fetal tone nor amniotic fluid index was significantly affected Mean biophysical profile (SD) on days 0 to 5 was 9.9 (±5.55), 6.1 (±1.4), 8.5 (±1.45), 9.8 (±0.55) and 9 (±0.55) respectively. Individual values of the biophysical profile score were 56, whereas on 24, 48 and 72 hours, 16% (4/25), 76% (19/25), 16% (4/25) of them were 56 respectively (p<0.05). Moreover 3 of these healthy fetuses had a BPS of 4 (12%) on 48 hours showing the profound effect of steroids especially on this day

CONCLUSION: Maternal betamethasone administration can cause a significant but transient reduction in fetal body movements, breathing movements and fetal heart rate reactivity Misinterpretation of post-steroid biophysical depression as evidence of fetal compromise could lead to the unwarranted delivery of a premature fetus.


OBJECTIVE: Chronic cigarette smoking causes fetal growth restriction and fetal hypoxia. The effects of acute exposure to cigarette smoke on fetal cerebral and umbilical flows have not been established. We propose that fetal cerebral and umbilical blood flow may be altered as a result of an alteration of umbilical blood flow.

STUDY DESIGN: Doppler evaluation of blood flows in the umbilical artery, middle cerebral artery and common carotid artery were performed in 40 normally grown fetuses at a mean gestational age of 35.5±0.9 weeks following an episode of maternal tobacco smoking. All mothers were chronic smokers (>5 yrs duration). We used an ATL HDI 5000 scanner with color doppler to visualize blood vessels and measure blood flow velocities. The interval between assessing blood flows and the last cigarette smoked (hrs) was compared to the umbilical and cerebral blood flow velocities.

RESULTS: The interval since smoking the last cigarette was significantly inversely correlated with the systolic-diastolic (S/D) ratio in the middle cerebral artery (r=−0.40, p=0.002). None of the other parameters were significantly altered.

CONCLUSION: In the absence of fetal growth restriction, fetal cerebral blood flow may be reduced following cigarette smoking and the effects decline with time after smoking. The mechanisms are apparently independent of alterations in umbilical blood flow.

313 MATERNAL DRUG USE AND POLYHYDRAMNios. A Pustong Kemph, T Nguyen, J. Castro, Dept Obst/Gyn, Univ of IL, Chicago, IL.

OBJECTIVE: Drug use during pregnancy is known to produce central nervous system (CNS) depressive effects both in the fetus (decreased biophysical profile (BPP) scores), and the neonate (poor feeding). Drug effects on the amniotic fluid index (AFI), one variable of the BPP, are not well documented. Our objective was to determine the effects of maternal drug use on the AFI, specifically, if there was an increased incidence of polyhydramnios.

METHODS: Over a 12 month period from 07/97 to 12/98, consecutive cases of women with toxicology positive drug use during pregnancy, in whom there was at least one antenatally recorded AFI during the affected pregnancy, were identified. Data were retrieved from a prospectively maintained ultrasound and delivery database, and cases complicated by conditions known to cause polyhydramnios were excluded (diabetes mellitus, multiple gestation, congenital anomalies, placental abnormalities, twinanamnestic). AFI values in substance users were compared to those obtained during the same time period in over 5000 controls without a history of drug use, who were subjected to the same exclusion criteria.

RESULTS: Of the 92 toxicology positive cases identified, 63 had at least one quadrant AFI measured during the affected pregnancy. AFI values in drug users ranged from 14 to 41 cm, with an average (mean ±SEM) of 25.6±0.8 cm, at 52.0±6.8 weeks gestation, versus AFI values in controls which averaged 17.9±1.1 cm, p<0.01. There was a significantly higher incidence of polyhydramnios (AFI>24cm), 28% (18/63) in substance users, than that seen in controls, 3.9% (p<0.005). There were no differences in the mean AFI values among the various groups of substances users studied, though the incidence of polyhydramnios was significantly higher (p<0.005) in cocaine users, as illustrated below.

Drug (number) | AFI (mean±SEM) | % polyhydramnios
---|---|---
cocaine (16) | 24.5±1.7 | 44% (7/16)
opiates (14) | 22.5±1.6 | 14% (2/14)
marijuana (17) | 21.0±1.3 | 24% (4/17)
opioid analogue (16) | 22.0±1.5 | 31% (5/16)

CONCLUSIONS: 1) There appears to be a trend towards increased AFI's in pregnancies complicated by maternal drug use 2) Maternal drug use is associated with a significantly higher incidence of polyhydramnios, and should be considered a possible etiologic factor in women with apparent idiopathic polyhydramnios.
MEASUREMENT OF FETAL UMILCordial CORD CIRCUMFERENCE AS AN ESTIMATE OF BIRTH WEIGHT. M. Zaatari, D. Gahm, G. Olson, G. Hankins, G. Saade, Deps. of Ob/Gyn, University of Texas Medical Branch, Galveston, TX.

OBJECTIVE: To evaluate the relationship between umbilical cord circumference and birthweight.

STUDY DESIGN: Gravidae between 32 and 42 weeks admitted in labor and who delivered within 72 hours were included. Pregnancies with known chromosomal or structural anomalies were excluded. Ultrasound measurement of umbilical cord circumference was obtained from a cross-sectional, vessel-view loop of the cord. The relationships between umbilical cord circumference, birthweight and gestational age were analyzed using Pearson correlation, multiple linear regression and receiver operating characteristics (ROC) curves. A P <0.05 was used to denote statistical significance.

RESULTS: Five-hundred and sixty-two were included. There was no significant correlation between age and cord circumference in the gestational range studied. Cord circumference correlated with birthweight (R=0.5, P=0.0001). This relationship persisted even after controlling for gestational age and diabetes (P=0.0001). Cord circumference was predictive of birthweights ≥ 4250 g (r=0.79, P=0.0001) as well as ≥ 4500 g (r=0.52, P=0.0001). Sensitivity and specificity of a circumference ≥ 5.0 cm were, respectively, 100% and 71% for predicting birthweight ≥ 4250 g and 100% and 68% for predicting birthweight ≥ 4500 g. The best performance was obtained when a composite score including gestational age as well as cord circumference and based on the equation of the multivariate regression was used for prediction of birthweight ≥ 4250 g (solid line in figure; r=0.837; P=0.0001); best-cutoff sensitivity 100%, specificity 87% or ≥ 4500 g (dashed line in figure; r=0.72; P=0.0001); best-cutoff sensitivity 99%, specificity 87%. For each gestational age, a best-cutoff for cord circumference was generated for prediction of birthweight ≥ 4500 g.

CONCLUSION: Umbilical cord circumference, measured by ultrasound prior to delivery, may be helpful in predicting birthweight. Combining this measurement with other data may improve detection of large fetuses.

MECONIUM PASSAGE IN TERM PREGNANCY OCCURS INDEPENDENT OF AMNIOTIC FLUID VOLUME. C.A. Carreia, S.C. Blackall, S.S. Hassan, M. Redman, Y. Sorokan, S.M. Berry, H.M. Wolfe. Dept. of Ob/Gyn, Hutzel Hospital/Wayne State University, Detroit, MI.

OBJECTIVE: Meconium stained amniotic fluid (MSAF) has been reported to occur more frequently in the presence of oligohydramnios. However, specific effects related to meconium passage related to amniotic fluid volume (AFV) are not well described. The purpose of this study was to determine the relationship between meconium passage and AFV as a function of gestational age and fetal growth.

STUDY DESIGN: Liveborn singleton gestations ≥ 37 weeks with an amniotic fluid index (AFI) performed in our ultrasonic department within 7 days of delivery from 1995-1998 were studied. AFV was categorized as oligohydramnios (< 50 mm), decreased (51-80 mm), normal (81-180 mm), increased (181-240 mm), and polyhydramnios (> 240 mm). Meconium passage for each AFV category was calculated then compared by ANOVA and, after controlling for GA at delivery and neonatal ponderal index [PI] (BW/length), by discriminant function analysis (DFA).

RESULTS:

<table>
<thead>
<tr>
<th>AFV Status</th>
<th>N</th>
<th>GA 37-39 wks</th>
<th>GA 40-41 wks</th>
<th>GA ≥ 42 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSAF</td>
<td>%</td>
<td>MSAF</td>
<td>%</td>
<td>MSAF</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>285</td>
<td>12.5</td>
<td>25.9</td>
<td>22.0</td>
</tr>
<tr>
<td>Decreased</td>
<td>235</td>
<td>10.1</td>
<td>28.4</td>
<td>25.0</td>
</tr>
<tr>
<td>Normal</td>
<td>885</td>
<td>15.2</td>
<td>26.3</td>
<td>22.6</td>
</tr>
<tr>
<td>Increased</td>
<td>154</td>
<td>20.7</td>
<td>29.8</td>
<td>40.0</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>63</td>
<td>16.7</td>
<td>42.1</td>
<td>50.0</td>
</tr>
<tr>
<td>Total</td>
<td>1622</td>
<td>167/588</td>
<td>165/588</td>
<td>25/94</td>
</tr>
</tbody>
</table>

There were no statistically significant differences in the rate of MSAF by AFV category at any GA. Advancing GA at delivery and increasing neonatal PI were the only factors correlated with meconium, with no significant contribution from AFV.

CONCLUSION: Our data suggests that meconium passage is not associated with amniotic fluid volume but rather events related to fetal maturity and growth.

A RANDOMIZED CONTROLLED CLINICAL TRIAL COMPARING NON-STRESS TEST VERSUS DOPPLER VELOCIMETRY AS A SCREENING TEST IN A HIGH RISK POPULATION. K. Williams, D. Farquharson, M. Bebbington, J. Dassanech, F. Galerneur, R. Wilson, D. Shaw and N. Keeler. University of British Columbia, Diag. and Ambul. Prog., B.C. Women's Hospital, 4500 Oak Street, Van., B.C. V6H 3V5, Canada.

OBJECTIVE: To evaluate the ability of different antepartum testing modalities to screen for the presence of peripartum morbidity and mortality.

STUDY DESIGN: During a one-month period, all patients referred to the fetal assessment unit at B.C. Women's Hospital for fetal assessment at a gestational age ≥ 32 weeks, were approached to participate in this study. Patients were randomly allocated to either receive umbilical artery Doppler ultrasound or a non-stress test (NST) as a screening test for fetal well being. If either the Doppler or NST was normal, patients were reassessed according to departmental protocol. If the Doppler showed a S/D ratio > 9th or the NST was abnormal, i.e., variable decelerations or non-reactive an amniotic fluid assessment (AFI) index was done as a back-up test. If the AFI was normal, delivery was recommended. If the Doppler showed absent end diastolic flow or the NST was abnormal, delivery was recommended. Comparison between the groups was done using the chi-square statistic.

RESULTS: 1240 patients were randomized with 16 being lost to follow up. 605 patients received Doppler and 621 received NST. Mean number of visits to the Doppler group, 2.3 ± 2.4 for the NST group. Major indications for assessment included post-dates 43%, hypertension 11%, decreased fetal movement 22% and IUGR 7%.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Doppler (n=605)</th>
<th>NST (n=621)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillborn</td>
<td>0</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Meconium</td>
<td>112 (18%)</td>
<td>120 (19%)</td>
<td>NS</td>
</tr>
<tr>
<td>1 min agger &lt; 4</td>
<td>22 (3.6%)</td>
<td>19 (3.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>5 min agger &lt; 7</td>
<td>7 (1.2%)</td>
<td>7 (1.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>C/section for fetal distress</td>
<td>26 (4.3%)</td>
<td>36 (5.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Admission NICU</td>
<td>14 (2.3%)</td>
<td>19 (3.1%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CONCLUSION: Both NST and umbilical artery Doppler as screening tests used in conjunction with a management protocol in a high risk population, are adequate in their ability to predict peripartum morbidity.

ULTRASOUND ASSESSMENT OF AMNIOTIC FLUID VOLUME: DISTRIBUTION OF LARGEST VERTICAL POCKET MEASUREMENTS. F. Manning, CR. Harmon, SM. Menticoglou, A. Dayal, Dept. Ob/Gyn, Albert Einstein College of Medicine, Bronx, NY, University of Maryland, University of Maryland.

OBJECTIVE: Amniotic fluid volume is generally held to be predictive of perinatal outcome although this concept has been recently challenged (Maguin et al Am J Obstet Gynec 1999;180:1350). The object of this study was to define the distribution of AFV by largest pocket method, to determine the effect of gestational age on distribution, and to examine the relationship of perinatal mortality (PNM) to AFV.

STUDY DESIGN: AFV by largest pocket method was recorded prospectively in all patients referred for fetal assessment. The fetal assessment database contains all AFV measurements, gestational age at measurement, and perinatal mortality. Between 1987 and 1991 inclusive, these data were extracted and correlated.

RESULTS: In the 5 year study interval 84,740 AFV measurements were recorded among 19,685 patients (mean 4.5 per patient, range 1-8). Gestational age ranged from 24-44 weeks. The distribution was skewed left with a mean of...
316 THE ALPHA-OMEGA THEORY: EVIDENCE OF THE ALPHA EFFECT. 
FA Manning, CR Harman, S Memtougou, A Dayal, Dept Ob/Gyn, Albert Einstein College of Medicine, Bronx, NY, University of Maryland, University of Minnesota.

OBJECTIVE: The Alpha-Omega theory posulates that fetal responses to intrauterine insult(s) may manifest as postnatal diseases across the lifespan. The omega effect, that is late onset adult disease of prenatal origin, was first reported by Barker (BMJ 1989; 298:564) and has subsequently been confirmed by others. An attempt to identify the alpha effect, this is early onset childhood disease of prenatal origin, was the object of this study.

STUDY DESIGN: The prevalence of 5 discrete childhood conditions (cerebral palsy (CP), attention deficit disorder (ADD), mental retardation (MR) and emotional disorders (EDOC)) and comparative rates between BPP tested and non-tested fetuses was determined by integration of 3 independent comprehensive databases (ICD-9 claims, obstetric outcome, fetal assessment). In tested infants the relationship between risk and last BPP was calculated.

RESULTS: In a 9 year study interval (1984-1992 inclusive) outcome data was collected from 153,593 liveborns.

<table>
<thead>
<tr>
<th>Prevalence per 1000</th>
<th>Outcome</th>
<th>Non-tested</th>
<th>Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All cases (n=153,593)</td>
<td>Non-tested (n=117,255)</td>
<td>Tested (n=36,388)</td>
</tr>
<tr>
<td>ADD</td>
<td>20.3</td>
<td>28.1</td>
<td>4.74*</td>
</tr>
<tr>
<td>CP</td>
<td>3.73</td>
<td>4.74</td>
<td>1.33*</td>
</tr>
<tr>
<td>MR</td>
<td>2.83</td>
<td>5.1</td>
<td>0.9*</td>
</tr>
<tr>
<td>CR</td>
<td>0.94</td>
<td>1.04</td>
<td>0.66*</td>
</tr>
<tr>
<td>EDOC</td>
<td>1.01</td>
<td>1.0</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*p<0.01

CONCLUSION: By comparison, tested fetuses were significantly less likely to develop childhood disorders of presumed asphyxial origin and for each of these there was a significant inverse exponential relationship between last BPP and risk. Since BPP reflects fetal adaptation and is an accurate proxy for fetal pH, these data are evidence of the alpha effect.

319 THE PREVALENCE OF NON-SPECIFIC EMOTIONAL DISORDER OF CHILDHOOD IS UNRELATED TO ADVERSE PERINATAL FACTORS. 
F.A. Manning, C.R. Harman, S. Memtougou, A. Dayal, J. Xie, Dept Ob/Gyn, Albert Einstein College of Medicine, Bronx, NY, University of Maryland, University of Manitoba, March of Dimes.

OBJECTIVE: Emotional disturbances of childhood (EDOC) is a distinct ICD-9 coded condition, distinct from attention deficit disorder and other neurological conditions. The etiology of EDOC is unknown. The object of this study was to determine the relationship to fetal and obstetric factors, to determine the prevalence of EDOC among infants followed from birth, to contrast the prevalence between pregnancies subjected to serial fetal biophysical profile (BPP) testing to non-tested pregnancies and to determine the relationship if any between last BPP result and risk of EDOC.

STUDY DESIGN: Index cases of EDOC and subsequent relevant clinical case data were obtained by integration of 3 independently-maintained prospective comprehensive data bases (ICD-9 claims data base, obstetric outcome data base and fetal assessment data base). Verification of diagnosis and clinical data was done by review of hospital and office records of index cases. Follow-up by ICD-9 claim data base was for a maximum of 12 years (1984-1996).

RESULTS: In a 9 year study interval (1984-1992 inclusive) 436 cases of MR occurred among 153,593 live births (prevalence 2.84 per 1000). 117 of 436 cases of MR (26.8%) were associated with genetic/developmental anomalies and 52 cases (11.9%) were associated with postnatal causes including infection, anoxia, hemorrhage and trauma. In 267 cases (61.3%) the etiology could not be assigned. The prevalence of MR increased directly with duration of follow-up such that at age 8 years the prevalence was 4.5 per 1000. (385 of 85,574 live borns). Among 8 year olds or older the prevalence of MR varied according to the presence or absence of antepartum BPP testing. In tested pregnancies the prevalence was 2.85 per 1000 (56 of 19,682) as compared to 4.32 in non-tested patients (289 of 65,892) (p<0.01). A highly significant inverse exponential relationship between last BPP and the risk of MR was observed. (R^2 0.79 p<0.01)

CONCLUSION: These data indicate that MR is a condition of diverse etiology that does not approach a stable prevalence until age 8 years or more. The lower prevalence of MR among tested patients and the relationship between BPP and risk may imply an antenatal asphyxial origin for some cases of MR.

CONTINUOUS MONITORING OF FETAL pH, PO2 AND PCO2 USING A FIBEROPTIC MULTIPARAMETER SENSOR IN ANIMAL MODELS. 
S. Haberger, E. Gratacé, J. Wu, N. Yesildaglar, Y. Arsen, J. Dequest, Center for Surgical Technologies, Faculty of Medicine, Kath. Univ. Leuven, Belgium and the Eurofetus group.

OBJECTIVES: To evaluate the feasibility and accuracy of continuous fetal monitoring with a multi-parameter intravascular sensor (MPIS), in animal models mimicking the fetal metabolic status.

STUDY DESIGN: First, the accuracy of the MPIS in hypoxic conditions was tested in adult rabbits (N=6). The carotid artery (N=4) or vein (N=2) was catheterized with a 20g cannula, housing a 500µm Neotrend ® fiberoptic sensor for pH, PO2, PCO2 and temperature. Second, the feasibility of continuous fetal fiberoptic sensing was tested during experimental fetoscopic surgery in lambs (N=4). An identical sensor was introduced in a chorionic artery and readings were compared to ABG analyses of fetal blood samples.

RESULTS: The overall bias and precision in the first experiment (147 measurement pairs) were, respectively, -4.2 and 10.9 for pH (mmHg), +1.6 and 8.2 for PO2 (mmHg) and -0.015 and 0.031 for PCO2. In the sheep experiments, continuous readings for all parameters were only available during 50 % of the observation time, mainly due to disturbances induced by movement, contact with vessel wall and intense endoscopic light. 20 sample pairs were obtained, resulting in an overall bias and precision of -5.9 and 4.5 for PO2 (mmHg), -0.74 and 3.68 for PCO2 (mmHg) and -0.0082 and 0.0624 for pH.

CONCLUSION: Fiberoptic micro-sensors are accurate and potentially useful for monitoring acid-base status in the low pH range typical for fetal life. The sensor is however prone to manipulation and light interference resulting in the inability to obtain continuous readings during half of fetoscopic surgery time.
TWIN Discordance With or Without a Small For Gestational Age Fetus and Perinatal Outcome. / Chu, W Persatte, H Galan, D Gioffi-Ragan*, L Schultz*, J Hobbins, Dept of Ob/Gyn, Univ of Colorado JBSIC, Denver, CO

OBJECTIVE: It is widely accepted that a 20% discrepancy between fetal weights is associated with high perinatal morbidity and possibly mortality. The purpose of this study was to determine if this concept is true only for twin pregnancies involving discordal for gestational age fetuses.

STUDY DESIGN: Two twin pregnancies complicated by a 20% or greater discrepancy in birth weight were identified from the perinatal database at the University of Colorado Health Sciences Center. These pregnancies were categorized according to sibling combinations of small-, large- and appropriate for gestational age (SGA, LGA and AGA, respectively) growth patterns. SGA was defined as birth weight less than the 10th percentile and LGA was defined as birth weight greater than the 90th percentile as determined by birthweight growth charts. Patients were divided according to presence or absence of SGA growth pattern: group 1) AGA/AGA or AGA/LGA and group 2) SGA/AGA or SGA/AGA twin combinations. These endpoints, gestational age (GA) at delivery, neonatal length of stay and perinatal death were compared between groups.

RESULTS: Of 350 twin pregnancies delivered from January 1992 to August 1999, 36 pregnancies were complicated by a 20% or greater discrepancy in birth weight. The following numbers of twin growth patterns were seen: group 1) 9 AGA/AGA and 1 AGA/LGA, group 2) 5 SGA/AGA and 21 SGA/AGA. Two pregnancies with an SGA/LGA sibling pairs were complicated by severe twin transfusion syndrome and fetal hydrops. The mean GA at delivery for groups 1 and 2 was 36.3 (29-39) and 35.1 (28-38) weeks (wks), respectively. The GA at time of delivery is significantly greater for group 1 compared with group 2 (p=0.027, MW test). Neonatal length of stay was ascertainment for 56 newborns. The mean neonatal length of stay in groups 1 and 2 was 6.1 (1-20) and 23.4 (1-70) days, respectively (p=0.01, t test). Two siblings in group 2 were stillborn (4.2%) at 20 weeks. None of the newborns in group 1 died. (NS)

CONCLUSION: Twin pregnancies complicated by a discrepancy for weight of 20% do not appear to be at risk for poor outcome unless the pregnancy involves a small for gestational age twin. These data may be considered when monitoring twins for fetal growth with ultrasound.

MANAGEMENT OF RhesOIMMUNIZATION USING THE QUEENAN AMNIOtic FLUID AOD450 CURVES. / C. Spong, A. Porter*, J. T. Queenan, Division of MFM, Georgetown University Medical Center, Washington DC and SDEMP, LDC, NICHD, NIH, Bethesda, MD

OBJECTIVE: Evaluation and management of patients with multiple maternal antibody isoimmunization is unclear. The presence of ≥ 1 maternal antibody may suggest a worse scenario. The objective of this study was twofold, first to determine if multiple antibodies are more severe than single and second to determine the utility of the Queenan curves in evaluating multiple antibody isoimmunization.

STUDY DESIGN: Amniotic fluid AOD450 measurements were obtained from the antenatal testing logbook and confirmed by chart review. Cases were categorized by antibody type and outcomes obtained by chart review.

RESULTS: 24 pregnancies with isoimmunization and multiple maternal antibodies were identified, of these 18 had two antibodies (anti-D-C in 13, D-E in 1, D-Jka in 1, little c-e-Jka in 1) and 6 had ≥ 2 antibodies (anti-D-C-E in 4, D-C-N in 1, little c-e-FYA in 1). 11 (46%) required at least one intrauterine fetal transfusion (mean initial fetal hematocrit 15% (range 4.9-24%). In those not transfused, there were no AOD450 measurements in the Queenan "fetal death risk" zone. Poorest outcomes (multiple transfusions/hydrops/fetal demise) were in patients with anti-D, anti-C, with or without anti-E. The absence of anti-D was associated with no need for fetal transfusions. The overall transfusion rate was significantly higher compared to a group of 57 isoimmunization patients with only anti-D (46% vs 25%, P<0.05).

CONCLUSIONS: The presence of anti-D appears to be the most significant factor guiding the course of isoimmunization with multiple antibodies. The presence of another antibody with anti-D appears to significantly increase the need for intrauterine fetal transfusions.

Deja Vu: Patterns of Salivary Estriol in Pregnant Women Whose Pernites Suffered Intrauterine Fetal Demise or Intrauterine Growth Retardation. / McGregor JA, Hseng CS, Engel LE, Univ of Colorado School of Medicine, Denver Health and Hospital, Denver CO, Biex, Dublin CA

OBJECTIVE: Evaluate and characterize salivary estrol (sES) in prospectively evaluated mothers whose perinates suffered intrauterine fetal demise (IUFD) or intrauterine growth retardation (IUGR)

STUDY: We prospectively compiled sES levels weekly in 956 singleton pregnancies beginning at 22 weeks gestation and continuing through delivery. Unconjugated sES was analyzed using a sensitive and specific enzyme-linked immunoassay (Blex, Dublin, CA). This multi-center study evaluated use of sES as a biochemical marker of fetal well-being as well as a signal of impending parturition (≥21 mg/ml), using descriptive statistics.

RESULTS: IUFD: There were 7 stillbirths (0.7%) in the study population. Three subjects had only 1 sample collected and were not analyzed further. Four subjects demonstrated two distinctive patterns of sES: A) persistently low (≤1 SD) sES levels preceding fetal death (n=3) and B) normal sES levels with expected increase followed by sudden decline and fetal demise (n=1). IUGR: There were 15 subjects determined clinically to be IUGR (≤10% birthweight) at study centers. Four patterns of sES were described: A) persistently low sES with no ascribable clinical antecedent/course noted (n=6), B) persistently low sES with ascribable clinical condition, i.e. PIH (n=3), C) antiphospholipid antibody (n=1), and D) normal sES pattern with commonly ascribable course of growth retardation noted (n=5).

CONCLUSION: Three of four cases of IUFD demonstrated persistently low sES. Clinical IUFD was also associated with persistently low sES in 9 out of 15 cases. These findings recapitulate prior studies employing difficult to measure urinary estriol measurements. Serial sES determination may allow practitioners to recognize perinates at risk for death or growth retardation associated with fetal/maternial endocrine metabolism and well-being.
A ROLE FOR SALIVARY ESTRIOL IN PREDICTING POST-TERM PREGNANCIES

McGregor JA, Hastings C, Dullien V, Engel L. University of Colorado School of Medicine, Denver Health and Hospital, Denver CO, Biex, Dublin, CA.

OBJECTIVE: We examined the role of salivary estradiol (sE2) in predicting post-term pregnancies. We compared the difference in sE2 values prior to 39 weeks in term and post-term pregnancies.

METHODS: In a prospective, multi-centered trial, 615 term and 27 post-term singleton pregnancies with spontaneous labor onset provided a standardized 1cc sample of saliva collected weekly from 22 to 25 weeks to term. Unconjugated sE2 values were determined using an established ELISA (Biex, Dublin, CA). We evaluated sE2 levels in term and post-term patients using descriptive statistics.

RESULTS: A positive sE2 (>21 ng/ml) prior to 39 weeks had a positive predictive value of 98% for delivery prior to 42 weeks. For term deliveries, 59% of subjects had a positive sE2 prior to 39 weeks, whereas only 33.5% of post-term deliveries had a positive sE2 prior to 39 weeks (2-tailed Fisher’s Exact test p <0.04). Mothers and fetuses destined to undergo parturition >42 weeks demonstrated 1) persistently lower sE2 levels and 2) did not demonstrate a “surge” prior to 39 weeks.

CONCLUSION: Patients destined to deliver post term obtain their sE2 surge later than subjects who deliver at term or preterm. For a patient who has a positive test (>21 ng/ml) by 39 weeks, there is a 98% chance that the patient will deliver prior to 42 weeks gestational age.

INTRAPARTUM FETAL PULSE OXIMETRY IN THE SECOND STAGE LABOR: CORRELATION BETWEEN UMBILICAL ARTERY pH AT BIRTH.

Ev Marnick, JM Mathi, Deps Ob/Gyn, Federal University of Santa Maria, Santa Maria, RS, and University of Caxias do Sul, Caxias do Sul, RS, Brazil.

OBJECTIVE: To study the correlation between fetal arterial oxygen saturation values (FSpO2) measured by pulse oximetry in the second stage of labor, and umbilical artery pH at birth.

STUDY DESIGN: Oxygen saturation was monitored by fetal pulse oximetry during last thirty, twenty and ten minutes of second stage of labor in fifty-eight singleton pregnancies at term, with vertex presentation. Criteria for exclusion were multiple gestations, gestational age <37 weeks, placenta previa, chorioamnionitis, vaginal bleeding of unknown origin, uterine anomalies, sexually transmitted diseases, and birth weight <2500 gm. All fetuses showed SpO2 >90% during the whole labor. Umbilical blood was sampled immediately after delivery for subsequent measurement of venous and arterial blood gases and pH with use of an ABG 500 gas analyzer (Rathometer, Copenhagen). The FS-14B fetal oxygen sensor (Neon Puritan Bennett Inc., Pleasanton, CA) and a Corometrics Medical Systems Inc fetal monitor, 129F model, were used.

RESULTS: The fetal mean percent SpO2 correlated significantly with umbilical artery pH at birth when measured in the last 30 (p<0.01), 20 (p<0.01) and 10 minutes (p<0.01) of second stage of labor. There was no significant relationship between FSpO2 and the oxygen saturation of umbilical artery at birth.

CONCLUSION: Fetal oxygen saturation measured by pulse oximetry in the second stage of labor showed a significant correlation with umbilical artery pH at birth, in cases of normal FSpO2 during the whole labor.

EPIDURAL ANALGESIA ASSOCIATED WITH INCREASED RATE OF ANTIBIOTIC USE IN LABOR.


OBJECTIVE: To examine the rate of antibiotic use and the indications for use in women with and without epidural analgesia.

STUDY DESIGN: We analyzed 1235 women with singleton term pregnancies with cephalic presentation who presented in spontaneous labor with a temperature of <95.9. Any antibiotic use during admission was recorded and categorized according to indication for use. Chorioamnionitis was based on MD diagnosis, generally in the presence of fever. Surgical prophylaxes included use for cesarean section, 4th degree lacerations and manual placental extraction. Postpartum use included endometritis and fever of unknown origin. Medical use was defined as any non-obstetric indication.

RESULTS: 59.0% of women received epidural analgesia. There was no difference in admission temperature (98.1 vs 98.1), or rates of PROM (17.9% vs 15.9%), cesareans (16% vs 6%), and 4th degree lacerations (15% vs 15%). The rate of antibiotic use was significantly higher in women receiving epidural (28% vs 10.8%). After adjusting for confounders using logistic regression, epidural use was associated with a relative risk of 2.6 (95% CI 2.0; 3.4) for antibiotic treatment. This increased risk was due to significantly higher rates of antibiotic treatment for chorioamnionitis (9.0% vs 0.4%) and surgical prophylaxes (12.8% vs 5.4%) in the epidural group. Overall, 98% of antibiotic treatment for chorioamnionitis and 45% of antibiotic use for surgical prophylaxes was associated with epidural use. These higher rates are likely due to more frequent (17% vs 9.0%), cesareans (15% vs 6%), and 4th degree lacerations (21% vs 15%) in the epidural group. No increased rates of antibiotic treatment were seen for medical or postpartum indications.

CONCLUSION: We found no evidence that women who receive epidural analgesia have sub-clinical infections at admission or at epidural placement. Epidural use was associated with increased rates of antibiotic prophylaxes for the clinical diagnosis of chorioamnionitis (because of a higher rate of fever with epidural), and for surgical prophylaxes (because of higher rates of cesarean and 4th degree lacerations).
**330 CAN THE NICHD GUIDELINES FOR FETAL HEART RATE MONITORING INTERPRETATION DECREASE INTEROBSERVER DIFFERENCE?**

**R. Bonduelle, A. Fleming, C. Buechert, V. Haynatzka (Creighton University School of Medicine, Omaha NE).**

**OBJECTIVE:** In 1996, the NICHD convened a research planning workshop to develop a Clinical Opinion for the interpretation of fetal heart rate (FHR) monitoring in research in hopes of increasing the reliability. The objective of this study was to determine if using the specific guidelines developed by the NICHD study group could significantly reduce the interobserver variability of FHR interpretation compared to "traditional" interpretation.

**STUDY DESIGN:** A prospective cohort study was conducted, with 8 physicians recruited. Forty high-risk FHR monitor strips consisting of 20 antepartum (30 min long) and 20 intrapartum (60 min long) strips were reviewed. The FHR strips were evaluated for FHR baseline, variability, and decelerations which, if present, were evaluated for type and reactivity. The physicians were initially given the strips and asked to interpret them without any instructions. One week later they were given instructions on interpreting FHR monitor strips recommended by the NICHD study group and then asked to interpret the same strips again using the specific instructions for FHR monitor interpretation. Proportion of agreements and kappa analysis was performed.

**RESULTS:** Table 1 = "traditional" interpretation; Table 2 = NICHD guidelines

<table>
<thead>
<tr>
<th>Variable Decelerations</th>
<th>Late Decelerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antepartum</strong></td>
<td></td>
</tr>
<tr>
<td>PA 0.78</td>
<td>Kappa 0.75-0.82</td>
</tr>
<tr>
<td>0.29</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>Intrapartum</strong></td>
<td></td>
</tr>
<tr>
<td>PA 0.73</td>
<td>Kappa 0.76-0.77</td>
</tr>
<tr>
<td>0.45</td>
<td>0.81</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable Decelerations</th>
<th>Late Decelerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antepartum</strong></td>
<td></td>
</tr>
<tr>
<td>PA 0.75</td>
<td>Kappa 0.71-0.78</td>
</tr>
<tr>
<td>0.36</td>
<td>0.97</td>
</tr>
<tr>
<td><strong>Intrapartum</strong></td>
<td></td>
</tr>
<tr>
<td>PA 0.69</td>
<td>Kappa 0.65-0.73</td>
</tr>
<tr>
<td>0.37</td>
<td>0.86</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** The implementation of the NICHD FHR monitoring guidelines for interpretation of FHR strips did not decrease interobserver variability as measured by proportion of agreement and Kappa. Thus, in this study, reliability of clinicians interpreting FHR monitor strips was not improved with NICHD guidelines.

**331 THE RELATIONSHIP BETWEEN MECONIUM PASSAGE, AMNIOTIC FLUID VOLUME AND THE NEED FOR CESAREAN DELIVERY FOR NON-REASSURING FETAL STATUS.**

**R. Weber, S.C Blackwell, H.L. Wolfe, C.A. Carreno, S.S. Hassan, S.M. Berry, Y. Soyokai. Dept. of Ob/Gyn, Hutan Hospital, Wayne State University, Detroit, MI.**

**OBJECTIVE:** Meconium stained amniotic fluid (MSAF) has been reported to occur more frequently in the presence of oligohydramnios. The concept that the presence of MSAF is a marker of non-reassuring fetal status (NRFS) has been recently challenged. (Obstet General 1996; 87; 181-4). The purpose of this study was to evaluate the impact of MSAF and amniotic fluid volume (AFV) on the risk for cesarean delivery (C/S) for NRFS.

**STUDY DESIGN:** 1626 liveborn singleton gestations who delivered after 37 weeks within 7 days of an assessment of amniotic fluid volume (AFV) in our ultrasound department from 1995-1998 were included. C/S rates for NRFS were compared and odds ratios were calculated comparing patients with clear amniotic fluid (AF) and those with MSAF stratified by gestational age (GA) (37-39 weeks, 40-41 weeks, and ≥42 weeks).

**RESULTS:** The presence of MSAF was associated with an increased rate of C/S for fetal indications, regardless of gestational age.

<table>
<thead>
<tr>
<th>AFV Category</th>
<th>C/S NRFS (%)</th>
<th>MSAF C/S NRFS (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligohydramnios</td>
<td>11/283 (4.7%)</td>
<td>7/32 (13.5%)</td>
<td>3.14 (1.28-7.85)</td>
</tr>
<tr>
<td>Decreased</td>
<td>8/194 (4.1%)</td>
<td>5/41 (12.2%)</td>
<td>3.2 (99-10.4) NS</td>
</tr>
<tr>
<td>Normal</td>
<td>33/711 (4.6%)</td>
<td>17/174 (9.8%)</td>
<td>0.68 (0.36-1.3)</td>
</tr>
<tr>
<td>Increased</td>
<td>11/116 (9.5%)</td>
<td>5/38 (7.9%)</td>
<td>1.22 (0.28-5.1)</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>1/47 (2.1%)</td>
<td>0/10 (0%)</td>
<td>6.6 (0.8-57.8)</td>
</tr>
<tr>
<td>Total</td>
<td>64/1900 (3.4%)</td>
<td>34/321 (10.6%)</td>
<td>2.45 (1.63-3.8)</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Although the overall rate of C/S for non-reassuring fetal status is increased in patients with meconium, this effect is most significant with decreased amniotic fluid volumes. Our findings support the concept that meconium is an "environmental hazard" in pregnancies possibly complicated byUpstained fetal reserve, rather than an indicator of fetal compromise.

**332 EFFICACY OF SECOND TRIMESTER GENETIC ULTRASOUND – A 2 YEAR COMMUNITY BASED EXPERIENCE.**

**R. Wax, J. Guibbert, J. Mather, C. Chen, D. Rower, J.D. Steinfeld, C.J. Ingargiola. Dept. Ob/Gyn, Hartford Hospital, Hartford, CT.**

**OBJECTIVE:** To prospectively assess the efficacy of genetic ultrasound in detecting chromosomally abnormal fetuses in a high-risk population and determine independent markers of aneuploidy.

**STUDY DESIGN:** Patients 218 years old and 14-54 weeks’ gestation were included if referred for maternal age ≥35, increased Down syndrome or trisomy 18 risk by second trimester serum screen, or prior affected offspring. All women had a targeted ultrasound (US) between April 1997 and June 1999 and were offered fetal chromosomal analysis. Markers of aneuploidy and pregnancy outcomes were prospectively recorded. The primary outcome was prenatally or postnatally detected chromosomal abnormalities.

**RESULTS:** 789 of 1030 fetuses seen during the study had outcome data available and comprised the study group. 691 (87.6%) were normal, 73 (9.2%) had 1 marker present, 17 (2.2%) had 2 markers present, and 5 (0.6%) had 3 markers present. Fourteen of 17 (82.3%) aneuploid fetuses had an abnormal US, including 5 of 7 (71.4%) with Down syndrome. When ≥1 marker was present, the sensitivity, specificity, positive and negative predictive values were 82.4%, 89.1%, 14.9%, and 96.6%, respectively. When ≥2 markers were seen, these values were 58.8%, 98.4%, 45.4%, and 99.1%. For 23 markers, the values were 25.3%, 99.8%, 80.6%, and 98.3%. Univariate analysis showed hydrocephalus, cardiac anomaly, intracardiac echogenic focus (ICEF), echogenic bowel, renal pelvis dilation, short humerus, short femur, chromody, structurally abnormal, and abnormal amniotic fluid volume significantly associated with aneuploidy. Logistic regression showed hydrocephalus, cardiac anomaly, and ICEF to be significant aneuploidy markers. The amniosentesis rate was 354/1030 (34%) and increased with the number of US markers noted (p < 0.05). 14.8%, 2-66.7%, 33-80%)

**CONCLUSION:** Genetic US is highly effective in identifying chromosomally abnormal fetuses in a community based practice. The amniosentesis rate and US sensitivity increase with the number of US markers present.

**333 SHORT CERVICAL LENGTH IMPLIES HIGH RISK OF CHORIOAMNIONITIS.**

**Abbasus SMF, Barba EJN, Dekker GA, van Geijn HP, Hummel PD, Dept. Ob/GYN and pathology, Free University Hospital, Amsterdam, the Netherlands.**

**OBJECTIVE:** To compare the incidences of chorioamnionitis in patients with a cervical length < 25 mm and in patients with a longer cervical length before a gestational age of 27 weeks.

**STUDY DESIGN:** Cervical length was measured serially by transvaginal ultrasonography in patients with high risk of cervical incompetence. When cervical length < 25 mm was measured before 27 weeks’ gestation, patients were randomized to receive a McDonald cerclage or not. All pregnancies were examined by one pathologist. Student’s test, Fisher’s Exact test and Mann-Whitney test were used and p < 0.05 was considered significant.

**RESULTS:** Ultrasound follow-up of cervical length was performed in 75 patients and a cervical length < 25 mm before a gestational age of 27 weeks was found in 32 patients. Of the 32 patients with the short cervix (SC group) and the 43 patients with the long cervix (LC group) were similar for age, number of pregnancies, parity, history of abortions, history of D&C and history of preterm delivery. Significantly more chorioamnionitis was found in the SC group, 19 patients (59%) versus 14 patients (33%) (p <0.05; RR=1.6, 95%CI 1.0-2.5). Furthermore, significantly more stage III chorioamnionitis was found in the SC group, 14 patients (41%) versus 1 patient (7%) (p=0.0002; RR=10.8, 95%CI 1.6-73.5). Mean gestational age at delivery was significantly lower (p<0.001) in the SC group 31.5/7 (95%CI 28.5/7-34.4/7) versus 38.5/7 weeks (95%CI 37.5-39.0/7) and neonatal survival was significantly lower in the SC group 29/32 versus 43/43 (p<0.0001; RR=2.05, 95%CI 2.1-4.2). In the SC group no significant difference (p>0.3) in the incidence of chorioamnionitis was found between patients treated with a cerclage (11/19) and patients not treated with a cerclage (8/13).

**CONCLUSIONS:** A cervical length < 25 mm measured by transvaginal ultrasonography before a gestational age of 27 weeks means a high risk of chorioamnionitis, especially stage III and a high risk of preterm delivery with poor neonatal outcomes. Chorioamnionitis might rather be a complication of a short cervical length than of the application of a cervical cerclage.
334 SONOGRAPHIC VISUALIZATION OF AMNION CHORION SEPARATION BETWEEN 15-21 WEEKS GESTATION IN PREGNANCIES WITH NORMAL FETUSES. W Canek, C Sullivan, F Gallasso, Division of Maternal-Fetal Medicine, The Stamford Hospital, Stamford, CT.

OBJECTIVE: To evaluate the frequency of amnion chorion separation (ACS) in pregnancies with normal fetuses between 14-18 weeks gestation.

STUDY DESIGN: From 7/98 to 6/99, singleton, well-dated gestations presenting to our antenatal unit for targeted fetal evaluation between 14-20.9 weeks gestation were assessed for ACS. Patients with any sonographically detected fetal structural and/or chromosomal abnormalities were excluded. Separation was considered to be present if any portion of the amnion was non-fused. For patients undergoing amniocentesis, separation was determined prior to the procedure. Chi-square analysis was used to evaluate for differences in ACS across gestational age.

RESULTS: A total of 306 patients met the inclusion criteria. The mean maternal age (+SD) at the time of the study was 30.4 (+5.0) years. The median (range) gravidity and parity were 2 (1-10) and 1 (0-5), respectively. The frequency of ACS across gestational age was as follows:

<table>
<thead>
<tr>
<th>Gestational Age (weeks)</th>
<th>n</th>
<th>ACS Present (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.0-14.9</td>
<td>14</td>
<td>9 (64%)</td>
</tr>
<tr>
<td>15.0-15.9</td>
<td>43</td>
<td>15 (35%)</td>
</tr>
<tr>
<td>16.0-16.9</td>
<td>64</td>
<td>12 (19%)</td>
</tr>
<tr>
<td>17.0-17.9</td>
<td>129</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>18.0-18.9</td>
<td>157</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>19.0</td>
<td>99</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

CONCLUSION: The frequency of sonographically detected ACS decreases with advancing gestational age in the early second trimester. No cases of ACS were seen after 18.9 weeks gestation. Knowledge of these data is essential when examining the potential association between ACS and fetal structural and chromosomal abnormalities.

335 AMNION CHORION SEPARATION BETWEEN 15-19 WEEKS: A POTENTIAL MARKER OF FETAL ANEUPLOIDY. W Canek, C Sullivan, F Gallasso, Division of Maternal-Fetal Medicine, The Stamford Hospital, Stamford, CT.

OBJECTIVE: 1) to evaluate the frequency of amnion chorion separation (ACS) between 15-19 weeks gestation in pregnancies with fetal chromosomal abnormalities and 2) to determine if the frequency of ACS is higher in pregnancies with fetal aneuploidy vs. pregnancies with euploid fetuses.

STUDY DESIGN: Between 5/98-9/99, ACS was recorded in patients undergoing prenatal ultrasound evaluation. ACS was considered to be present if any portion of the amnion was non-fused. For patients undergoing amniocentesis, separation was determined prior to the procedure. The frequency of ACS between 15-19 weeks in pregnancies with fetal aneuploidy diagnosed during the study period was compared to the frequency of ACS in a previously reported group of patients with normal fetuses evaluated during the study period. Chi-square analysis was used to evaluate for differences between groups. Significance was set at p<0.05.

RESULTS: The mean maternal age (+SD) at the time of the study was 35.3 (+4.4) years. The median (range) gravidity and parity were 3 (1-4) and 1 (0-5), respectively. ACS was reported in 13/19 pregnancies in which fetal chromosomal abnormalities were diagnosed. Overall, ACS was seen in 6/13 (46.2%) pregnancies with fetal aneuploidy.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>n</th>
<th>Singleton</th>
<th>Twins</th>
<th>Triplets</th>
<th>P&lt;</th>
<th>P&lt;</th>
<th>P&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>3.7±0.5 (17)</td>
<td>3.6±0.5 (9)</td>
<td>3.6±0.5 (14)</td>
<td>0.7</td>
<td>0.7</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>3.5±0.4 (14)</td>
<td>3.5±0.4 (12)</td>
<td>3.5±0.5 (16)</td>
<td>0.1</td>
<td>0.9</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>3.6±0.4 (15)</td>
<td>3.5±0.6 (14)</td>
<td>3.5±0.4 (12)</td>
<td>0.5</td>
<td>0.3</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>3.6±0.6 (20)</td>
<td>3.6±0.5 (56)</td>
<td>3.5±0.4 (15)</td>
<td>0.9</td>
<td>0.6</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>3.6±0.5 (16)</td>
<td>3.5±0.6 (23)</td>
<td>3.5±0.6 (21)</td>
<td>0.2</td>
<td>0.6</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>3.5±0.6 (20)</td>
<td>3.2±1.0 (28)</td>
<td>2.8±1.3 (16)</td>
<td>0.4</td>
<td>0.1</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>3.3±0.1 (16)</td>
<td>3.2±1.0 (22)</td>
<td>2.8±1.4 (22)</td>
<td>0.7</td>
<td>0.2</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>3.4±0.1 (21)</td>
<td>3.5±0.6 (5)</td>
<td>2.6±1.3 (15)</td>
<td>0.9</td>
<td>0.000</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>3.5±0.5 (11)</td>
<td>3.6±1.1 (44)</td>
<td>3.1±0.9 (20)</td>
<td>0.1</td>
<td>0.2</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>3.5±0.5 (30)</td>
<td>3.7±1.5 (35)</td>
<td>2.9±1.2 (22)</td>
<td>0.001</td>
<td>0.02</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

GA, gestational age; Pa, singleton vs twins; Pb, singleton vs triplets; Pc, twins vs triplets.

CONCLUSION: In comparison to singleton gestations, cervical length in twin gestations are shorter at ≥23 weeks' gestation and this trend reached significance at 24 weeks' gestation. Cervical length in triplet gestations are shorter in comparison to singleton gestations at ≥25 weeks' gestation and this reached significance at 26 weeks' gestation. However, there was no significant difference in cervical length between twin and triplet gestations.

336 A COMPARISON OF SONOGRAPHIC CERVICAL LENGTH BETWEEN 15 AND 24 WEEKS' GESTATION IN SINGLETON, TWIN AND TRIPLET GESTATIONS. E Cuzan, CV Ananth, NB Merozov, W Kinzler, J Nigam, AM Vintzileos, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: To compare sonographic cervical length between 15 and 24 weeks' gestation in singleton, twin and triplet gestations.

STUDY DESIGN: Transvaginal sonographic measurement of cervical length was performed in 81 singleton, 117 twin and 51 triplet gestations on 180, 295 and 180 occasions respectively between 15 and 24 weeks' gestation. The data was obtained longitudinally. The shortest of 3 measurements was obtained and the mean and standard deviation (SD) of measurements was determined. Unpaired t-test was performed to determine differences between the types of gestation.

RESULTS:

<table>
<thead>
<tr>
<th>Mean ±SD centimeters (number of measurements)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA months</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>17</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>21</td>
</tr>
</tbody>
</table>

CONCLUSION: In this prospective blinded study, various residents performed clinical and ultrasonographical estimations of fetal weight (EFW) on admission to labor and delivery. Actual birth weight (all patients delivered within 24 hours), gravidity, parity, gestational age, body mass index (BMI), presence or absence of diabetes and hypertensive diseases, presentation and amniotic fluid index (AFI) were recorded. All EFW were divided into 3 groups: Morning shift (0 am to 4 pm), evening shift (4 pm to midnight) and night shift (midnight to 8 am). Accuracy of fetal weight estimation as compared with actual birthweight was analyzed per shift by using ANOVA test Multivariate analysis was performed to evaluate the factors mostly and independently affecting the weight evaluations.

RESULTS: Statistically significant changes were found between the clinical EFW and the birth weight along the working shifts (505g, 387g and 354g for the morning, evening and night shifts, respectively p=0.008). In the clinical EFW the overall trend was to underestimate the fetal weight. No significant changes were shown in the accuracy of the sonographic EFW during the shifts (50g, 115g and 105g, respectively). In all shifts the sonographic EFW was more accurate than the clinical EFW. Using multivariate analysis AFI was found to affect the clinical and sonographic EFW and BMI was found to affect only the sonographic EFW.

CONCLUSIONS: Time of the day that the EFW was done affects the accuracy of clinical but not sonographic EFW. The clinical EFW performed during the day shift was the most inaccurate. Therefore, it seems that residents' level of alertness is not the cause for inaccuracies in EFW.
**338**

**RISK FACTORS FOR PRETERM BIRTH IN PRIMIGRAVIDAE WITH TWIN GESTATION AND THE ROLE OF TRANSVAGINAL ULTRASONOGRAPHIC ASSESSMENT OF THE CERVIX.** B. Weiss, M.D., D. Soriano, M.D., D., DS. Soudan, M.D. E. Schiff, M.D., S. Lipietz, M.D., R. Achiron, M.D. Dept. Ob/Gyn, Sheba Medical Center, Tel-Hashomer, and Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

**OBJECTIVE:** To identify the risk factors for preterm birth in primigravida with twin gestation and the role of transvaginal ultrasonographic assessment of the cervix.

**STUDY DESIGN:** Between January 1996 and December 1996, 50 consecutive twin pregnancies were prospectively enrolled. All women were at their first pregnancy. All had a normal cervical curve, evaluated by hysterologicpapignography (HSG) or hysteroscopy. Multiple logistic regression analysis was used to evaluate the association between the length of the cervix at 18-24 weeks of gestation and outcome variables, controlling for possible confounding factors.

**RESULTS:** The mean±SD maternal age was 30.9±3.3 years (range 22-46) among patients (29.5%) who delivered prematurely (defined as spontaneous delivery at or before 34 weeks of gestation). There was no significant difference between women who delivered before or after 34 weeks of gestation in regard to maternal age, body mass index (BMI), weight gain in pregnancy, smoking and work during pregnancy. The mean cervical length of patients who delivered before 34 weeks of gestation (30.1±6.1 mm) was significantly shorter than that of patients who delivered after 34 weeks of gestation (42.2±6.2 mm) (p<0.001). Cervical length longer than 35 mm predicted delivery after 34 weeks of gestation with sensitivity and specificity of 88.5% and 88.9%, respectively. The positive and negative predictive values were 96.9% and 67.0%, respectively.

**CONCLUSION:** A transvaginal ultrasonic measurement of the cervix >35 mm at 18-22 weeks in twin gestation can identify patients at low risk for delivery before 34 weeks. Maternal age, BMI, weight gain, smoking and work during pregnancy did not influence the duration of the pregnancy.

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**340**

**NEITHER AMNIOTIC FLUID INDEX NOR SINGLE-DEEPEST POCKET METHODS ACCURATELY REFLECT ABNORMAL AMNIOTIC FLUID VOLUMES.** E. Magann, S. Chauhan, G. Barrilleaux. NS Whitworth, JN Martin Jr. Dept. Ob/Gyn, Univ. Mississippi Medical Center, Jackson, MS.

**OBJECTIVE:** The amniotic fluid index (AFI) has been reported to be a more accurate ultrasonic technique than the single-deepest pocket method (SDP) in the identification of abnormal amniotic fluid volumes (AFV). However, these 2 ultrasonic techniques have only been compared to each other, not to actual AFV. The purpose of this investigation was to determine if the AFI is superior to SDP in the identification of actual abnormal AFV.

**STUDY DESIGN:** One-hundred seventeen singleton pregnancies underwent an ultrasonic estimation of AFV using both AFI and SDP techniques. Following the ultrasonic measurements, all women then underwent an ultrasound-directed amniocentesis. A dye-dilution technique and spectrophotometric analysis were used to determine the actual AFV.

**RESULTS:** In this prospective investigation, true AFV were low (<50th percentile for gestational age) in 62, normal (5th to 95th percentile) in 100, and high (>95th percentile) in 17 pregnancies.

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**339**

**INTER- AND INTRA-OBSERVER VARIATIONS IN THE MEASUREMENT OF SONOGRAPHIC CERVICAL PARAMETERS BEFORE AND AFTER CERCLAGE PLACEMENT.** C. Walter, ER Guzman, CV Ananth, CV Benito, LYeo, S Shinar, AM Vancaillie, UMNDL-Robert Wood Johnson Medical School/Saint Peter’s University Hospital, New Brunswick, NJ.

**OBJECTIVES:** To determine inter- and intra-observer variations in the measurement of funnel width (FW), funnel length (FL), and cervical length (CL) before and after placement of a cervical cerclage.

**STUDY DESIGN:** 50 transvaginal sonographic images of the cervix demonstrating funneling were collected. Twenty-five were obtained before and 25 after cerclage placement. Three physicians and 2 registered diagnostic medical sonographers were asked to measure the FW, FL and CL of these images, on two separate occasions, one week apart. All cervical images showed some degree of funneling. Measurements were obtained using calipers and the measurement scale on still films. Inter- and intra-observer variations in FW, CL, and FL were examined separately for measurements taken before and after cerclage placement. Statistical analysis was based on the analysis of variance (ANOVA), and P-values are reported based on the F-test. In the ANOVA models for FW, CL and CL, indicator variables for examiner (physicians (P) versus sonographers (S)) and measurement (measurement 1 (M1) versus measurement 2 (M2)) were included. Statistically significant differences between measurements obtained by physicists and sonographers would indicate inter-observer variation, while significant differences in measurements obtained between measurements 1 and 2 would indicate intra-observer variation. All measurements are reported in centimeters.

**RESULTS:** The table summarizes results:

<table>
<thead>
<tr>
<th>Ultrasound Technique</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR</th>
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<tr>
<td>AFI &gt;5.0 cm to differentiate</td>
<td>(32%-90%)</td>
<td>(94-98%)</td>
<td>(67-70%)</td>
<td>(95-71%)</td>
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<tr>
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<tr>
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<td>(62-89%)</td>
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<td>(90-99%)</td>
<td>(81-94%)</td>
<td>(81-94%)</td>
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</tr>
</tbody>
</table>

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**341**

**ASSESSING THREE DIMENSIONS IN TWO: WHICH DEPTH MEASUREMENT TO USE FOR FETAL BLADDER VOLUME.** S. E. Menta, M. Fracese*, M.G. Ross, Dept. Ob/Gyn, Haror-UCLA Med Ctr, Torrance, CA.

**OBJECTIVE:** Ultrasound measurement of fetal urine flow is useful for the assessment of fetal well being. However, there is controversy regarding technique and formula for bladder volume quantification. Specifically, a fetal bladder depth as obtained from both scan views of the bladder with potential discrepancies. We sought to determine the optimal bladder depth measurement(s) to quantify bladder volume.

**STUDY DESIGN:** Informed consent was obtained from 29 pregnant patients between 18 and 40 weeks with anatomically normal fetuses and intact membranes. Bladder scans were obtained every 5-6 minutes for 45-60 min. Bladder longitudinal-transverse or coronal-sagittal views provided one (1) length, one (1) width and two (2) depth measurements. Using the ovoid technique and formula, bladder volume was calculated four different ways using length, width and depth measurements. Due to the potential error of a single measure, the mean of the two depth measurements was utilized for the calculation of bladder volume. The hourly urine fetal production rate increased throughout gestation from a mean value of 5 ml/hr at 20 weeks to 85 ml/hr at term (Figure).

**RESULTS:** Calculated bladder volume and urine flow rates were not significantly different among the four different combinations of depth measurements. Due to the potential error of a single measure, the mean of the two depth measurements was utilized for the calculation of bladder volume. The hourly urine fetal production rate increased throughout gestation from a mean value of 5 ml/hr at 20 weeks to 85 ml/hr at term (Figure).

**CONCLUSIONS:** 1) Mean bladder depth is an appropriate measure for calculation of fetal bladder volume. 2) An increase in both fetal urine output towards term suggests that the normally observed decrease in amniotic fluid volume is not a result of decreased fetal urine flow.
A PROSPECTIVE STUDY OF ANEUPLOIDY IN 499 CASES WITH INTRA-CARDIAC ECHOCARDIC FOCUS. AA Miyasaka, FA Salzman, O Gomez-Mann, JN Guillaume, AM Astra, VH Gonzalez, Q R, and D Martin, Departments of Obstetrics & Gynecology, Epidemiology & Public Health, and Pediatrics, University of Miami School of Medicine, Miami, FL.

OBJECTIVE: To determine the overall incidence of chromosomal abnormalities in fetuses and neonates with an intracardiac echogenic focus (IEF) identified on antenatal ultrasound examination, and compare fetuses with, versus without risk factors for aneuploidy.

STUDY DESIGN: During a 44-month study period, the location and number of IEF seen on obstetrical ultrasounds were prospectively recorded. The patients were divided into two groups: a) Low risk (LR) group: fetuses with isolated IEF, b) High risk (HR) group: fetuses with risk factors for aneuploidy, including advanced maternal age, positive triple test screen, family history, and/or associated sonographic findings. All patients had genetic counseling and were offered amniocentesis for karyotyping. Analyses were performed using chi-square techniques, odds ratios and their 95% confidence intervals (95% CI).

RESULTS: A total of 499 fetuses were identified with IEF, 358 in the LR and 141 in the HR group. Prenatal karyotype was performed on 182 (36.5%) fetuses, 85 (46.7%) in the LR and 97 (68.4%) in the HR group. The remaining 317 cases (273 in the LR group and 44 in the HR group) had neonatal follow up with a comprehensive physical exam that was completely normal with no evidence of dysmorphic features. The overall incidence of fetal aneuploidy in the presence of an IEF was 2.4%. The incidence of an abnormal karyotype was 2.35% (0.6%) in the LR group [twinomy 13 and trisomy 21] and 10.1% (7.1%) in the HR group [trisomy 21, 1 trisomy 18 and 1 trisomy 15]. Among the 182 patients with prenatal karyotype the odds ratio for an abnormal karyotype when comparing the HR versus the LR groups was 4.77 (95% CI: 1.01, 22.4). The overall odds ratio for aneuploidy when comparing the HR versus the LR groups was 13.6 (95% CI: 5.9, 62.9).

CONCLUSION: In the presence of IEF, patients at high risk of chromosomal aberrations can be counseled of a thirteen fold increase in the risk of fetal aneuploidy. Risk of fetal loss following amniocentesis should be weighted against the low incidence of aneuploidy in low risk patients with isolated IEF.

CERVICAL HYDROSONOGRAPHY: A NOVEL TECHNIQUE FOR THE MEASUREMENT OF CERVICAL LENGTH USING TRANSABDOMINAL ULTRASOUND. JN. Robinson, K.E. Economy, D. Rodriguez-Thompson, E.R. Norris, A.B. Feunenberg, Dept. of Ob/Gyn, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: To evaluate a simple technique for the measurement of cervical length using transabdominal ultrasound in later pregnancy.

STUDY DESIGN: Cervical length in the second trimester was predictive of preterm delivery. Transvaginal sonography has become the gold standard for the measurement of cervical length using transabdominal ultrasound correlates well with transvaginal measurements but only if the cervix can be adequately visualized. We hypothesized that an inadequate transabdominal scan could be converted into an adequate scan by introducing sterile water into the vagina thereby creating a hydro-acoustic window between the vaginal lumen and the cervix. Women were recruited for study if they were not in labor, had a cephalic presenting fetus after 26 weeks’ gestation, intact membranes, an unscarred cervix by transabdominal scan, and cervical length documented by transvaginal scan within 24 hours. Real time, gray scale, transabdominal ultrasound was performed after the introduction of 60 mL sterile water into the vagina through a 30 mL Foley catheter, and cervical measurements were taken. Sonographers were blinded as to the cervical measurements by transvaginal scan. The kappa statistic was used to assess the accuracy of the measurements.

RESULTS: Six patients were studied (4 singleton, 1 twin, and 1 triplet pregnancy). In all cases, the previously indistinguishable cervix could be adequately visualized and measured. There were no complications, and the procedure was not perceived to be uncomfortable by any of the patients. Statistical analysis generated a kappa value of 0.66 which represents a good agreement between transabdominal cervical hydrosonography and transvaginal measurements.

CONCLUSIONS: Introduction of water into the vagina at transabdominal ultrasound can convert an “invisible” cervix into one which can be well visualized, with measurements of cervical length comparable with that achieved by transvaginal scan. This simple technique can be used to measure cervical length in settings where transvaginal scans may not be readily available such as in the office or on Labor and Delivery.

GESTATIONAL TIMING FOR ACCURATE PRENATAL DIAGNOSIS OF DISCORDANCY IN TWIN GESTATIONS. H. Saker, D. Shah, M. Schluchter, R. Kwi, N. Saker, Department of Obstetrics & Gynecology, University MacDonald Women’s Hospital, Case Western Reserve University, Cleveland, Ohio.

OBJECTIVE: To define the earliest gestational age for accurate prenatal diagnosis of discordant twins by ultrasound.

STUDY DESIGN: All the twin gestations (n=240) delivered at the University MacDonald Women’s Hospital between January 1996 and July 1998 were included in the study. A retrospective review of maternal and infant pair charts was conducted. Definitive diagnosis of discordancy was based on postnatal birth weight data (15% weight difference). Prenatal diagnosis of discordancy using the 15% weight difference criteria was tested against postnatal diagnosis of discordancy to define the accuracy of prenatal diagnosis. All prenatal ultrasound data were categorized into five gestational age groups using 5-week intervals. Sensitivities and specificities were calculated from the number of true positives (discordant EFW and discordant birth weight), false positives (discordant EFW and concordant birth weight), and false negatives (concordant EFW and discordant birth weight) and true negatives (discordant EFW and discordant birth weight).

RESULTS: The overall sensitivity and specificity for prenatal diagnoses of discordance among twins by estimated fetal weight at various gestational age intervals were: < 20 weeks 14 & 94, 21-25 weeks 15 & 97, 26-30 weeks 15 & 90, and 31-34 weeks 42 & 92, and 35+ weeks 50 & 93. The best interval for prenatal diagnosis of discordancy was gestational age interval 21-25 weeks (area under ROC curve 0.76 and 0.62).

CONCLUSION: Early diagnosis of discordance is best made at the 21-25 week ultrasound evaluation.

ASYMMETRIC HEAD-TO-ABDOMEN CIRCUMFERENCE AND ADVERSE OUTCOME IN CONCORDANT TWIN PREGNANCY. JS Dashe, DD McIntire, KJ Leveno, Dept Ob/Gyn, UT Southwestern Med Ctr, Dallas, TX.

OBJECTIVE: To determine whether asymmetry of the fetal head-to-abdomen circumference (HC/AC) is a useful marker for pregnancy complications in monochorionic and dichorionic twins with birthweight discordance.

STUDY DESIGN: All the twin gestations (n=240) delivered at the University MacDonald Women’s Hospital between January 1996 and July 1998 were included in the study. A retrospective review of maternal and infant pair charts was conducted. Definitive diagnosis of discordancy was based on postnatal birth weight data (15% weight difference). Prenatal diagnosis of discordancy using the 15% weight difference criteria was tested against postnatal diagnosis of discordancy to define the accuracy of prenatal diagnosis. All prenatal ultrasound data were categorized into five gestational age groups using 5-week intervals. Sensitivities and specificities were calculated from the number of true positives (discordant EFW and discordant birth weight), false positives (discordant EFW and concordant birth weight), and false negatives (concordant EFW and discordant birth weight) and true negatives (discordant EFW and discordant birth weight).

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OUTCOME IN CONCORDANT TWIN PREGNANCY. JS Dashe, DD McIntire, KJ Leveno, Dept Ob/Gyn, UT Southwestern Med Ctr, Dallas, TX.

OBJECTIVE: To assess the association between the discordance by EFW and discordance at birth for each interval. Receiver operator characteristic (ROC) curve graphs plotting sensitivity and 1-specificity were developed for each gestational age intervals.

RESULTS: The overall sensitivity and specificity for prenatal diagnoses of discordance among twins by estimated fetal weight at various gestational age intervals were: < 20 weeks 14 & 94, 21-25 weeks 15 & 97, 26-30 weeks 15 & 90, and 31-34 weeks 42 & 92, and 35+ weeks 50 & 93. The best interval for prenatal diagnosis of discordancy was gestational age interval 21-25 weeks (area under ROC curve 0.76 and 0.62).

CONCLUSION: Early diagnosis of discordance is best made at the 21-25 week ultrasound evaluation.

SYMPTOMATIC HEAD-TO-ABDOMEN CIRCUMFERENCE AND ADVERSE OUTCOME IN CONCORDANT TWIN PREGNANCY. JS Dashe, DD McIntire, KJ Leveno, Dept Ob/Gyn, UT Southwestern Med Ctr, Dallas, TX.

OBJECTIVE: To determine whether asymmetry of the fetal head-to-abdomen circumference (HC/AC) is a useful marker for pregnancy complications in monochorionic and dichorionic twins with birthweight discordance.

STUDY DESIGN: All the twin gestations (n=240) delivered at the University MacDonald Women’s Hospital between January 1996 and July 1998 were included in the study. A retrospective review of maternal and infant pair charts was conducted. Definitive diagnosis of discordancy was based on postnatal birth weight data (15% weight difference). Prenatal diagnosis of discordancy using the 15% weight difference criteria was tested against postnatal diagnosis of discordancy to define the accuracy of prenatal diagnosis. All prenatal ultrasound data were categorized into five gestational age groups using 5-week intervals. Sensitivities and specificities were calculated from the number of true positives (discordant EFW and discordant birth weight), false positives (discordant EFW and concordant birth weight), and false negatives (concordant EFW and discordant birth weight) and true negatives (discordant EFW and discordant birth weight).

RESULTS: The overall sensitivity and specificity for prenatal diagnoses of discordance among twins by estimated fetal weight at various gestational age intervals were: < 20 weeks 14 & 94, 21-25 weeks 15 & 97, 26-30 weeks 15 & 90, and 31-34 weeks 42 & 92, and 35+ weeks 50 & 93. The best interval for prenatal diagnosis of discordancy was gestational age interval 21-25 weeks (area under ROC curve 0.76 and 0.62).

CONCLUSION: Early diagnosis of discordance is best made at the 21-25 week ultrasound evaluation.

OBJECTIVE: To evaluate whether asymmetry of the fetal head-to-abdomen circumference (HC/AC) is a useful marker for pregnancy complications in discordant twins.

STUDY DESIGN: Retrospective cohort study of asymmetric and symmetric twins with ≥25% birthweight discordance, comparing their outcomes with those of symmetric twins <25% discordant. Only liveborn twin pairs without malformations were included. Pregnancies were termed asymmetric based on HC/AC ≥95th percentile for gestational age on sonograms performed within 4 weeks of delivery. Gestational age-specific HC/AC nomograms for twin pregnancies were derived from our sonographic database. Statistical analysis was performed using chi-square.

RESULTS: Neonatal morbidities, including respiratory distress, intraventricular hemorrhage, and necrotizing enterocolitis were not significantly different between groups with and without diabetes.

CONCLUSIONS: Discordant twins with HC/AC asymmetry are at increased risk for adverse pregnancy outcome. However, discordant symmetric twins were not at increased risk when compared with concordant twins.

348 FETAL ULTRASOUND BIOMETRY IN PREGNANCIES COMPROMISED BY DIABETES COMPARED TO THOSE WITHOUT DIABETES. BM Casey, DD McIntire, KJ Leveno. Dept. Ob/Gyn, Univ. of Texas Southwestern Med Ctr, Dallas, Texas.

OBJECTIVE: To compare fetal biometric differences in pregnant women with and without diabetes.

STUDY DESIGN: Pregnancies examined sonographically between January 1, 1989 and September 30, 1996 were analyzed. Women were classified as a non-diabetic (ND), a non-insulin requiring diabetic (A1), or an insulin-treated diabetic (A2/B-FR). Fetal biometrics were compared among these groups according to gestational age at sonogram. Adjustments were made for maternal age, race, parity, and weight. Statistical analysis was performed using chi-square, and ANCOVA.

RESULTS: 25,520 pregnancies were included. 717 (2.8%) of these were classified as A1 and 908 (3.5%) were A2/B-FR. AC was significantly different in each of the three groups (P<0.001) and is depicted below. Similar results were found for EFW, HC/AC, and FL/AC. BPD was not different among the three groups.

CONCLUSIONS: AC and EFW were significantly increased as the classification of diabetes worsened. HC/AC and FL/AC both decreased as the classification of diabetes worsened.

347 FACTORS INFLUENCING SUBOPTIMAL LEVEL II ULTRASOUNDS IN A TERTIARY CARE CENTER. AP Martha1, KA Boggess1, AH James2, EL Livingston1, J. Bowie3, Dept of OB/GYN and Radiology, Duke University Medical Center, Durham, NC.

OBJECTIVE: The objective of this investigation was to determine whether gestational age at the time of the ultrasound, the type of background of the ultrasound examiner (radiology vs. perinatology), and examiner experience influence the proportion of level II ultrasounds interpreted as suboptimal.

STUDY DESIGN: All ultrasounds performed in a recent 3 month period were reviewed. Cases included singleton gestations between 16 and 22 weeks receiving their first anatomy scan. A standard list of anatomy to be visualized was reported as normal, suboptimally seen, abnormal, or not seen. Data collected included anatomy that was suboptimally seen, gestational age at the time of exam, area of specialty of the examiner (radiology vs. perinatology), and level of experience of the examiners based on the number of years interpreting ultrasounds. Of those ultrasounds from this time period, 60 (30 normal and 30 suboptimal studies) were re-examined at random to be re-examined by the most experienced reviewers who were blinded to the objective of the investigation. Data were analyzed using Chi square or Fisher exact test with significance defined as P<.05.

RESULTS: Of the 370 scans reviewed 94 (24%) were read with at least one anatomic feature suboptimally seen. There were significantly more ultrasounds with a report of one or more anatomic features as suboptimal when the gestational age was <18 weeks when compared to those ≥18 weeks (P<.0001). There was no difference in the proportion of ultrasounds read suboptimally when radiologists were compared to perinatologists (P=.68). Of the 66 studies re-examined by the most experienced reviewers, 52% initially interpreted as suboptimal were subsequently interpreted as normal (P<.0001).

CONCLUSION: The results of this investigation suggest that, if possible, level II ultrasounds should be delayed until after 18 weeks gestation to reduce the number of suboptimal studies. In addition, when an ultrasound is interpreted as suboptimal, consideration should be given for review by a more senior examiner.

349 GROWTH PATTERNS IN DISCORDANT TWINS. W.H. Persutte, J.K. Chyu, J.C. Hobkins. Dept. Ob/Gyn, Univ. of Colorado Health Sci Center, Denver, CO.

OBJECTIVE: The prenatal ultrasound findings of twin neonates complicated by birth weight discordancy (≥20% or more) were studied. Our objective was to determine whether divergent growth occurred in early or late pregnancy. This information was then correlated with outcome data. All patients had serial examinations with a mean of 3.8 ± 1.6 examinations per patient. Based on ultrasound biometry, patients were assigned to one of two groups, depending upon when a 20% discordance in estimated fetal weight was initially noted. Group 1 were patients in which a discordancy was first identified between 20 and 30 weeks gestation and Group 2 were those in which the discordancy was not observed until after 36 weeks gestation. Outcome variables included time of delivery and hospital days.

RESULTS: Eight patients were in Group 1 and 16 were in Group 2. The median length of gestation in Group 1 was 33.4 weeks and in Group was 35.5 weeks (p=0.040). Average number of neonatal days in the hospital were 40 in Group 1 and 19 in Group 2. The average time that a discordancy surfaced in Group 2 (after a concordant early scan) was 34.4 weeks. Variations in discordancy were significant in a follow-up analysis.

OBJECTIVE: Twin pregnancies are at risk for preterm delivery. Endovaginal (TVS) ultrasound cervical assessment has been shown to be useful in the identification of the singleton pregnancy at risk for preterm delivery (PTD). We examined our patient population to determine whether cervical length (CL) was helpful in the identification twin pregnancies that delivered early.

STUDY DESIGN: This prospective, cross-sectional study included all patients referred to our Center with a twin pregnancy between 1/1/96 and 1/15/98. Participants were limited to those with spontaneous onset of labor and vaginal delivery. One hundred five women were investigated at 20-32 weeks' gestation. In each patient, the entire curvilinear length of the cervix was measured using TVS sonography. All CL measurements were assessed for gestational age using a nomogram previously constructed from singleton data. Delivery information included age, indication, and type of delivery. CL measurements were compared in those who had a PTD (<37 wks, n=72) with those who delivered at term (≥37 wks, n=33).

RESULTS: We observed no difference in the CL measurements for gestational age between patients with twins who delivered spontaneously at term and term singletons. However, twins who delivered early had shorter CL measurements. The Figure below shows CL measurements for gestational age in those that delivered at term (circle) and those that delivered early (triangle). Regression shows the mean of the two groups differed significantly (p<0.05). Using a 25mm CL measurement as the lower limit of normal, we found 75% of patients who delivered at <35 wks had a CL <25mm.

CONCLUSION: Women with twin pregnancies destined to deliver at term had CL measurements similar to singletons. However, those who are predisposed to spontaneous early labor and delivery have shorter cervixes.

351 EARLY SECOND TRIMESTER Discordant Fetal Growth and Clinical Outcome of Twin Gestation. V. Kiran, N. Strobel, P. Vergalli, D. Consolini (§). Department of Ob/Gyn, ISBM S.Gerardo, Monza, and EI) Istituti Clinici di Perfezionamento, University of Milan, Italy.

OBJECTIVE: To test if early second trimester sonographic finding of intertwin abdominal circumference (AC) discordance has a predictive value on the clinical course of pregnancy, in order to establish optimal sonographic monitoring of twin gestation during the third trimester.

STUDY DESIGN: Retrospective analysis of computerized data file of all twin pregnancies delivered between Jan 1982 and Dec 1998 at the Division of Ob/Gyn of S Gerardo Hospital. Ultrasound screening studies performed during two gestational age (GA) periods, 16-19.6 and 29-23.6 weeks respectively (groups A and B), were analyzed to evaluate if an intrapair difference of 22 cm in AC measure was a predictor of subsequent poor clinical outcome.

RESULTS: Group A consisted of 153 gestations. An intrapair CA discordance ≥2 cm predicted and increased risk of twins-to-twin transfusion at birth (20% vs. 0.8%, p=0.01), with a sensitivity of 67%. Sonographic observation of GA discordance during the period 16-19.6 weeks of GA did not predict other adverse outcomes (perinatal death, high prematurity, cesarean section rate), although a trend of increased NICU admission was found (13/29 vs. 10/125, p=0.05). Group B consisted of 190 pregnancies, in which interpair CA discordance ≥2 cm during the period 20-23.6 weeks correctly predicted higher rates of intrapair fetal death (3/32 vs. 1/346, p=0.02), NICU admission (21/32 vs. 129/346, p=0.007), cesarean section (13/16 vs. 89/173, p=0.02), twins-to-twin transfusion (4/16 vs. 2/173, p=0.0001), and high prematurity (delivery <32 weeks in 5/16 vs. 14/173, p=0.005).

CONCLUSION: Interpair CA discordance ≥2 cm observed during the period 20-23.6 weeks of GA could be considered a marker of a subgroup of twin pregnancies that present higher risk of adverse outcome, and require intensive clinical and sonographic monitoring.

352 NUCHAL INDEX: A GESTATIONAL AGE INDEPENDENT MARKER FOR THE DETECTION OF DOWN SYNDROME. R. I Lim*, D. Pugash*, J. Dandeneau#, RD Wilson*, British Columbia Women's Hospital* and The Victoria General Hospital** University of British Columbia, Vancouver, British Columbia, Canada.

OBJECTIVES: To determine if nuchal index is gestational age independent, and determine its sensitivity for Down Syndrome (DS).

METHODS: Prospective. A prospective database of fetal biometry and soft markers of aneuploidy was searched for fetuses with the following criteria: confirmed gestational age, at least two measurements of nuchal thickness and biparietal diameter, no major fetal anomalies and either normal karyotype or normal post-natal exam. Nuchal Index (NIx) was defined as 100 x (mean nuchal thickness [mm]) / (mean biparietal diameter [mm]). Thus cohort was systematically divided into two groups according to the last digit in their hospital identification number. Initial analysis was carried out in the first group (analysis group), with the second group (normal group) used to test the results prospectively. A prospective cohort of pre or post-natally diagnosed DS fetuses with at least two prospective nuchal thickness measurements constituted the abnormal study group. P value < 0.05 was considered significant.

RESULTS: 887 fetuses constituted the control group with 455 in the analysis group and 432 in the normal study group. Fetal coefficient and Anova confirm that for 14/40 to 22/6 weeks gestation, NIx is reasonably independent of gestational age. For the analysis group, mean NIx was 7.72 SD = 2.93 and a threshold value of 11.0 yielded a theoretical specificity of 94.5%, 45 Down syndrome fetuses made up the abnormal study group. Mean NIX = 17.69 (SD = 15.9) for the abnormal study which was highly significant (P < 0.00001). Using a threshold of 11.0, Sensitivity for Down Syndrome was 62% (32/52) and Specificity was 95% (402/420).

CONCLUSIONS: Nuchal index can be assumed to be constant between 14-40 and 22-6. Using a threshold of 11.0, Sensitivity for Down syndrome was 62% with a specificity of 95%. NIX would seem to be a useful, gestational age independent marker for Down Syndrome.


OBJECTIVE: To establish the correlation of sonographically thick placenta with increased mortality and morbidity by determining placental thickness throughout pregnancy.

STUDY DESIGN: Placental thickness was determined by routine sonographic examination throughout pregnancy in 561 singleton pregnancies. Thick placenta was determined as placenta that was above the 95th percentile. Gravidae between 20 to 22 weeks' gestation (n=193) and 32 to 34 weeks (n=75) were then divided into two groups according to placental thickness. The study group consisted of 44 gravidae with thick placenta. The control group included 151 gravidae with placental thickness in the range of 10th and 90th percentile. A comparison of perinatal mortality and morbidity rates as well as the incidence of small and large for gestational age neonates was conducted.

RESULTS: A linear increase of placental thickness was found to correlate with gestational age throughout pregnancy. No statistical differences were observed between the two groups with regard to obstetrical variables such as maternal age, parity, or gestational age at delivery. No correlation was found between placental thickness and maternal age or parity.

<table>
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<tr>
<th>Thick placentas</th>
<th>Controls</th>
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<th>95% CI</th>
</tr>
</thead>
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<tr>
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<td>N=151</td>
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<tr>
<td>Perinatal mortality</td>
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</tr>
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<td>Birthweight ≥2500g</td>
<td>13.3%</td>
<td>7.3%</td>
<td>0.03</td>
</tr>
<tr>
<td>Fetal anomalies</td>
<td>9.1%</td>
<td>3.97%</td>
<td>ns</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Sonographically thick placenta may be associated with increased risk of perinatal mortality and morbidity. Placental thickness is independent of both small for gestational age and large for gestational age infants at term.
PRENATALLY DIAGNOSED UNILATERAL VENTRICULOMEGALY. Wil. Knauer, JC Simulian, DA McLean, ER Guzman, AM Vintzileos, UMDNJ- Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVES: The purpose of this study was to 1) determine the frequency of prenatally detected unilateral ventriculomegaly (UVM), 2) determine how often this finding is associated with other fetal abnormalities, and 3) evaluate neonatal outcomes in these patients. STUDY DESIGN: Women having prenatally detected unilateral ventriculomegaly at our institution from 10/94-99 and diagnosed with a fetal central nervous system abnormality were identified from a computerized ultrasound database. All patients noted to have UVM, defined as one lateral ventricle measuring >1.0 cm or the presence of a dangling choroid plexus when seen in an axial plane, were included for review. Follow-up ultrasounds, in addition to maternal and neonatal records, were reviewed. The Denver II developmental screening tool was used to evaluate social, fine motor, language and gross motor skills of these children.

RESULTS: UVM was diagnosed in 16/211,722 (0.08%) pregnancies, including two with aural width <1.0 cm and a dangling choroid plexus. The mean ± standard deviation (SD) maximum width of the lateral ventricle was 1.37 ± 0.27 cm and the left side predominated (14/16 or 87.5%). The mean gestational age at diagnosis was 28 ± 6.9 weeks. The majority (12/16 or 75%) were isolated findings. Associated anomalies included one fetus each with 1) pyleocele (pelvic kidney), 2) Dandy Walker (DW) variant, 3) clubfoot, 4) polyhydramnios, and 5) micrognathia. Microcephaly, craniosynostosis, cataracts, microphthalmia, and 8 cleft palate were identified. Proportions of the fetal face profile included the forehead; the orbits and lens, the nose, the lips and palate, and the chin.

THE FETAL FACE PROFILE IN THE DIAGNOSIS OF CONGENITAL ABNORMALITIES. L. Goldstein, A.E.Reece, I. Tamir, J. Isonkowitz-Eldor* Department of Obstetrics and Gynecology, Ramah Medical Center, The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel and Department of Obstetrics, Gynecology & Reproductive Sciences, Temple University School of Medicine, Philadelphia, PA.

OBJECTIVE: To characterize the fetal face proportions in defining in utero the normal fetal face and to rule out fetal anomalies. Fetal development was assessed in only 5/14 patients (21.4%), one of which was the DW malformation, and resolved in 4/14 (28.6%). There were equal numbers of male and female infants. Neonatal follow-up was available in 12 infants, of which 9 had postnatal cranial imaging. The prenatal finding of ventricular asymmetry was confirmed in 5/9 (55.6%). One infant had surgical intervention (for a large arachnoid cyst with brainstem compression diagnosed prenatally as a DW variant) and died at 2 years of age.

CONCLUSIONS: UVM is an uncommon finding on prenatal ultrasound and is usually isolated. Preliminary data suggest that UVM has no adverse effect on early developmental outcome.
358 SONOGRAPHIC DETECTION OF FETAL TRISOMIES. A. Hatt, A. Tramouxi, H. Brown, D. Zimmer, Dep. Ob. Gyn, St. Vincent Hospital, Indianapolis, IN

OBJECTIVE: To determine the sensitivity of genetic ultrasound in the detection of fetal trisomy.

STUDY DESIGN: Genetic sonoanography was introduced at our institution on Jan. 6, 1997 and followed prospectively through Mar. 12, 1999. The indications for the exams included maternal age > or =35, abnormal triple screen, and history of prior trisomic fetus. The following markers were used to screen for the presence of fetal trisomy structural malformations, increased nuchal fold thickness, short femur, short humerus, echogenic bowel, polydactyly, choroid plexus cysts, hand and finger anomalies, two vessel umbilical cord, and cardiac echogenic foci.

RESULTS: 1104 genetic ultrasound examinations were prospectively followed. The mean gestational age at the time of the examination was 17.4 weeks. The incidence of trisomy was 2.1%. 318 (16.4%) genetic ultrasounds had at least one abnormality. 367 of 925 (39.8%) patients with a normal ultrasound exam and 79 of 181 (43.7%) patients with an abnormal genetic ultrasound underwent amniocentesis. 25 trisomies were diagnosed (16 trisomy 21, 3 trisomy 15, and 4 trisomy 18). 21 (91.5%) trisomic fetuses had one or more ultrasound markers. 15 (65.2%) of the trisonic fetuses had two or more markers. 14 of 16 fetuses with trisomy 21 had at least one marker present. All fetuses with trisomy 13 or 18 had two or more markers present. The sensitivity, specificity, positive predictive value, and negative predictive value when one marker was present were 91.3%, 83.2%, 11.6%, and 99.6%, respectively. The false positive rate was 14.5%. The sensitivity, specificity, positive predictive value, and negative predictive value when two or more markers were present were 95.2%, 95.6%, 23.8%, and 99.2%, respectively. The false positive rate was 4.3%.

CONCLUSIONS: Genetic ultrasound performed in a thorough systematic fashion can detect the majority of trisomic fetuses in an “at risk” population.

359 ABDOMINAL CIRCUMFERENCE: A SINGLE MEASURE VERSUS A RATE OF GROWTH IN THE PREDICTION OF INTRAPARTUM CAESAREAN SECTION FOR FETAL DISTRESS. K. Williams, Nwachukwu Nwobue, University of British Columbia, Division of Maternal Fetal Medicine, B.C. Women’s Hospital, 4500 Oak Street, Vancouver, B.C. Canada, V6H 3W3.

OBJECTIVE: The fetal abdominal circumference is the most sensitive ultrasound bionetry measure to predict intrapartum growth restriction which is associated with an increased risk of intrapartum fetal distress. We sought to evaluate and compare whether a third trimester ultrasound measurement of abdominal circumference done within 1 week of delivery better predicts operative delivery for fetal distress when compared with the growth velocity of the abdominal circumference in the third trimester.

STUDY DESIGN: Retrospective analysis of prospectively collected ultrasound data on 117 patients with singleton gestations who had at least two ultrasound assessments performed in the third trimester with the last ultrasound performed within 1 week of delivery, was done. Ultrasound biometry had to be performed less than 6 weeks apart. The abdominal circumference value of the last ultrasound prior to delivery was placed into 3 categories, 5%, 5-10%, and 10-90%ile for gestational age. The growth velocity of the abdominal circumference per week was placed in 3 categories < 5mm/week, 5-10mm/week and > 10mm/week. The chi-squared statistic was used to compare differences between the incidence of fetal distress between the groups.

RESULTS: The incidence of c/section for fetal distress with a single measure of the abdominal circumference: (AC) < 5%tile = 8/23 (35%), (AC) 5-10%tile, 3/12 (25%) and (AC) >10%ile = 8/81 (10%) (p < .05). The incidence of c/section for fetal distress with an abdominal circumference growth velocity rate < 5mm/week = 9/55 (16%), AG growth 6-10mm/week 4/11 (18%) and ≥ 11mm/week = 8/34 (10%) (p > .05). The incidence of c-section for fetal distress with an abdominal circumference growth velocity rate < 5mm/week = 9/55 (16%), AG growth 6-10mm/week 4/11 (18%) and ≥ 11mm/week = 8/34 (10%) (p > .05).

DISCUSSION: A single measure of the fetal abdominal circumference done within one week of delivery is superior to an assessment of growth rate of the fetal abdomen in the third trimester in discriminating patients who require caesarean section for fetal distress.


OBJECTIVE: To determine whether early antenatal detection of a nuchal cord is clinically useful.

STUDY DESIGN: Fetuses diagnosed sonographically with a nuchal cord at less than 28 weeks’ gestation at our tertiary prenatal diagnosis unit, over a 15 month period were included in the study. Multiple gestations and fetuses with prenatally diagnosed structural or chromosomal abnormalities were excluded. A prenatal diagnosis of nuchal cord was made whenever color Doppler or Power Doppler imaging demonstrated a continuous loop of cord on at least three sides of the fetal neck in transverse and longitudinal sections. All included pregnancies were followed prospectively until delivery. The presence of a nuchal cord was not reported to clinicians and it did not alter obstetrical management. Data were collected on presence of a nuchal cord at delivery, oligohydramnios, fetal growth restriction, mode of delivery, gender, Apgar scores and neonatal outcome.

RESULTS: Forty two patients met inclusion criteria. Mean gestational age at prenatal diagnosis was 22 weeks (range 15-28SD 4 weeks). Mean maternal age was 28.2 years (SD 6.2) and 41% of patients were multiparous. No fetuses developed intrauterine growth retardation and six (15.6%) developed oligohydramnios. Four patients (9.1%) ruptured membranes prior to delivery. One fetus (2%) had severe variable decelerations in labor. Mean gestational age at delivery was 37.8 weeks (SD 3.6) and thirty eight patients (86.4%) were delivered vaginally. Only twelve patients (27.3%) had a nuchal cord at delivery, 11 had a single loop and 1 had 3 loops. All 5 minute Apgar scores were greater than 7. There were no perinatal deaths.

CONCLUSION: Nuchal cords can be detected very early in pregnancy. However as shown in this study, the majority of them result in spontaneous resolution. Those that persist appear to have little, if any impact on neonatal outcome. This suggests that there is limited clinical utility in routine antenatal screening for nuchal cords before 28 weeks.

361 OUTCOME AFTER PRENATAL DIAGNOSIS OF FETAL HYPOPLASTIC LEFT HEART SYNDROME. R. Levy, D. Gray, G. Leguizamon, A. Sharkey, Deps of Ob/Gyn and Pediatrics, Washington University, St. Louis, MO.

OBJECTIVE: To assess the survival and morbidity of infants diagnosed prenatally with hypoplastic left heart syndrome (HLHS).

STUDY DESIGN: We reviewed the charts of all women with a prenatal diagnosis of HLHS referred to our center between 1991-1998. Surviving infants had follow-up into late infancy (1-2 years of age). Primary outcome measures were long-term survival and the incidence of major neurological disabilities.

RESULTS: Diagnosis of HLHS was made antenatally in 54 fetuses. The diagnosis was confirmed by autopsy or postnatal echocardiography in all but one newborn who was found to have transposition of the great vessels. Twenty-four women elected to undergo termination of the pregnancy. Thirteen of their fetuses had major extra-cardiac anomalies, and two had trisomy 18. Two patients had antepartum fetal death. Nine of the 27 infants who survived after delivery underwent heart transplant. All nine infants survived surgery, yet two of them died from rejection and one from sepsis. The six surviving infants (66%) were all maintained on cyclopenic (but not steroids) and were free of major neurological disabilities at follow-up at 2.9 years of age. 11 infants underwent a Norwood operation. Three of these infants survived for more than 2 years (28%), were free of major neurological disabilities and required no medications (ages 2-3 years). Of the remaining 7/27 infants, two infants died before surgery and two were not offered surgery because of a diagnosis of trisomy 18 in one and major extra-cardiac anomalies in the other. The parents declined surgery in the remaining three infants. All seven infants died before the age of 12 months.

CONCLUSION: The long-term survival with no major neurological disabilities of infants prenatally diagnosed with HLHS was 37.5% after excluding termination of pregnancy, and those that were not candidates for or declined surgery. Infants who underwent heart transplantation had the best long-term outcome.
**362 ACCURACY OF SONOGRAPHIC ASSESSMENT OF LUNG-TO-HEAD RATIO IN FETUSES WITH CONGENITAL DIAPHRAGMATIC HERNIA.**


**OBJECTIVE:** The sonographic determination of lung volume using a lung-to-head ratio (LHR) is a predictive outcome in fetuses with congenital diaphragmatic hernia (CDH). The purpose of this study was to assess the accuracy of the LHR measurement by comparing the predictive value of two techniques of caliper positioning, as well as assessing inter-observer and intra-observer variability.

**STUDY DESIGN:** The sonographic records of 25 fetuses referred to our institution for evaluation of CDH between 23 and 29 weeks' gestation were reviewed by four experienced sonologists blinded to the outcome of the pregnancy. They determined the LHR at two time points 3 months apart. Three images were made for each fetus. Fetuses that underwent fetal intervention, or had been diagnosed with additional anomalies were excluded from this study. Outcome variables assessed were neonatal survival, and need for extracorporeal membrane oxygenation (ECMO). To determine lung size, calipers were placed either in the anterior-posterior margin of the identified contralateral lung, or across its largest diameter. The second set of calipers was placed perpendicular to the first. Regression analysis and Receiver-Operator curve were used for data analysis.

**RESULTS:** LHR measurements generated by the two protocols for caliper positioning across the lung correlated closely (r²=0.98). Values generated by using the largest diameter of lung were consistently greater than when the anterior-posterior diameter was used. There were no significant differences between observers in predicting outcome, and intra-observer variability was small and did not reach statistical significance. 

**CONCLUSION:** Either method of LHR determination was equally predictive of survival and the need for ECMO support in fetuses with CDH. Different cut-off values to determine prognostic criteria are appropriate for each technique. Small intra-observer variability and no difference in predictive value between observers indicate that LHR may be measured accurately, and is a reliable prognostic factor.

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**363 THE AMOUNT OF ALCOHOL CONSUMED AT CONCEPTION CORRELATES WITH THE SIZE OF THE FRONTAL LOBE OF THE FETAL BRAIN.**

W. H. Persutte, J. Nesbitt, T. Wass, J. C. Hoblins, Dept. of Ob/GYN, Univ. of Colorado Health Sciences Center, Denver, CO

**INTRODUCTION:** The diagnosis of Fetal Alcohol Syndrome (FAS) is based on strict objective signs seen in the neonate/infant. However, other than a finding of fetal microcephaly in heavy alcohol partakers, no investigation has addressed the effect of alcohol on specific portions of the fetal brain.

**METHOD:** 151 women were interviewed by one investigator (TW), regarding alcohol consumption at the time of conception, and categorized into 3 groups according to average alcohol consumption/day (AA/D). Each patient then had at least one detailed ultrasound examination by a “blinded” examiner after the 20th week of gestation (average 4, 1-6) in which measurements of BPD, head circumference (HC) and other standard biometric measurements were made. In addition, measurements of the transccerebellar diameter (TCD), thalrusus-calvarium (L2C) and frontal lobe (FL), made from the back of cavum septi pellucidi to the inner table of the calvarium, were documented. Each measurement plotted against normative data for gestational age developed in our laboratory and expressed as a percentile.

**RESULTS:** Alcohol consumption - patients enrolled had intakes of AA/day of between 0-20 ounces Group 1 (controls) 92 pts = 0/23 AA/Day (60/99); Group 2 (moderate) 34 pts = 1 86 AA/Day (1,6-2,8), Group 3 (heavy) 29 pts. 8,16 AA/Day (3,5-8,8). (Table: Findings – No fetus had evidence of microcephaly. There was no statistical correlation between TCD or T2C and alcohol consumption. However, there was a highly significant relationship between FL and alcohol consumption. For example, 20% of group 1, 25% of group 2, and 46% of group 3 were below the 10th percentile. 

**CONCLUSION:** Regression analysis showed a disproportionate effect on FL. A cohort of 66 infants in this study are undergoing cognitive function testing at three months to compare in utero findings with functional brain development.

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**364 CERVICAL LENGTH AND THE RISK OF PRETERM DELIVERY AMONG MULTIPLE GESTATIONS.**

A. Braumo, A. Bhattacharuka, E. Kuczyński, A. Reharber, M. Pádiás, C. Lockwood, Dept Ob/Gyn, New York University School of Medicine, NY, NY

**OBJECTIVE:** To examine whether cervical length measured across gestational age is predictive of preterm delivery (PTD) among multiple gestations.

**STUDY DESIGN:** A retrospective chart review was utilized to examine all multiple gestations delivered at our institution between 3/95-6/99. We examined the mean cervical length across specific gestational age intervals. Additionally, we assessed whether cervical length measurements at 26 to 31 weeks were predictive of preterm delivery. Obstetric and neonatal outcomes were also examined.

**RESULTS:** There were 107 sets of twins and 20 triplet gestations delivered during the study interval. Demographic variables are displayed in the table below.

<table>
<thead>
<tr>
<th>Demographic Variables (%) or mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triplets (n=20)</td>
</tr>
<tr>
<td>Maternal age, years</td>
</tr>
<tr>
<td>Nulliparity (%)</td>
</tr>
<tr>
<td>Race (% White)</td>
</tr>
<tr>
<td>Gest age at delivery, weeks</td>
</tr>
<tr>
<td>Cervical length in cm</td>
</tr>
</tbody>
</table>

Cervical length in the 26-31 week interval was positively associated with gestational age at delivery for both twin and triplet gestation groups (r=0.47, p=0.04 and r=0.24, p=0.02, respectively). A cervical length of 2.7 cm predicted delivery at <34 weeks in triplets with sensitivity 0.5 and specificity 0.5, while in the twin group, a length of 3.1 cm had sensitivity of 0.4 and specificity of 0.4.

**CONCLUSIONS:** Between 26 and 31 weeks’ gestation, cervical length predicts gestational age at delivery in both twin and triplet gestations.

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**365 PROGNOSTIC ROLE OF Oligohydramnios IN PREMATURE RUP-TURE OF MEMBRANES AT <26 WEEKS.**


**OBJECTIVE:** To evaluate whether oligohydramnios in extreme preterm premature rupture of membranes (PROM) is associated with poor perinatal and long-term neurologic outcome.

**STUDY DESIGN:** Included were all singleton pregnancies between 1/91 and 6/98 with PROM at <26 weeks, lasting ≥4 days, and managed expectantly. Amniotic fluid (AF) volume was assessed bi-weekly. Pregnancy outcome of women with persistent oligohydramnios (median cord-free pocket of AF ≥2x2 cm) (n=25) was compared with that of women with a median AF pocket ≤2x2 cm (n=135) using Wilcoxon Ranksum test and Fisher’s exact test for categorical variables. Pulmonary hypoplasia was diagnosed based on strict clinical, radiological and pathological criteria. Neurological outcome was assessed at 1 year of age using the Milan-Compartèti & Gidoni score.

**RESULTS:**

<table>
<thead>
<tr>
<th>AF pocket ≥2 cm</th>
<th>AF pocket ≤2 cm</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.A. at PROM (wks)</td>
<td>21.0 (16.0-26.0)</td>
<td>19.3 (14.0-25.0)</td>
</tr>
<tr>
<td>G.A. at delivery (wks)</td>
<td>22.5 (20.4-35.0)</td>
<td>24.4 (17.0-29.0)</td>
</tr>
<tr>
<td>Birth-weight delivery (grams)</td>
<td>94 (7-119)</td>
<td>22 (10-105)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Pulmonary hypoplasia</td>
<td>0/12</td>
<td>13/21</td>
</tr>
<tr>
<td>Neonatal survival</td>
<td>12/13 (92%)</td>
<td>6/25 (24%)</td>
</tr>
<tr>
<td>Poor neurologic outcome</td>
<td>9/12</td>
<td>2/6</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Residual AF volume in pregnancies with PROM at ≤26 weeks identifies cases at higher risk for poor perinatal and long term neurologic outcome.
366 THE RELATIONSHIP BETWEEN OLIQOHYDRAMNIOSES AND THE ONSET OF PRETERM LABOR IN PRETERM PREMATURE RUPTURE OF THE MEMBRANES. JS Park1, BH Yoon, R Romero, VA Kim2, JR Jeon3, HC Shin3, Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea.

OBJECTIVE: To examine if a reduced amniotic fluid volume is a risk factor for amniotic fluid infection and the onset of preterm parturition in patients with preterm premature rupture of membranes (PROM).

STUDY DESIGN: Amniotic fluid index (AFI) was determined before the conduction of transabdominal amniocentesis in 129 patients with preterm PROM (gestational age less than 35 weeks) Amniotic fluid was cultured for aerobic and anaerobic bacteria as well as Mycoplasma. Survival techniques were used for analysis.

RESULTS: 1) The prevalence of a positive amniotic fluid culture was 24.8% (32/132). 2) Patients with a positive amniotic fluid culture had a significantly lower median AFI and higher rate of an AFI of <5cm than those with a negative culture (median 4.65 cm [range 0.175] vs median 8.40 cm [range 0.31 9]; p<.05, 50.0% [16/32] vs 22.7% [22/97], p<.01, respectively). 3) Patients with an AFI of <5 cm had a significantly shorter amniocentesis-to-delivery interval than those with an AFI of >5 cm (median 38 hours [range 0-21310] vs median 100 hours [range 0.1-2017]; p<.01). 4) Cox proportional hazards model analysis demonstrated that an AFI of <5 cm was a significant predictor of the duration of pregnancy after the adjustment for gestational age and the results of amniotic fluid culture (odds ratio 2.4, 95% confidence interval 1.439 6 p<.001).

CONCLUSIONS: Patients with preterm PROM and an AFI of <5 cm are at increased risk for amniotic fluid infection and shorter interval to delivery.

368 ENDOVAGINAL ULTRASOUND IN THE MANAGEMENT OF INCOMPETENT CERVIX TREATED WITH CERCLAGE. J Byers, S Chupek1, J Tolosa, Div. of Maternal Fetal Medicine, Thomas Jefferson Univ. and Pennsylvania Hospital, Philadelphia, PA.

OBJECTIVE: To assess the impact of transvaginal cervical ultrasound on the evaluation, management, and outcome of pregnancies treated with cerclage.

STUDY DESIGN: A retrospective study was performed dividing 171 patients with McDonald cerclages into 2 cohorts differing by the use of endovaginal ultrasound for cervical surveillance. The following 3 previously described sonographic signs were studied for their value in predicting and impacting the outcomes of pregnancies attended by multiple perinatologists in a clinical setting: funneling >1 cm, funneling within 1 cm of the cervix, and funneling to the cervix. Outcome and utilization variables included perinatal loss rate, birthweight, length of gestation, hospital and tocolytic days, and corticosteroid use.

RESULTS: 98 patients managed between 1991 and 1993 (Group 1) averaged 1 post cerclage cervical ultrasound per 10 weeks of pregnancy. 75 patients managed between 1994 and 1997 (Group 2) were scanned every 2.5 weeks (p<0.01). Though insensitive, funneling of membranes to the cervix was the most useful parameter (sens=88, spec=91, pp 75, npv=88). Differences in utilization variables were limited to an increase in steroids given to women who ultimately delivered at term. Outcome variables were similar between groups.

The overall best predictors for birth weight and fat percent were abdominal circumference, estimated fetal weight, and AD-BPD (abdominal diameter minus biparietal diameter). These parameters may therefore be useful adjuncts in ultrasonic evaluation of patients with diabetes.


OBJECTIVE: To identify which sonographic parameters are most predictive of neonatal body composition and birth weight.

METHODS: Infants of diabetic (n=22) and non-diabetic mothers (n=25) underwent ultrasonographic evaluation at term within one week of delivery. Usual biometry parameters were obtained, as well as humeral thickness, chest circumference, liver length, midfemoral (thigh) thickness, thigh circumference, and check-to-cheek diameter. After delivery, the following measurements were obtained: birth weight, length, circumferences of the head, chest, shoulders, and extremities; length of the extremities; and triceps, subscapular, flank, and thigh skinfolds. Body fat mass and percent fat were calculated using the method described by Dauncey.

RESULTS: Correlations between ultrasonographic parameters with percent fat and birth weight are listed below.

<table>
<thead>
<tr>
<th>Percent fat</th>
<th>Birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>AD-BPD</td>
<td>0.46 &lt;0.0001</td>
</tr>
<tr>
<td>AC</td>
<td>0.55 &lt;0.0001</td>
</tr>
<tr>
<td>FL</td>
<td>0.00 NS</td>
</tr>
<tr>
<td>EFW</td>
<td>0.58 &lt;0.0001</td>
</tr>
<tr>
<td>Thigh Thickness</td>
<td>0.18 NS</td>
</tr>
<tr>
<td>Chest Circumference</td>
<td>0.17 NS</td>
</tr>
<tr>
<td>Check-to-check</td>
<td>0.19 NS</td>
</tr>
<tr>
<td>Humeral thickness</td>
<td>0.22 NS</td>
</tr>
<tr>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

No significant differences in these relationships were observed when the patients were further stratified by presence or absence of maternal diabetes. Only femoral thickness correlated with birth weight in infants of non-diabetic mothers.

CONCLUSIONS: The overall best predictors for birth weight and fat percent were abdominal circumference, estimated fetal weight, and AD-BPD (abdominal diameter minus biparietal diameter). These parameters may therefore be useful adjuncts in ultrasonic evaluation of patients with diabetes.

369 THE ABILITY TO DETECT CONGENITAL HEART DEFECTS BETWEEN 12-14 WEEKS' GESTATION IN HIGH-RISK POPULATION. Z. Wexner1, Y Goldberg2, N Zohar3, E. Shalev4, Dept. of Ob/Gyn, Haemek Medical Center, Afula, Israel.

OBJECTIVE: To observe the accuracy of detecting congenital heart defects (CHD) as early as 12-14 wks in high-risk patients.

STUDY DESIGN: All high-risk patients undergoing fetal echocardiography between January 1995 and March 1999 were included. Indications for fetal echocardiography included: 1) Suspicious cardiac findings on a routine fetal scanning; 2) Pre-gestational diabetes; 3) Previous pregnancy with CHD; 4) Maternal CHD; 5) Exposure to a known teratogen causing CHD; 6) Fetal arrhythmia. The first fetal echocardiography was offered to all high-risk patients between 12-14 wks. However, according to the indication, women were also referred for fetal echocardiography at 14-16 and 20-24 wks. Normal fetal echocardiography examinations performed at 12-14 wks were repeated at 14-16 and at 20-24 wks. Final diagnosis of cardiac anomalies observed at 12-14 wks was always established at 14-16 wks or later. Normal fetal echocardiography examinations performed at 14-16 wks were repeated at 20-24 wks' gestation. Ascertainment of cardiac anomalies was obtained by postnatal echocardiography or by pathological examinations of the fetal heart.

RESULTS: Nine (3.5%) major CHD were correctly diagnosed, 4 (1.6%) minor CHD were incorrectly diagnosed, and 12 (4.7%) CHD were correctly diagnosed. 3 (0.9%) CHD were incorrectly diagnosed, and 2 (0.7%) CHD were correctly diagnosed, and 3 (0.5%) minor CHD were not diagnosed out of 610 fetal echocardiography examinations performed between 20-24 wks.

CONCLUSIONS: The overall accuracy of detecting congenital heart defects between 12-14 wks. When fetal echocardiography is normal or a minor CHD is diagnosed, the examination should be repeated.
370 PERINATAL OUTCOME IN PRENATALLY DIAGNOSED SITU S INVER-SUS, A Johnson, R Pysko, AD Gilbert, PJ Stockman, E Bawle, MI Evans, MC Treadwell, IE Zador, Dept of Ob/Gyn, Hutzel Hospital/Wayne State University and Deps of Pediatric Surgery and Genetics, Children’s Hospital of Michigan, Detroit, MI.

OBJECTIVE: To determine the spectrum of anomalies associated with prenatally diagnosed situs inversus (SI) and perinatal outcome in affected cases. 

STUDY DESIGN: A prospectively entered antenatal ultrasound database was utilized to identify all cases of SI detected from 1/93-6/99. Perinatal outcome was obtained from the maternal and neonatal records.

RESULTS: Of 14 cases identified (4-totals, 10-partial) 3 were isolated (2-totals, 1-thoracic) and 11 (2-totals, 1-thoracic and 9-abdominal) had additional anomalies. Seven cases were diagnosed as asplenia/polysplenia syndrome due to the presence of a complex congenital heart defect (CHD) and SI (1-totals, 1-thoracic and 5-abdominal). In 3 of these cases the gestational age was an IEDD. The additional structural anomalies seen included an increased molar yold (NF) (5), mild ventriculomegaly (2), single umbilical artery (2), horseshoe kidney (1), clubfeet (1) and diaphragmatic hernia (1). The mean gestational age at diagnosis was within range (12-38). Four asplenia/polysplenia cases elected TAB. One case with abdominal SI and mild ventriculomegaly diagnosed at 32 wks was lost to follow up. In the continuing pregnancies, 1 asplenia/polysplenia case with clubfeet and increased NF diagnosed at 17 weeks ended as IUFD at 32 wks. The neonates required surgical intervention, 2-cardiothoracic and 3-bowel obstructions.

CONCLUSION: In this series, 70% of cases with SI had additional anomalies, with 64% being CHD. While the perinatal survival rate reported here approached 90%, further cases are necessary to determine if early detection will improve long term outcome. The finding of IEDD in 42% of the asplenia/polysplenia cases, provides further support to the potential teratogenicity of carbohydrate intolerance.

371 EFFECTS OF BLEEDING ON UTERO- AND UMBILICOPLACENTAL HEMODYNAMICS DURING THE FIRST TRIMESTER OF PREGNANCY. K Makitalho, A Tekaya, P Jouppila, Dept Ob/Gyn, University of Oulu, Finland.

OBJECTIVE: To determine the effects of acute vaginal bleeding on utero- and umbilicoplacental circulation. 

STUDY DESIGN: A total of 26 patients entered this longitudinal study 1-2 days after the beginning of vaginal bleeding and were re-examined every 1-2 weeks. In 3/26 cases vaginal bleeding occurred at 5+ weeks, in 13/26 at 7+ weeks, in 9/26 at 8+ weeks and in 1/26 at 10+ weeks. Subchorionic hematoma was documented in one case at 5+, in 9 at 7+ and 8+ weeks and in 7 cases at 10+ weeks. Four pregnancies ended in miscarriage. Blood flow waveforms of the umbilical artery and umbilical (UA) arteries were obtained by transvaginal pulsed Doppler ultrasonography and peak systolic velocities (Vp) and pulsatility indices (PI) were calculated. Control group consisted of 16 uncomplicated pregnancies.

RESULTS: At 7+ weeks, RA PI-values were significantly (p=0.04) higher in pregnancies with vaginal bleeding (1.6±1.3) compared to control group (1.5±1.0). UA, AA, SA and UA PI-values were similar between the groups. Vaginal bleeding at 5+ weeks did not affect UA, AA, RA, SA or UA blood flow parameters. Subchorionic hematoma at 7+ weeks was associated with significantly greater (p=0.03) RA PI-values compared to control group (1.0±0.0 vs 1.4±0.6). Persistence of subchorionic hematoma until 10+ weeks did not affect UA, AA, RA, SA or UA hemodynamics compared to control group. Doppler ultrasonography could not predict pregnancies ending in miscarriage.

CONCLUSION: Acute vaginal bleeding with or without subchorionic hematoma formation is associated with increased RA impedance at 7+ weeks. This may reflect RA sensitivity to vasoactive substances released by the bleeding. Persistence of subchorionic hematoma does not affect uteroplacental circulation. Miscarriage could not be predicted by parameters describing utero- and umbilicoplacental circulation.

372 HUMAN FETAL CARDIAC FUNCTION DURING THE FIRST TRIMESTER OF PREGNANCY. K Makitalho, P Jouppila, J Rasanen, Dept Ob/Gyn, University of Oulu, Finland.

OBJECTIVE: To test the hypothesis that the systolic and diastolic functions of the human fetal heart change significantly during the first trimester of pregnancy.

STUDY DESIGN: By using transvagal pulsed Doppler ultrasonography in major and minor blood vessels waveforms of the heart were obtained longitudinally at 6+, 7+, 8+, 9+ and 10+ gestational weeks in 12 uncomplicated pregnancies. The proportions (%) of the isovolumetric relaxation (IRT: diastolic function) and isovolumetric contraction (ICT: systolic function) times of the total cardiac cycle were measured. Time-velocity integrals (TVI) of the outflow (OF) and inflow (IF) waveforms and fetal heart rate (FHR) were measured and the mean velocities (Vmean) were calculated (TVIxFHR). Presence of atroventricular valve regurgitation (AVR) was noted and the shape of the inflow waveform (mono- or biphasic) was documented.

RESULTS:

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>IRT (%)</th>
<th>ICT (%)</th>
<th>OF-Vmean (cm/s)</th>
<th>IF-Vmean (cm/s)</th>
<th>AVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>6+</td>
<td>15.4±1.2</td>
<td>17.5±1.3</td>
<td>9.0±2.8</td>
<td>7.6±1.4</td>
<td>0/12</td>
</tr>
<tr>
<td>7+</td>
<td>17.4±2.3</td>
<td>17.2±1.4</td>
<td>8.4±2.0</td>
<td>7.5±2.8</td>
<td>0/12</td>
</tr>
<tr>
<td>8+</td>
<td>17.4±2.3</td>
<td>13.2±3.8</td>
<td>8.4±2.0</td>
<td>6.7±1.4</td>
<td>0/12</td>
</tr>
<tr>
<td>9+</td>
<td>15.0±2.1</td>
<td>9.0±2.8</td>
<td>9.8±1.8</td>
<td>6.7±1.4</td>
<td>0/12</td>
</tr>
<tr>
<td>10+</td>
<td>12.4±1.1</td>
<td>7.3±1.8</td>
<td>8.4±1.7</td>
<td>7.6±1.7</td>
<td>6/12</td>
</tr>
</tbody>
</table>

*p<0.05 (compared to 6+ gestational weeks)

CONCLUSION: A significant improvement in the diastolic function between 6+ and 7+ gestational weeks is accompanied by simultaneous increase in the mean velocities across inflow and outflow tracts. Systolic function changes significantly at 9+ weeks which is associated with the appearance of biphasic inflow pattern. AVR is a common finding at 9+ and 10+ weeks of gestation.

373 VALIDATION OF A NON-INVASIVE TRANSCRANIAL DOPPLER AND BLOOD PRESSURE BASED FORMULA FOR THE ASSESSMENT OF CEREBRAL PERFUSION PRESSURE IN PREGNANT WOMEN. M Behler, C Tookle-Miller, K Jolley, J Fulmer, M Varner, K Diggs, G Saade, GA Bland, H Neele, C Grunewald, JA Herd, Dept Ob/Gyn, University of Utah Medical School, Salt Lake City, UT, Dept Medicine, Baylor College of Medicine, Houston, TX, Univ Texas, Galveston, Karolinska Institute, Sweden.

OBJECTIVE: To develop a Doppler based formula for estimation of cerebral perfusion pressure (CPP) using Fourier analysis of Doppler and radial artery pressure data. We modified this formula using the area under the curve and non-across acquired blood pressure (BP) waveform. Our objective was to evaluate our formula in pregnant women.

METHODS AND MATERIALS: Patients with an epidural in-situ had transtemporal Doppler (TCD) of the middle cerebral artery (MCA) to measure systolic, diastolic and mean velocities (V). A pressure transducer (Utah Medical) was connected to the epidural catheter and pressure was recorded Systolic (SBP), diastolic (DBP), and mean (MAP) blood pressure were taken with a Dinamap monitor. Doppler estimated CPP (mmHg) = (Vmean / (Vmean*Vdiastolic)) x (MAP - DBP). Directly measured CPP(mmHg)= MAP - epidural pressure. Data were plotted on a Bland-Altman graph and in linear and polynomial regression analyses.

RESULTS: 19 healthy women were studied. 17 had normal pregnancies, one had preclampsia, and one had Von Willebrand disease. Mean maternal age was 27±4 yrs and mean gestational age was 30±2 weeks. Mean maternal MAP was 79±8 mmHg. The Bland-Altman plot showed a mean difference of 1.3 mmHg at a mean CPP of 69±12 mmHg with a standard deviation of 5.2 mmHg. The absolute difference was 4.2±3.3 mmHg as a mean CPP of 69±12 mmHg. The regression analysis showed an R=0.92, R²=0.85, and a p<0.0001.

CONCLUSIONS: Our modified formula allows estimation of CPP using a simple calculation and non-invasively acquired data. This validates the use of our method in pregnant women and will allow frequent, easy, and accurate CPP and intracranial pressure establishment. We believe that this methodology will have significant research and clinical applications.

OBJECTIVE: To examine the effects of steroids on the Doppler parameters of umbilical (UM) and middle cerebral artery (MCA) on healthy fetuses, and the time period when this effect (if any) starts and finishes.

STUDY DESIGN: Twenty one singleton pregnancies between the gestational ages of 27 and 33 weeks, and mean (SD) 30.9 weeks (±3.4) who were given betamethasone to accelerate pulmonary maturation were prospectively studied. After Doppler flow velocity waveforms of umbilical and MCA were documented, patients received two doses of 12mg betamethasone. 24th apart Doppler studies were performed at 0 (presteroid) 24, 48, 72, and 96 hours. Peak systolic velocity (PSV), end diastolic velocity (EDV), PI, RI, S/D ratios of both MCA and umbilical artery, and PE-UM/PI-MCA ratio were compared with one way analysis of variance of repeated measures. Statistical significance defined as p < 0.05.

RESULTS: Mean (SD) delivery time was 36.7 (±5.4) weeks (range 32 to 40). 3 Min APGRs were 9.5 (± 47) (range 8 to 10) no neonatal death or neonatal infection was documented. Compared with the control day before steroid administration (hour 0) each of the indices was found to be unaffected by steroid administration. P values were as UMPSV p=0.952, UMRI p=0.991, MCAV p=0.566, UMEDV p=0.837, LMA-B p=0.990, MCAFSV p=0.918, MCAPI p=0.818, MCAPI p=0.930, MCAEDV p=0.779, MCA-A/B p=0.905, UMPI / MCAPI=0.892.

CONCLUSION: As maternal betamethasone administration can significantly affect components of the biophysical profile, other parameters for determining fetal well-being should be investigated. The middle cerebral and umbilical artery Doppler indices were found to be unaffected suggesting the reliability of this modality for evaluating fetuses previously exposed to antenatal steroids.
FETAL CARDIAC FLOW VELOCITY WAVEFORMS BETWEEN 14 AND 16 WEEKS’ GESTATION IN NORMAL PREGNANCIES, David Pelg, Moshe Ben-Ami, Department of Obstetrics and Gynecology, Portia Government Hospital, Tiberias, Israel.

OBJECTIVE: To establish normal values for flow velocity waveforms in fetuses at 14 to 18 weeks’ gestation.

STUDY DESIGN: Doppler waveforms were recorded in 89 normal fetuses at 14 to 16 weeks’ gestation. All scans were performed transvaginally. Peak velocities at E (passive atrial filling) and A (atrial contraction) waves were obtained from tricuspid and mitral flow velocity waveforms. Peak systolic velocities for the ascending aorta and pulmonary artery were also calculated. Linear regression analysis was performed.

RESULTS:

<table>
<thead>
<tr>
<th>Velocity</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricuspid valve peak E-wave velocity (cm/sec)</td>
<td>25.3±4.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Tricuspid valve peak A-wave velocity (cm/sec)</td>
<td>42.7±5.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Mitral valve peak E-wave velocity (cm/sec)</td>
<td>23.0±4.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Mitral valve peak A-wave velocity (cm/sec)</td>
<td>39.9±5.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Aortic peak systolic velocity (cm/sec)</td>
<td>38.5±6.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Pulmonary peak systolic velocity (cm/sec)</td>
<td>38.6±6.9</td>
<td>-0.14</td>
</tr>
</tbody>
</table>

There was no significant correlation between any of the velocities and gestational age.

CONCLUSION: Fetal cardiac function by Doppler waveform analysis remains unchanged between 14 and 16 weeks’ gestation in normal pregnancies.

SHORT-TERM EFFECTS OF GLUCOCORTICOIDS (STGC) ON FETAL RIGHT AND LEFT VENTRICULAR EARLY AND LATE DIASTOLIC FILLING, EC Pryce, JC Veille, Dept of Obs/Gyn, Wake Forest University School of Medicine, Winston-Salem, NC.

INTRODUCTION: Glucocorticoids (GC) are beneficial in reducing perinatal mortality. STGC have also been shown to increase fetal blood pressure and vascular resistance (VR) transiently in experimental animals (within 24-48 hours). Abnormal patterns of left ventricle (LV) diastolic filling have been shown in children with mild systemic hypertension.

AIM: To document the effect of STGC on right ventricle (RV) and LV diastolic filling pattern.

STUDY DESIGN: Nine patients were enrolled in this ongoing prospective study. Gestational age varied between 25 and 38 weeks at enrollment. All fetuses received GC to enhance lung maturation. Two-dimensional directed pulsed Doppler fetal echocardiograms were obtained prior to administration of GC and at 36-48 hours post-steroideal administration. Doppler tracings of RV and LV waveforms were subsequently analyzed with a digitizing table. Parameters to assess the diastolic phase of ventricular filling were analyzed: time-velocity integral (TVI), E and A wave velocities.

RESULTS:

<table>
<thead>
<tr>
<th>SES</th>
<th>Pre</th>
<th>36-48 Hours Post</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV TVI</td>
<td>6.29±0.56</td>
<td>6.20±0.74</td>
<td>0.92 (NS)</td>
</tr>
<tr>
<td>LV TVI</td>
<td>5.69±0.52</td>
<td>5.72±0.55</td>
<td>1.00 (NS)</td>
</tr>
<tr>
<td>RV 1st 1/2 TVI</td>
<td>2.22±0.27</td>
<td>2.39±0.35</td>
<td>0.16 (NS)</td>
</tr>
<tr>
<td>LV 1st 1/2 TVI</td>
<td>2.24±0.49</td>
<td>2.71±0.36</td>
<td>0.28 (NS)</td>
</tr>
<tr>
<td>RV 2nd 1/2 TVI</td>
<td>3.87±0.38</td>
<td>3.70±0.31</td>
<td>0.16 (NS)</td>
</tr>
<tr>
<td>LV 2nd 1/2 TVI</td>
<td>3.05±0.29</td>
<td>3.26±0.39</td>
<td>0.45 (NS)</td>
</tr>
</tbody>
</table>

CONCLUSION: STGC do not have a significant effect on TVI, E and A wave velocities of the LV or RV which suggests that antenatal GC may not affect the diastolic filling pattern in the fetus. Additional studies are necessary to confirm these findings. (Supported by NIH HL 39886)
SHORT-TERM EFFECTS OF GLUCOCORTICOIDS (STGC) ON FETAL SYSTOLIC FUNCTION. E.C. Pryor, J.C. Veille, Dept. of Ob/Gyn, Wake Forest University School of Medicine, Winston-Salem, NC.

INTRODUCTION: Glucocorticoids (GC) are beneficial in reducing perinatal mortality and the incidence of intraventricular hemorrhage. STGC have also been shown to increase fetal blood pressure and vascular resistance (VR) transiently in experimental animals (within 24-48 hours). These changes may affect ventricular diastolic filling pattern.

AIM: To document the STGC on right ventricle (RV) and left ventricle (LV) diastolic filling pattern.

STUDY DESIGN: Nine patients were enrolled in this ongoing prospective study. Gestational age varied between 25 and 35 weeks at enrollment. All fetuses received GC to enhance lung maturation. Two-dimensional directed range-gated pulsed Doppler examinations were obtained prior to administration of GC and at 36-48 hours post-steroi administration. Doppler tracings of RV and LV waveforms were subsequently analyzed with a digitizing table. Parameters to assess the diastolic phase of ventricular filling were analyzed: E/A ratio (the ratio of the early (E) peak which represents passive filling to the A peak which represents the atrial contraction in diastole), deceleration time of the ventricle for early filling, and isovolumetric relaxation time (IVRT). Paired t-test was utilized for statistical analysis (mean±SEM).

RESULTS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre</th>
<th>36-48 Hours Post</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV E/A</td>
<td>0.67±0.05</td>
<td>0.92±0.07</td>
<td>0.03</td>
</tr>
<tr>
<td>LV E/A</td>
<td>0.74±0.05</td>
<td>0.75±0.05</td>
<td>NS</td>
</tr>
<tr>
<td>RV DT</td>
<td>105.7±51</td>
<td>105.14±67</td>
<td>NS</td>
</tr>
<tr>
<td>LV DT</td>
<td>105.02±6.84</td>
<td>105.96±11.17</td>
<td>NS</td>
</tr>
<tr>
<td>RV IVRT</td>
<td>45.71±5.80</td>
<td>40.56±24.24</td>
<td>NS</td>
</tr>
<tr>
<td>LV IVRT</td>
<td>47.09±3.28</td>
<td>59.93±35.35</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CONCLUSION: RV E/A and LV IVRT are increased which suggests that STGC may affect diastolic function. More studies are necessary to confirm these findings. (Supported by NIH HL 38296).

384 SHORT-TERM EFFECTS OF GLUCOCORTICOIDS (STGC) ON FETAL SYSTOLIC FUNCTION. E. C. Pryor, J. C. Veille, Dept. of Ob/Gyn, Wake Forest University School of Medicine, Winston-Salem, NC.

INTRODUCTION: Glucocorticoids (GC) are beneficial in reducing perinatal mortality and the incidence of intraventricular hemorrhage. STGC have also been shown to increase fetal blood pressure and vascular resistance (VR) transiently in experimental animals (within 24-48 hours). These changes may affect cardiac systolic function.

AIM: To document the effect of STGC on fetal systolic function.

STUDY DESIGN: Nine patients were enrolled in this ongoing prospective study. Gestational age varied between 25 and 35 weeks at enrollment. All fetuses received GC to enhance lung maturation. Two-dimensional directed range-gated pulsed Doppler examinations were obtained prior to administration of GC and at 36-48 hours post-steroi administration. Doppler tracings of ascending aorta (AO) and pulmonary artery (PA) waveforms were subsequently analyzed with a digitizing table. Parameters analyzed included time-velocity integral (TVI), acceleration to ejection time (AC/ET), and peak flow velocity (PFV). Paired t-test was utilized for statistical analysis (mean±SEM).

RESULTS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre</th>
<th>36-48 Hours Post</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA TVI (cm/s)</td>
<td>8.71±0.48</td>
<td>7.60±0.88</td>
<td>0.44 (NS)</td>
</tr>
<tr>
<td>PA PFV (cm/s)</td>
<td>70.60±4.49</td>
<td>61.74±6.97</td>
<td>0.25 (NS)</td>
</tr>
<tr>
<td>PA AC/ET</td>
<td>0.17±0.04</td>
<td>0.33±0.06</td>
<td>0.24 (NS)</td>
</tr>
<tr>
<td>AO TVI (cm/s)</td>
<td>3.62±0.49</td>
<td>7.20±1.19</td>
<td>0.07 (NS)</td>
</tr>
<tr>
<td>AO PFV (cm/s)</td>
<td>51.08±24.44</td>
<td>49.52±7.47</td>
<td>0.72 (NS)</td>
</tr>
<tr>
<td>AO AC/ET</td>
<td>0.50±0.05</td>
<td>0.33±0.06</td>
<td>0.75 (NS)</td>
</tr>
</tbody>
</table>

CONCLUSION: STGC do not significantly affect TVI, PFV, or AC/ET of the PA or AO which suggests that arterial GC may not affect systolic function in the fetus. Additional studies are necessary to confirm these findings. (Supported by NIH HL 38296).

385 EVIDENCE OF FETAL CEREBRAL BLOOD FLOW REDISTRIBUTION IN IDIOPATHIC HYDRAMNIIOS. H. Roshkovits, B. Furman, A. Bashiri, M. Hallak, A. Smolin, M. Mazor; Dept. OB/GYN, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

OBJECTIVE: Idiopathic hydranmios is an independent risk factor for perinatal morbidity and mortality, although the precise mechanism is unknown. (Eur J Obstet Gynecol Reprod Biol 1996;70:41-7, 1998;77 157-61). Hydramnios may alter oxygen delivery to the human fetus. Middle cerebral artery (MCA) pulsatility index (PI) is a sensitive parameter to detect blood flow redistribution “centralization”. The aim of this study was to determine if idiopathic hydramnios is associated with changes in the PI of the MCA and the umbilical artery (UA).

STUDY DESIGN: PI of MCA and UA was determined prospectively in 46 consecutive pregnant women with singleton pregnancies and idiopathic hydranmios (study group) and in 72 matched control patients with normal growth in sheep.

RESULTS: An abnormal MCA PI was found in 30.4% (14/46) of patients in the study group and in 5.5% (4/72) of patients in the control group (OR=5.48; p=0.002; 95% CI 1.55-21.2) Fig. 1 displays the MCA PI descriptive statistics in the study and control group and Fig. 2 the relationship between MCA PI and AFI.

A significant correlation was found between MCA PI and AFI. In contrast there were no significant differences between the UA PI (0.95 (0.57-2.06) vs.1.0 (0.49-1.48), (p=0.201) and MCA/UA (0.86 (0.57-2.06) vs. 2.15 (0.86-4.11), (p=0.141) in both groups.

CONCLUSIONS Our observations provide evidence of cerebral blood flow redistribution in fetuses with idiopathic hydranmios.

SHORT-TERM EFFECTS OF GLUCOCORTICOIDS (STGC) ON FETAL MIDDLE CEREBRAL ARTERY (MCA) AND UMBILICAL ARTERY (UA) HEMODYNAMICS. E.C. Pryor, J.C. Veille, Dept. of Obstetrics and Gynecology, Wake Forest University School of Medicine, Winston-Salem, NC.

INTRODUCTION: Glucocorticoids (GC) are beneficial in reducing the incidence of intraventricular hemorrhage. However, GC have been associated with a reduction in head circumference and decreased birth weight ratio (birth weight divided by the median birth weight for the gender and gestational age) Single course GC have been shown to retard fetal brain growth in sheep.

AIM: Effect of STGC on MCA and UA hemodynamics.

STUDY DESIGN: Nine patients were enrolled in this ongoing prospective study. Gestational age varied between 25 and 35 weeks at enrollment. All fetuses received GC to enhance lung maturation. Two-dimensional directed range-gated pulsed Doppler examinations were obtained prior to administration of GC and at 36-48 hours post-steroi administration. Doppler tracings of MCA and UA waveforms were subsequently analyzed with a digitizing table. Parameters analyzed included pulsatility index (PI), time velocity integral (TVI), and acceleration to ejection time (AC/ET). Paired t-test was utilized for statistical analysis (mean±SEM).

RESULTS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre</th>
<th>36-48 Hours Post</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA PI</td>
<td>1.90±0.26</td>
<td>1.56±0.12</td>
<td>0.45 (NS)</td>
</tr>
<tr>
<td>MCA TVI</td>
<td>5.54±0.55</td>
<td>4.21±0.58</td>
<td>0.28 (NS)</td>
</tr>
<tr>
<td>MCA AC/ET</td>
<td>0.24±0.03</td>
<td>0.25±0.03</td>
<td>0.38 (NS)</td>
</tr>
<tr>
<td>UA PI</td>
<td>1.19±0.09</td>
<td>1.19±0.09</td>
<td>0.96 (NS)</td>
</tr>
</tbody>
</table>

CONCLUSION: STGC do not significantly affect PI, TVI, or AC/ET in MCA or UA. Additional studies are necessary to confirm these findings. (References: 1) Am J Obstet Gynecol 1999;180:114-21; 2) Obstet Gynecol 1999;94:213-8) (Supported by NIH HL 38296).
UMBILICAL VENOUS BLOOD FLOW IS REDUCED IN IUGR FETUSES: A LONGITUDINAL STUDY. J Chyu*, H Hobbins*, B Beaty*, J Chyu*, H. Galan*, Department of Obstetrics and Gynecology, Denver Health Medical Center, Denver, CO, and the Departments of *Ob/Gyn & *Biometrics and *Pediatrics at UCHSC, Denver, CO, and Departments of Obstetrics and Gynecology, Denver Health Medical Center, Denver, CO, and Departments of Obstetrics and Gynecology, Denver Health Medical Center, Denver, CO.

OBJECTIVE: 1) To compare umbilical venous flow (UVF; ml/min) per kg fetal weight between Denver and Milan; 2) To compare UVF per kg in intermediate growth-restricted (IUGR) fetuses to normally grown fetuses in Denver.

STUDY DESIGN: In this longitudinal study, normally grown fetuses in Denver (n=15) and Milan (n=21) had UVF (ml/mm) calculated which was corrected for fetal weight. Umbilical vein diameter and mean velocity were measured on a perpendicular and longitudinal section of free cord, and corrected for fetal weight.

RESULTS: In normally grown fetuses, Denver fetuses compared to Milan, when corrected for fetal weight, there was no effect of group (Denver or Milan) on UVF. The two groups were combined for comparison to IUGR fetuses. IUGR UVF had significantly reduced UVF compared to normal fetuses (p<0.01).

CONCLUSION: The lower absolute flow in fetuses from Denver is consistent with the lower weight fetuses which result from the genetic mix seen in Denver. When corrected for fetal weight, no differences were detected in UVF between Denver and Milan fetuses. UVF was significantly reduced in IUGR fetuses compared to the normal fetuses and may become a useful tool for antenatal surveillance of the IUGR fetus. (Supported by MOD 6-FY97-0174 and AAOG)

CIRCULATORY CHANGES IN GROWTH RESTRICTED FETUSES OF DIFFERENT SEVERITY: A LONGITUDINAL STUDY. J Chyu*, H Hobbins*, B Beaty*, J Chyu*, H. Galan*, Department of Obstetrics and Gynecology, Denver Health Medical Center, Denver, CO, and the Departments of *Ob/Gyn & *Biometrics and *Pediatrics at UCHSC, Denver, CO.

OBJECTIVE: The severity of IUGR has been previously stratified into groups by umbilical artery pulsatility index (PI) and fetal heart rate tracing characteristics: Group 1-normal PI and FRH, and Group 2-normal PI and abnormal FRH and PI. Group 2 fetuses have a significantly lower risk of acidemia than Group 3 (14% vs 68%, NEJM, 1995). The purpose of this study was to compare the circulatory changes between fetuses in Groups 1 and 2.

STUDY DESIGN: 33 singleton IUGR pregnancies were categorized into Group 2 (n=8) and Group 3 (n=25). Doppler measurements were recorded every three days and included ductus venous (DV) S/A ratio, middle cerebral artery pulsatility index (MCA PI), ductus venous (DV) S/A ratio, tricuspid valve (TV) E/A ratio and mean velocity (MV) E/A ratio. Doppler measurements were corrected for abdominal circumference (AC). Perinatal outcome data are presented as mean ± SEM, and analyzed with Student’s t-test and Fisher’s Exact test.

RESULTS: Group 2 had a significantly greater number of perinatal deaths than Group 2 (11 vs 0; p=0.05). Analysis showed that there was a significant interaction between days prior to delivery and group for the DV S/A ratio (p<0.001). The DV S/A ratio became abnormal in 66% (15/22) of fetuses in Group 2 and normal in 24% (6/25) of fetuses. Data were corrected for abdominal circumference and plotted against days prior to delivery. Doppler measurements were compared between groups using mixed effects modeling (SAS Proc MIXED).

CONCLUSION: We conclude that the DV S/A ratio becomes abnormal earlier and remains abnormal compared to other central circulatory parameters. This may represent the earliest sign of cardiac decompensation in IUGR fetuses and may occur earlier than an abnormal FHR tracing. Studies are in progress to evaluate this potentially helpful tool. (Supported by MOD and AAOG)


OBJECTIVE: Chronic high altitude exposure changes the hematologic and hemodynamic profiles in human fetuses, and reduces birthweight. Our objective was to explore Doppler velocimetry of the peripheral and central circulations in normal fetuses is not affected by relatively high altitude. Denver (CO; 1660m) compared to sea level (Milan, Italy, 40m).

STUDY DESIGN: In this cross-sectional study, 119 patients (55 Denver, 66 Milan) with normal singleton pregnancies underwent Doppler waveform analysis of the following vessels: umbilical artery (UA) S/A ratio, uterine artery (UA) S/A ratio, middle cerebral artery pulsatility index (MCA PI), ductus venous (DV) S/A ratio, tricuspid valve (TV) E/A ratio and mean velocity (MV) E/A ratio. Doppler measurements were corrected for abdominal circumference (AC). Statistical analysis was performed by General Linear Models Procedure (SAS Systems) taking into account the variables of group (normal or IUGR), gestational age and the interaction of group and gestational age. A p value of <0.05 was considered significant.

RESULTS: Relative to Milan, patients at Denver’s altitude had a significant decrease in the DV S/A (p=0.02; see graph). Gestational age had no significant effects on Doppler indices that were the same at Milan and Denver’s altitudes. The TV E/A ratio and the TV E/A ratio significantly increased with gestational age (p<0.01), while the UA S/D ratio and the UA S/D ratio decreased with gestational age (p<0.01).

CONCLUSION: Gestational age has the same effect on the Doppler indices at both high and low altitude. Fetuses at Denver’s altitude had significant decreases in the DV S/A. We speculate that the DV may be sensitive to slight changes in PO2 and may represent an adaptation by the fetus to the lower PO2 in Denver. This is an ongoing study of the Doppler indices of the umbilical artery (UA) and may identify patients at risk for preclampsia and intrauterine growth restriction. However, the reported sampling sites have varied along the length of the UA. The purpose of this study was to compare UA Doppler indices at Denver’s altitude to those sampled distal to the external iliac vessel.

STUDY DESIGN: 3 singleton pregnancies consisting of both normal and complicated patients were included in the study. Doppler velocimetry was performed on the UA proximal and distal to the external iliac vessel for both right and left sides of the patient. Doppler parameters included the systolic/diastolic ratio (S/D) and the resistance index (RI).

RESULTS: A total of 36 measurements were obtained at proximal and distal locations for each right and left UA. There was a strong correlation and no significant differences between the proximal and distal Doppler measurements for either UA. The Doppler indices were compared on either the right or left side of the patient. Comparisons were not made between right and left sides. Data are presented as mean ± SEM. Proximal and distal Doppler indices were compared by linear regression and paired t-test.

CONCLUSIONS: We conclude that there are no differences in UA Doppler indices sampled near and far from the external iliac vessels. This should reassure physicians and investigators when comparing published studies in which the methodologies differ in the sampling site of the umbilical artery. One should feel comfortable sampling the site on the uterine artery that is best visualized. (Supported by the AAOGF)
ACUTE FETAL CARDIOVASCULAR RESPONSES TO AMNIOINFUSION

OBJECTIVE: To study the effects of maternal position on the uterine and umbilical artery Doppler velocimetry indices.

STUDY DESIGN: In consenting women with singleton pregnancies at >20 weeks' gestation with no identified maternal or fetal complications (n=90), pulsed Doppler flow measurements for the right and left uterine arteries and umbilical arteries were obtained 5 minutes after standing, 15 minutes after lying in the left lateral position, and 15 minutes after lying supine in a semi-Fowler position. Resistance index (RI) and pulsatility index (PI) were obtained in the left lateral position, and 15 minutes after lying supine in a semi-Fowler position.

RESULTS: Data are presented as mean ± standard deviation.

<table>
<thead>
<tr>
<th>Position</th>
<th>Left uterine RI</th>
<th>Right uterine RI</th>
<th>Umbilical artery PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>0.50±0.11</td>
<td>0.41±0.11</td>
<td>1.12±0.27</td>
</tr>
<tr>
<td>Left lat.</td>
<td>0.52±0.11*</td>
<td>0.51±0.10*</td>
<td>1.13±0.26</td>
</tr>
<tr>
<td>Supine</td>
<td>0.52±0.09*</td>
<td>0.54±0.10*</td>
<td>1.07±0.24</td>
</tr>
</tbody>
</table>

*p<0.001 compared with standing position; no difference between left lateral and supine position (right uterine artery p=0.15, left uterine artery p=0.78).

CONCLUSIONS: In the absence of obstetric complications, orthostatic position is associated with a significant decrease in impedance to flow in the uterine arteries compared to left lateral and supine positions.

CHANGES IN UTERINE ARTERY IMPEDANCE TO FLOW WITH MATERNAL POSITION

OBJECTIVE: To study the effects of maternal position on the uterine and umbilical artery Doppler velocimetry indices.

STUDY DESIGN: In consenting women with singleton pregnancies at >20 weeks' gestation with no identified maternal or fetal complications (n=90), pulsed Doppler flow measurements for the right and left uterine arteries and umbilical arteries were obtained 5 minutes after standing, 15 minutes after lying in the left lateral position, and 15 minutes after lying supine in a semi-Fowler position. Resistance index (RI) and pulsatility index (PI) were calculated. Statistical analysis was performed using one-way analysis of variance with Bonferroni correction. A p<0.05 was considered significant.

RESULTS: Data are presented as mean ± standard deviation.

<table>
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CONCLUSIONS: In the absence of obstetric complications, orthostatic position is associated with a significant decrease in impedance to flow in the uterine arteries compared to left lateral and supine positions.

PRENATAL TREATMENT WITH ACUPUNCTURE AND LABOR

OBJECTIVE: To evaluate the so far controversially discussed influence of prenatal acupuncture (AP) on the duration of labor

STUDY DESIGN: Fifty-seven women with AP treatment and vaginal delivery of a singleton pregnancy at term were included in our study. The control group consisted of 63 women. The following parameters were assessed: duration of the first stage of labor, defined as the time interval between 5 cm of cervical dilatation and complete dilatation, duration of the second stage of labor, the use of analgesics (pethidine) during labor, administration of epidural anesthesia, and intravenous application of oxytocin during the first and second stages of labor.

RESULTS: Median duration of the first stage of labor was significantly abbreviated after AP, 106 minutes vs. 291 minutes (P<0.0001). Median duration of the second stage of labor was 57 minutes in both cohorts. Controls received significantly more often oxytocin during the first stage of labor compared with the study group (85% and 15%, respectively, P=0.01) and during the second stage (72% and 28%, respectively, P=0.03). The use of epidural anesthesia and analgetics was equal in both groups.

CONCLUSIONS: Our study suggests that AP treatment is a recommendable form of childbirth preparation due to its positive effect on the first stage of labor.

MATERNAL HEMODYNAMICS AFTER OXYTOCIN BOLUS VERSUS INFUSION IN THE THIRD STAGE OF LABOR

OBJECTIVE: To determine whether oxytocin bolus given in the third stage of labor is associated with maternal hypotension compared to oxytocin infusion.

STUDY DESIGN: In a randomized double-blinded fashion 201 women received either an oxytocin bolus (B) (10 IU push) or an infusion (I) (10 IU in 500 cc saline at 125 cc/h) immediately after vaginal delivery. Maternal arterial pressures (MAP) and heart rates (HR) were recorded over 30 minutes.

RESULTS: The B group (N=99) and the I group (N=102) were similar in the first stage of labor:

- Mean arterial pressure: B 80±10 vs. I 81±10
- Mean heart rate: B 75±10 vs. I 76±10

No significant differences were found in MAP and HR between the two groups. Analgesia was similar in both groups.

CONCLUSION: Maternal hemodynamics after oxytocin bolus versus infusion in the third stage of labor differ significantly, with the use of oxytocin infusion showing lower maternal blood pressures compared to bolus oxytocin.
Further study is required to determine the relative safety and efficacy of these formulations. Of the 25 who delivered vaginally (77%), there was no difference in the interval to delivery between groups (group 1, 1775±1084; group 2, 1186±600; group 3, 1818±600; p=0.32). Thirty-five per cent (8/23) delivered vaginally in response to misoprostol alone. Between groups, there was no significant difference in route of delivery or rate of tachysystole. There were no cases of hyperstimulation in any group. There were no differences in parity, epidural or oxytocin usage, blood loss, or short-term neonatal outcome between groups.

CONCLUSIONS: Each of the three low dose oral misoprostol regimens tested was able to induce labor without causing high rates of clinically significant tachysystole, hyperstimulation or need for cesarean delivery. Further study is required to determine the relative safety and efficacy of these regimens.

CONCLUSIONS: The use of low dose oral misoprostol to induce labor in the third trimester is a safe and effective treatment for resolving dystocia in women in labor and is a preferred alternative to oxytocin.

CONCLUSIONS: Primary vaginal delivery, fetal weight above 4.8 kg, and pudendal or epidural analgesia prospectively help to identify low-risk singleton patients at greatest risk for severe perineal tear. During delivery of these patients usage of vacuum (instead of forceps) and restricting the use of midline episiotomy might reduce the incidence of severe perineal tear. In cases where episiotomy seems crucial the use of a mediolateral episiotomy will reduce the likelihood of severe perineal tear.
REGULARITY OF UTERINE CONTRACTIONS AS AN INDICATOR OF THE OUTCOME OF LABOR. J. W. Oppenheimer, E.S. Rand*, W. Shiue Wenyss
Division of Maternal-Fetal Medicine, *Department of Mathematics, University of Ottawa.** Laboratory Centre for Disease Control Ottawa, ON, Canada.

OBJECTIVE: To examine the correlation between the regularity of uterine contractions and the outcome of labor in terms of oxytocin usage and cesarean section for dystocia.

STUDY DESIGN: Data was extracted from the Ottawa General Hospital labor and delivery database which contained over 8,000 records including demographic data and electronically archived cardiotocographic (CTG) labor traces. All cases meeting the following criteria were identified: primigravida in spontaneous labor, singleton pregnancy, vertex presentation, 37 - 42 weeks gestation, cesarean section for failure to progress, minimum of 3 hours of analzyable CTG prior to onset of the second stage. Cases with cesarean section for dystocia were matched 1:2 with controls delivering vaginally. The peak of each contraction was visually identified and electronically marked on each CTG trace, using customized software. A moving average (MTIME) and standard deviation (SDTIME) of 5 interpeak times was calculated for successive 30 minute periods and plotted against cervical dilatation for each group. Statistical analysis was performed using SAS.

RESULTS: 65 cases of cesarean section for failure to progress were matched with 130 controls. Overall, both MTIME and SDTIME fell as labor progressed. These changes were more marked in the vaginal delivery group. In women requiring oxytocin, the rate of fall MTIME and SDTIME was significantly greater following oxytocin in the group delivering vaginally (slope of MTIME, 2.71 pre-oxytocin and 28.95 post-oxytocin, p = 0.0045; slope of SDTIME -4.44 and -6.44, p = 0.002). No such change was seen in the cesarean section group.

CONCLUSION: As normal labor progresses there is a shortening of the inter-contraction interval (MTIME) and an increase in contraction regularity (SDTIME). A successful response to oxytocin augmentation may be predicted by the change in contraction pattern following treatment.

399 INCREASED RISK OF ADVERSE MATERNAL OUTCOMES WITH INDUCTION OF LABOR IN WOMEN WITH A HISTORY OF PREVIOUS CESAREAN DELIVERY. S. Fleischma*, K.A. Bennett*, L. Elmore*, K. Demasio, D. Jones, J. A. Copel. Dept. Ob/Gyn, Yale University, New Haven, CT.

OBJECTIVE: To compare maternal morbidity and mortality with induction of labor compared to spontaneous labor in women who attempted vaginal delivery after prior cesarean delivery.

STUDY DESIGN: Data for this retrospective cohort study were obtained from the database of the Yale New Haven Hospital, New Haven, Connecticut for the years 1995 through 1999. The cohort consisted of all women who attempted vaginal delivery after prior cesarean delivery. The study group consisted of all women with an unfavorable cervix (Bishop score < 7) who underwent induction of labor after prior cesarean delivery. The control group consisted of all women who labored spontaneously at term with a similar Bishop score (< 7). Randomization to induction or spontaneous labor was not performed. Categorical data were compared using the chi-square test, while the Student t-test or ANOVA were used for continuous data.

RESULTS: Among 283 patients included, 76 were induced with prostaglandin and 127 with oxytocin. Bishop score was not significantly different in women who received prostaglandin compared to those who received oxytocin. The mean time (+ standard deviation) to delivery was 1317 (+ 328) minutes with prostaglandin compared with 615 (+ 376) minutes with oxytocin (p < 0.001). The cesarean rate was 48.1% in the prostaglandin group and 41.9% with oxytocin (p = 0.39; odds ratio [OR] = 1.28, confidence interval [CI] [0.79 - 2.06]). Uterine rupture occurred in 0.8% of patients who received prostaglandin compared with 2.4% of patients who were given oxytocin (p = 0.02; OR = 4.86, CI (1.54 - 16.39)). Misoprostol and dinoprostone did not differ significantly in time to delivery nor in rate of uterine dehiscence.

CONCLUSION: Induction with prostaglandin, compared with oxytocin, in women with prior cesarean delivery results in a significantly increased time to delivery and risk of uterine rupture.

398 PROSTAGLANDIN INDUCTION IN WOMEN WITH A PRIOR CESAREAN DELIVERY INCREASES INDUCTION TIME AND RISK OF UTERINE RUPTURE. K.A. Bennett, L. Elmore, S. Fleischman, K. Demasio, D. Jones, J. A. Copel. Dept. Ob/Gyn, Yale University, New Haven, CT.

OBJECTIVE: To compare oxytocin with prostaglandins for induction of labor and cesarean section in women with unfavorable cervixes and a history of prior cesarean delivery.

STUDY DESIGN: Data for this retrospective cohort study were obtained from the database of the Yale New Haven Hospital, New Haven, Connecticut for the years 1995 through 1999. The cohort consisted of all women with prior cesarean delivery with unfavorable cervixes (Bishop score < 7) who underwent induction of labor and attempted vaginal delivery. The first study group included all women who were induced using dinoprostone or misoprostol, while the second consisted of all who were induced using only oxytocin. The principal outcome measure was time to delivery. Cesarean rate and the occurrence of uterine rupture were considered secondary outcomes. Categorical data were compared using the chi-square or Fisher exact tests, while the Student t-test or ANOVA were used for continuous data.

RESULTS: Among 880 patients included, 560 patients presented in spontaneous labor. Two hundred and thirty-one patients were induced with oxytocin and 414 with prostaglandins. Oxytocin was associated with a significantly increased rate of cesarean delivery and uterine rupture.

CONCLUSION: Induction with oxytocin for induction of labor and cesarean section in women with unfavorable cervixes and a history of prior cesarean delivery results in a significantly increased time to delivery and risk of uterine rupture.

389 A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL OF OXYTOCIN AT THE BEGINNING VERSUS THE END OF THE THIRD STAGE OF LABOR FOR PREVENTION OF POSTPARTUM HEMORRHAGE. W. Hub*, D. Cheilamen*, F.D. Malone. Dept. of Ob/Gyn, Tufts University School of Medicine, New England Medical Center, Boston, MA.

OBJECTIVE: To evaluate the effect of giving oxytocin at the beginning or at the end of the third stage of labor on the incidence of postpartum hemorrhage (PPH), and on other objective measures of blood loss.

STUDY DESIGN: A prospective double-blinded, trial was performed in which patients with singleton pregnancies delivering vaginally were randomized to one of two different third stage of labor treatment algorithms. All patients received two injections. Injection A (either 10 units of oxytocin or the same volume of normal saline) was given intramuscularly after delivery of the anterior shoulder of the fetus. Injection B (10 units of oxytocin if the patient previously received normal saline during injection A or vice versa) was given following delivery of the placenta. Injections appeared identical and were prepared in advance by the pharmacist. The primary outcome measure was the incidence of PPH (estimated blood loss >500 ml). Blood loss was objectively measured by weighing the delivery collection drapes, and comparing admission and postpartum day #2 hemoglobin and hematocrit (Alhgb/Hemc). Visual estimation of blood loss and length of the third stage of labor were also recorded.

RESULTS: 51 patients were enrolled into the trial, with 27 receiving oxytocin at delivery of the anterior shoulder and 24 receiving oxytocin following delivery of the placenta. The incidence of PPH was 0% when oxytocin was given after delivery of the placenta, but was 14.8% when oxytocin was given at delivery of the anterior shoulder (P < 0.05).

CONCLUSION: The incidence of PPH is lower when oxytocin is given at the end, rather than the beginning, of the third stage of labor. The optimal time to administer oxytocin during the third stage of labor may be after delivery of the placenta is complete.
**402**

**THE USE OF DNA MICRO-ARRAY TECHNOLOGY TO IDENTIFY GENES UNIQUELY EXPRESSED BY THE LABORING MYOMETRIUM. J. Spino, J. Jenebol and Y. Dadavis. Dept Of Ob/Gyn, Univ. Of Utah Health Sciences Center, Salt Lake City, UT.**

**Objective:** Our understanding of the gene cascade responsible for the induction of human labor remains limited at best, due in part to the fact that genes expressed preferentially or even exclusively in the laboring myometrium have thus far been identified on a case-by-case basis. However, now molecular technologies now permit a systematic approach capable of establishing the complete repertoire of differentially-expressed genes in the laboring human myometrium at term. The purpose of the current study was to employ DNA microarray technology to identify DNA sequences uniquely expressed in the myometrium during labor.

**Methods:** Samples of laboring myometrium were obtained from women at ≥ 26 weeks gestation experiencing regular uterine contractions (≥ 3 UC/10 min) associated with a change in cervical dilation or effacement on sequential cervical exams. Quiescent samples were obtained from patients, not in labor as documented by the absence of regular uterine contractions, who underwent elective cesarean section for obstetric indications. mRNA populations derived from laboring and myometrial samples were differentially labeled with CyDye-labeled cDNA pools and hybridized with a glass matrix converted to cDNA in the presence of dCTP/rL-CyDye-5. The two mRNA populations were detected with CyDye-labeled cDNA pools and hybridized with a glass matrix converted to cDNA in the presence of dCTP/green-CyDye-5 while mRNA from quiescent myometrium were detected with CyDye-labeled cDNA pools and hybridized with a glass matrix arrayed with 4,000 unique human DNA sequences. The fluorescence emission induced by lasers of the appropriate wavelength (552 nm and 630 nm) were detected by a confocal lens system. Any sequence with a ratio of given to red emission that was 2 standard deviation above the mean was considered to be differentially expressed.

**Results:** Approximately 18,400 unique cDNA sequences were screened for differential expression using this technique. A total of 213 DNA sequences, including 90 EST and unnamed sequences, were found to be up-regulated in laboring myometrium.

**Conclusion:** The DNA microarray technique is a useful method that allows a rapid means of screening large numbers of unique sequences to identify differentially expressed genes. The use of this technique will lead to a more complete understanding of the initiation and progression of the labor process in humans.

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**403**

**SUCCESS OF INDUCTION OF LABOR AMONG WOMEN WITH ECLAMPSIA IN THE UNITED STATES. M. Menkes, C. V. Ananth, J. F. Simon, D. Vimtiklis, U.M.D.N.J.-Robert Wood Johnson Medical School/Saint Peter’s University Hospital, New Brunswick, N.J.**

**Objectives:** To establish success rates for induction of labor in eclamptic women by gestational age (GA) and to determine if the presence of eclampsia has any impact on the likelihood of successful vaginal delivery.

**Study Design:** Data was derived from the national linked birth/infant death data sets for 1995 and 1996 assembled by the National Center for Health Statistics. Analyses was restricted to women having an induction of labor who delivered singleton liveborns between 24 and 42 completed weeks of gestation. For analyses, births were grouped by parity, placenta previa, implantable GAs and women with pregnancy associated hypertension without eclampsia were excluded. The state of eclampsia was defined in the data set as convulsions in women with signs and symptoms of preeclampsia. Inductions were considered successful if they resulted in vaginal delivery. Rates of successful induction for eclamptic and non-eclamptic women were calculated, stratifying by GA at delivery. Multivariable logistic regression models were fit to derive relative risks (RR) and 95% confidence intervals (CI) after adjusting for confounders, including maternal age, race, gravidity, previous cesarean delivery or infant >4000 grams, diabetes, birthweight, premature rupture of membranes, cord prolapse and fetal distress.

**Results:** The analysis included 1,089,662 women who underwent induction of labor, of which 6,217 (0.6%) had eclampsia. Success rates for induction of labor in eclamptic and non-eclamptic women for each GA category are presented below.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>Successful induction</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eclamptic women</td>
<td>Non-eclamptic women</td>
<td></td>
</tr>
<tr>
<td>24-27</td>
<td>65%</td>
<td>76.0%</td>
</tr>
<tr>
<td></td>
<td>41.7%</td>
<td>75.5%</td>
</tr>
<tr>
<td>33-36</td>
<td>69.9%</td>
<td>85.5%</td>
</tr>
<tr>
<td>37+</td>
<td>71.1%</td>
<td>84.1%</td>
</tr>
</tbody>
</table>

**Conclusions:** Eclamptic women have lower rates of successful induction than non-eclamptic women at all GAs. Induction success increases markedly in eclamptic women, and to lesser extent in non-eclamptic women, with advancing GA. This may reflect a tendency among the earlier GAs to discontinue an induction in the presence of eclampsia.

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**404**

**INCREASED RISK OF ADVERSE NEONATAL OUTCOMES WITH INDUCTION OF LABOR IN WOMEN WITH A HISTORY OF PREVIOUS CESAREAN DELIVERY. L. Elmore, K.A. Bennett, S. Fleischman, K. Demaino, D. Jones, J.A. Copel. Dept. Ob/Gyn, Yale University, New Haven, CT.**

**Objective:** To examine maternal mortality and morbidity with induction of labor compared to spontaneous labor in women who attempted vaginal delivery after prior cesarean delivery.

**Study Design:** Data for this retrospective cohort study were obtained from the database of the Yale-New Haven Hospital, New Haven, Connecticut for the years 1995 through 1999. The cohort consisted of all women who attempted vaginal delivery after prior cesarean delivery. The study group consisted of all women with an unfavorable cervix (Bishop score < 7) who underwent induction of labor. All women who labored spontaneously were considered controls. Categorical data were compared using the χ⁴ or Fisher exact tests, while the Student t-test or ANOVA were used for continuous data. Gestational age, birth weight, maternal age, congenital anomalies and respiratory distress syndrome were examined for interaction and confounding. Multivariate logistic-regression analysis was used to control for the simultaneous effects of covariates. Adjusted odds ratios and 95% confidence intervals were derived from the estimated regression coefficients.

**Results:** Among 765 pregnancies in women with a history of prior cesarean delivery, 360 patients presented in spontaneous labor. Two hundred and three patients with unfavorable cervixes underwent induction of labor with oxytocin, dinoprostone or misoprostol. Neonatal complications found to be increased with induction included: admission to neonatal intensive care (28.1% compared to 17.7%, p = .002; odds ratio [OR] = 1.52, confidence interval [CI] (1.25 - 1.84)), ten minute Apgar score below five (1.0% compared with 0.2%, p = .17; OR = 5.56, CI (0.66 - 47.21)), neonatal sepsis (3.4% compared to 2.7%, p = .57; OR = 1.30, CI (0.52 - 3.25)). Two neonates in the induction group and one in the spontaneous labor group met ACOG criteria for birth asphyxia. No cases of neonatal death occurred.

**Conclusions:** Induction of labor in women with prior cesarean delivery is associated with a significantly increased rate of admission to neonatal intensive care and increased neonatal morbidity.

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**405**

**THIRD- AND FOURTH-DEGREE LACERATIONS: THE ROLE OF PHYSICIAN EXPERIENCE. H.N. Simkan, R.P. Hencz, Dept. of Ob/Gyn/RS, Division of Maternal-Fetal Medicine, Magee-Womens Hospital, Pittsburgh, PA.**

**Objective:** To determine the effect of operator experience (resident vs. attending physician) on the risk of third- and fourth-degree rectal injury (RI) during vaginal delivery.

**Study Design:** A computerized perinatal database at our institution was used to identify 1825 women with a singleton gestation, vertex presentation, and no prior cesarean delivery who underwent a vaginal delivery from 1995 to 1997. Of these women, 3977 were resident patients and 14384 were private patients. The risk of RI was determined using multivariate analysis for both of these groups, adjusting for parity, birthweight, operative vaginal delivery, and the use of midline episiotomy.

**Results:** The table depicts the overall adjusted risk of RI for both resident and private physicians.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Private OR (95% CI)</th>
<th>Resident OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity 3+</td>
<td>0.67 (0.64-0.71)</td>
<td>1.05 (0.95-1.15)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>0.72 (0.69-0.75)</td>
<td>1.03 (1.00-1.06)</td>
</tr>
<tr>
<td>Birthweight &gt;4000 g</td>
<td>2.2 (1.92-2.6)</td>
<td>2.1 (1.93-2.3)</td>
</tr>
<tr>
<td>Forceps</td>
<td>2.4 (2.1-2.9)</td>
<td>2.7 (2.5-3.0)</td>
</tr>
<tr>
<td>Vacuum</td>
<td>1.4 (1.3-2.2)</td>
<td>1.6 (1.5-2.0)</td>
</tr>
<tr>
<td>Episiotomy</td>
<td>3.3 (2.8-3.9)</td>
<td>4.0 (3.7-4.3)</td>
</tr>
</tbody>
</table>

**Conclusion:** The protective effect of increased parity on the risk of RI is present regardless of operator status. The increase in risk of RI with birthweight >4000 g, operative vaginal delivery, and the use of midline episiotomy was noted in both the resident and private groups.
CRITERIA FOR FAILED LABOR INDUCTION: PROSPECTIVE EVALUATION OF A STANDARDIZED PROTOCOL. O. Rouse, J. Owens, J.C. Hauth. The University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To assess the safety and efficacy of a protocol which mandated at least 12 hrs of oxytocin administration after membrane rupture (ROC prior to cesarean (CS) in the latent phase for failed labor induction.

STUDY DESIGN: Prospective evaluation of term gravidas undergoing indicated induction with dilation ≤ 2 cm. If the fetal heart rate pattern was reassuring, CS was not permitted prior to the active phase of labor (4 cm and ≥ 90% effacement or 5 cm) unless the membranes had been ruptured and oxytocin administered for at least 12 hrs. In women ≤ 2 cm dilated without ROM, extra-amniotic saline infusion for cervical ripening was begun in consultation with oxytocin.

RESULTS: Of 430 women managed by protocol, 20% had a CS. The median interval from oxytocin initiation to ROM for the 305 women who began with intact membranes was 5.9 hrs. After 6 hrs of oxytocin and ROM, 85% of women had progressed to the active phase or had delivered, vs 92% after 9 hrs, and 96% after 12 hrs. The subsequent CS rate for women still in the latent phase after 6 hrs was 35%, vs. 60% after 9 hrs and 84% after 12 hrs. Other than CS, chorioamnionitis was the only maternal outcome that correlated with latent phase duration, increasing from 13% for women still in the latent phase after 6 hrs of oxytocin and ROM, to 23% after 12 hrs. No woman had a serious complication. Serious neonatal morbidities (e.g. sepsis, seizures, asphyxia, or death) did not occur: in infants born to women still in the latent phase after 6, 9, or 12 hrs of oxytocin and ROM,

RATES OF NEONATAL MORBIDITIES (e.g. antibiotics, assisted ventilation) were unrelated to latent phase duration. The sole infant with proven sepsis was born to a mother who was in the active phase of labor at 6 hrs.

CONCLUSIONS: These data suggest that our criteria for failed induction, based on duration of oxytocin after ROM and time to progression to the active phase, were efficacious and safe. A definition of failed labor induction which includes a requirement for at least 12 hrs of oxytocin after ROM could serve as a useful clinical standard.

407 PROVIDER AND NOT OBSTETRIC FACTORS DICTATE RATES OF EPI-SOTOMY AND SEVERE PERINEAL TRAUMA. J.N. Robinson*, R.E. Nowitz, A.P. Cohen, E.S. Lieberman*, Dept. of Obst/Gyn, Brigham & Women's Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Midline episiotomy is associated with an increased incidence of severe perineal trauma (3rd and 4th degree lacerations). This study was performed to determine factors associated with the use of episiotomy at spontaneous vaginal delivery.

STUDY DESIGN: We studied 1619 consecutive low-risk, term, singleton, spontaneous vaginal deliveries in nulliparous women at Brigham & Women's Hospital between December 1, 1994 and July 31, 1995. The association of demographic variables (maternal age, maternal race) and obstetric factors (obstetric provider, length of second stage, fetal distress, meconium, epidural analgesia, birth weight) with the rate of episiotomy use were examined. Adjusted odds ratios were determined using logistic regression. Midline episiotomy is the usual practice at our institution.

RESULTS: The overall rate of episiotomy was 49.6% (657/1319). The provider was identified in 97.3% (1357/1361) of cases. Midwives performed episiotomy at a lower rate (21.4% [121/565]) than faculty/resident (33.3% [64/192]) and private providers (55.6% [55/98]) (p < 0.001; x² test). In a logistic regression controlling for provider type, birth weight, maternal age, maternal race, and obstetric factors (prolonged second stage of labor, fetal distress, meconium), factors which had a significant independent effect on the rate of episiotomy included a private (OR, 4.4; 95% CI, 3.5-5.8) or faculty/resident provider (OR, 1.8; 95% CI, 1.2-2.7) and prolonged second stage of labor (OR, 1.4; 95% CI, 1.2-1.5). Epidural analgesia was associated with a significant increase in episiotomy rate, but only among midwives who perform fewer episiotomies overall (OR, 1.8; 95% CI, 1.2-2.9). Birth weight, maternal race, meconium, and fetal distress were not associated with the incidence of episiotomy. The use of episiotomy was associated with an increased rate of 3rd and 4th degree lacerations at delivery in all three provider groups: 4.9-6.6% (2.9% to 14.1%) among midwives, 3.5-4.6% (6.3% to 21.9%) among faculty/resident, and 2.8-5.0% (5.2% to 14.1%) among private providers.

CONCLUSIONS: In this cohort, the strongest determinant of whether or not an episiotomy was performed was the type of obstetric provider. This association could not be explained by identifiable obstetric or demographic factors. The rate of 3rd and 4th degree lacerations correlated with higher use of midline episiotomy. Both obstetrician and parturient should be aware of these associations when planning the management of the second stage of labor.

OBJECTIVE: To determine the effect of decreasing temperature on spontaneous contraction activity and responses to activating and inhibitory agents in the isolated myometrium from nonpregnant and term pregnant women.

STUDY DESIGN: Strips of myometrium obtained at the time of surgery from nonpregnant and term pregnant non-laboring women were equilibrated in Krebs buffer for isometric recording of spontaneous contractile activity. The temperature of the organ chamber solution was progressively reduced from 37°C by 2°C steps at 30 min intervals until the desired change in temperature was determined as the integral activity for 30 min using an on-line data acquisition and analysis system. Concentration-response relationships to positive chloride, oxytocin and isoproterenol were also compared at 37°C and 32°C.

RESULTS: Lowering the temperature significantly reduced spontaneous uterine contractility, especially in pregnancy. Decreasing temperature did not influence the response to agents acting at the receptor level, but attenuates the effect of isoproterenol were not significantly different at 37°C vs 32°C. The sensitivity of the myometrium to oxytocin and isoproterenol was low at either temperature.

CONCLUSIONS: Lowering the temperature effectively inhibits uterine contractility, especially in pregnancy. Decreasing temperature does not influence the response to agents acting at the receptor level, but attenuates the effect of membrane depolarization. Subtle changes in temperature at the tissue level may have an important impact in a number of clinical situations such as preterm labor and amniotamn.

411 INDUCTION OF CERVICAL RIPENING IN PREGNANT GUINEA PIGS BY INTRACERVICAL APPLICATION OF SODIUM NITROPRUSSIDE GEL. C. Fitchett, S.Q. Shi, L. Mackay, E. Bythuicnse, G. Saade, R. Garfield, Dept. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To investigate the effect of intracervical application of the nitric oxide (NO) donor sodium nitroprusside (SNP) on cervical collagen as measured by light induced fluorescence (LIF) in pregnant guinea pigs.

STUDY DESIGN: Term pregnant guinea pigs at midgestation (day 42) were randomly allocated to receive 0.2 ml of 25 mg SNP/ml in 10% methylcellulose gel (n=5) or vehicle (n=7) applied intracervically. The cervical content of cross-linked collagen was measured using light-induced fluorescence (LIF) on a xenon lamp with a selective filter. A selective filter system was used as the excitation light source (340 nm). The excitation light was carried through optical silica fibres to the tip of a probe which was placed in contact with the cervix. The fluorescence emitted from the tissue was collected into a spectrograph and CCD (charge coupled device) detector and monitored by an on-line computer. The fluorescence spectrum at 390 nm (peak wavelength of the collagen spectrum) was determined. For standardization, the ratio of count at 390 nm over reference counts was used in the final analyses as an indicator of cross-linked collagen content. The measurements were performed before and 8 hours after application of the gel under metofane anesthesia. Paired students t-test was used for statistical analysis.

RESULTS: As compared to baseline, LIF decreased in both SNP (12.5 ± 1.3 vs 3.27 ± 0.84) and control groups (13.89 ± 1.65 vs 9.02 ± 1.72), but the difference was statistically significant only after SNP (P=0.007, Figure). On average, local application of SNP reduced the fluorescence of cervical collagen by 71% versus 30% after vehicle application. Four of the 5 animals receiving SNP delivered premature (5 lived 5 days and 1 after 5 days), while only 2 of the 7 animals receiving the vehicle delivered prematurely (both within 48 hours).

CONCLUSION: Intracervical application of the NO-donor SNP induces cervical ripening in guinea pigs by decreasing the content of collagen crosslinks.

412 CHANGE IN CERVICAL COLLAGEN FOLLOWING MISOPROSTOL VERSUS PREPIDIL APPLICATION. C. Olson, C. Pitkows, G. Saade, F. Martin, R. Garfield, Dept. of Ob/Gyn, The Univ of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To compare cervical collagen content before and after the application of misoprostol versus prepidil for cervical ripening prior to induction of labor.

STUDY DESIGN: Gravida at ≥ 37 weeks gestation and undergoing induction of labor with misoprostol (50 µg intravaginal) or prepidil (0.5 mg intracervical) were included. Lighr induced fluorescence (LIF) was used to measure cervical content of cross-linked collagen prior to and 4 hours after prostaglandin application. A xenon lamp with a selective filter was used as the excitation light source (540 nm). The light was focused through a fused silica lens at the end of an optical wand that was placed in contact with the cervix. The fluorescence emitted from the tissue was collected into a grating monochromator and the signal was directed to an optical multichannel analyzer connected to an on-line computer. The fluorescence spectrum at 390 nm (peak wavelength of the collagen spectrum) was determined. For standardization, the ratio of count at 390 nm over reference count was utilized. Data were tested for normality and are reported as mean ± SD or median [interquartile range].

RESULTS: Twenty three women received misoprostol and 17 received prepidil. There was no significant difference between the groups (misoprostol vs prepidil) for maternal age (26.0 ± 5.9 vs 27.7 ± 7.7 yr, P=0.43), gestational age (41.0[41.0-42.0] vs 41.0[39.8-41.3] weeks; P=0.16), gravidity (2.0[2.0-4.0] vs 2.0[1.8-3.3]; P=0.17) or parity (0[0-1.0] vs 1.0[1.0-2.0]; P=0.05). The Bishop score before and after prostaglandins was significantly different between the two groups (misoprostol before: 5.0[4.0-5.7] vs prepidil before: 2.0[2.0-4.0]; P<0.001). LIF did not significantly differ between the groups before or after placement of the prostaglandin agent. The change in LIF was larger for misoprostol compared to prepidil, indicating increased collagen fragmentation, but the difference did not reach statistical significance (9.14[6.0-15.6] vs 0.84[0.21-29.0]; P=0.41). Two-way repeated-measures ANOVA confirmed a trend for an effect of type of ripening agent on LIF before and after (P=0.07).

CONCLUSIONS: Prostaglandins applied to the cervix decreased collagen cross-linking. The effect of specific prostaglandins on cervical collagen may be more pronounced than others, which characteristics which may have clinical implications. The collagen may be a useful tool to monitor cervical ripening at the time of labor induction.

413 EFFECT OF MIFEPRISTONE ON CERVICAL RIPENING AND LABOR INDUCTION IN PREGNANCIES BEYOND 41 WEEKS’ GESTATION. Di Wang, MJ Fassett, D. R. Mitchell, Jr., Dept. of Ob-Gyn, University of Southern California School of Medicine, Los Angeles, CA.

OBJECTIVE: To evaluate the influence of mifepristone (RU-486) on cervical ripening and labor induction in the prolonged pregnancy.

METHODS AND MATERIALS: 180 women with pregnancies beyond 41 weeks’ gestation and uninduced, unfractured cervixes were randomly assigned to receive either 200 mg of mifepristone 25 mg was then administered orally for cervical ripening, or intravenous oxytocin was given to augment labor.

RESULTS: 97 women received mifepristone and 83 women received placebo. The average interval from start of induction to delivery was 2208±780.8 (SD) seconds for mifepristone-treated subjects and 2671±2885.7 minutes for placebo-treated subjects (P<0.01, log transformed data). 12 (12.6%) mifepristone-treated women and 7 (10.8%) of placebo-treated subjects delivered vaginally within the first 24 hr (P=0.60) (RR 1.27, 95% CI 0.53-5.02). After 24 hr, the median Bishop score for both groups was 5 (0-11). P=0.05, 61 (67.9%) misoprostol-treated women, and 66 (75.1%) placebo-treated women required misoprostol (P=0.06). 86 subjects required oxytocin. 45 (44.5%) of the mifepristone treatment group, and 42 (50.6%) in the placebo treatment group (P=0.48). The mean oxytocin requirement was 294±8452.5 mU for misoprostol-treated women and 4897±6517.5 mU for placebo-treated women (P=0.04). 153/180 or 85% were delivered vaginally. There were nine Cesareans in the mifepristone-treated group, and 18 Cesareans in the placebo-treated group (P=0.02). There was no fetal distress and uterine contraction abnormalities in the subjects who received mifepristone. There were no differences in neonatal outcomes between the two groups.

CONCLUSIONS: Mifepristone had a modest effect on cervical ripening when given 24 hr prior to labor induction. Fewer mifepristone-treated women required misoprostol for cervical ripening, and mifepristone-treated women required less oxytocin than placebo-treated women. Further studies are needed to assess the full benefit of mifepristone for pre-induction cervical ripening in term pregnancies.
414 THE EFFECT OF PARITY ON LABOR PAIN. J.M. Alexander, SK Sharma, DD McIntire, J. Wiley, RJ Leveno, Dept of Ob/Gyn and Dept of Anesthesiology, Univ of Texas Southwestern Medical Center, Dallas, TX.

**OBJECTIVE:** To assess the effect of parity on labor pain.

**STUDY DESIGN:** Secondary analysis of a previously reported randomized investigation into the effects of epidural analgesia during labor compared with patient-controlled intravenous meperidine in women who received patient-controlled intravenous meperidine identified for this analysis. All women were term with singleton gestations in spontaneous active labor. The pain scores and analgesia requirement of nulliparous women were compared with multiparous women.

**RESULTS:** Nulliparous women were younger (38.2 ± 2.7 yrs, p < 0.01), not as heavy (71 ± 76 kg, p < 0.01), and had longer labors (7.5 ± 6 hrs, p < 0.01). There was no difference in EGA (30.6 ± 39.9 wks, p = NS), cervical examination on admission (5.6 ± 3.0 cm, p = NS), oxytocin augmentation (24 ± 21%, p = NS), forceps use (5% vs 8%, p = NS), or cesarean delivery (3.6% vs 6.1%, p = NS) in the two groups. There were no differences in VAS pain scores and meperidine use.

<table>
<thead>
<tr>
<th></th>
<th>Nulliparous</th>
<th>Multiparous</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS score;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>prior to analgesia*</td>
<td>8.9 (2)</td>
<td>8.2 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>during labor*</td>
<td>4.7 (2)</td>
<td>5.4 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>at delivery*</td>
<td>5 (1.6)</td>
<td>5 (1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Meperidine (meg/hr)*</td>
<td>21 (2)</td>
<td>24 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Women requiring &gt;50mg/hr</td>
<td>15 (17)</td>
<td>35 (20)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*mean±SD

**CONCLUSION:** Using VAS pain scores and meperidine use as markers, parity does not have a measurable effect on labor pain.

415 ACTIVE MANAGEMENT OF LABOR: A META-ANALYSIS. C. McIntrach, E. Monzertowski, Dept Ob/Gyn, Univ of Michigan, Ann Arbor, MI

**OBJECTIVE:** To compare active management of labor with traditional management with respect to cesarean section rate, rate of operative deliveries, length of labor leading to a vaginal delivery, and 5 minute Apgar score less than 7.

**STUDY DESIGN:** The English-language literature in MEDLINE and Cochran Database were searched using the term “active management of labor.” The Cochrane Database was also searched using the terms “oxytocin” and “labor management.” Included studies had controls who received traditional management and an intervention group who received active management of labor. Active management of labor included the following tenets:

1. Patterns were admitted in labor.
2. Aminotransferase was performed soon after admission unless the patient presented with ruptured membranes in labor.
3. If indicated, oxytocin was used.

Studies with similar controls compared to the intervention group were excluded. Quality scores were assigned using modified criteria of Reulini and Goldzieher. Observational studies with quality assessment scores less than or equal to 8 were excluded. Randomized controlled trials with a quality assessment score less than or equal to 2 out of 3 were excluded. Randomized controlled trials with a quality assessment score less than or equal to 2 out of 3 were excluded. Data were extracted from a total of 16 articles with 4,419 women in the active management group and 4,321 in the traditional management group.

**RESULTS:** Meta-analysis using the random effects method revealed that cesarean deliveries were significantly less common in women receiving active management of labor than in those receiving traditional management (odds ratio [OR] 0.64, 95% confidence interval [CI] 0.51, 0.78). Similar analysis revealed that active management of labor resulted in significantly fewer operative deliveries than traditional management (OR 0.81, 95% CI 0.67, 0.97). There was no difference in the proportion of infants with 5 minute Apgar scores less than 7 (OR 0.95, 95% CI 0.87, 1.04). Time to vaginal delivery was reduced in the group receiving active management of labor (weighted mean difference, -0.31 hours, 95% CI, [-0.41, -0.22]).

**CONCLUSIONS:** Active management of labor resulted in significantly fewer cesarean sections, operative vaginal deliveries, and reduced time to vaginal delivery. Active management of labor did not significantly affect the number of neonates with 5 minute Apgar scores less than 7.

416 THROMBIN STIMULATED MYOMETRIAL CONTRACTIONS OCCUR BOTH IN VITRO AND IN VIVO. M. Phillips, J. Banoff, M. Elorza, MFM Section. Dept. Ob/Gyn. Univ of Chicago, Chicago, IL.

**OBJECTIVE:** Previously reported in vitro studies have demonstrated that thrombin stimulates myometrial contractions mediated by the activation of the phosphatidylinositol signaling pathway similar to those occurring in response to classic uterotonic agents. These studies sought to test the hypothesis that thrombin stimulates myometrial contractions occur not only in vitro but also in vivo and can be suppressed by hirudin, a thrombin antagonist.

**STUDY DESIGN:** In vitro contraction studies were performed using uterine tissue from Sprague-Dawley rats. The myometrial tissues were exposed to increasing concentrations of thrombin (1 to 100 U/mL) with and without pretreatment with hirudin. An in vivo contractile model was created after midline laparotomy, pressure transducers and infusion catheters were placed into each uterine horn. With each animal, one horn received thrombin while the other horn received equal volume of vehicle alone. Contraction data were acquired and statistically analyzed.

**RESULTS:** In the in vitro experiments, thrombin increased myometrial contractions in a dose-response fashion. In vivo, myometrial contractions were suppressed with thrombin combined with hirudin compared to thrombin alone. In vitro, in non-pregnant animals, thrombin significantly increased myometrial contractions compared to equal volumes of saline (p < 0.05). In vivo experiments with pregnant rats further confirmed the uterotonic properties of thrombin.

**CONCLUSIONS:** The uterotonic properties of thrombin are of physiologic importance and can be observed in vivo as well as in vitro. The uterotonic effects of thrombin are suppressed with the addition of a specific thrombin antagonist. These studies confirm that thrombin is a potent uterotonic similar to classic uterotonic agents; small doses can elicit a significant contractile response in vivo. Thrombin stimulated contractions may be responsible for such events as early pregnancy cramping associated with threatened abortion and/or preterm contractions associated with intrauterine bleeding as occurs with placental abruption or subchorionic hemorrhage.

417 INFLUENCE OF OCCIPITO-POSTERIOR POSITION ON DELIVERY OUTCOME. M. Fitzpatrick, R. McQuillan, C. O’Herlihy, Dept of Obstetrics, National Maternity Hospital and University College Dublin, Ireland.

**OBJECTIVE:** To assess delivery outcome associated with intrapartum occipito-posterior position (OPP) of the fetal head in nulliparous and multiparous labors and particularly the influence of epidural analgesia.

**STUDY DESIGN:** Delivery details of 246 women diagnosed with OPP in labor (1.8%) were prospectively recorded over a 2 year period and compared with 13,543 contemporaneous labors with fetal occipito-anterior position. Comparisons were made using Chi-square analysis. *p < 0.001, ** p < 0.01.

**RESULTS:**

<table>
<thead>
<tr>
<th></th>
<th>Nullip OA (n=141)</th>
<th>Nullip OP (n=141)</th>
<th>Multip OA (n=7728)</th>
<th>Multip OP (n=105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Delivery</td>
<td>4245 (78%)</td>
<td>41 (29%)</td>
<td>7187 (93%)</td>
<td>58 (55%)</td>
</tr>
<tr>
<td>Cesareas</td>
<td>525 (9%)</td>
<td>37 (26%)</td>
<td>309 (4%)</td>
<td>18 (17%)</td>
</tr>
<tr>
<td>Cesareas for dystocia</td>
<td>199 (38%)</td>
<td>27 (13%)</td>
<td>138 (18%)</td>
<td>16 (20%)</td>
</tr>
<tr>
<td>Forceps</td>
<td>407 (7%)</td>
<td>41 (29%)</td>
<td>77 (11%)</td>
<td>22 (21%)</td>
</tr>
<tr>
<td>Vacuum</td>
<td>649 (11%)</td>
<td>22 (16%)</td>
<td>155 (2%)</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>Epidural analgesia</td>
<td>4070 (70%)</td>
<td>121 (16%)</td>
<td>2241 (29%)</td>
<td>62 (59%)</td>
</tr>
</tbody>
</table>

The cesareans performed because of dystocia with OPP constituted 12% of all cesareas for dystocia (33/275) during the study period; 26/43 (60%) were performed at the cervical dilation, or more. In multiparas OPP contributed more frequently to cesareas for dystocia, when compared with primiparas OPP was documented prior to cesarean in only 10/43 (23%).

**CONCLUSIONS:** Although OPP occurred in only 1.8% of deliveries, it contributed disproportionately to operative delivery; fewer than 50% of OPP labors ended in normal delivery. OPP incidence has not increased despite a recent 10-fold rise in epidural rates. Recognition of OPP occurred infrequently prior to cesareans performed because of dystocia.
WHAT PROCESSES OF CARE DURING LABOR AFFECT THE CESAREAN SECTION (C/S) RATE? WM Calbert, J Melnikow, P Romano, M Schember, J Keyzer, RL Kravitz. Dept of OB/GYN and Center for Research in Primary Care, Univ of CA, Davis, Sacramento, CA.

OBJECTIVE: To determine which processes of care during labor result in lower C/S rates.

STUDY DESIGN: Using 1992-93 State data, 51 hospitals with high (HI), medium (MED), and low (LO) C/S rates, after adjustment for various demographic and clinical risk factors, were randomly sampled. 1278 randomly sampled medical records of women who attempted labor were abstracted to examine processes of care during labor and delivery that might influence C/S rate.

RESULTS: Overall C/S rates for the HI, MED, and LO hospitals were 30%, 27%, and 25%, respectively. The use of intravenous pressure catheters (IVPC), which is a lower dosage than previous studies, is both safe and effective with a lower incidence of hypotension and cesarean delivery. These findings suggest that further study of vaginal misoprostol as a method of outpatient induction of labor at term would be appropriate.

THE EFFICACY AND SAFETY OF ORAL VERSUS VAGINAL MISOPROSTOL FOR THE INDUCTION OF TERM LABOR. T.R. Dyson, R. Greg, R. Cummings, K. Nichols, Dept of Ob/Gyn, Greenville Memorial Hospital (GH), Greenville, SC.

OBJECTIVE: To compare the safety and efficacy of oral versus vaginal misoprostol for the induction of labor at term.

STUDY DESIGN: All women referred to GMH for induction of labor at term from the resident teaching service between 12/1/97 and 6/30/97. The study was random to either vaginal misoprostol at a dosage of 50 μg every 4 hours for a maximum of 6 doses with continuous EHR monitoring. The oral dosage was increased to 100 μg after 2 doses if there was no significant response. Outcome variables were time to delivery, C/S rate, and incidence of tachysystole and hyperstimulation. Data were analyzed using intention to treat analysis with continuous variables compared by t-test and categorical variables by chi square with Yates correction with a p value < 0.05 considered significant.

RESULTS: A total of 153 patients were randomized (77 to vaginal and 76 to oral misoprostol). The mean time to delivery was 968 minutes in the vaginal group and 1222 minutes in the oral group (p = 0.005). Tachysystole was significantly less common in the oral vs the vaginal group (20% vs 44%, p = 0.01) as was the incidence of hyperstimulation (7% vs 20%, p = 0.09). The C/S rate was 15% with oral vs 27% with vaginal, however, this was not statistically significant (p = 0.14). No adverse neonatal outcomes were noted in either study group.

CONCLUSIONS: These data suggest that vaginal misoprostol at the 50 mcg dosage is a safe and effective form of labor induction but has a high incidence of hyperstimulation. However, the use of 50-100 μg oral misoprostol, which is a lower dosage than previous studies, is both safe and effective with a lower incidence of hypotension and cesarean delivery. These findings suggest that vaginal misoprostol as a method of outpatient induction of labor at term would be appropriate.
422 RANDOMIZED CLINICAL TRIAL OF EARLY VS LATE AMNIOTOMY FOLLOWING CERVICAL RIPENING WITH A FOLEY CATHETER. B Levy, A Ben-Ariex, B Pavez, I Hazanx, I Blicksteinx and Z Hagayo, Dept of Ob/Gyn, Kaplan Medical Center, Rehovot, Israel.

OBJECTIVE: Ripening of the cervix with a Foley catheter commonly results in cervical dilatation without contractions. We examined the outcome of labor in women that underwent induction of labor using a Foley catheter, followed by either (a) early amniotomy, or (b) augmentation of labor by oxytocin and late amniotomy.

STUDY DESIGN: We conducted a prospective randomized clinical trial of pregnant women at 38-42 weeks with singleton gestations and unscarred uteri. All participants had vertex presentations, intact membranes, and exhibited no regular contractions. All women underwent cervical ripening using a Foley catheter. Following removal of the catheter, women were randomly assigned to either early amniotomy (n=89) or augmentation of labor by oxytocin, and amniotomy after regular contractions and progressive dilatation occurred (n=88). Primary outcome measures were duration of labor and method of delivery.

RESULTS: There was no difference (p=0.21) in duration of labor (8.2 hours ±8.8 vs 7.9 hours ±2.9). The rate of cesarean section was significantly higher (p<0.001) between the groups and five minutes Apgar scores were >7 in all the infants.

CONCLUSION: In women who undergo cervical ripening with a Foley catheter, a protocol of augmentation of labor by oxytocin followed by amniotomy during active labor results in a lower rate of cesarean delivery for infants.

424 DOES COMBINATION PHARMACOLOGIC AND MECHANICAL PREINDUCTION CERVICAL RIPENING IMPROVE RIPENING TO DELIVERY INTERVAL? Orion Rust MD, Mary Greymbush DO, Robert Atlas MD, James Balditucci, MD, Kelly Jones BS

OBJECTIVE: To determine if the addition of a mechanical ripening agent (transcervical Foley) to a pharmacologic agent (intravaginal misoprostol) improves the efficiency of preinduction cervical ripening.

STUDY DESIGN: Singleton patients with an indication for delivery, unscarred cervix (Bishop score ≥5) and no contraindication to labor were randomly assigned to 2 groups: Misoprostol alone (25 μg intravaginally q3 hr for no more than 12 hr) or combination therapy (25 μg transcervical Foley inflated to 50cc of sterile water with identical intravaginal misoprostol dosing). All patients received a history and physical exam including Bishop score, preripening ultrasound, electronic fetal heart rate and contraction monitoring to rule out spontaneous labor and document fetal well-being. Multiple variables of interest were collected which included the main outcome variables of ripening to delivery time and C-section rate.

RESULTS: During August 98 to August 99, 81 patients were randomized: 40 Misoprostol Alone and 41 to combination therapy. The following table summarizes the results:

<table>
<thead>
<tr>
<th>Therapy</th>
<th>n=40</th>
<th>n=41</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (yr)</td>
<td>25.0±6.7</td>
<td>26.8±5.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Primiparous (%)</td>
<td>57.5</td>
<td>51.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Bishop Score (median, range)</td>
<td>2.0-5</td>
<td>2.0-5</td>
<td>0.2</td>
</tr>
<tr>
<td>Gestational Age (wk)</td>
<td>37.0±3.8</td>
<td>36.3±3.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Birth Wt. (gmt)</td>
<td>2834±905</td>
<td>2763±736</td>
<td>0.7</td>
</tr>
<tr>
<td>Ripen - Delivery time (min)</td>
<td>1300±518</td>
<td>984±471</td>
<td>0.5</td>
</tr>
<tr>
<td>C-Section Rate (%)</td>
<td>27.5</td>
<td>29.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Tachysystole Rate (%)</td>
<td>35.0</td>
<td>24.0</td>
<td>0.09</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The addition of mechanical ripening with a transcervical Foley to intravaginal misoprostol did not improve the efficiency of preinduction cervical ripening. Mechanical and pharmacologic cervical ripening agents appear to act independently rather than synergistically.

423 INTRAVAGINAL MISOPROSTOL IN PRELABOR RUPTURE OF MEMBRANES AT TERM. N Thomas, S A Longo, P J Runneya, M P Nageotte, T Asrat, Division of Maternal-Fetal Medicine, Women's Hospital, Long Beach Memorial Medical Center, Long Beach, University of California, Irvine, CA.

OBJECTIVE: Given the lack of published studies comparing vaginal misoprostol to placebo in women with prelabour spontaneous ruptured membranes beyond 36 weeks gestation, our purpose was to evaluate its effectiveness as a labor induction agent in these patients.

STUDY DESIGN: Women with term prelabour spontaneous ruptured membranes, reassuring fetal status and vertex presentation were randomized to intravaginal misoprostol 50μg or placebo vaginal suppository (double-blinded). If active labor did not occur within 6 hours, a second suppository was placed. Oxytocin was initiated if there was no active labor at 12 hours.

RESULTS: 27 women were randomized to misoprostol and 25 to placebo. Nulliparous accounted for 59% of the misoprostol group and 63% of the placebo group. Mean interval (± standard deviation [SD]) from induction to delivery was shorter in the misoprostol group (15.8 ± 7.3 hours vs 19.9 ± 6.7 hours, p=0.05). Need for oxytocin was less in the misoprostol group (79.4% vs 88.0%) (Odds Ratio[OR]=0.32, 95% Confidence Interval [CI] 0.08-1.40). Incidence of cesarean was lower in the misoprostol group (25% vs 35.0%, p=0.02) between the groups and five minutes Apgar scores were > 7 in all the infants.

CONCLUSION: In women who undergo cervical ripening with a Foley catheter, a protocol of augmentation of labor by oxytocin followed by amniotomy during active labor results in a lower rate of cesarean delivery for infants.

425 PATIENT ACCEPTANCE OF OUTPATIENT PREINDUCTION CERVICAL RIPENING WITH THE FOLEY BULB. M Pollock, B Maa, M Muench, A Sciscione, Division of Maternal-Fetal Medicine, Christiana Hospital, Newark, DE. USA.

OBJECTIVE: As the United States continues to focus on quality healthcare and cost effectiveness, there will be continued movement to move certain inpatient procedures to the outpatient setting. Pre-induction cervical ripening (PICR) is amenable to this healthcare trend. Although the focus has been on cost savings, safety, and efficacy, there has been little focus on patient perception and experience. We sought to describe our patient's acceptance and experience with outpatient preinduction cervical ripening.

STUDY DESIGN: A randomized prospective trial was conducted from May 1998 to August 1999. Women with a low-risk term pregnancy in the vertex presentation, and a Bishop score ≤ 5 were screened for inclusion. After insertion of the Foley bulb, a reactive non-stress test, without evidence of hypertonus, and an amniotic fluid index > 5th percentile were required for randomization. Patients in the outpatient group received detailed oral and written instructions prior to discharge. Twenty-four hour phone access to a physician was provided. The women were given a postpartum survey to list their feelings and experiences with the induction process.

RESULTS: Of 50 women in the outpatient group, 37 (74%) completed the questionnaire. The mean age of the women was 29.2 years, with a mean gestational age of 40.0 weeks at the time of induction. Most women (52%) were primigravidas. Twenty-seven of 35 (77.1%) reported satisfaction with outpatient preinduction cervical ripening. Seven women had inpatient PICR with a previous pregnancy. Of those women, 5 (71.4%) described the outpatient experience as being better. Overall, 34 of 37 women (92%) were satisfied with their induction experience. Patients were asked to rank their comfort level from 1 to 10 using a Lickert scale. Scores ≥ 7 were considered comfortable. A total of 72.4% ranked the score > 7 with the mean score of 4.7 (SD = 2.6). Thirty-three of 37 (89.2%) patients were able to remain at home without discomfort for randomization. Patients in the outpatient group received detailed oral and written instructions prior to discharge. Twenty-four hour phone access to a physician was provided. The women were given a postpartum survey to list their feelings and experiences with the induction process.

CONCLUSIONS: The addition of mechanical ripening with a transcervical Foley to intravaginal misoprostol did not improve the efficiency of preinduction cervical ripening. Mechanical and pharmacologic cervical ripening agents appear to act independently rather than synergistically.

CONCLUSION: The presence of morbidity and overall positive patient response to outpatient cervical ripening supports the consideration of this as an alternative for PICR in a low risk population.

OBJECTIVE: Degradation of extracellular matrix is a cardinal feature of parturition. This process is mediated by a group of enzymes collectively known as matrix metalloproteinases (MMPs). Collagenases, a sub-group of MMPs, includes MMP-1 (interstitial collagenase), MMP-8 (neutrophil collagenase) and MMP-13 (collagenase-3). This study was conducted to explore the changes in collagenase concentration in the maternal and fetal compartments during human parturition at term.

MATERIALS AND METHODS: A cross-sectional study was conducted where maternal and cord plasma were assayed by a sensitive immunomassay for MMP-1, MMP-8 and MMP-13 in the following two groups: 1) term, not in labor (n=30); and 2) term, in labor (n=30). Maternal and cord plasma samples were drawn from patients with uncomplicated pregnancies undergoing elective cesarean section and patients in active labor at term who had a vaginal delivery (>37 weeks gestation). Non-parametric tests were used for analysis. MMP-1, 8 and 13 were determined with sensitive and specific immunomasses.

RESULTS: 1) Levels of maternal plasma concentrations of MMPs were significantly higher in maternal plasma than in cord plasma. There was no difference in MMP-8 levels (no labor: median 6.4 ng/ml, range 1.0-38 n/ml vs. labor: median 9.7 ng/ml, range 3.5-260 ng/ml, p<0.02). 2) In contrast, labor was not associated with changes in MMP-1 concentration in maternal plasma (no labor: median 5.1 ng/ml, range 1.4-231 ng/ml vs. labor: median 6.2 ng/ml, range 1.0-75.0 ng/ml, p>0.05). 3) There were no demonstrable changes in fetal MMP-1 and MMP-13 concentrations with labor. For MMP-1, maternal plasma (no labor: median 12.9 ng/ml, range 1.9-297 ng/ml vs. labor: median 15.3 ng/ml, range 6.5-37.6 ng/ml, p>0.05); fetal plasma (no labor: median 16.1 ng/ml, range 2.1-387 ng/ml vs. labor: median 10.2 ng/ml, range 0.9-47.6 ng/ml, p>0.05). For MMP-13, fetal plasma (no labor: median 0.1 ng/ml, range 0.0-0.04 ng/ml vs. labor: median 0.99 ng/ml, range <0.05-0.22 ng/ml, p>0.05). MMP-13 was detectable in only 10% (6/60) and 92% (55/60) of fetal and maternal plasma, respectively. In contrast, MMP-1 and MMP-8 were detectable in all maternal and cord blood samples.

CONCLUSIONS: 1) Normal spontaneous labor is associated with an increase in the fetal, but not maternal, plasma concentration of MMP-8 or neutrophil collagenase; and 2) Our data suggest that the human fetus may play a role in the control of extracellular matrix degradation during parturition.
THE IMPACT OF EPIDURAL ANALGESIA ON UTERINE CONTRACTILE STRENGTH.

R Driggers, N Hueppchen, JN Kopelman, AJSatin, Dept Ob/Gyn, National Naval Medical Center, Bethesda, MD

OBJECTIVE: Several studies have suggested an association between epidural analgesia and labor dystocia. We specifically sought to evaluate the effect of epidural analgesia on uterine contraction intensity.

STUDY DESIGN: This case-control study involved term gravidas delivering at our institution over a two-year period. Included were patients monitored with an intrauterine pressure catheter (IUPC) for at least one-hour prior and following epidural dosing whose epidural analgesia was initiated in active labor (4-9 cm dilation). The Montevideo units (MVUs) were calculated for 6 ten-minute segments prior to and after epidural dosing by two senior authors. The examiners were blinded as to which two IUPC tracings corresponded to a patient and which was pre- or post-epidural. Descriptive statistics and paired t-test data analysis were used.

RESULTS: 59.5% (25/42) had a decrease in average MVUs in the hour following epidural dosing compared to the hour prior. 67.7% (21/31) of patients who received ropivacaine had a decrease in average MVUs. The average decrease in MVUs was 19.2% and ranged from 1.5 to 66.3%. The average MVUs prior to and following epidural dosing were 153 and 141, respectively (p<0.05). Those patients with decreased contraction intensities were more likely to require cesarean delivery for labor dystocia (23.1 vs 7.9%). There was no significant difference in average birth weight (3615 vs 3520gm), maternal age (27.6 vs. 28.1yr), or cervical dilation at epidural bolus (5.1 vs 5.5cm).

CONCLUSION: Controversy exists regarding the manner in which epidural analgesia influences the incidence of labor dystocia. Our results suggest that epidural analgesia administered in active labor is associated with decreased uterine contraction pressures. Those women experiencing a decrease in contraction intensity following epidural dosing are more likely to undergo cesarean delivery.
POSTER SESSION IV

Friday, February 4, 2000
3:30 pm - 5:30 pm

Fontainebleau Ballroom A/B

CATEGORIES
Clinical Obstetrics
Operative Obstetrics
Medical/Surgical Complications

Poster Numbers
431-543

Judges:
John R. Barton, MD
Baha M. Sibai, MD
Robert Silver, MD
PERINATAL OUTCOMES FROM THE AUSTRALIAN AND NEW ZEALAND TWIN-TWIN TRANSFUSION SYNDROME REGISTRY Jan E Dickenson, Sharon F. Evans* University of Western Australia and The Women and Infants Research Foundation, King Edward Memorial Hospital, Perth, Western Australia.

OBJECTIVE: To assess contemporary management strategies and perinatal outcomes in pregnancies antenatally identified as complicated by twin-twin transfusion syndrome utilizing a national registry.

STUDY DESIGN: Tertiary perinatal centers in Australia and New Zealand voluntarily notified cases of severe twin-twin transfusion syndrome to the national registry between 1995 and 1998. The obstetric and neonatal outcomes were evaluated.

RESULTS: 112 cases were reported from 16 centers. The median gestation at diagnosis was 21.5 weeks (range 14.4-34.6 weeks). The most common presentation was the oligohydramnios/polyhydramnios sequence (84%). Therapeutic amnioreduction was used in 92 cases (82.1%); the median number of procedures per case was 2 (range 1-23). The median amniotic fluid volume removed was 8575 ml/case (range 300-50,000 ml). The complication rate directly attributable to the procedure of amnioreduction was 3.2%.

Median gestation at delivery was 29 weeks (range 18-38 weeks). The overall perinatal survival was 62.5%. Absence of umbilical artery diastolic flow was a predictor of poor perinatal outcome; with perinatal demise in 56.4% of cases, and IVH or PVL in 52.9% of survivors. The pretterm birth rate was 90.2%, and 58.9% were delivered <30 weeks gestation. Neonatal survival was low <28 weeks gestation (54.5%). The principal neonatal complications were those secondary to prematurity; and gestation at birth was the predominant factor determining outcome. 27.9% of liveborn infants had an abnormal cranial ultrasound and 10.8% PVL. The median hemoglobin difference between live-born twin pairs was 3.7 g/dl (IQ 1.5 to 6.3 g/dl).

When analyzed according to outcome (no complications vs neonatal complications vs death), increased gestational age at delivery, the presence of umbilical artery diastolic flow, and prolonged duration from final amnioreduction to delivery were positively associated with the delivery of live fetuses without complications.

CONCLUSION: Twin-twin transfusion syndrome remains a condition associated with high perinatal mortality and morbidity. In this national series, antenatally identified cases were managed primarily by serial amnioreduction, with outcomes comparable to those published from other international centers.

A POLICY OF ELECTIVE CESAREAN DELIVERY FOR FETAL MACROSOMIA IS NOT EFFECTIVE IN REDUCING BRACHIAL PLEXUS INJURY. R Gonen1, B Budert2, M Ajami2, Departments of Obstetrics and Gynecology1 and Neonatology2, Buun Zion Medical Center, Faculty of Medicine, Haifa, Israel.

OBJECTIVE: To examine the impact of a policy of elective CS for fetal macrosomia on the incidence of brachial plexus injury and on CS rate. 2. To estimate the number of unnecessary cesarian deliveries required to prevent a single case of brachial plexus injury.

MATERIALS & METHODS: In 1995 we implemented a policy by which we recommend CS whenever macrosomia, defined as estimated fetal weight >90th percentile for gestational age, was suspected. Weight estimation is carried out whenever macrosomia is suspected. Women with either diabetes or previous CS were excluded from the study.

RESULTS: During the study period there were 10,416 deliveries, of which 135 (0.8%) were of macrosomic infants that met our inclusion criteria. Macrosomia was correctly predicted in 21/135 (15.3%). Of the remaining 112 women, 13 were delivered by emergency CS, and 99 were delivered vaginally, three of which (3%) sustained brachial palsy. Another 14 non-macrosomic infants sustained brachial palsy following cephalic delivery. Macrosomia was suspected in 87 women and confirmed in 21 (45%). Forty-five of these women underwent CS, contributing 0.15% to our cesarean rate. Assuming a 5% risk for brachial palsy in macrosomic infants, vaginal delivery of these 21 macrosomic infants should result in an access of 0.6 case of brachial palsy. Seventy-eight cesarean deliveries would have been required to prevent one single case of brachial palsy, moreover, prevention of a single case of permanent neurological deficit would require approximately 780 cesarean deliveries.

CONCLUSIONS: A policy of elective CS for fetal macrosomia is not effective in reducing the incidence of brachial plexus injuries, however, its contribution to the CS rate is small. The number of CS required to prevent a single case of permanent brachial injury is probably unjustified.


OBJECTIVE: To evaluate the effect of a prenatal nutrition and educational intervention program on obstetric outcomes in twinning.

STUDY DESIGN: This was a prospective intervention study of women pregnant with twins who participated in a prenatal nutrition and education program (Program Pregnancies, PP) at the University of Michigan Medical Center and delivered between 5/96-9/99, compared with non-participants who delivered during the same time period (Non-Program Pregnancies, NPP). Selection criteria for PP included enrollment in the program prior to 25 weeks gestation, and at least four program visits. NPP must not have had any prenatal visits, all twin pairs must have both been liveborn and without major congenital anomalies. The study sample included 70 PP (140 infants) and 126 NPP (252 infants).

RESULTS: PP mothers tended to be older (32.3 ± 5.0 years vs 30.2 ± 5.3 years, p<.01), had higher education (4 years vs 27.4 lbs vs 25.2 lbs) and higher rates of pregravid BMI (24.0 vs 24.2), or parity. Controlling for gestational age and maternal age, PP mothers were less likely to deliver preterm (<37 weeks, 61% vs 72%), or vaginal infections. Birthweight and gestation for PP and NPP was 2,488 \( \pm \) 1,057 for reduced from 3, and 3,043 \( \pm \) 1,037 for reduced from > 3. The proportion of birthweight zscores < -1 paralleled advancing gestation, even after controlling for other factors, with consistently higher proportions among reduced pregnancies (p<.001). Controlling for gestation, race, parity, infertility treatments, smoking, pregravid weight, and weight gain, reduced pregnancies were significantly more likely to have birthweight zscores < -1 (adjusted odds ratio, AOR, 2.98, 95% CI, 1.26-7.02).

CONCLUSIONS: Despite comparable length of gestation and maternal weight gain, selective reduction results in significant residual growth retardation in twin gestations, particularly with starting numbers \( \geq 4 \).

EFFECT OF SELECTIVE REDUCTION ON INTRAUTERINE GROWTH, BIRTHWEIGHT, AND WEEKS GESTATION IN TWIN PREGNANCIES B Luke, L Min, RB Newman, JC Mauldin, FR Witter, MJ O'Sullivan. Univ Michigan Med School, Ann Arbor, MI, Medical Univ South Carolina, Charleston, SC, Johns Hopkins Univ School of Medicine, Baltimore, MD, Univ Miami School of Medicine, Miami, FL.

OBJECTIVE: To evaluate the effect of selective reduction on growth, length, gestation, and birthweight discordance in twin pregnancies.

STUDY DESIGN: This historical cohort study was based on 2,029 pregnancies of liveborn twins from Ann Arbor, Charleston, Baltimore, and Miami (42 reduced and 1,987 non-reduced). The reduced group included 31 pregnancies reduced from three or two and 11 pregnancies reduced from four or more fetuses to two.

RESULTS: Women who underwent reductions were more likely to be primiparous (74% vs 39%, p<.0001), white (79% vs 35%, p<.0001), older [(33 years vs 27 years, p<.0001), of low or normal pregravid BMI (bmi mass index \( \leq 20, 81% \) vs 61%, p<.009), and to have had infertility treatment (98% vs 11%, p<.0001), cerclage (7% vs 2%, p<.01), and to develop gestational diabetes (GDM, 12% vs 4%, p<.02). There were no significant differences in rates of preterm labor (38% vs 28%), preterm premature rupture of membranes (10% vs 16%), or preeclampsia (12% vs 17%). Based on analysis of variance and controlling for race, maternal age, parity, BMI, and weight gain, GDM, and infertility treatments, weeks gestation was 35.8 \( \pm \) 2.9 for non-reduced, 35.7 \( \pm \) 2.7 for reduced from 3, and 34.5 \( \pm \) 4.3 for reduced from 2.4, twin pair birthweight was 2,450g \( \pm \) 525g for non-reduced, 2,406g \( \pm \) 514 for reduced from 3, and 2,167g \( \pm \) 1,072 for reduced from > 3. The proportion of birthweight zscores < -1 paralleled advancing gestation, even after controlling for other factors, with consistently higher proportions among reduced pregnancies (p<.001). Controlling for gestation, race, parity, infertility treatments, smoking, pregravid weight, and weight gain, reduced pregnancies were significantly more likely to have birthweight zscores < -1 (adjusted odds ratio, AOR, 2.98, 95% CI, 1.26-7.02).

CONCLUSIONS: Comparing length of gestation and maternal weight gain, selective reduction results in significant residual growth retardation in twin gestations, particularly with starting numbers \( \geq 4 \).
NEONATAL MORBIDITY AMONG TWINS: EFFECT OF BIRTHWEIGHT, GESTATIONAL AGE, AND BIRTHWEIGHT-FOR-GESTATIONAL AGE

OBJECTIVE: To evaluate the effect of birthweight, length of gestation, and birthweight-for-gestational-age (birthweight zscore) on neonatal morbidity, as newborn length of stay (NBLOS) and hospital charges among twins.

STUDY DESIGN: This historical cohort study was based on 856 twin pregnancies of >28 weeks’ gestation (1,672 liveborn twin infants) from Baltimore, Miami, Charleston, and Baltimore, and Charleston, SC; Univ Miami School Medicine, Miami, FL.

RESULTS: The lowest neonatal morbidity for twins as achieved at birthweights of >2,500 g at 36-37 weeks and >2,800 g at 38-39 weeks. Twin births and >40 weeks (3,824 ± 665 g) were associated with a significant increase in newborn morbidity, as evidenced by longer hospital stays and higher charges.

CONCLUSIONS: Newborn hospital charges were region- and inflation-adjusted. Differences in mean NBLOS and hospital charges were evaluated using analysis of variance across gestational categories by birthweight and by birthweight zscore. Birthweight zscores were generated using gestation-specific normal weight (19.8-26.0), overweight (26.1-29.0), and obese (>29.0). Rates of maternal weight gain and fetal growth were modeled using multiple regression for the gestational periods of 0-20 weeks (early), 20-28 weeks (mid), and 28-36 weeks (late) (projected as necessary). Optimal rates of fetal growth were defined as between the twin and singleton 50th and 90th percentiles at 28-28 weeks and between the twin 75th and 90th percentiles at 36-36 weeks. Optimal birthweight was defined as between the singleton 50th and twin 90th percentiles at 36 weeks (2,700-2,800 g). Multiple regression was used to model fetal growth and average twin birthweight, controlling for potentially confounding factors.

RESULTS: The pregravid BMI status of the study population was 14% underweight, 55% normal weight, 10% overweight, and 21% obese. The racial and ethnic composition was 36% white, 43% black, 20% Hispanic, and 1% Asian; 9% were primiparas, 10% smoked during pregnancy. Average twin birthweight was 2,944 ± 665 g at 35.8 ± 2.9 weeks, with 42% of birthweights ≥ 2,900 g and 22% ≥ 2,800 g. 54% of births were caesarean sections. Optimal rates of fetal growth and optimal birthweights were associated with rates of maternal weight gain (lbs/week) as follows:

<table>
<thead>
<tr>
<th>BMI Group</th>
<th>Early</th>
<th>Mid</th>
<th>Late</th>
<th>Total Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>1.25-1.75</td>
<td>1.50-2.00</td>
<td>1.25</td>
<td>47-17 lbs</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>1.00-1.50</td>
<td>1.25-1.75</td>
<td>1.00</td>
<td>38-52 lbs</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.75-1.00</td>
<td>1.00-1.5</td>
<td>0.75</td>
<td>29-34 lbs</td>
</tr>
</tbody>
</table>

CONCLUSIONS: These findings indicate that comparable, optimal fetal growth and birthweight is achieved at rates of maternal weight gain which vary with maternal pregravid BMI status.

IMPROVING OUTCOMES IN TWIN PREGNANCIES: MATERNAL AND NEONATAL HOSPITAL CHARGES AND LENGTH OF STAY

OBJECTIVE: To evaluate the effect of a prenatal nutrition and education program on maternal antenatal admissions, birth admission length of stay (LOS), newborn LOS, and hospital charges.

STUDY DESIGN: This was a prospective study of women, pregnant with twins who participated in a prenatal nutrition and education program (Program, PP) and delivered between 5/96/5/99, compared with non-participants who delivered during the same time period (Non-Program Pregnancies, NPP). Gestational age (GA) was defined as the start of the pregnancy or the last menstrual period (LMP), whichever was sooner. GA was calculated from LMP or LMP + 14 days for PP and NPP, respectively. GA was calculated from LMP or LMP + 14 days for PP and NPP, respectively. GA was calculated from LMP or LMP + 14 days for PP and NPP, respectively. GA was calculated from LMP or LMP + 14 days for PP and NPP, respectively. GA was calculated from LMP or LMP + 14 days for PP and NPP, respectively.

RESULTS: PP versus NPP did not differ significantly in their rates of antepartum admissions (28% vs 26%) or excessive birth admission LOS (29% vs 21%). Maternal birth admission LOS did not differ for PP versus NPP by LOS (4.5 ± 0.7 days vs 5 ± 0.7 days), hospital charges ($7,773 ± 748 vs $9,601 ± 1,139), or charges/day ($2,115 ± 325 vs $2,775 ± 340). Twin pair newborn LOS, hospital charges, and charges/day for PP versus NPP were 12.9 ± 3 days vs 32 ± 4 days ($2,925 ± 425 vs $7,773 ± 748). Regression analysis indicated that PP newborns had lower birthweights (435.3 g, p=0.001), longer gestations (13.1 days, p=0.006), shorter LOS (7.4 days, p=0.006); newborn savings due to program participation was $52,555 per twin pair, p=0.003.

CONCLUSIONS: These findings indicate that participation in a prenatal nutrition and education program for mothers pregnant with twins is associated with dramatic reductions in neonatal morbidity, as evidenced by shorter newborn LOS and lower newborn hospital charges.

REPRODUCTIBILITY OF THE BISHOP SCORE IN TERM PREGNANT WOMEN.

OBJECTIVE: The Bishop score is widely used to evaluate the cervix before induction of labor, but its reproducibility was never assessed. We evaluated the agreement within two pairs of experienced observers (AB and AC) regarding (1) the Bishop score; (2) a subjective global evaluation of the cervix (favorable or unfavorable). Method: A cervical examination was performed successively by two independent examiners in term pregnant women. The Bishop score and the subjective global evaluation of the cervix were recorded by each examiner, blinded to the other’s evaluation. We calculated the proportion of agreement and Cohen’s kappa coefficient. Results: The proportion of agreement was 87% (95%CI 83-91). When the Bishop score was 7, the cervix was usually described as unfavorable. Kappa coefficients for each pair of observers are shown below:

<table>
<thead>
<tr>
<th>A-B (n=48)</th>
<th>A-C (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa</td>
<td>95% CI</td>
</tr>
<tr>
<td>Bishop score</td>
<td>74%</td>
</tr>
<tr>
<td>Bishop score</td>
<td>74%</td>
</tr>
<tr>
<td>Favorable cervix</td>
<td>66%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Agreement between two observers evaluating the Bishop score was considered good to fair. The differences observed remained in a clinically acceptable range. The subjective evaluation of the cervix seems to be as reproducible as the formal evaluation by the Bishop score.
THE EFFECT OF INCREASING MATERNAL BODY MASS INDEX ON MATERNAL AND FETAL MORBIDITY

Robert K. Silverman, M.D., and Constantine G. Binas, M.D.1
Martha A. Wojtowycz, Ph.D.
SUNY, Syracuse, NY

METHODS: A total of 20,064 women who gave birth in Central New York in 1999 were identified using a perinatal registry. A retrospective analysis was performed to ascertain the impact of progressively increasing BMI (kg/m²) on four categories: Maternal medical conditions, including hypertension, diabetes mellitus and chronic lung disease, Perinatal and postpartum complications, such as preeclampsia, macrosomia, number of hospitalizations, Cesarean section rates, chorioamnionitis, and postpartum hemorrhage. Finally, neonatal intensive care unit (NICU) admissions, low APGAR scores (<6 at 5 minutes), and meconium-stained fluid (MSF) were used as a guide to perinatal morbidity. BMI categories were based on criteria determined by the Institute of Medicine.

RESULTS: A significant correlation was found between obesity (BMI 29-35) and morbid obesity (BMI>35), and a spectrum of maternal and fetal parameters. Both obese and morbidly obese patients are at increased risk for hypertension (OR 5.81; P<0.0005), chronic lung disease (OR 1.48; P<0.0005), and diabetes (OR 2.5; P<0.002). Amongst others, their pregnancies were further complicated by increased cesarean section rates (OR 1.92; P<0.0005), and sterile infections (OR 1.84; P<0.0005). In terms of neonatal complications, infants were found to have a greater number of NICU admissions (OR 1.27; P<0.0005) significantly depressed APGAR scores at 5 minutes (BMI >35; OR 2.13; P<0.0005) and moderate to thick MSF (BMI >35; OR 1.25; P<0.001). No association was found between obesity and morbid obesity in relation to postpartum complications such as atony, chorioamnionitis and fever. This is in contrast to findings reported in some of the literature. Infants did not have increased risk for anomalies and preterm delivery.

CONCLUSION: This large, retrospective analysis provides strong evidence that excessive maternal BMI is associated with significant maternal and fetal complications. This evidence argues strongly that BMIs in the obese and morbidly obese range should be an independent factor when risk stratifying a pregnancy.

UMBILICAL CORD BLOOD COLLECTION BEFORE PLACENTAL DELIVERY DURING CESAREAN SECTION INCREASES CORD BLOOD VOLUME AND NUCLEATED CELL NUMBER AVAILABLE FOR TRANSPLANTATION

A. Gebhart, F Voca, C. Steinmann, A. Tichelli, S. Schatt, S. Hahn, A. Gratwohl, W. Holtgreve
Departments of Obstetrics & Gynecology and Pathology, Mount Sinai Medical Center, NYC, NY

OBJECTIVE: To determine if umbilical cord blood collection during cesarean section can be improved by collecting cord blood before delivery of the placenta.

STUDY DESIGN: Patients undergoing cesarean section were randomly assigned to cord blood collection before or after placental delivery. Closed sterile collection systems were used for blood sampling. Cord blood characteristics as well as maternal outcome parameters were compared between the two groups.

RESULTS: A total number of n = 40 patients were available for analysis. No differences in maternal and neonatal characteristics were found. A larger amount of cord blood volume (mean ± SEM, 98 ± 7.5 mL vs 66 ± 6.0 mL, p = 0.015) and total nucleated cell number (11.1 ± 1.2 × 10⁷ vs. 7.4 ± 0.8 × 10⁷, p = 0.026) was obtained in the samples collected before compared to after placental delivery. Similarly, there was a trend towards higher total CD34⁺ cell number in samples collected in situ (30.9 ± 6.0 × 10⁶ vs. 17.4 ± 2.4 × 10⁶, p = 0.07). Estimated intraoperative blood loss, the difference between pre- and postpartum hemoglobin values, operating time as well as perinatal infections were similar in both groups.

CONCLUSION: Cord blood collection during cesarean section is improved if sampling is performed before delivery of the placenta. This collection method seems beneficial and safe, and might therefore be preferred for targeted related cord blood stem cell transplantation.

PRETERM BIRTH AND CORD BLOOD AVAILABLE FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION

D. V. Supek, W. Holtgreve, C. Steinmann, S. Hahn, A. Gratwohl, W. Holtgreve
Departments of Obstetrics & Gynecology, Hematology, and Experimental Hematology, University of Basel, Switzerland

OBJECTIVE: Cord blood from deliveries at term can be used for stem cell transplantation. The objective was to determine the amount of cord blood nucleated cells and progenitor cells collectable from preterm deliveries.

STUDY DESIGN: Cord blood collected from preterm deliveries between 22 and 36 gestational weeks was compared regarding volume, nucleated cell count and CD34⁺ cell count per cord blood sample between different gestational age.

RESULTS: We found a correlation between gestational age and nucleated cell count (r=0.52; p<0.001) and an inverse relation between gestational age and CD34⁺ cell count (r=-0.68; p<0.001). The total CD34⁺ cell content per cord blood sample was independent of gestational age (r=-0.13; p=NS). In contrast to findings reported in some of the literature, no significant difference between early (22-28 weeks) and late (33-36 weeks) preterm deliveries was found (p=0.970). Comparison with data from cord blood transplantations revealed that up to one third of preterm samples would have been suitable for transplantation. Median nucleated cell number or CD34⁺ cell number transplanted, and 77% (42%) of all preterm samples contained enough nucleated cells (CD34⁺ cells) for transplantation in a recipient of 20 kg body weight, based on lower threshold of 1x10⁶ nucleated cells/kg in the graft.

CONCLUSION: We conclude that preterm delivery should not be a reason to exclude cord blood collection if allogeneic cord blood transplantation in a sibling is planned.

MECONIUM INDUCED VASCULAR SMOTH MUSCLE NECROSIS: TIMING AND ULTRASTRUCTURE IN AN INVITRO MODEL

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Dept OB/GYN, Pathology, Mount Sinai Medical Center, NYC, NY and Dept. Pathology, Columbia University, NYC, NY

OBJECTIVE: To investigate the light microscopic and ultrastructural effects of meconium exposure on the umbilical cord.

STUDY DESIGN: Umbilical cords were obtained at elective cesarean section from term, singleton infants born to mothers without systemic or pregnancy related diseases. Meconium was collected from term, healthy neonates within 18 hours of delivery, and was suspended as a 10% solution in sterile medium. Cord segments were ligated at both ends with suture to prevent intrafunicular meconium exposure, were submerged in either sterile medium (controls) or meconium solution, and were incubated in a 5% CO² incubator at 37°C. Samples were removed at intervals, and prepared for light and electron microscopy (EM). Preparations were evaluated blinded for integrity of umbilical epithelium, and viability of histiocytes of Wharton’s jelly and of vascular smooth muscle (VSM). Cord epithelium detachment, and necrosis of histiocytes and VSM injury were graded on a 0-4 scale. Contingency tables and analyses of repeated measures were considered significant if p<0.05.

RESULTS: 53 umbilical cord segments were analyzed from 5 separate experiments. Cords were studied at 0, 2, 4, 8, 12, 24 hours. At each time interval, more VSM injury was seen in meconium exposed cords (p<0.001). Umbilical VSM injury was identified within 2-4 hours of meconium in 2 trials, and by 8 hours in the remaining 3 trials. VSM injury was not seen uniformly in all cords, until 12-14 hours. The severity of VSM injury was not related to epithelial or histiocyte pathology in either meconium or control cords. On EM, the smooth muscle cells showed nuclear pyknosis, cell shrinkage, and changes suggestive of apoptosis.

CONCLUSION: An in vitro model demonstrates time-dependent cord VSM injury after exposure to meconium, and may indicate myocyte apoptosis as a mechanism.
443 IS INHERITED THROMBOPHILIA A MAJOR CAUSE IN UNEXPLAINED RECURRENT FETAL LOSS? O Dovü, C Baykal, A AP, T Darukau, A Gurel, I Onderoglu, Dept Ob/Gyn, Hacettepe Univ School of Medicine Ankara - TURKEY.

OBJECTIVE: To determine the role of inherited thrombophilias in unexplained recurrent fetal loss (RFL).

STUDY DESIGN: Patients presenting to our institution from 10/98 to 8/99 with RFL were preconceptionally evaluated. Recurrent abortion was defined as 3 or more abortions and not more than a live birth Unexplained 2nd trimester fetal loss was defined as at least two fetal losses above the 20th week. All patients were evaluated by obtaining, history, physical examination, parental karyotypes, TSH, prolactin, diabetes screening tests, antiphospholipid antibody panel, diagnostic hysterosalpingogram/hysteroscopy, placental pathology and/or autopsy from previous losses if available. After excluding other probable factors, 86 patients underwent thrombophilic screening panel including tests of mutation for Factor V Leiden and Factor II protein S and C activity, and Antithrombin III deficiency. A control group of 70 healthy volunteers without any obstetric and thrombolic complications were tested for inherited thrombophilia as a control group.

RESULTS: A total of 88 patients who had unexplained recurrent fetal losses were evaluated. At least one of the thrombophilias was found in 51.1% (45/88) of the study group compared with 7.1% (5/70) among controls (p=0.001) 13.6% (12/88) of the patients had two and 5.7% (5/88) of patients had three thrombophilic disorder. Number of thrombophilic patients for each group is displayed below.

<table>
<thead>
<tr>
<th>Study</th>
<th>%</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>19</td>
<td>26.2</td>
</tr>
<tr>
<td>Antithrombin III deficiency</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Factor II mutation</td>
<td>2</td>
<td>2.3</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>29</td>
<td>33.0</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>16</td>
<td>18.2</td>
</tr>
</tbody>
</table>

CONCLUSION: The results indicate that thrombophilias may be a contributory factor in recurrent pregnancy loss. These thrombophilias like Factor V Leiden, Factor II mutation, Protein C and Antithrombin deficiencies should be a part of routine screening tests in patients with unexplained recurrent fetal loss.


OBJECTIVE: To evaluate chorionicity and zygosity as possible risk factors for preterm birth, perinatal death, and other adverse perinatal outcomes.

STUDY DESIGN: A population-based retrospective cohort study of all twin gestations in Nova Scotia from 1988 to 1997 was conducted using the Nova Scotia Atlee Perinatal Database. Intrauterine fetal deaths were excluded except for the perinatal death analysis. Chorionicity was established by histologic examination. Monozygosity was defined by monochorionicity and/or twins of same sex and blood type. Logistic regression analysis was used to determine adjusted odds ratios (OR) and 95% confidence intervals (CI).

RESULTS: The cohort included 289 monochorionic twins and 280 dichorionic twins of which 58.9% were monzygotic and 41.1% were dizygotic. The adjusted OR (CI) for preterm birth before 28, 32, and 37 weeks for monochorionic twins relate to dichorionic twins were 0.69 (0.26-1.82), 0.67 (0.38-1.1), and 0.98 (0.73-1.31) respectively. Medically indicated preterm delivery before 37 weeks was more likely to occur in monochorionic than dichorionic twins (OR 1.57, CI 0.9-2.68). Adjusted OR (CI) for spontaneous and medically indicated preterm birth before 28, 32, and 37 weeks were not statistically significant for monochorionic twins. The adjusted OR (CI) for perinatal death of at least one twin was 2.32 (1.17-4.64) for monochorionic twins. Zygotis was not associated with perinatal death. Monochorionic and monzygotic twins were at increased risk of intrauterine growth retardation (IUGR) compared to dichorionic and dizygotic twins respectively (p<0.05).

CONCLUSION: Monochorionic twins are at increased risk of perinatal death and IUGR. Monzygotic twins are at increased risk of HUGR. Spontaneous preterm birth does not appear to be influenced by chorionicity or zygosity.

445 THE NEONATAL AND ECONOMIC IMPACT OF ELECTIVE PRETERM DELIVERY IN TWIN GESTATIONS. MA Kalcherbauer, NK Bergauer, D Jacques, SK Coleman, GJ Stanzano, Rockford Regional Perinatal Center, Rockford, IL; Matera Healthcare, Murieta, GA.

OBJECTIVE: While many view 36 weeks as a term in twin pregnancies (TW), these infants are still classified as preterm (PT), and impact the reported national PT birth rate. Our objective was to identify the neonatal and economic consequences of elective delivery (ELD) of TW.

STUDY DESIGN: TW with induced labor or cesarean (CS) delivery, without maternal or fetal indications, were identified in a perinatal database. Delivery route, infant birth weight, frequency of NICU admission, and nursery days were collected. A cost model was applied to estimate nursery charges. Data were compared between those with ELD at a gestational age (GA) of 35-36 weeks (group 1), vs. those with ELD at 37-39 weeks (group 2), using Student's t and p-values as required.

RESULTS: 954 mothers with 1908 infants met inclusion criteria. Mean GA at delivery for infants of group 1 was 36.1±0.5 (n=976), while mean GA at delivery for group 2 was 37.3±0.5 (n=932). More infants of group 1 were delivered by CS (7.1% vs. 2.7%, p<0.001). Overall, 62.8% of group 1 had scheduled CS vs. 57.5% of group 2 (p=0.131). Neonatal and cost data are below.

<table>
<thead>
<tr>
<th>Study</th>
<th>%</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight gms</td>
<td>2464±370</td>
<td>2801±376</td>
</tr>
<tr>
<td>LBW %</td>
<td>55.5</td>
<td>20.8</td>
</tr>
<tr>
<td>NICU adm %</td>
<td>28.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Ventilator %</td>
<td>3.5</td>
<td>0.4</td>
</tr>
<tr>
<td>NICU days</td>
<td>2.5±6.1</td>
<td>0±1.8</td>
</tr>
<tr>
<td>Nursery days</td>
<td>5±5.6</td>
<td>3.4±1.8</td>
</tr>
<tr>
<td>Nursery cost $</td>
<td>5906±1154</td>
<td>211±2838</td>
</tr>
</tbody>
</table>

Data means SD, or percentage as indicated. 'Total' Per infant

CONCLUSION: This data suggests that the practice of ELD prior to 37 weeks' gestation has a profound economic impact. Nursery costs for each infant in a TW with ELD prior to 37 weeks were approximately $3800.00 more, when compared to an infant delivered between 37-39 weeks.

446 PREGNANCY COMPLICATIONS IN WOMEN OF ADVANCED MATERNAL AGE: A POPULATION-BASED STUDY IN THE UNITED STATES. AC Raman, CV Ananth, JC Smallman, AM Vintzileos, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: To determine the risk of adverse pregnancy outcomes among women with advanced maternal age in the United States.

STUDY DESIGN: The data for this study were derived from the national linked birth/infant data sets for 1995 and 1996 provided by the National Center for Health Statistics. Analyses were restricted to singleton live births occurring after 20 weeks gestation. Absolute risks for pregnancy complications in the 35-39, 40-44 and 45-49-year-old age groups were compared to those in the 25-34 year old age group, and their association expressed as relative risk (RR).

RESULTS: In the US, there were 7,505,099 singleton births, of which 30.4% (n=3,784,314) occurred in women aged 25-34, 9.2% (n=744,435) in 35-39, 50.4% (n=3,784,314) occurred in women aged 25-34, 9.2% (n=744,435) in 35-39, 9.2% (n=744,435) in 40-44 and 0.1% (n=4,994) in women 45-49. Absolute risk and RR for adverse pregnancy outcomes by age group is shown below.

<table>
<thead>
<tr>
<th>25-34 yrs</th>
<th>35-39 yrs</th>
<th>40-44 yrs</th>
<th>45-49 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>% (RR)</td>
<td>% (RR)</td>
<td>% (RR)</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>8.5</td>
<td>10.0 (1.2)</td>
<td>11.6 (1.4)</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>1.8</td>
<td>3.4 (1.1)</td>
<td>10.9 (1.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.9</td>
<td>4.7 (1.5)</td>
<td>6.3 (2.5)</td>
</tr>
<tr>
<td>PIH</td>
<td>3.1</td>
<td>3.3 (1.1)</td>
<td>4.2 (1.4)</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>0.2</td>
<td>0.3 (1.1)</td>
<td>0.4 (1.4)</td>
</tr>
<tr>
<td>Abnormal labor</td>
<td>2.9</td>
<td>2.9 (1.0)</td>
<td>3.2 (1.6)</td>
</tr>
<tr>
<td>Abruption</td>
<td>0.5</td>
<td>0.7 (1.2)</td>
<td>0.8 (1.6)</td>
</tr>
<tr>
<td>PPROM</td>
<td>0.9</td>
<td>1.2 (1.3)</td>
<td>1.3 (1.5)</td>
</tr>
<tr>
<td>Placenta praevia</td>
<td>0.7</td>
<td>0.7 (1.0)</td>
<td>0.9 (1.2)</td>
</tr>
<tr>
<td>Post-term (&gt;29wks)</td>
<td>8.9</td>
<td>7.0 (0.8)</td>
<td>6.7 (0.7)</td>
</tr>
</tbody>
</table>

25-34 year old group used as a reference for RR calculation.
*Indicates 95% CI for RR includes unity.

CONCLUSION: Pregnancy beyond 35 years of age increases the likelihood of untoward obstetric complications. Women intending to become pregnant beyond 35 years of age should be counseled about the risk of adverse pregnancy outcomes and monitored for maternal complications.
FREQUENCY OF ADOPTIVE PREGNANCY OUTCOMES IN MULTIPLE GESTATIONS. AC Ramadan, CV Ananth, JC Sondell, UMNIJ,Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: Adoptive pregnancy outcomes are more frequent among patients with multiple gestations when compared to singleton gestations. However, data have been limited to studies with inadequate study size. We present population-derived data on the frequency of adverse pregnancy outcomes in pregnancies with increasing numbers of fetuses.

STUDY DESIGN: The data for these analyses were derived from the national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics in the United States. We compared obstetric complications for 7,179,990 live births including singleton, 104,910 twins, 9,619 triplet, 909 quadruplet and 126 quintuplet or greater gestations. Patients were excluded if birth weight and/or gestational age (GA) data were missing or if GA was less than 20 weeks at delivery. Risks of maternal complications including PPRM >12 hours, abortion, excessive bleeding, diabetes, preclampsia and placenta previa were presented using simple percents and relative risks (RR) using singleton gestations as the referent.

RESULTS: The mean (±SD) gestational age at delivery was 39.0 ± 2.5 weeks for singletons, 35.6 ± 3.7 weeks for twins, 32.3 ± 4.0 weeks for triplets, 30.4 ± 3.8 weeks for quadruplets and 24.1 ± 5.6 weeks for quintuplets or greater.

RR were derived with singleton gestations as the referent.


OBJECTIVE: To discriminate risk factors during delivery that influence neonatal mortality and morbidity in twin infants.

STUDY DESIGN: Retrospective cohort study of all twin pregnancies (n=7,884) delivered at a gestational age >22 weeks at the Academic Medical Center from 1988 through 1998. Excluded were 54 twins with lethal congenital abnormalities or antepartum death of one or both infants. Mortality was defined as death during or after delivery until discharge from hospital; morbidity was defined by respiratory distress syndrome, bronchopulmonary dysplasia, intracerebral hemorrhage >grade 2, or sepsis. Factors analyzed were presentation of the infant (cephalic or noncephalic), birth order, chorionic separation of the gestational sac, parity (nulliparous, multiparous), ethnic origin (Caucasian or non-Caucasian), corticosteroids 24 hours before preterm delivery, gestational age (4 week interval), mode of delivery (vaginal spontaneous, vaginal operative or cesarean section), birth weight (500 gram interval) and gender of the infant. The factors were analyzed by multivariate logistic regression analysis.

RESULTS: Although infants of monochorionic twins and infants born in breech presentation had a higher mortality and morbidity these differences disappeared after adjustment for gestational age and birth weight. Statistically significant factors influencing mortality were gestational age (OR 0.2 (95% CI 0.14-0.4) for each 4 weeks increase), birth weight (OR 0.4 (95% CI 0.29-0.6) for each 500 g increase), female gender (OR 0.5 (95% CI 0.3-0.9)) and corticosteroids before preterm labor (OR 0.3 (95% CI 0.2-0.5)). Morbidity was influenced by gestational age (OR 0.2 (95% CI 0.2-0.5) for each 4 weeks increase), birth weight (OR 0.7 (95% CI 0.6-0.9) for each 500 g increase), corticosteroids before preterm labor (OR 1.7 (95% CI 1.2-2.2)), non-Caucasian origin (OR 0.5 (95% CI 0.3-0.9)) and the presence of congenital abnormalities (OR 4.2 (95% CI 0.04-87)).

CONCLUSION: Fetal presentation and birth order were not related to neonatal outcome. Neither was vaginal operative delivery (extraction by vacuum or forceps, breech extraction or internal version and extraction)

450 TEENAGE PREGNANCY: RISK FACTORS FOR ADVERSE PERINATAL OUTCOME. I. Coetzee-Usborne, M. Hallak, I. Shoham-Vardi, E. Press, and M. Katz. Depis Of Obst/Gyn, Wayne State University School of Medicine, Detroit, MI. The obstetrics and gynecology department at the University of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel.

OBJECTIVE: To determine whether the high rate of low birthweight (LBW) that is associated with teenage pregnancy is due to biological maternal age or is the consequence of demographic and/or medical factors as well.

STUDY DESIGN: All singleton first deliveries to mothers of age 16-24 years were included. The deliveries were subdivided into three groups according to maternal age (16-17, 18-19 and 20-24 yrs.). The oldest age group served as a reference group because of its favorable prognosis. These women were matched to 318 women 20-30 years of age within 20% of the gestational age of the infant. Statistical analyses included student t and chi-square tests.

RESULTS: Gravida and parity were significantly higher in the cases compared to controls (5.1 vs 3.2) and (3.2 vs 1.8) respectively. Mean gestational age at delivery was 38.2 ± 3.2 weeks in cases versus 38.8 ± 2.9 weeks in controls (p<0.01). Advanced maternal age, compared to younger age, was associated with significantly higher rates of preterm delivery (7.6% vs 16.4%), cesarean delivery (CS) (31.1% vs 13.8%) and antepartum complications [gestational diabetes, intrauterine growth restriction, intrapartum fetal heart abnormality and meconium passage] (3.7% vs 1.8%). Mean birth weight was no different than that among controls (3168 ± 708 g vs 3257 ± 586 g) and a similar number of babies born to both groups had an Appgar score ≤ 7 at 5 min. Although more cases required induction compared to controls (14.5% vs 9.5%), there was no significant difference in operative vaginal delivery (25.1% vs 29.4%) or in the duration of labor (377.8 ± 242 min vs 371.3 ± 281 min). When the two groups were subdivided according to parity, rates of preterm delivery, CS, preecclampsia, gestational diabetes, RUP and labor induction were significantly higher among older multiparas (14.3, 30.9, 4.2, 5.5, 5.3 & 14.7%, respectively) compared to rates among control multiparas (8.0, 14.5, 0.0, 1.5, 1.3 & 7.7%, respectively). However, only preterm and CS rates were found to be significantly higher in older nulliparous women (22.6 and 32.1%, respectively) compared to (7.7 and 9.6%) in younger nulliparas.

CONCLUSION: Multiparous, and not nulliparous, women age 40 or more seem to have a higher antepartum complication rate than younger women. However, preterm and cesarean delivery rates are higher in nulliparous and multiparous older women compared to younger women. These data may be helpful when counseling women 20 years or over who are considering pregnancy. 

Risk factors: Adjusted OR (95% CI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>16-17 y/o</th>
<th>18-19 y/o</th>
<th>20-24 y/o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Values in %</td>
<td>n=600 (52.2%)</td>
<td>n=2087 (18.2%)</td>
<td>n=8799 (66.4%)</td>
</tr>
</tbody>
</table>

LOPC 24.8* 14.4 6.9
Bedridden incontinence 76.8* 70.4* 38.1
PTCD (≥7 days) 14.2* 7.8 8.8
Malformations 3.8* 3.2 2.6
LBW 15.3* 11.9 9.8
Very LBW 3.2* 1.8 1.6

Multivariate logistic regression analyses for LBW.

CONCLUSIONS: Teenage pregnancy was found to be associated with adverse outcomes, such as LBW, preterm delivery and malformations. The risk for LBW in teenage pregnancy was affected independently mainly by demographic (maternal ethnicity, LOPC) and medical (PIH, malformations) factors.
453 PREGNANCY COMPLICATIONS AND OBSTETRICAL INTERVENTIONS IN WOMEN OF YOUNG MATERNAL AGE: A POPULATION-BASED STUDY IN THE UNITED STATES. AC Rampn, CV Ananth, JC Smulian, AM Vintzileos, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ.

OBJECTIVE: To determine the risk of adverse pregnancy outcomes and obstetric interventions in the United States among women of young maternal age.

STUDY DESIGN: The data for this study were derived from the national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics Analyses were restricted to singleton live births occurring after 20 weeks gestation. Absolute risk for pregnancy complications were calculated in the 11-14, 15-19, and 20-24 year old age groups were compared with those in the 25-34 year old age group, and their association was expressed as relative risk (RR).

RESULTS: There were 7,505,099 singleton live births, of which 3% (n=22574) occurred in women age 11-14, 12.9% (n=9641565) in women 15-19, 24.7% (n=3151535) in women 20-24 and 50% (n=7384314) in women 25-34 years in the older. The absolute and relative risk for adverse pregnancy outcomes by maternal age is shown below. The referent group is the 25-34 year age group.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>11-14 years</th>
<th>15-19 years</th>
<th>20-24 years</th>
<th>25-34 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (RR)</td>
<td>% (RR)</td>
<td>% (RR)</td>
<td>% (RR)</td>
<td></td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>9.3 (3.5)</td>
<td>12.7 (1.5)</td>
<td>10.0 (1.2)</td>
<td>8.5</td>
</tr>
<tr>
<td>PPROM</td>
<td>1.4 (1.6)</td>
<td>1.0 (1.0) *</td>
<td>1.9 (1.0) *</td>
<td>0.9</td>
</tr>
<tr>
<td>PPROM</td>
<td>2.1 (1.4)</td>
<td>2.1 (1.2)</td>
<td>1.0 (0.6)</td>
<td>1.7</td>
</tr>
<tr>
<td>PPH</td>
<td>5.3 (1.7)</td>
<td>4.9 (1.5)</td>
<td>8.4 (1.1)</td>
<td>3.1</td>
</tr>
<tr>
<td>Vacuum</td>
<td>0.5 (1.3)</td>
<td>0.5 (1.3)</td>
<td>0.4 (1.3)</td>
<td>0.5</td>
</tr>
<tr>
<td>Intrapartum fever</td>
<td>2.1 (1.3)</td>
<td>1.9 (1.6)</td>
<td>1.7 (1.1)</td>
<td>1.6</td>
</tr>
<tr>
<td>Meconium</td>
<td>7.1 (1.3)</td>
<td>6.3 (1.4)</td>
<td>5.9 (1.0) *</td>
<td>5.7</td>
</tr>
<tr>
<td>I cesarean</td>
<td>1.3 (1.1)</td>
<td>1.2 (1.3)</td>
<td>1.6 (1.8)</td>
<td>1.2</td>
</tr>
<tr>
<td>CDPP</td>
<td>2.6 (1.0) *</td>
<td>2.3 (0.9) *</td>
<td>2.9 (0.9)</td>
<td>2.0</td>
</tr>
<tr>
<td>Forceps</td>
<td>4.3 (1.3)</td>
<td>3.8 (1.1)</td>
<td>5.1 (1.0) *</td>
<td>3.4</td>
</tr>
<tr>
<td>Vacuum</td>
<td>7.2 (1.2)</td>
<td>6.8 (1.1)</td>
<td>5.9 (1.0) *</td>
<td>6.2</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>5.0 (1.3)</td>
<td>4.6 (1.1)</td>
<td>4.2 (1.1) *</td>
<td>4.0</td>
</tr>
<tr>
<td>Induction of labor</td>
<td>12.1 (0.7)</td>
<td>14.8 (0.9)</td>
<td>16.2 (0.9)</td>
<td>17.4</td>
</tr>
</tbody>
</table>

*Indicates 95% CI for RR includes unity.

CONCLUSIONS: Pregnancy prior to age 20 increases the likelihood of untoward obstetric complications. When pregnancy occurs in a teenager, increased pregnancy surveillance should be initiated. Public policy should continue to address teenage pregnancy rates because of the increased risk of obstetric complications. This is particularly true at the youngest ages.

454 PREGNANCIES IN DIABETIC WOMEN - IS PERINATAL OUTCOME IMPROVED? U Lang, G Braems, M Zygmunt, K Munstedt, W Kunzel, Universitätshospital Schleswig-Holstein, Germany.

OBJECTIVE: Management of pregnancies in diabetic women (PD) with strict glucose control and intensive fetal monitoring in specialized centers has been advocated since the 1970s. To determine whether improvement of perinatal outcome of PD, data from the Hessische Perinatalerhebung (HEPE), a state wide data collection on obstetrical care in the State of Hesse, Germany (Pop. 5,9 million) was used to assess a total of 2901 PD recorded from 1982-1988 in three and four year subgroups and compare them with each other and to the non-diabetic population.

STUDY DESIGN: Patient histories, pregnancy risks, birth risks and complications. The majority of pregnancies in diabetic women (PD) with strict glucose control and intensive fetal monitoring in specialized centers has been advocated since the 1970s. To determine whether improvement of perinatal outcome of PD, data from the Hessische Perinatalerhebung (HEPE), a state wide data collection on obstetrical care in the State of Hesse, Germany (Pop. 5,9 million) was used to assess a total of 2901 PD recorded from 1982-1988 in three and four year subgroups and compare them with each other and to the non-diabetic population.

RESULTS: The percentage of PD with gestational diabetes and the percentage of maternal infants of diabetic mothers remained nearly unchanged and significantly higher than in the non-diabetic population. Overall, 52% had an adverse perinatal outcome (8% when MSAP < 2.5). Anomalies not identified by US were grouped A (polyductaly), group B (miscellaneous). Of 27 patients with karyotype results available, 8% (1/27) were abnormal: inversion of chromosome nine (n=1) with no anomalies at birth. Seven percent (6/22) of the unexplained elevated MSAP patients had true cord knots on pathology; of these, 67% (4/6) had normal perinatal outcomes, while 33% (2/6) had IUGR and oligohydramnios. CONCLUSIONS: Patients with higher values of unexplained elevated MSAP are more likely to have preterm births, perinatal deaths, intrauterine growth restriction/low birth weight infants and oligohydramnios than those with lower values. Interestingly, the incidence of true cord knots was higher than what is reported in normal populations.

452 POSTTERM PREGNANCY: SHOULD THE DEFINITION OF 42 WEEKS BE RECONSIDERED? M Flugel, M Hallak, T Silberstein, M Flugel, M Katz, M Mazor, Dept. Obs/Gyn, Wayne State University, Detroit, MI, and Epidemiology, Sarkova Medical Center, Faculty of Health Science, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

OBJECTIVE: To determine the occurrence of maternal and fetal complications in risk of postterm pregnancy (PTP) and to reevaluate the acceptable cutoff (42 weeks) for induction of labor.

STUDY DESIGN: 36,100 low risk pregnancies with good dating (LMP & early US) were included. Fetal and maternal complications were evaluated, including group non-progressive labor (NPL), cervical tear, retained placenta, postpartum hemorrhage, vacuum delivery, cesarean section (CS), macrosomia, meconium, fetal distress, ante-, intra- and postpartum death. Pregnancy outcomes at different gestational ages were compared using univariate and multivariate analyses (MVA) and ROC's.

RESULTS: NPL stage I & II, retained placenta, CS, macrosomia, meconium and fetal distress were found to be significant in the univariate analysis. These parameters were evaluated using MVA. The following parameters were found to be significant in MVA and were assessed using ROC's.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=39 wks</th>
<th>N=40 wks</th>
<th>N=41 wks</th>
<th>N=42 wks</th>
<th>N=43 wks</th>
<th>N=44 wks</th>
<th>ROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPL stage I</td>
<td>1%</td>
<td>1.2%</td>
<td>1.8%</td>
<td>3.2%</td>
<td>5.6%</td>
<td>42 wks</td>
<td></td>
</tr>
<tr>
<td>NPL stage II</td>
<td>1.4%</td>
<td>1.8%</td>
<td>2.1%</td>
<td>3.1%</td>
<td>4.9%</td>
<td>42 wks</td>
<td></td>
</tr>
<tr>
<td>Macrosomia</td>
<td>8.4%</td>
<td>9.0%</td>
<td>10.5%</td>
<td>15.1%</td>
<td>23.0%</td>
<td>41 wks</td>
<td></td>
</tr>
<tr>
<td>Meconium</td>
<td>12.5%</td>
<td>17.0%</td>
<td>21.0%</td>
<td>32.5%</td>
<td>37.5%</td>
<td>41 wks</td>
<td></td>
</tr>
<tr>
<td>CS</td>
<td>6.1%</td>
<td>5.4%</td>
<td>5.8%</td>
<td>7.9%</td>
<td>8.2%</td>
<td>41 wks</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: The rates of non-progressive labor stage I&II, meconium stained amniotic fluid, macrosomia and CS were significantly higher with increasing gestational age. In order to decrease the rate of these complications induction of labor should be performed before 42 weeks for non-progressive labor and before 44 weeks for macrosomia, meconium and CS. Therefore, we suggest that the definition of 42 weeks and beyond as postterm should be reconsidered.
PHARMACOKINETICS OF TOTAL AND IONIZED MAGNESIUM IN PRETERM LABOR AND PIH SUBJECTS. E. Tauer, L. Tan, M. Ross, C. Chao. Dept Ob/Gyn, Elbou-UCLA Med Ctr, Torrance CA.

OBJECTIVE: Magnesium sulfate (MgSO4) has demonstrated efficacy in the treatment of preterm labor (PTL) and preeclampsia (PIH). However, the precise therapeutic range of plasma levels and the active agent (total (tMg) or ionized (IMg) magnesium) remain uncertain. To aid in developing improved use of MgSO4, we sought to determine the initiation and elimination pharmacokinetics of both tMg and IMg during MgSO4 infusion to patients with PTL and PIH.

STUDY DESIGN: 39 singleton pregnant patients who were candidates for MgSO4 were studied (11 PTL, 8 PIH). MgSO4 dosages were tailored clinically with loading doses of 4 or 6 gms, followed by maintenance dosages of 2.0-3.5 gms/hr. Multiple serial blood samples were taken over 4 hours prior to and during initiation of MgSO4 and over 4 hours following discontinuation of infusion. tMg and IMg were analyzed with spectrophotometric assays and non-selective electrodes (NOVA 8), respectively. Apparent volumes of distribution (VOD) were determined by standard pharmacokinetic modeling. PTL and PIH groups were compared by unpaired T test.

RESULTS: Among all patients, the mean tMg and IMg levels at 30 minutes were 5.03±0.32 and 2.21±0.17 mg/dl, respectively, with a linear relationship (IMg:0.34 tMg:0.17, r=0.60). However, IMg levels varied 2-fold (1.9 to 3.7 mg/dl) at therapeutic IMg levels (5 to 6 mg/dl). For PTL subjects, the time to steady state (SS) for IMg and tMg was reached by 50 min, with mean IMg and tMg levels of 5.0±0.35 and 2.5±0.21 mg/dl, respectively. The time to SS for the PIH group was 45 min, with mean IMg and tMg levels of 4.7±0.30 and 2.0±0.16 mg/dl, respectively. The initial VOD was significantly greater for the patients with PIH as compared to PTL (28.98±8.431 vs. 16.17±2.924 ml; p<0.01).

CONCLUSION: Using the combined bolus and constant infusion protocol, magnesium steady state levels are reached within 30 to 45 min. IMg and tMg levels are closely correlated within patients, though the IMg/tMg ratio may differ between patients. Despite a known reduced plasma volume and renal clearance in PIH, the increased Mg VOD and time to SS may have important clinical implications.


OBJECTIVE: To compare therapies with and without heparin in patients with a history of prior pregnancy loss and negative antiphospholipid antibody status.

STUDY DESIGN: This was a retrospective review of the pregnancy outcomes of 44 patients with a prior second or third trimester fetal death and negative antiphospholipid antibodies specifically lupus anticoagulant and anticardiolipin (IgG) antibody. Patients with a history of an incompetent cervix or a history of thromboembolic disease requiring anticoagulation were excluded.

RESULTS: For those patients were the subjects of this study. Twenty-four (55%) patients received heparin (prophylactic dose) and aspirin (low dose) therapy, and 17 received either aspirin (low dose) or no medical therapy. Only four patients in each group had a previous liveborn, a nonsignificant difference, p=7. There were no significant differences between the two groups regarding maternal age, cigarette or recreational drug use, or history of previous preterm birth. There were 40 liveborns and 1 fetal demise (on heparin). The mean gestational age at delivery was 35.5±4.27 weeks in the group that received heparin and 38.9±5.1 weeks in the nonheparin group, p=0.03. Delivery prior to 37 weeks occurred in 12 patients, 11 of whom received heparin, p=0.02. The mean birthweight was significantly decreased in the group that received heparin, 2605±842 grams versus 3296±526 grams, p=0.05, a finding reflecting the difference in gestational age. Complications of therapy included two cases of abortion and two cases of hematuria, all occurring in the group that received heparin.

CONCLUSIONS: For patients with a history of a prior second or third trimester fetal demise and negative antiphospholipid status, empiric treatment with heparin resulted in a significantly earlier gestational age at delivery and a higher rate of complications compared to no treatment or treatment with aspirin. We suggest that in this population, use of heparin is not efficacious and may be harmful.

CORRELATION BETWEEN PRENATAL AND NEONATAL BIRTH ORDER IN TWIN PREGNANCY. ST. Chasen, HR Al-Kouzaly, New York Presbyterian Hospital/Cornell, Department of Obstetrics and Gynecology, New York, NY

OBJECTIVE: The objective of this study was to determine whether birth order in twin pregnancies corresponds to the order of presentation early in pregnancy.

STUDY DESIGN: All twin pregnancies in which amnioncensis was performed from 1996-1998 were identified. Those with discordant genders (one male and one female) that delivered at our hospital were included. In considering only these cases, we could correlate the in utero and neonatal identification of the twins with certainty. Among the 44 patients, the presenting twin was denoted "Twin A" and the non-presenting twin was denoted "Twin B." The cytogenetics laboratory also used these designations. Delivery data were obtained from review of medical records. Statistical comparison was done using two-tailed Fisher's exact test and Student's t test.

RESULTS: There were 60 patients who met inclusion criteria. The mean gestational age at amnioncensis was 16.4±1.5 weeks (range 15-21 weeks), and the mean gestational age at delivery was 36.2±2.1 weeks. The mean interval to delivery was 37.5±3.6 years. A total of 49 patients (81.4%) underwent cesarean delivery of both twins. A lower transverse uterine incision was performed in all cases of cesarean delivery. Birth order corresponded to the order at the time of amnioncensis in 35 cases (91.4%) There was no difference in the rate of discordance of prenatal and neonatal birth order in twins delivered vaginally compared to those delivered abdominally (90.0% vs. 91.8%, p=0.91). Cases with discordant prenatal and neonatal birth order had similar maternal ages, gestational ages at amnioncensis and delivery, and fetal presentation at delivery, as cases with concordant birth orders.

CONCLUSION: In dichorionic twin pregnancies, birth order is established relatively early in gestation in greater than 90% of cases. This is not affected by mode of delivery. This data may assist in correlating certain prenatal sonographic findings present in only one twin with postnatal outcome when genders are concordant.
RELATIONSHIP BETWEEN INFANT SHOULDER MORPHOLOGY AND BIRTHWEIGHT.

M. Zlatnik, G. Olson, G. Saade. Dept of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: Body morphology as well as weight may influence the occurrence of shoulder dystocia. Larger infants may be less flexible ultimately altering the dynamics of vaginal delivery. The objective of this study was to determine if infant morphology correlates with birthweight.

STUDY DESIGN: Neck length (distance between the superior aspect of the deltoid to inferior mandible while in the military or neutral position), shoulder width (bicoronal distance including soft tissue) and neck circumference were measured within the first 2 days of life in normal singletons born between 37 and 42 weeks gestation. Maternal and infant records were reviewed for birthweight, maternal diabetes and complications of delivery. Multiple linear regression, Pearson correlation, and receiver operating characteristics (ROC) curves were used for data analyses. A composite score was created based on the multivariate regression equation using gestational age, presence or absence of diabetes, shoulder width and neck circumference.

RESULTS: Neck circumference and shoulder width were significantly correlated with birthweight. A trend was seen with neck length, but this did not reach significance.

Shoulder width predicted BW ≥2425g (z=8.94, p<0.0001) and BW >4250g (z=7.28, p<0.0001)

Neck circumference predicted BW ≥2425g (z=15.70, p<0.0001) and BW >4500g (z=4.47, p<0.0001)

The composite score was the best predictor of BW ≥2425g (dashed line in figure, z=10.30, p<0.0001) with best cutoff sensitivity 100% and specificity 75%, and BW >4500g (solid line in figure, z=8.47, p<0.0001) with best cutoff sensitivity 100% and specificity 98%.

CONCLUSIONS: Shoulder width and neck circumference positively correlate with birthweight and are predictive of large infants. Infant shoulder and neck morphology may be as significant a role as birthweight in dystocia cases. Antenatal evaluation of shoulder and neck biometry may further refine our ability to detect the fetus at risk.

USING COLOR-FLOW DOPPLER TO AID IN THE MEASUREMENT OF ANOMNIOTIC FLUID INDEX OVERESTIMATES OLIGOHYDRAMNIONS.

M. Zlatnik, R. Bukowski, G. Olson, G. Saade. Dept. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To determine if using color-flow Doppler (CFD) to identify amniotic bands affects amniotic fluid index (AFI) measurements.

STUDY DESIGN: 507 AFIs measured between 24-42 weeks’ gestation in singleton gestations with no known or suspected fetal anomalies and <14 days discrepancy between menstrual and ultrasonographic dating were included. CFD was used to identify loops of amniotic cord and exclude them from the measurement. Polynomial regression was used to generate mean and variability of amniotic fluid index according to a standard nomogram derived without using CFD (Moore & Cayle, AJOG, 1990) were calculated.

RESULTS: The AFI decreased significantly over gestational age, starting at ≥31 weeks (p<0.05 by ANOVA). The relationship between AFI and gestational age was best modeled by a 2nd degree polynomial (figure A; p<0.01), lines represent mean as well as 2.5, 5, 95 and 97.5%iles. The proportion of AFIs that fell outside the ranges of the standard nomogram would have been (given as median [range]): 6%[2.5-3.5]% for ≤2.5%ile, 9.9%[3.2-7.5]% for ≤5%ile, 3.4[0.5-3.0]% for ≤95%ile, and 1.8[0.2-2.0]% for ≥97.5%ile. The 2.5 and 97.5%iles using the current data were lower than those of the standard and the difference increased with advancing gestation (Figure B). Upper 95%ile were also different (not shown).

CONCLUSION: AFI measured using CFD overestimates oligohydramnions and may underestimate polyhydramnions when a standard AFI table obtained without CFD is used. Differences in populations may represent an alternative explanation to the findings. Normal values specific for measurement method and population should be used for reference.

PLACENTAL PATHOLOGY IN GRAVIDAS WITH OLIGOHYDRAMNIONS.

S Schueler*, M Inceeti, Z. Pavlovic. Departments of Ob/Gyn and Pathology, USC School of Medicine, Los Angeles, CA.

OBJECTIVE: Oligohydramnions, defined as an amniotic fluid index <5.0 cm, occurs in 3-5% of pregnancies at term. While this decrease in amniotic fluid may be due to decreased fetal oxygenation with subsequent shunting of blood away from the kidneys, there is little objective evidence to support this. The goal of this study was to determine whether there is an increase in placental pathology in patients with oligohydramnions at term.

STUDY DESIGN: Patients admitted to our labor and delivery suite were eligible for this study if they met the following inclusion criteria: a singleton pregnancy with an estimated gestational age ≥36 weeks, intact membranes, no evidence of fetal aneuploidy, and an amniotic fluid index <5.0 cm. Informed consent was obtained and the placentas were examined by a single investigator, who was blinded to the obstetrical history. These were then compared to a cohort of historical control patients without oligohydramnions. Placentas were examined grossly for the presence of injuries, amnion nodosum, cord abnormalities, and meconium. They were then examined microscopically for evidence of sclerosis, deciduium, villitis, chronic villitis, chorangiosis, chorangiosis, syncytial knots, and nucleated red blood cells. Over a 6 month period, we collected 47 cases and compared these to 52 controls. Statistical analysis was performed with Chi-square and Fisher’s exact test when appropriate. Confounders such as gestational age and infant weight were studied with regression analysis.

RESULTS: Our cases and controls did not differ significantly regarding gestational age, gravity, parity, route of delivery, infant weight, APGAR scores, or rates of meconium passage. We found a significant increase in hypoxic changes in the oligohydramnions group. These were defined as increased syncytial knots, chorangiosis, and nucleated red blood cells. These changes were found in 27/47 (57%) of study patients, versus 9/52 (17%) of control patients (p<0.05).

CONCLUSION: We found a statistically significant increase in hypoxic changes in placentas of patients with oligohydramnions at term. This lends objective evidence to the theory that hypoxia is an underlying etiology of oligohydramnions, and supports our current policy of induction of labor for these patients.

IS HISTORY OF A PREVIOUS LIVEBIRTH A PREDICTOR OF AN ABNORMAL FETAL KARYOTYPE FOLLOWING A PREGNANCY LOSS? D. Rodriguez-Thompson, F.R. Biebert*, A. Thomas, E.S. Lieberman*, J.A. Hill. Dept. Ob/Gyn, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: To evaluate whether history of a previous livebirth (PLB) is associated with the presence of an abnormal fetal karyotype overall, and in women with and without a history of recurrent pregnancy losses.

STUDY DESIGN: Reproductive history, maternal age, and gestational age were abstracted from the medical records of 502 consecutive women who had tissue submitted for karyotype analysis following a spontaneous pregnancy loss prior to twenty weeks of gestation between April, 1994 and February, 1997.

RESULTS: Of the 502 women identified, 154 (30.8%) were successfully karyotyped. Samples with missing data points were excluded thus 410 (90.3%) samples were analyzed. One third (n=131) were from women with a history of three or more pregnancy losses, termed recurrent aborters. In the overall population, 52/55 (n=217) of the samples were abnormal. Advanced maternal age (AMA) (<age 35) (62% vs 43% p<0.001) and early gestational age (EGA) (>12 weeks) (65% vs 25%, p<0.001) were associated with a higher rate of abnormal fetal karyotype. The proportion of abnormal karyotype was the same in patients with a history of a PLB and those without (54.4% vs 51.8%, p=0.9).

In separate logistic regression analyses, history of a PLB was not significantly associated with an abnormal fetal karyotype in patients with either recurrent or sporadic losses.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recurrent Aborters (≥2 losses) n=131</th>
<th>Sporadic Aborters (1-2 losses) n=279</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMA</td>
<td>1.38 (0.93, 2.09)</td>
<td>1.56 (0.93, 2.62)</td>
</tr>
<tr>
<td>EGA</td>
<td>5.18 (1.89, 14.18)</td>
<td>5.54 (3.05, 10.11)</td>
</tr>
<tr>
<td>PLB</td>
<td>2.06 (0.93, 4.55)</td>
<td>1.35 (0.79, 2.38)</td>
</tr>
</tbody>
</table>

CONCLUSION: Chromosomal anomalies are an important cause of failure in spontaneous abortions. A history of a previous livebirth is not independently associated with an abnormal fetal karyotype. Fetal karyotype analysis is important to identify patients with cupido pregnancy losses who may benefit from further evaluation.
463 THE EFFECT OF FETAL GROWTH RESTRICTION ON NEONATAL OUTCOME IN POSTTERM PREGNANCY, JM Alexander, DD McNamara*, RJ Leveno Dept. of Ob/Gyn, Univ. of Texas Southwestern Medical Center, Dallas, Texas.

OBJECTIVE: To compare neonatal outcomes of postterm infants with a birthweight ≤ third percentile to gestational age-matched controls with a normal birthweight.

STUDY DESIGN: Retrospective analysis of 14875 women who underwent labor induction at or beyond 42 weeks’ gestation between 1 January 1988 and 31 December 1998. Women with diabetes, hypertension and prior cesareans were excluded. Infants with anomalies were also excluded. Birthweight percentiles were derived from the obstetrics population at our hospital. Statistical analysis was performed using chi-square.

RESULTS:

<table>
<thead>
<tr>
<th>POSTTERM INFANTS</th>
<th>Birthweight ≤3rd percentile</th>
<th>Birthweight ≥3rd percentile</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean for fetal distress</td>
<td>26 (11%)</td>
<td>540 (4%)</td>
<td>.001</td>
</tr>
<tr>
<td>Neonatal intensive care</td>
<td>7 (2%)</td>
<td>82 (1%)</td>
<td>.001</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>8 (22/1000)</td>
<td>22 (1/1000)</td>
<td>.001</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>0 (0)</td>
<td>8 (0)</td>
<td>.66</td>
</tr>
</tbody>
</table>

CONCLUSION: Morbidity and mortality is significantly increased in infants of postterm pregnancy whose birthweights are at or below the third percentile. Indeed, one fourth of the stillbirths attributable to postterm pregnancy were found in the ≤3rd percentile group.


OBJECTIVE: To compare the five-year growth and neurologic development between first and second twin pairs.

STUDY DESIGN: Forty-seven sets of twins were recruited prenatally for a longitudinal study of growth and neurologic development. Extensive maternal demographic, risk assessment, and antepartum data were compiled on each individual. Comprehensive anthropometric measurements were obtained on each infant at birth. Infants were followed through five years of age for assessment of growth and neurologic development. Extensive anthropometric measurements and neurodevelopmental tests (including tests for IQ (Weschler Preschool/Primary Scales of Intelligence-Revised), motor function (Peabody Fine-/ Gross Motor Scales), and psycholinguistic ability (Test for Auditory Comprehension of Language-Revised)) were obtained at the five-year assessment. Statistical analyses included the paired Student's t-test and McNemar's test when appropriate.

RESULTS: Of the initial 47 sets of twins identified, 37 sets completed follow-up testing through 5 years. Average delivery gestational age (mean ± SD) for the study cohort was 35.6 ± 2.2 weeks. No significant differences were noted between the first and second born twin with regard to one and five minute Apgar scores, birthweight, infant sex, or incidence of respiratory distress syndrome. Additionally, birth anthropometric measurements were not significantly different between the first and second born twin. No significant differences were noted between the first and second born twin with respect to IQ, language, gross motor skills, and fine motor performance at the five-year testing assessment. Of the seven anthropometric measures assessed at five years, only arm circumference (A 1.0 ± 0.1 cm, p<0.05) and subcapular skin fold measurements (A 1.0 ± 0.4 cm, p<0.05) were significantly different between the two groups, with the first born twin measuring larger.

CONCLUSION: Overall, five-year anthropometric and neurodevelopmental outcomes are similar between first and second born twins.

465 OUTCOME OF QUINTUPLET PREGNANCY. K. Francois*, A. Alperin*, J.P. Elliott. Dept. of OB/GYN, Good Samaritan Regional Medical Center, Phoenix, AZ.

OBJECTIVE: Quintuplet pregnancy usually results from assisted reproductive technologies. Once the diagnosis of five embryos is made by ultrasound, the patient must decide between two choices: selective embryo reduction or attempting to carry the quintuplet pregnancy. This report details the outcome of quintuplet gestations in the United States.

STUDY DESIGN: Cases were identified within the 50 United States from women who contacted two large support groups for high order multiple gestations: The Triplet Connection and Mothers of Super Twins (MOST). The pregnancies were registered with these groups prospectively usually in the first or second trimester. The database of the two support groups was accessed and individual patients and their physicians were contacted for further information.

RESULTS: Ninety-nine women were identified as being diagnosed with a quintuplet gestation in the first trimester. Selective reduction of one or more embryos was elected in 22 patients, 77 patients attempted to carry the quintuplet gestation. Prior to 24 weeks gestation, 31 patients had a fetal demise of 1-5 fetuses (1st trimester: 1 fetus; N=11; 2 fetuses, N=11; 3 fetuses, N=4) (2nd trimester: 1 fetus, N=1; 2 fetuses, N=5; 3 fetuses, N=7). Thirty-two patients reached a gestational age of 24/7 weeks with five living fetuses. Complete data was unable to be collected on the remaining 15 patients. The mean gestational age of delivery for these quintuplet pregnancies was 29.03 weeks. The mean gestational age of delivery for multiples and parous patients was 28.5 weeks and 30.0 weeks, respectively. Sixteen-five quintuplet pregnancies reported preterm labor at a mean gestational age of 22.5 weeks. Pre-ecmalpasia was reported in 48.0% of quintuplet gestations (36/75).

CONCLUSION: Quintuplet pregnancy is complicated by multiple adverse pregnancy outcomes. Spontaneous abortion of 1-3 fetuses in the 1st or 2nd trimester occurs in 40.2% of pregnancies. The mean gestational age of delivery for patients reaching 24/7 weeks with 5 living fetuses is 29.03 weeks. Preterm labor and pre-eclampsia occur frequently.


OBJECTIVE: To determine whether the incidence of cesarean delivery (CS) differs among women with severe pre eclampsia (PE) who receive either epidural versus intravenous patient-controlled analgesia (PCA) during labor.

STUDY DESIGN: We conducted a randomized clinical trial of epidural analgesia (n=58) versus intravenous PCA with meperidine (n=52) for labor in women with severe PE at ≥24 weeks’ gestation. The primary outcome was the CS rate, and our sample size was calculated using an estimated baseline rate of 50%. Data were analyzed by intent to treat.

RESULTS: Of the 105 women enrolled, eight did not receive the assigned treatment because of rapid labor progress, and two women assigned to PCA also received epidural analgesia. The groups were similar regarding age, weight, race, parity, medical conditions, gestational age and initial cervical dilation.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Epidural (#58)</th>
<th>PCA (#52)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean, N (%)</td>
<td>9 (17)</td>
<td>6 (12)</td>
<td>.43</td>
</tr>
<tr>
<td>Maternal Epidurine, N (%)</td>
<td>5 (10)</td>
<td>0 (0)</td>
<td>.03</td>
</tr>
<tr>
<td>Neonatal Naloxone, N (%)</td>
<td>5 (10)</td>
<td>28 (54)</td>
<td>.001</td>
</tr>
<tr>
<td>Average Pain Score*</td>
<td>4.2±3.6</td>
<td>6.8±2.7</td>
<td>.0001</td>
</tr>
<tr>
<td>Satisfaction Score**</td>
<td>2.8±1</td>
<td>2.2±1</td>
<td>.01</td>
</tr>
</tbody>
</table>

*p=none to 10=worst possible; **1=poor to 4=excellent

Birthweight, umbilical cord arterial pH, NICU admissions and neonatal death were also similar between the two groups.

CONCLUSIONS: Compared to intravenous PCA, epidural analgesia for relief of labor pain in women with severe PE did not increase the low CS rate observed at our level III center, and it provided enhanced pain relief.
PREGNANCY OUTCOME IN HISPANIC PATIENTS WITH UNEXPLAINED POSITIVE TRIPLE MARKER SCREENING FOR DOWN SYNDROME. CS. Naylor, B. Cohen, M. Porta, TJ. Garite. Dept. Ob/Gyn, University of California Irvine, Orange, CA

OBJECTIVE: Recent studies have shown that Caucasian, African-American, and Asian women whose Triple Marker Screen (TMS) is falsely positive for Down syndrome are at higher risk than the general population for adverse pregnancy outcomes. Since ethnicity has been demonstrated to be an independent pregnancy risk, the objective of this study is to compare pregnancy outcomes in Hispanic patients with a positive serum TMS and different racial-ethnicities, Hispanic patients with an unexplained positive TMS for Down syndrome of less than 1 in 190. Adverse pregnancy outcomes were compared to ID: PTL-50.5%, PROM-17%, Maternal diabetes-10%, and fetal anomalies-3% for TMS positive patients. The study group consisted of 40 Hispanic patients with an unexplained positive serum TMS for Down syndrome. The control group consisted of 100 women whose TMS indicated a risk for Down syndrome with reduced labor or scheduled cesarean (CS). Data were divided and analyzed by week delivered.

RESULTS: There were 3786 TW (7572 infants) analyzed. ID: PTL-50.5%, DD-20.6%, preterm PROM-16%, MAT-10.5%, and FET2.5%. The overall CS rate was 88%. 71.9% of infants were <2500g and 5.8% were <1500g. 50.1% were admitted to NICU, and 9.1% required assisted ventilation. For those with DD, 77.5% were CS. 43.5% were admitted to NICU, with 7.2% requiring ventilator assistance. The mean GAD at DD was 35+4 with a mean nursery LOS of 8.4±10.4 days. 66.4% in this group were <2500g. See table for all groups by week delivered.

CONCLUSION: The majority of PTD’s are related to PTL, preterm PROM, MAT or FET indications, though for >20% PTD is discretionary; it is important to consider neonatal morbidity and costs related to GAD when choosing DD.

WEEK N DD% BW DAVIS NICU%
50 254 8.5 1439±37 35±18.8 91 9
51 258 11.8 1838±318 27.6±15.2 95.3
52 546 12.1 1794±310 19.7±11.1 89.4
53 874 10.2 1974±355 15.4±11.5 83.5
54 1542 16.7 2187±360 19.7±14.7 26.3
55 1830 21.5 2385±348 9.5±10.2 38.2
56 2468 27.5 2583±362 4.1±4.4 20.5

Data mean aSD, or percentage as indicated. Total Nursery Level 2 & 3

508 consecutively twins at gestational age of >32 weeks were analyzed. ID: PTL-50.5%, DD-20.6%, preterm PROM-16%, MAT-10.5%, and FET-2.5%. The overall CS rate was 88%. 71.9% of infants were <2500g and 5.8% were <1500g. 50.1% were admitted to NICU, and 9.1% required assisted ventilation. For those with DD, 77.5% were CS. 43.5% were admitted to NICU, with 7.2% requiring ventilator assistance. The mean GAD at DD was 35+4 with a mean nursery LOS of 8.4±10.4 days. 66.4% in this group were <2500g. See table for all groups by week delivered.

CONCLUSION: The majority of PTD’s are related to PTL, preterm PROM, MAT or FET indications, though for >20% PTD is discretionary; it is important to consider neonatal morbidity and costs related to GAD when choosing DD.
SMOKING CESSATION PROGRAM EFFECTIVENESS DURING PREGNANCY. A. Hiett, S. Brazaas, J. Hedberg, H. Brown, Dept Ob/Gyn, St. Vincent Hospital, Indianapolis, IN.

OBJECTIVE: To compare the effectiveness of a structured smoking cessation program to conventional methods in an obstetric population.

STUDY DESIGN: Women enrolling for prenatal care were asked to participate in a smoking cessation program. Each woman completed the Fagerstrom profile, used to quantify dependence. Women were randomized into two groups and followed prospectively. Women in the study group were enrolled in a smoking cessation program consisting of education and at least 8 encounters with a program counselor. Urine cotinine levels were obtained at the first visit and at delivery. Number of cigarettes smoked per week, peak flow values and carbon monoxide levels were obtained at each prenatal visit. Peak flow values and carbon monoxide levels were shared with the study patients. Neatly used urine cotinine levels were also obtained at delivery. Women in the control group received identical care; except, they were not enrolled in the smoking cessation program. Peak flow values and carbon monoxide levels were not disclosed to the control patients.

RESULTS: 49 patients have completed the program and delivered (26 study group, 23 control group). The groups were similar with regard to maternal age, Fagerstrom scores, initial peak flow values, and initial urine cotinine levels. Women in the study group had significantly higher median peak flow values when compared to controls during the course of their prenatal care (305 L/min vs 365 L/min, p<0.05, respectively). There were no significant differences between the two groups with respect to number of cigarettes smoked per week (self-reported), carbon monoxide levels, and maternal urine cotinine levels at delivery. Significantly more women in the study group stopped smoking based on negative neonatal urine cotinine levels at delivery (29% study vs 6% control, p=0.05).

CONCLUSIONS: Women enrolled in a prenatal smoking cessation program had better lung function during their prenatal care as measured by peak flow values. Significantly more women were able to quit smoking when enrolled in a comprehensive smoking cessation program.


OBJECTIVE: Vaginal bleeding during pregnancy is a risk factor for adverse pregnancy outcome (e.g., SGA, preterm premature rupture of membranes [PROM], preterm labor). Yet, the etiology of most cases of vaginal bleeding is unknown. The purpose of this study was to determine the frequency and clinical significance of microbial invasion of the amniotic cavity in patients presenting with "idiopathic" vaginal bleeding.

STUDY DESIGN: Amniocentesis was performed to determine the microbial state of the amniotic cavity of patients presenting with vaginal bleeding between 22 and 34 weeks. Amniotic fluid was cultured for aerobic and anaerobic bacteria as well as Mycoplasmas. Patients with preterm labor, preterm PROM, placenta previa, cervical bleeding and clinical cervical incompetence were excluded. Analysis was conducted with non-parametric statistics.

RESULTS: 32 patients met the entry criteria. Microbial invasion of the amniotic cavity was present in 13% of cases (4/32). The microorganisms isolated from the amniotic fluid were Ureaplasma urealyticum (n=3), candida species (n=1) and staphylococcus species (n=2). All patients with microbial invasion of the amniotic cavity had an early preterm delivery (<32 weeks).

CONCLUSIONS: Subclinical microbial invasion of the amniotic cavity was detected in 15% of patients with "idiopathic" vaginal bleeding and was associated with early preterm delivery (<32 weeks). We propose that ascending intrauterine infection in the chorionicdecidual interphase may cause vaginal bleeding.

ANTENATAL FACTORS AFFECTING SURVIVAL AND NEONATAL MORBIDITY IN THE FETUS AT THE Cusp OF VIABILITY. M. Fleischer, M. Malde, Brown Univ, Dept. Ob/Gyn, Providence, RI.

OBJECTIVE: To determine which demographic and antenatal factors are associated with survival and short-term morbidity (STM) in newborns of 22 to 25 weeks gestation.

STUDY DESIGN: We performed a retrospective cohort study of all (n=82) non-surgical cases, known to have documented heart activity within 24 hours of hospital admission, born at 22.0 to 25.0 weeks' gestation from 1/1996 through 12/98. We used univariate and multivariate analyses to compare survivors at hospital discharge with nonsurvivors, including stillbirths (SB), and those with and without STM. Gestational age at delivery (GAD) was based on menstrual and ultrasound dates consistent with newborn exam. STM was defined by the presence of: grade 3 or 4 intraventricular hemorrhage, an oxygen requirement on discharge, respiratory distress syndrome (Stage 2) or necrotizing enterocolitis requiring surgery.

RESULTS: 26 (42%) infants survived to discharge. Survival rates were 6%, 46%, and 67% at 22, 23 and 24 completed weeks, respectively. Survivors were older (24.1±2.6 vs 23.2±0.8, p<.001) than nonsurvivors. On multiple logistic regression analysis, GAD (p<.001), physician's expectation of survival (p<.001), and steroid exposure >24 hours (p<.001) were associated with survival. Steroid exposure was no longer significant upon analysis of covariance. Only 7% (2/26) of surviving infants were deemed viable, vs 67% (24/36) of nonsurvivors (8% (6/26) of survivors were discharged without STM). STM occurred in 67% (9/12) and 71% (10/14) of survivors at 23 and 24 completed weeks, respectively. Clinical chorioamnionitis (p=0.055) and rupture of membranes (ROM) >24 hours (p=0.005) were positively associated with STM. Presentation and mode of delivery did not affect survival or outcome.

CONCLUSION: Survival of infants born in the perinatal period is most dependent on gestational age at delivery and physician expectation of survival figures prominently. STM >24 hours and clinical chorioamnionitis were the only obstetric factors associated with an increased risk of STM. Critical assessment of gestational age is the most important factor in devising a strategy of counseling and management of a periviable gestation.

TWIN Discordance: Long Term Outcome. James Baldiucos, MD, D. Sokolowska MD, Amy Bosamse, MS, Michael Patterson BS, Robert Atlas MD, Orson Rust MD

OBJECTIVE: To determine whether increasing discordance in twins is associated with increased short or long term morbidity in children.

METHOD: A retrospective chart review was performed on the 350 sets of twins who are now school age and delivered at Lehigh Valley Hospital from Jan 84 to 92. Chart reviews of 334 complete sets with analysis of short term morbidity. Surveys were mailed to parents concerning current growth and function of their twins. Repeat mailings and follow-up phone calls netted 112 (33.5%) completed surveys. Variables analyzed included birth weight percentile and or <10 percentile and mental or learning disabilities. A psychosocial screening checklist was completed on twins with >20% (n=15) discordance and compared to a matched for GA group of twins with <20% discordance (n=14). All data sets were stratified according to GA at delivery and degree of discordance.

RESULTS: Degree of Discordance

<table>
<thead>
<tr>
<th>GA at De:</th>
<th>0-10%</th>
<th>11-20%</th>
<th>21-30%</th>
<th>31-40%</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-25wks</td>
<td>35</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>55</td>
</tr>
<tr>
<td>26-39wks</td>
<td>39</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>57</td>
</tr>
<tr>
<td>30-39wks</td>
<td>59</td>
<td>9</td>
<td>7</td>
<td>6</td>
<td>97</td>
</tr>
<tr>
<td>31-44wks</td>
<td>86</td>
<td>15</td>
<td>6</td>
<td>9</td>
<td>167</td>
</tr>
<tr>
<td>Total</td>
<td>184</td>
<td>99</td>
<td>32</td>
<td>9</td>
<td>324</td>
</tr>
</tbody>
</table>

Analysis of short term morbidity demonstrated a significant inverse relationship with GA at birth (p<.0001) and no correlation with degree of discordance (r=.01). With respect to long term morbidity, early GA (≤24 weeks) showed an inverse correlation with learning disabilities (p=.02) but no association with discordance (p=.8). When each low birth wt twin was compared to its sibling with higher birth wt, no difference was noted in short or long term complications. Psychosocial screening showed no difference in twins with <20% or >20% discordance (p=0.9).

CONCLUSION: Birth weight discordance has little impact on short or long term morbidity. Early GA and delivery are significant predictors short or long term childhood complications. Antenatal testing in discordant twins should be tailored to obtain the maximum GA for optimal outcome. Prospective trials are indicated prior to determining the degree of discordance as a risk factor for adverse short or long term outcome.
475 UTERINE EVACUATION COMPLICATED BY HystECTOMY: AN ASsoCIATION WITH PRIOR CESAREAN DELIVERY. J Y. Lu, C.C. Hartley, G.D. Wendel, Dept. Ob/Gyn, Univ TX Southwestern Medical School, Dallas, TX

OBJECTIVE: There is an association between previous cesarean delivery, abnormal placentation and increased morbidity at delivery requiring hysterectomy. We hypothesized that this association would extend to first and second trimester uterine evacuations.

DESIGN: A retrospective case-control study was undertaken from Jan 1, 1990 to Aug 15, 1999. Surgical logsbooks at Parkland Hospital were reviewed to identify all cases of first or second trimester uterine evacuation and subsequent emergent hysterectomies. The preceding and succeeding uterine evacuations were controls (2:1 match). Planned abortion-hysterectomies were excluded. We compared the groups using t-tests, χ² tests, and odds ratios (OR) where appropriate.

RESULTS: We identified 18 hysterectomy cases and 36 controls. All 18 cases, and 30 of 36 controls records were located and reviewed. All 18 hysterectomies were performed for post-abortion hemorrhage. Only one case was known to have a previa preoperatively. The rate of at least one previous cesarean delivery was 11 of 18 (61%) in the hysterectomy cases and 6 of 30 (20%) in the controls (P = 0.01; OR 6.29, 95% CI 1.44, 28.4). The difference in the rate of 2 or more prior cesarean deliveries was even more striking, 8 of 18 (44%) in hysterectomy cases and 1 of 30 among controls (P < 0.001; OR 23.2, 95% CI 2.42, 1063). Eight of 18 (44%) cases had abnormal placentation (3 previas, 4 accretas, and 1 percreta); 1 (6%) had invasive gestational trophoblastic tumor; 3 (17%) had uterine perforations; and 6 (33%) had no diagnoses identified. Seven of the 8 abnormal placentation (87%) occurred in the eleven prior cesarean deliveries (64%) compared with 1 of 7 (14%) without cesareans (P = 0.07).

CONCLUSIONS: We found a significant association with prior cesarean delivery and emergency hysterectomies for post-abortion hemorrhage. These findings confirm that the risk of hysterectomy is present in women with prior cesarean deliveries even at time of uterine evacuation. Further prospective studies are indicated to quantify the magnitude of risk.

476 DES-EXPOSED PRIMIGRAVID PATIENT: TO STITCH OR NOT TO STITCH: A FIFTEEN YEAR EXPERIENCE. J Ludmir, G Wong Depts of OB/GYN, Univ of Pennsylvania Health System, Philadelphia, and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston

OBJECTIVE: To determine if an expectant management protocol of delayed cerclage placement based on sonographic parameters, results in the same pregnancy outcome as prophylactic early cerclage prior to 1990.

STUDY DESIGN: Forty-eight singleton pregnancies in DES-exposed primigravid patients managed with prophylactic early cerclage prior to 1990 (Group A) were compared to a cohort of 126 patients after 1990, managed expectantly. Each patient had frequent cervical assessment by vaginal ultrasound and therapeutic cerclage, if sonographic cervical change was detected (Group B). Pregnancy outcome was analyzed by student T-test and Chi-square for statistical significance (p<0.05).

RESULTS: Thirty-four patients in Group B (72%) received a prophylactic cerclage at a mean gestational age of 19.3 weeks. The following table describes the pregnancy outcome for both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Gest age at delivery</th>
<th>Delivery &lt; 35 weeks</th>
<th>Perinatal deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>37</td>
<td>37 ±1.5 wks</td>
<td>1/48</td>
<td>0/48</td>
</tr>
<tr>
<td>B</td>
<td>36</td>
<td>36 ±1.8 wks</td>
<td>4/126</td>
<td>2/126</td>
</tr>
</tbody>
</table>

The two perinatal deaths in Group B occurred at 21 and 25 weeks secondary to premature rupture of membranes within a week of a normal cervical exam.

CONCLUSIONS: In our experience, an expectant management protocol utilizing cerclage only for sonographic cervical change, results in the same good pregnancy outcome, as the use of early cerclage for all DES-exposed primigravid patients irrespective of cervical appearance.

477 EPIDERMAL GROWTH FACTOR INHIBITS HYPOXIA-INDUCED APOPTOSIS IN HUMAN TERM CULTURED TROPHOBLASTS. R Levy, SD Smith*, G Leguzamion*, V Sadovsky, BM Nelson, Dept of Ob/Gyn, Washington University School of Medicine, St. Louis, MO

OBJECTIVE: Preeclampsia and fetal growth restriction (FGR) are associated with placental hypoperfusion and villous hypoxia. The villous response to these stimuli includes altered trophoblast differentiation and apoptosis via an unknown mechanism. We have demonstrated that hypoxia limits differentiation and induces apoptosis in cultured term human trophoblasts. Epidermal growth factor (EGF) promotes trophoblast differentiation and inhibits cytokine-induced apoptosis in cultured trophoblasts. We therefore tested the hypothesis that EGF blocks apoptosis induced by hypoxia in term cultured trophoblasts.

METHODS: Trophoblasts from placenta of term uncomplicated human pregnancies were cultured up to 48 hours in standard (pO₂=120mmHg) or hypoxic conditions (pO₂<15mmHg) in the presence or absence of EGF. Control we used transforming growth factor (TGF)-β which does not promote differentiation. Apoptosis was measured by DNA ladder, TUNEL, staining, and morphologic evaluation of hematoxylin-eosin staining. Media hCG level, a measure of cell differentiation was analyzed by ELA.

RESULTS: Trophoblasts cultured for 24 hours of hypoxia exhibited markedly enhanced apoptosis when compared to trophoblasts cultured in standard conditions. Addition of EGF to trophoblasts during hypoxia significantly diminished the level of apoptosis (p<0.01). Furthermore, addition of EGF 24 hours before exposure to hypoxia increased hCG production and reduced the level of apoptosis (p=0.02). In contrast, TGFβ had no effect on hCG production or on the level of apoptosis.

CONCLUSION: Exposure to hypoxia-induced apoptosis in term human trophoblasts in vitro EGF may play a role in vivo to protect trophoblasts from hypoxic injury in pregnancies complicated by preeclampsia and FGR.


OBJECTIVE: Many states now use vaginal birth after cesarean (VBAC) rates to "grade" providers. To calculate this, all women with a previous C-section (C/S) are included in the denominator; including those not eligible for a trial of labor (TOL). However, tertiary level hospitals and Maternal Fetal Medicine services (MFM) may have a disproportionate number of noncandidates. Therefore we evaluated the impact of patient population on VBAC rates.

STUDY DESIGN: Patient charts were reviewed for all women with a previous C/S delivering during 1998 (n=305). Noncandidates for TOL were defined as: prior classical or T-shaped incision, prior uterine surgery entering the cavity, placenta previa, previous uterine rupture, 3 or more previous C/S, active herpes lesion, macrosomia (>4200 grams) in a diabetic, non-vergent presentation other than frank breech, congenital anomalies, maternal medical conditions, previous cesarean section (CS), previous vaginal surgery, pelvic tumor obstructing outlet, abdominal cecreage, and very low birth weight infant in breech presentation. For the MFM, clinic and private services the percentage of noncandidates, the VBAC rate and adjusted VBAC rate were analyzed with chi-square or Fisher’s exact test.

RESULTS:

<table>
<thead>
<tr>
<th>Service</th>
<th>VBAC Rate</th>
<th>Noncandidate Rate</th>
<th>Adjusted VBAC Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>MFM</td>
<td>92 (24%)</td>
<td>26 (28%)</td>
<td>36%</td>
</tr>
<tr>
<td>Low risk clinic</td>
<td>121</td>
<td>68 (56%)</td>
<td>17 (14%)</td>
</tr>
<tr>
<td>Private</td>
<td>92</td>
<td>37 (49%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>Total Hospital</td>
<td>305</td>
<td>129 (42%)</td>
<td>46 (15%)</td>
</tr>
</tbody>
</table>

*Adjusted VBAC rate = Total Hospital rate - (Low risk clinic rate + Private rate)

CONCLUSIONS: To accurately compare VBAC rates among providers and institutions, accounting for patient risk status in the VBAC definition by eliminating noncandidates for TOL is essential.
THE EFFECT OF MAGNESIUM SULFATE ON THE BLEEDING TIME OF NORMAL GRAVIDAS: A RANDOMIZED, PLACEBO CONTROLLED TRIAL. J. Martinez-Poy, M. Hallak, T. Russell, K. Poole-Bryan, Y. Sorokin. Division of MFM, Dept. of Ob/Gyn, Hutzel Hospital/Wayne State University, Detroit, MI.

OBJECTIVE: The maternal administration of magnesium sulfate (MgSO4) has been anecdotally associated with increased blood loss at delivery. Our objective was to determine whether MgSO4 affected bleeding time in normal pregnant women.

STUDY DESIGN: 13 patients with singleton pregnancies > 30 weeks' gestation were randomized to receive either saline or MgSO4 in unlabeled IV bags. Patients received boluses of either saline or 6 g of MgSO4 in 20 minutes, followed by maintenance infusions of placebo or 2 g/hr of the medication for 3 hours. Blood was drawn at baseline, 1 and 3 hours of the infusions for determination of platelets, serum electrolytes and ionized calcium & magnesium. Bleeding time was measured by a modified method, at baseline, 1 and 3 hours of the infusion. Measurements were expressed as change from baseline values. Statistical analyses included Student's t-test and ANOVA.

RESULTS: Six patients were randomized to MgSO4 and 7 to saline. There were no differences attributable to demographics, platelet count, ionized calcium or electrolytes between the two groups. MgSO4 levels were significantly elevated at 1 and 3 hours in the study group only. The bleeding time was clinically prolonged (> 9.5 min) at 3 hours in 4 of 6 (67%) patients in the MgSO4 group as compared to 1 of 7 (14%) in the saline group (p=0.0001). CONCLUSIONS: Short-term administration of MgSO4 is associated with clinically significant prolongation in bleeding time. These results are consistent with our previously reported in vitro MgSO4-related decrease in platelet aggregation and release.

RECEIVER OPERATING CHARACTERISTIC (ROC) CURVE ANALYSIS OF AMNIOTIC FLUID INDEX (AFI) FOR PREDICTION OF Oligohydramnios or MECONIUM in PROLONGED PREGNANCIES. C. O'Reilly-Green, Dept. of Ob/Gyn, Montefiore Medical Center, Bronx, NY, and Lenox Hill Hospital, New York, NY.

OBJECTIVE: To evaluate decreasing AFI as a predictor of oligohydramnios or meconium at rupture of membranes in patients with prolonged pregnancy, using ROC curve analysis.

STUDY DESIGN: AFI was evaluated within 4 days of admission in 643 patients. Fluid at rupture of membranes was classified as normal, oligohydramnios, or meconium. ROC curves for AFI as a predictor of outcome were constructed.

RESULTS:

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>Area SE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligohydramnios</td>
<td>0.84</td>
<td>0.021</td>
</tr>
<tr>
<td>Thick Meconium</td>
<td>0.55</td>
<td>0.06</td>
</tr>
<tr>
<td>Thick/Moderate Meconium</td>
<td>0.46</td>
<td>0.051</td>
</tr>
</tbody>
</table>

Area = area under the ROC curve; SE = standard error; p value = p value for Area in comparison with an area of 0.5 (i.e., the area under the ROC curve for a useless test). The inflection point on the ROC curve for predicting oligohydramnios occurred at an AFI ≤ 7.8. Using this value, the sensitivity was 81%, the specificity was 73%, and the relative risk for oligohydramnios was 7.85 (95% confidence intervals 4.84, 12.75; p < 0.00001 by Yates correction of the Mantel-Haenszel chi-square test).

CONCLUSION: AFI is a useful test for predicting oligohydramnios, but not meconium, at rupture of membranes, in patients with prolonged pregnancy. While meconium is known to be associated with poor perinatal outcome, the finding of oligohydramnios alone may be physiologic in prolonged pregnancies. The optimal AFI for predicting oligohydramnios by ROC analysis is 7.5. This value may be used in designing a prospective randomized trial of the morbidity associated with using AFI as an indication for delivery in prolonged pregnancy.


OBJECTIVE: The absence of fetal pulmonary maturity in patients with preterm premature rupture of the membranes (pPROM) at 32-34 weeks is often considered as an indication for conservative management. The purpose of this study was to examine the clinical utility of biochemical pulmonary maturity assessment in patients with pPROM between 32st and 34th weeks gestation.

STUDY DESIGN: We conducted a retrospective chart review of all cases of pPROM at 32st to 34th weeks with biochemical fetal pulmonary maturity testing from 1995-1998. Amniotic fluid was obtained by either amniocentesis or vaginal pool collection. The presence of phosphatidylglycerol (PG) or an FLM > 54 mg/g was considered mature. Patients with medical disorders (diabetes, hypertension, preeclampsia), multiple gestations, fetal anomalies, or evidence of intra-amniotic infection were excluded. Survivors at < 72 hours of life, need for mechanical ventilation or supplemental oxygen, NICU days, and total hospital days were compared between neonates with mature and immature biochemical indices.

RESULTS: There were no cases of neonatal death, intraventricular hemorrhage or necrotizing enterocolitis. There were no differences in seizure rates or days in the NICU.

COMPARISON OF EXTERNAL CEPHALIC VERSION IN MULTIPAROUS WOMEN WITH AND WITHOUT PRIOR HISTORY OF CESAREAN SECTION. R. Charn, M. Frank, Dept. OB/GYN, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA.

OBJECTIVE: To compare the success rate, mode of delivery, and complications of external cephalic version (ECV) in multiparous women with and without previous cesarean section.

STUDY DESIGN: Data was collected retrospectively on all multiparous women undergoing ECV at our medical center between January 1, 1985 and April 30, 1990. Data included maternal age, parity, gestational age at time of ECV, description of prior delivery route(s), success or failure of the ECV, mode of delivery, and procedure related complications such as prolonged observation, immediate cesarean section, uterine rupture, or fetal demise. Comparisons were made using Chi-square analysis with significance set at p<0.05.

RESULTS: There were 672 multiparous women who underwent ECV during the study period, of which 132 had a prior cesarean, and 540 had no history of cesarean. There was no significant difference in maternal age, parity, and gestational age between the two groups. ECV was more likely to be successful in women with a prior history of cesarean section (73% vs 62%, p<0.022), but these women had a decreased rate of delivering vaginally (46% vs 56%, p=0.041). There was no significant difference in the complication rate between the two groups (3.8% vs 3.3%, p=NS). One intrauterine fetal demise occurred before the onset of labor in a patient without history of prior cesarean section. No clinically evident uterine rupture occurred.

CONCLUSION: ECV is a reasonable option for patients with a history of cesarean section.
483 AMNIOTIC FLUID INDEX IN THE UNCOMPLICATED TERM PREGNANCY: PREDICTION OF OUTCOME. M Rainford1, R Adams2, A Scialli1, A Giuliano, C F Spong, Dept Obst/Gyn, Georgetown University Med Ctr, SDMP, NCHD, NIH, Washington DC and Bethesda, MD.

**OBJECTIVE:** Studies of high-risk pregnancies have demonstrated an association between oligohydramnios and pregnancy outcome. The purpose of this study was to identify in the term, uncomplicated pregnancy if there is any difference in outcome in patients with a normal amniotic fluid index (AFI) and those with an AFI <5 cm.

**STUDY DESIGN:** Patients with singleton, term (≥37 wks), cephalic presentations with reactive non-stress tests and an AFI within 4 days of delivery between 1/94 and 9/98 were studied. Exclusion criteria were: maternal/fetal complications (e.g. diabetes, toxemia, growth restriction, PROM) or unavailable outcome information. The primary outcome measure was operative delivery (cesarean section or operative vaginal delivery) for non-reassuring fetal heart rate tracing. Statistical analysis included Fisher’s exact test (categorical data) and one way ANOVA (continuous data), with P<0.05 considered significant.

**RESULTS:** 232 women met inclusion criteria, of these 44 (19%) had AFI≤5 cm. There was no difference in the operative delivery rate for non-reassuring fetal heart rate tracing between those with normal AFI (39 [21%]) and AFI≤5 [5111%], p=0.65. In addition, there were no differences in NICU admissions or 5 min Apgar scores ≥7. The incidence rate was significantly lower in patients with normal AFI [96, 51% vs 42, 98%], p<0.001. The incidence of meconium stained amniotic fluid was higher with normal AFI (55 [35%] vs 7, 16%), p=0.01.

**CONCLUSIONS:** In the uncomplicated patient at term, an AFI ≤5 cm increase the incidence of induction but does not appear to affect the rate of operative delivery for abnormal fetal heart rate tracings. This sample size excluded a 2.9 fold difference for the primary outcome variable between the two groups with 80% power.

484 MATERNAL AND FETAL OUTCOMES IN SPONTANEOUS AND FERTILITY THERAPY-DERIVED MULTIPLE PREGNANCIES. E.P. Leone, E Fernaz, AM Macnab, A Bulfonix, AM Sison, G. Ragusa, G. Pardi, Department of Obst/Gyn at DMCO San Paolo, University of Milan, Italy.

**OBJECTIVE:** To compare maternal and fetal outcomes in dichorionic spontaneous twin pregnancies and fertility therapy-derived twin pregnancies.

**STUDY DESIGN:** The population in this retrospective study included 186 pregnant patients with twin pregnancies (372 fetuses) greater than 20 weeks of gestation managed in our tertiary care center from January 1991 and December 1996 using our computerized obstetrical performance, and the presence of acquired or inherited thrombophilia. There was no association of the individual markers of thrombophilia with recurrent pregnancy loss.

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gest age at delivery (wks)</td>
<td>36 (34-37)</td>
<td>34,5±3.3</td>
<td>34±5.6</td>
</tr>
<tr>
<td>Fetal death</td>
<td>2%</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Cerebral section</td>
<td>61%*</td>
<td>91%</td>
<td>99%</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>2284±660</td>
<td>2113±702</td>
<td>2094±675</td>
</tr>
<tr>
<td>Weight discordancy (&gt;20%)</td>
<td>30 (22%)</td>
<td>7 (22%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Apgar score &lt;7 at 5′</td>
<td>13%</td>
<td>17%</td>
<td>16%</td>
</tr>
<tr>
<td>Perinatal mortality rate</td>
<td>6%</td>
<td>8%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** After 20 weeks of gestation, maternal and fetal outcome of fertility therapy-derived and reduced twin pregnancies were not significantly different compared to spontaneous dichorionic twin gestations, except for doctors attitude toward the route of delivery.

485 PREVALENCE OF INHERITED AND ACQUIRED THROMBOPHILIA IN PATIENTS WITH RECURRENT AND ISOLATED FIRST TRIMESTER LOSS. H Itoyo, T. E. D. Abdelhak, M. P. B. A. Rebarber, C J Lockwood, Dept of OB/GYN NYU Medical Center.

**OBJECTIVE:** Our null hypothesis is that among women with recurrent first trimester losses the prevalence of thrombophilia is not increased compared to women with isolated first trimester losses.

**STUDY DESIGN** Historical cohort study of 93 consecutive women with first trimester losses and known fetal karyotype. Charts were reviewed for past obstetrical performance, and the presence of acquired or inherited thrombophilia, including: anticardiolipin antibody, lupus anticoagulant, factor V leiden mutation, protein C and protein S deficiencies, hyperhomocysteinemia and antithrombin III deficiency. Data were compared by student t test, x² analysis and Fischer exact test where appropriate. Power analysis required a sample size of 27 patients in each arm to detect a 30% difference in the prevalence at the p<0.05 level.

**RESULTS:** We report an unexpectedly high prevalence of thrombophilia in this cohort (32%) overall. There was no increase in the prevalence of thrombophilia in women with recurrent compared to isolated first trimester losses (33% vs. 30%), or compared to unexplained losses (25% vs. 29%). There was no association of the individual markers of thrombophilia with recurrent pregnancy loss.

**CONCLUSIONS:** Women referred to our high risk obstetrical practice for recurrent or isolated first trimester loss have an alarmingly high background prevalence of thrombophilia (32% of the tested cohort). This is a significant increase over previously reported values. While we were unable to reject the null hypothesis, further studies are being conducted to reduce the probability of type II error.

486 NUCHAL CORD ENCIRCLEMENTS AND RISK OF STILLBIRTH. J.C. Carr, W. Rayburn, Dept Obstet/Gynecol, Univ. Oklahoma, Oklahoma City, OK.

**OBJECTIVE:** To determine any association between stillbirth and single or multiple nuchal cord encirclements and stillbirth.

**STUDY DESIGN:** Data were retrieved from consecutive deliveries at our institution between January 1991 and December 1996 using our computerized perinatal database. Data included the presence or absence of a nuchal cord encirclement and the number of encirclements. Chi-square and multiple stepwise logistic regression were used for analysis.

**RESULTS:** A stillbirth occurred in 98 (0.7%) of the 15,757 deliveries. A single nuchal cord encirclement was found in 3,256 (23.6%) deliveries, while multiple encirclements were observed in 504 (3.7%). Stillbirths were not more common in the presence of a single or multiple nuchal cord entencirclement (p=0.86, chi-square). This risk did not increase if there was a double or triple encirclement. Multiple stepwise logistic regression showed an adjusted odds ratio of 1.03 (95% CI 0.64-1.60) for stillbirth if a nuchal cord was present after controlling for other factors associated with stillbirth.

**CONCLUSION:** The finding of a single or multiple nuchal cord encirclement is insufficient evidence to explain a stillbirth. Further evaluation, such as placental histologic examination, is suggested to adequately counsel the parents.
487 INTRAVENOUS MAGNESIUM AS A TREATMENT OF MIGRAINE IN PREGNANCY. M C Wilson, M C Williams, W F O Brien. Deps. of Neurology, Obstetrics, and Gynecology, University of South Florida, Tampa, FL.

OBJECTIVE: To determine the efficacy of intravenous magnesium sulfate in the treatment of migraine during pregnancy.

MATERIALS AND METHODS: Ten pregnant women presenting with migraine headache were classified according to the International Headache Society classification (IHS). The referral source included patients from the obstetrics ward and the emergency room over a period of six months. All of them received intravenous hydration and one gram of magnesium sulfate (MgSO4) in a 10% solution over five minutes. Headache intensity was assessed before and after infusion of the MgSO4, using a numeric analog scale 1 to 10 (NAS). Mann-Whitney test of ranks was used to evaluate the pain scores, with p<0.05 considered significant.

RESULTS: Patients had a baseline intensity headache of 7.9 using the NAS. Significant reductions in pain scores were observed after MgSO4 infusion (p<0.01). Total pain relief was reported by eight (80%) patients within 20 to 30 minutes. Two patients (20%) reported no significant improvement and received additional treatment with intravenous prochlorperazine. All patients reported resolution of migraine associated nausea, photophobia and phonophobia upon resolution of the headache. Minimal facial flushing and abdominal cramping occurred in two (20%) of the patients receiving magnesium.

CONCLUSION: It appears that intravenous magnesium sulfate may be an effective and safe treatment of migraine during pregnancy. A larger prospective study is planned to corroborate this preliminary finding.

488 MATERNAL METHADONE DOSE AND NEONATAL WITHDRAWAL. V Bergella, P Lam, J Cherpes, MK Hill, R Kaltenbach, RJ Wagner, Div of MFM, Dept of Obstetrics and Gynecology, and Family Center, Dept of Pediatrics, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: To determine if high (≥90mg) maternal methadone doses at delivery are correlated with more severe neonatal withdrawal compared to lower doses.

STUDY DESIGN: Retrospective review of all maternal and corresponding neonatal records of opioid-addicted pregnancies followed at our institution between 9/96 and 12/97. These pregnancies were followed by a multidisciplinary program, with admission to the hospital early in pregnancy for methadone stabilization starting at 20mg, with dose increases during pregnancy as needed when withdrawal symptoms occur. Methadone dosing was recorded daily, and urine drug screens (UDS) done at least weekly. Neonatal abstinence scores (NAS) and length of neonatal withdrawal treatment (NWT) were recorded. T-test for continuous variables and chi square for categorical variables were used for statistical analysis.

RESULTS: Fifty-one pregnancies were identified, with a mean dose of methadone before delivery of 83.4mg (range 50-165mg).

Methadone dose, UDS positive for opiates, Mean highest NAS, Mean NWT duration (in mg (ng))

Mean NWT duration (days)

<80 (25) 10 (38%) 12.1 19 (75%) 15.8
80-260 (25) 9 (36%) 12.2 20.8 (80%) 19.2
P value 0.9 6.9 20 0.4

CONCLUSIONS: High methadone doses often required by addicted pregnant women may not significantly worsen neonatal withdrawal compared to lower doses.

489 SALVARY ESTRIOL EXPRESSIN IN TWIN GESTATION. Hayashz, R, McGregor JA, Hansen L, Hastings C, Engel L, Stouch B, University of Michigan, Ann Arbor, MI, University of Colorado School of Medicine, Denver Health Medical Center, Denver CO, Biex, Dublin CA.

OBJECTIVE: Characterize salivary estriol (sE3) physiology in mothers with twin gestation from mid pregnancy until birth in order to assess possible difference vs. singleton pregnancies for baseline sE3 levels and timing of sE3 surge.

METHOD: We prospectively measured sE3 values at one to two week intervals from 22 weeks gestational age until birth. Unconjugated sE3 was assayed using a sensitive and specific enzyme-linked immunoassay (Biex, Dublin, CA). Subjects with twin gestations (n=34) submitted weekly or biweekly mailed samples (n=290) which were analyzed using descriptive statistics and student's t test (alpha = 0.05).

RESULTS: Each subject's maximum sE3 was calculated on a patient-specific basis for <4 weeks and 24 weeks prior to delivery. The arithmetic average (±SD) of sE3 levels ≥4 weeks prior to delivery was 2.9 ± 1.5 ng/ml. Correspondingly, the arithmetic average ±SD collected 24 weeks preceding birth was 2.4 ± 0.9 ng/ml. On a paired basis, the average intra-patient change (surge) <4 weeks prior to delivery was +0.49 ± 1.5 ng/ml (p = 0.03, paired t test). There was an average difference of a 21% increase in sE3 observed 24 weeks prior to birth. This analysis included subjects treated with beta-blockers, which had a suppressive effect on sE3.

CONCLUSION: sE3 values "surges" within 4 weeks of parturition in twin gestations, similar to findings in women with singleton pregnancies. Correspondingly, baseline "pre-surge" sE3 levels were not different from singleton pregnancies in this prospective study of 34 twin gestations. These observations suggest that 1) the mechanism of sE3 fetal-placental transfer/ placental endocrine signaling of parturition in twins is similar to singleton pregnancy and 2) serial sE3 determinations may inform practitioners and patients regarding impending parturition in twin gestation.

490 A RANDOMIZED PROSPECTIVE TRIAL OF TWO TYPES OF INTRAUTERINE PRESSURE CATHETERS AND THE RATE OF EXTRA-OVULAR PLACEMENT. A Sciacalone, A Bisce, A Dohl, M Pollock, B Mas, J Mantey, P Shlossman, W Mulla, GHC Colmorgen, Divs. of MFM of the Christiana Hospital, Newark, DE, and the Johns Hopkins Hospital, Baltimore, MD.

OBJECTIVE: Previous reports have noted an association between the occurrence of placental abruption and transfuter tipping. (TT) IUPC placement. We hypothesized that extra-ovular (between the amniotic membranes and uterus) catheter placement was the cause of placental separation. Our purpose was to determine if the newer air coupled sensor tip (AC) IUPCs have the same rate of extra-ovular placement as the TTUUPC, which are shorter and have larger tips.

STUDY DESIGN: A randomized prospective trial comparing a TTUUPC (Intraplus™, Utah Medical Products, Midvale, UT) to an ACIUPC (Koala™, Clinical Innovations, Murray, UT) was conducted from October of 1998 to August of 1999. Women were eligible if their attending physician decided to place an IUPC. Women with vaginal bleeding, chorioamnionitis, or known abruption were excluded. Our primary outcome variable was extra-ovular placement. The IUPC was left in place at the time of cesarean delivery (CD) and the position was documented. Women who did not have a CD were not included in the analysis of extra-ovular placement. Secondary outcome variables included IUPC associated placental abruption and difficulty in IUPC placement. Demographic characteristics and potential confounding variables were also recorded. Student's t-test, Chi-square analysis, Fisher's exact test, and a Kruskal-Wallis test were used where appropriate. A p value of < 0.05 was considered significant.

RESULTS: A total of 206 patients were entered into the trial. Twelve were excluded due to the removal of the TTUUPC before CD, which left 194 evaluable patients. Of the 194 patients (36 (36.9%) received a CD, with 22 in the ACIUPC group and 38 in the TTUUPC group. There was no significant difference in maternal age, gestational age, gravidity, duration of rupture of membranes, birthweight, Apgar scores, cord pH, cocaine use, tobacco use, Prinoc use, or catheter removal due to poor function. The TTUUPC was significantly more likely to be extra-ovular then the ACIUPC (0% vs. 21%, p < 0.02). Two patients with extra-ovular placement of the TTUUPC were noted to have a placental separation. TTUUPC was significantly more likely to be rated as difficult to place by the inserting physician (p < 0.001).

CONCLUSIONS: We found the TTUUPC was significantly more likely to be placed extra-ovular and to be more difficult to place. Two patients had a non-clinical placental separation from the TTUUPC that was apparent at documentation of position.
491 INTRAPARTUM INFLUENCES ON CAESAREAN DELIVERY IN MULTIPLE GESTATIONS. Keith Williams, France Galeraux, University of British Columbia, Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, B.C. Women’s Hospital, 650 Oak Street, Vancouver, B.C. Canada H8W 1W5

OBJECTIVE: To evaluate in a group of twin gestations eligible for vaginal delivery which intrapartum factors determine the method of delivery.

STUDY DESIGN: Over a 5 year period, all consecutive vaginal and/or caesarean deliveries were reviewed. The impact of the following intrapartum factors on the incidence of c/section was assessed: 1) presentation of the 2nd twin: vertex vs breech vs other, 2) experience of the obstetrician: ≤ 10 yrs vs > 10 yrs in practice, 3) difference in fetal weight between twin A and twin B ≤ ≤ 25% difference vs > 25% difference, 4) multiparas: nulliparas vs primiparas, 5) incidence of epidual usage, 6) induction vs spontaneous labor. The chi-square statistic was used to compare differences between the incidences of c/section between the groups.

RESULTS: The total incidence of c/section was 245/906 (27%). The incidence of caesarean section associated with various intrapartum factors were: primipara 153/460 (33%) vs multipara 92/146 (62%) (p < .008). Physician experience ≤ 10 yrs 367/1246 (29%) vs > 10 yrs 155/530 (29%) (p = .292). Presentation: vertex 150/540 (27%) vs breech 84/313 (27%) vs other 31/53 (58%) (p < .001). Twins admitted for spontaneous labor 44/244 (18%) were induced 196/662 (30%) (p < .001). Epidual yes 140/678 (21%) versus no epidual 155/530 (29%) (p < .001). Twin B ≤ 25% twin A’s weight, 208/806 (26%) vs Twin B ≥ 25%, Twin A’s weight, 37/109 (34%) (p < .001).

CONCLUSION: Twin gestations that were primiparas, induced or with a ≥ 25% discrepancy in the weight of twin B, were associated with a significantly increased c/section rate. Increased physician experience did not decrease the operative delivery rate. Non-vertex presentations of the 2nd twin other than breech, were associated with an increased in the c/section rate. The liberal use of epidual analgesia may improve the success rate in patients with twin gestations considered as good candidates for vaginal delivery.


OBJECTIVE: To determine if removal of cervical cerclage following preterm premature rupture of the membranes (PPROM) prior to 35 weeks’ gestation influences perinatal outcome. The only other study to address this issue (Ludmir et al, Obstet Gynecol, 1994 [n=27]) suggested a 7-fold increase in perinatal mortality with cerclage retention.

STUDY DESIGN: All gestations, ≥ 24 weeks’ gestation with non-pregnant membranes at gestational age ≥ 24.0 weeks gestation who presented to our institution between 24.0 and 33.9 weeks’ gestation were included. The impact of the following intrapartum factors on the incidence of c/section was assessed: 1) presentation of the 2nd twin: vertex vs breech vs other, 2) experience of the obstetrician: ≤ 10 yrs vs > 10 yrs in practice, 3) difference in fetal weight between twin A and twin B ≤ ≤ 25% difference vs > 25% difference, 4) multiparas: nulliparas vs primiparas, 5) incidence of epidual usage, 6) induction vs spontaneous labor. The chi-square statistic was used to compare differences between the incidences of c/section between the groups.

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493 CAN PLACENTAL ABORTION BE PREDICTED? Peter Buehmann, Christine Sticht, Hans-Joachim Friedrich, Dept. of Obstetrics and Gynecology, Wayne State University, Detroit, MI; Institute of Medical Statistics and Biomathematics, Medical University Luebeck, Schleswig-Holstein, Germany

OBJECTIVE: To identify correlates of placental abortion (PA) and to develop an analytic model to predict PA in singleton pregnancies.

STUDY DESIGN: 170 singleton birth records from 1991 to 1996 contained in the Schleswig-Holstein perinatal data base were analyzed. To determine their association with PA, 52 recognized obstetrical risk factors were subjected to univariate analysis employing contingency tables with χ²-testing, p-values, odds ratios (OR), and confidence intervals (CI) were calculated. Correlates of PA then underwent stepwise forward binary logistic regression (LR). A constant B0, coefficients B1, ..., Bp, OR, and CI for individual correlates were calculated using the statistical package SPSS.

RESULTS: PA occurred in 874/170,258 (0.5 %). Multiparous women (MP) had a slightly elevated risk as compared to primips (PP) (OR: 1.15, CI: 1.008 - 1.31). Of the 52 risk factors, 31 proved to be correlates of PA, 36 for PP, and 25 for MP. 10 correlates with the according coefficients B for PP, and 13 for MP, respectively, as well as constants B0 for the PP (z = 2.25) and the MP group (z = 4.25) entered from the LR, with 7 correlates shared by PP and MP as displayed in the table.

494 OUTPATIENT USE OF INTRACERVICAL PROSTAGLANDIN GEL IS A SAFE AND EFFECTIVE METHOD OF LABOR INDUCTION. RR Viscuso, S Grubbth, B Pfyfterich, K Baranger, Maternal Fetal Care, PC, Stamford, CT

OBJECTIVES: To determine the safety and efficacy of intracervical prostaglandin gel (PGG) for the outpatient reduction of labor.

STUDY DESIGN: During the study period, 198 outpatients underwent intracervical PGG-placement for labor induction. Post-PGG insertion, all patients had a BPP 28+30 and AF 35, and a Bishop’s score (BS) was performed. Following PGG insertion, FHR monitoring was performed for 90 to 120 minutes and a second BS was determined. If post-PG BS >10, the patient was sent to L&D, otherwise the patient was discharged to home. If delivery did not occur within 24 hours, reactivation was performed. Outcome data were obtained by hospital chart review. Perinatal outcome was compared for patients delivering after a single gel (Gep 1) and after 2 or more applications (Gep II), using Student’s T, and Chi square tests of analysis, where appropriate.

RESULTS: Ninety percent of patients (178/198) delivered after one PGG, 19 after two, and only 1 required 3 gel applications. There was no significant difference between Gep I and Gep II with respect to maternal age, parity, pre-PGG BS (5.6 ± 5.1), GA at delivery (39 2 ± 3 9 weeks), or BW (3503 ± 566 gms). Gep I had a mean time to delivery (TDD) of 8 hrs and 29 minutes. Statistically significant differences between Gep I and Gep II were noted in TDD (p<0.001) and rate of cesarean delivery (13% vs 55%, p<0.009), 4 complications (2%) occurred post-PGG: 3 uterine hyperstimulation (all resolved with 0.5mg Terbutaline) and 1 maternal hypersensitivity reaction which included DIC. There were no newborn complications.

CONCLUSIONS: Our data suggest that outpatient, intracervical administration of PGG is a safe and effective method of labor induction when performed in a carefully selected population with appropriate monitoring and supervision. If validated by further studies, this method would provide a more cost-effective alternative to in-patient induction without maternal or fetal compromise.
LEAVING THE HOSPITAL "AGAINST MEDICAL ADVICE": OBSTETRIC OUTCOMES. J Shimmy, F Ammon, W Holcomb, D Mostello, B Schwartz, H Wrin, Div Maternal-Fetal Medicine, Dept Ob/Gyn, St Louis University School of Medicine, St Louis, MO.

OBJECTIVE: To describe the characteristics of women who leave the hospital against medical advice (AMA) and their pregnancy outcomes.

STUDY DESIGN: Records of all women discharged from our obstetrical units from April 1995 through May 1998 with the status of "Discharge Against Medical Advice" were analyzed. Results were compared against concurrent State of Missouri birth data using Chi-square analysis.

RESULTS: 82 AMA discharges were reviewed. A total of 13,665 patients were delivered at our center during this period yielding an incidence of AMA discharge status of 0.6%. The characteristics of AMA population included mean maternal age = 24.7 yr, 6.0 (24.4% were >19 yr, 9% were >35 yr), African-American = 57%, unemployed = 85.4%, previously discharged AMA = 25%, nulliparous = 26%, primigravida = 14%, prior preterm birth = 34%, twin gestation = 6%. Mean gestational age on admission was 30.0wks±8.0wks. (11± wk) Comparing to the state-wide pregnancy population, AMA patients had significantly higher proportions of unmarried status (85.4%*), poor socioeconomic status (32.7%*), utilization of public aid programs including WIC (73% vs 40.2%*), food stamps (67.7% vs 19.1%*), and Medicaid insurance (86.6% vs 42.1%*). AMA patients were more likely to be undereducated; 63% had<12 yr of education vs 19.1% statewide, to have late prenatal care (67.5% vs 15.9%*), no prenatal care (16% vs 1%*), maternal smoking (53.7% vs 19.5%*). Of 75 newborns, 13% were <1000gm, 23% were <2500gm, 7% were >4000gm. Cesarean Section was performed in 27.1% (*=p<0.001)

CONCLUSIONS: The rates of prematurity and low birth weight are exceptionally high in this group of patients. The profile of obstetric patients leaving the hospital AMA is characterized by poor prenatal care, out-of-wedlock pregnancy, lack of high school education, and tobacco abuse.

CORTICOSTEROIDS IN TRIPLET GESTATIONS. JM Mastrobattista, ER Pichipirri*, MC Day*, LC Glastrep, Dept Ob/GYN, UT-Houston Medical School, Houston, TX.

OBJECTIVE: To assess the effects of antenatal maternal corticosteroid use in triplet pregnancies and to evaluate pregnancy outcomes.

STUDY DESIGN: We performed a review of 33 triplet pregnancies who delivered at our institution over the past 13 years. The women and their newborns were divided into two groups - those who received antenatal steroids (BMZ) for fetal maturation and those who did not. Primary outcome variables included maternal infection, preeclampsia, fetal growth disturbances, and birth weight. Umbilical cord artery pHs for triplets A, B, and C were also evaluated.

RESULTS: Thirty-three triplet gestations and 99 newborns were included for analysis. There were 15 (45%) mothers who received and 18 (55%) mothers who did not receive antenatal corticosteroids. The mean GA at delivery was 31.6 weeks (+3.6) and the mean BW was 1589 g (+501) at delivery. Paired T tests were used for statistical analysis.

CONCLUSIONS: There was no difference in perinatal outcomes between the 2 groups. If all patients with breech presentation had been allowed to enter labor spontaneously without an attempted ECV, the total cost can be assumed to have been the same cost of delivery as for those patients who had a failed ECV attempt ($3,795/patient) per patient over an approach routinely using ECV.

CONCLUSIONS: A previous report by our group showed that ECV was more cost beneficial than electively scheduled Cesarean Section. The data presented now demonstrate that routine attempts at ECV for breech presentation are not cost effective. Significant savings would accrue with a policy of allowing the patient to go into labor spontaneously without routine ECV.

COST EFFECTIVENESS OF ROUTINE EXTERNAL VERSION FOR BREECH PRESENTATION. LB Curet, CJ Gilsen, F Christensen, Dept of OB/GYN, Univ of New Mexico, Albuquerque, NM.

OBJECTIVE: Determine if routinely attempting external cephalic version (ECV) at 37 weeks gestation for breech presentation reduces the overall cost of delivery.

STUDY DESIGN: 120 patients underwent an ECV attempt at 37 weeks gestation as determined by LMP and early ultrasound. Success was achieved if the presentation was converted to vertex. End points analyzed included success rate, presentation at delivery, route of delivery, cost of the ECV, cost of the delivery, and total costs. All patients were allowed to go into labor spontaneously. Paired T tests were used for statistical analysis.

RESULTS:

<table>
<thead>
<tr>
<th>Successful</th>
<th>Failure</th>
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<tr>
<td>Number</td>
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</tr>
<tr>
<td>Presentation at Delivery</td>
<td></td>
</tr>
<tr>
<td>Breech</td>
<td>54 (45%)</td>
</tr>
<tr>
<td>Vertex</td>
<td>48 (40%)</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>36 (67%)</td>
</tr>
<tr>
<td>Cost of Version</td>
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<tr>
<td>Cost of Delivery</td>
<td>$8,779</td>
</tr>
<tr>
<td>Total Cost/pt</td>
<td>$9,302</td>
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<table>
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<tr>
<th>Successful</th>
<th>Failure</th>
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<tbody>
<tr>
<td>Number</td>
<td></td>
</tr>
<tr>
<td>Presentation at Delivery</td>
<td></td>
</tr>
<tr>
<td>Breech</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Vertex</td>
<td>66 (100%)</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>19 (20.4%)</td>
</tr>
<tr>
<td>Cost of Version</td>
<td>$525/pt</td>
</tr>
<tr>
<td>Cost of Delivery</td>
<td>$5,507/pt</td>
</tr>
<tr>
<td>Total Cost/pt</td>
<td>$6,080 (&lt;p&lt;0.05)</td>
</tr>
</tbody>
</table>

There was no difference in perinatal outcomes between the 2 groups. If all patients with breech presentation, had been allowed to enter labor spontaneously without an attempted ECV, the total cost can be assumed to have been the same cost of delivery as for those patients who had a failed ECV attempt ($3,795/patient). This approach would have resulted in savings of $3,795 per patient over an approach routinely using ECV.

CONCLUSIONS: A previous report by our group showed that ECV was more cost beneficial than electively scheduled Cesarean Section. The data presented now demonstrate that routine attempts at ECV for breech presentation are not cost effective. Significant savings would accrue with a policy of allowing the patient to go into labor spontaneously without routine ECV.

RELATIONSHIP OF SOCIAL, MEDICAL AND SUBSTANCE USE CHARACTERISTICS TO GESTATIONAL AGE IN POLYSUBSTANCE USING WOMEN. PL Willbrown, V Dornati, R Yebo, LB Curet, Dept of OB/GYN, Univ of New Mexico, Albuquerque, NM.

OBJECTIVE: The purpose of this study was to determine the relative importance of medical, social and substance use characteristics on gestational age. We hypothesize that variables from each domain will predict gestational age at birth.

STUDY DESIGN: Charts of women and children participating in a comprehensive perinatal program for pregnant substance abusers were reviewed to collect comprehensive information regarding medical, social and substance use variables. Because of the moderating effect of gestational age on other pregnancy outcome variables, it was selected as the focus of this report.

RESULTS: Significant univariate reductions in gestational age were associated with the percent of cocaine positive urine toxicologies (p<0005), substance use by other members of the woman’s family (p<002) and a maternal history of rape (p<0005). Relative to women using other substances, quantity of drinks per drinking day (p<010) and frequency (p=030) of drinking were associated with longer gestational age. Considering substance use in combination with lifestyle and treatment variables in a hierarchical, stepwise, multiple regression, a history of rape (p=0005), substance use by family members (p=005), and number of drinks per drinking day (p<024) continued to predict gestational age, accounting for 19% of the variability in gestational age.

CONCLUSIONS: Social and substance use characteristics predict reductions in gestational age in poly-substance using women, while medical characteristics (infections, weight gain, prenatal care) did not demonstrate a direct relationship with gestational age in this sample of poly-substance users. Furthermore, independent relationships between rape, use by members of the woman’s family, drinks per drinking day and gestational age were found. These results indicate that social and substance abuse characteristics are more important modulators of gestational age at birth than medical factors.
DOES THE INTERBIRTH INTERVAL AFFECT THE RISK FOR UTERINE RUPTURE? T. Shapp, C. Zelop, J. Repke, A. Cohen, E. Lieberman, Dept. of Ob/Gyn, Massachusetts General Hospital, Brigham and Women’s Hospital, Boston, MA.

OBJECTIVE: We sought to evaluate whether a short interpregnancy interval was associated with an increased risk of uterine rupture during a trial of labor after prior Cesarean delivery.

STUDY DESIGN: The medical records over a 12-year period, 7/84-6/96, of all women undergoing a trial of labor after a Cesarean delivery were reviewed. The current analysis was limited to women with only one prior Cesarean delivery, with no prior vaginal deliveries, delivering a term singleton, and whose medical records included the month and year of the prior delivery. The time in months between the prior Cesarean and the index trial of labor was determined, and the patients were divided into subgroups according to length of time between deliveries; these subgroups were compared with respect to symptomatic uterine rupture.

RESULTS: Two thousand four hundred nine women underwent a trial of labor after one prior Cesarean delivery and had adequate history available from the medical records. There were 29 uterine ruptures (1.2%) in the population. For an interdelivery interval of ≤18 months, the uterine rupture rate was 2.25% (7/311); for 19-36 months, the rupture rate was 1.07% (12/1,119); and for >36 months, the rupture rate was 1.62% (16/979). A multiple logistic regression was used to assess the risk for uterine rupture with an interdelivery interval of ≤18 months as compared with those >18 months, while controlling for oxytocin use, public assistance, length of labor, and maternal age. In this model, those women with an interdelivery interval of ≤18 months had an odds ratio of 2.95 (95% CI: 1.21, 7.17) for a symptomatic uterine rupture.

CONCLUSION: An interdelivery interval of ≤18 months is associated with an increased risk for uterine rupture during a trial of labor after Cesarean.

THE RISK FOR UTERINE RUPTURE WITH RESPECT TO THE DURATION OF A TRIAL OF LABOR AFTER CESAREAN? T. Shapp, C. Zelop, J. Repke, A. Cohen, E. Lieberman, Dept. of Ob/Gyn, Massachusetts General Hospital, Brigham and Women’s Hospital, Boston, MA.

OBJECTIVE: To determine whether the duration of labor is associated with an increased risk of uterine rupture during a trial of labor after prior Cesarean delivery.

STUDY DESIGN: The medical records of every gravida with a history of only one prior Cesarean section, delivering at term of a singleton gestation, attempting a trial of labor during a twelve-year period were reviewed. The rate of uterine rupture was determined by stage of labor and whether or not labor was induced. Logistic regression analysis was used to examine the association, controlling for potential confounding factors.

RESULTS: There were 30 uterine ruptures (1.1%) among 2,690 gravidas undergoing a trial of labor after a prior Cesarean delivery, 16 occurring in the first stage of labor and 14 occurring in the second stage. For those with uterine rupture in the first stage of labor, there was no relation between the risk of uterine rupture and the duration of the first stage of labor. Second-stage uterine rupture rates were as follows:

<table>
<thead>
<tr>
<th>Hours</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
<th>≥4</th>
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</thead>
<tbody>
<tr>
<td>All patients</td>
<td>0.25</td>
<td>0.52</td>
<td>0.94</td>
<td>0.89</td>
</tr>
<tr>
<td>Induced patients only</td>
<td>0.0</td>
<td>0.0</td>
<td>1.67</td>
<td>2.70</td>
</tr>
</tbody>
</table>

A logistic regression analysis was performed, controlling for Pcriticin use, birth weight, and year of birth. Each additional hour of the second stage of labor was associated with approximately a 4% increase in the risk of uterine rupture, (odds ratio = 1.03, 95% CI = 1.00, 1.06).

CONCLUSION: The risk for uterine rupture in the second stage of labor increases with increasing duration of the second stage and is highest for women with a second stage of greater than 4 hours, especially in those patients whose labors are induced.
503 ADMINISTRATION OF LOW MOLECULAR WEIGHT HEPARIN WITHIN TWO HOURS PRIOR TO CESAREAN SECTION INCREASES THE PREVALENCE OF WOUND HEMATOMA. H Wolf, J.M. Piek1, F.H. van Wijl1, H.R. Buller2, Dept. Ob/Gyn1 and Dept. Vascular Medicine2, Academic Medical Center, Amsterdam, The Netherlands.

**OBJECTIVE:** To evaluate if the prevalence of wound hematoma after cesarean section is influenced by the time interval between prophylactic administration of low molecular weight heparin (LMWH) and delivery of the infant.

**STUDY DESIGN:** In 1998, 312 women received 2850 Axa-IE LMWH subcutaneous prior to cesarean section for prophylaxis of postoperative thromboembolic complications. This prophylaxis was continued for five days. The maximum effect of LMWH is reached two hours after subcutaneous administration. We therefore used this time cut-off for analysis. A short interval was defined as within two hours prior to delivery of the infant. Wound hematoma were defined as minor (restricted hematomas without serious sequelae) and major (large subcutaneous or intra-abdominal hematoma with clinical sequelae). The co-influence of obstetric variables (primary vs. secondary cesarean section, indication fetal distress vs. other indications, repeat cesarean section, preeclampsia, intrauterine infection and gestational age <37 weeks vs. ≥37 weeks) was evaluated by logistic analysis.

**RESULTS:** 17 (7.2%) major and 12 (9.1%) minor hematomas were noted in 235 women with a short time interval and no major and 2 (2.6%) minor hematoma in 77 women with a long time interval after LMWH. The odds ratio for wound hematoma (minor and major) after administration of LMWH within two hours prior to delivery of the baby was 5.3 (95% CI 1.2-22.8). The obstetric variables did not influence this ratio. The difference for major hematomas reached statistical significance (p = 0.009) No thromboembolic complications were observed in 259 women who were operated under spinal analgesia, no neurological complications were observed in these women.

**CONCLUSION:** Administration of prophylactic LMWH within two hours prior to cesarean section increases the prevalence of wound hematoma and should be avoided. Administration shortly post operative might be preferable.

504 ELECTIVE REPEAT CESAREAN SECTION OR TRIAL OF LABOR: A META-ANALYSIS OF THE LITERATURE FROM 1989 TO 1999. E Mozurkewich, Dept Ob/Gyn, University of Michigan, Ann Arbor, MI, E Hutson1, University of Toronto, Canada.

**OBJECTIVE:** To compare trial of labor (TOL) with elective repeat cesarean section (ERC) in women with one or more prior cesarean deliveries.

**Study Design:** We searched Medline and EMBASE (1989-1999) using the following keywords: MESH headings: original birth as cesarean section, trial of labor, trial of scar, and uterine rupture. We also searched the Registry of Clinical Trials maintained by the Cochrane Pregnancy and Childbirth Group. We cross-checked the reference lists of all relevant reports.

We included all controlled trials from developed countries in which the control group of women receiving ERC had been eligible for trial of labor. To be included, trials had to report one or more of the following outcomes: uterine rupture, hysterectomy, maternal (fetal) morbidity, maternal mortality, 5-minute Apgar ≤7, and fetal or neonatal mortality not attributable to intrapartum fetal demise before labor, prematurity, or lethal anomaly. Pooled odds ratios were computed using the fixed effects method, and confirmed using the random effects method.

**RESULTS:** The meta-analysis identified 48 controlled studies of which 33 were included principally because some, or all, of the control women receiving ERC were not eligible for TOL. No randomized controlled trials (RCT) were found. Fifteen studies totaling 47,292 women [28,605 TOL and 18,597 CES] met the inclusion criteria. Of women undergoing TOL, 20,597 or 72% achieved vaginal birth. Symptomatic uterine rupture occurred more frequently in women undergoing TOL than ERC [OR 2.07, 95% CI 1.42, 3.04] but the absolute risk of this outcome was low (0.4% versus 0.2%). There was no difference in maternal mortality between the two groups [OR 1.52, 95% CI 0.96, 0.88]. Fetal or neonatal mortality was greater in the TOL group than the ERC group [OR 2.18, 95% CI 1.25, 3.87] although the absolute risk of this outcome was also small (0.2% with TOL versus 0.1% with ERC). The proportion of infants with Apgar score ≤7 at 5 minutes in the TOL group was not different when compared with the ERC group [OR 2.24, 95% CI 2.19, 3.88]. Mothers undergoing TOL were less likely to experience fetal morbidity [OR 0.70, 95% CI 0.54, 0.77], or to require blood transfusion [OR 0.57, 95% CI 0.42, 0.76] or hysterectomy [OR 0.40, 95% CI 0.27, 0.60].

**CONCLUSION:** Although uterine rupture may be more common among women undergoing TOL than ERC the absolute risk of this outcome is low. The trial of labor may result in small increases in fetal or neonatal mortality. Maternal morbidity including fetal morbidity, and need for transfusion or hysterectomy may be reduced with TOL compared with ERC. A RCT would be useful, as it would provide unbiased information on the true effects of TOL versus ERC.

505 NITROGLYCERIN VERSUS PLACEBO TO FACILITATE BREECH EXTRACTION OF THE NONVERTEX SECOND TWIN. BB Larmann, DA Terrone, BK Rinehart, HM Graham, JN Martin, Jr. Department of Ob/Gyn, University of Mississippi Medical Center, Jackson, Mississippi.

**OBJECTIVE:** To determine if nitroglycerin adds to breech extraction of the nonvertex second twin.

**STUDY DESIGN:** A prospective double blinded study comparing nitroglycerin to placebo to facilitate breech extraction of a nonvertex second twin. Inclusion criteria were estimated gestational age ≥32 weeks and estimated fetal weight ≥1800 gms. Exclusion criteria were maternal illness requiring cesarean delivery, contraindication to vaginal delivery, fetal distress, and patient refusal to participate. Anesthesiology personnel randomized the patient to receive either nitroglycerin or placebo. The patient and the obstetric team were both blinded to study medication. Patients received either nitroglycerin 100μg or an equal volume of normal saline every two minutes starting at the time of clamping of twin A's umbilical cord. Maternal heart rate and blood pressure were recorded every minute. The study drug was discontinued if the blood pressure dropped by more than 25% or if the maternal heart rate exceeded 130 bpm. The main outcome variables studied were difficulty of delivery, time interval between delivery of twin A and twin B, maternal blood loss, maternal heart rate and blood pressure, and other medication side effects, as well as other pertinent maternal and neonatal outcomes.

**RESULTS:** Statistical analysis included Student's t-test, Kruskal-Wallis, and chi-square analyses, as appropriate.

**CONCLUSION:** There were no statistically significant differences in maternal demographics, hypotensive episodes, maternal tachycardia, blood loss, or interval to delivery of twin B between the two groups. Birth weight, estimated age at delivery, neonatal complications, and length of stay were similar in both groups.

**Difficulty of Delivery**

<table>
<thead>
<tr>
<th>Nitroglycerin (N=10)</th>
<th>Placebo (N=11)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Mild</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>


**OBJECTIVE:** In May 1998, the US FDA issued a health advisory reporting neonatal injuries/deaths following vacuum delivery (5 events/year) and encouraged reports of future adverse events. We compared FDA reports of vacuum delivery adverse events prior to and following the advisory.

**METHODS:** We searched the FDA database (Maude) which was searched for vacuum deliveries using brand name, manufacturer name, and procedure "string searches". Cases were sorted by report date, source, and manufacturer. Neonatal morbidity was quantified as deaths, life threatening or non-life threatening. Cases prior to and following the FDA advisory was compared by t-test.

**RESULTS:** A total of 80 reported adverse cases were identified, after duplicate cases were consolidated, 25 were reported prior to the May 1998 FDA advisory and 55 in the immediate 6 month period following the advisory. There was a significant log-linear (R=0.89, p=0.012) increase in reported events from 1995 (N=1) to 1998 (N=53). The distribution of reporting sources changed significantly following the advisory with increased "manufacturer" (8 to 43%) and decreased "voluntary" reports (56 to 20%) All major brand names were represented. During the 6 months following the FDA advisory, there were 10 neonatal deaths, 30 life-threatening events, 12 non-life threatening events and 3 equipment related reports. Infant deaths were due to intracranial or subgaleal hematomas. Injuries included skull fracture, scalp abrasions, and cephalohematoma. The vast majority of adverse outcomes did not appear to be associated with devotions from standard of care.

**CONCLUSIONS:** The FDA advisory was associated with a 22-fold increase in the rate of reported adverse events. It is apparent that vacuum delivery is associated with greater neonatal morbidity/mortality than was previously recognized Thus, the adage that the vacuum is "designed to come off before damage occurs" appears unsubstantiated.
057  
MISOPROSTOL INDUCTION IN WOMEN WITH PRIOR CESAREAN.  
I. Osby-Hal, BD Raynor, Emory University, Dept Gyn/Oh, Atlanta, GA  
Several reports of uterine rupture in women with prior cesarean delivery receiving misoprostol for induction of labor have appeared.  
OBJECTIVE: To compare complications of labor induction using misoprostol in women with prior cesarean with those of women with an unscared uterus.  
STUDY DESIGN: A computerized database was searched for women undergoing induction of labor at term with a viable fetus using misoprostol during the period 1/96-12/98. Patients were given misoprostol 50 mcg q 4 hours. Data was analyzed on labor and delivery complications, 5 mm Aggar, route of delivery using chi square test.  
RESULTS: A total of 425 women were given misoprostol for induction of labor. 48 with a history of cesarean, 377 without. Women with a history of cesarean were more likely to be delivered by cesarean than women with an unscared uterus (56% vs 26%, p<.04). There was no difference in the overall rate of complications (2% scarred v 5% unscarred). Complications included placental abruption, retained placenta, uterine atony and blood transfusion. No maternal deaths occurred. Seventy percent of the cases required labor induction using prostaglandins.  
CONCLUSION: Misoprostol induction of labor in women with prior cesarean results in a higher rate of cesarean delivery than in women with an unscared uterus but not a higher incidence of complications. There were no uterine ruptures. While blood losses >500 cc occurred more often, this may be due in part to the cesarean rate and did not result in more transfusions.  

058  
NEONATAL AND SURGICAL OUTCOMES IN INFANTS WITH ABDOMINAL WALL DEFECTS: CESAREAN VS. VAGINAL DELIVERY. A. Schinco, T. McFadden, M. Muench, M. Pollock, B. Maza, J. Jenkins, J. Manley, P. Shlosman, M. Kaufmann, GHC, Colomgore, Divisions of Maternal-Fetal Medicine, Christiana Hospital, Newark, DE and Thomas Jefferson University, Philadelphia, PA.  
OBJECTIVE: The affect of mode of delivery on outcomes in infants with abdominal wall defects is controversial. We sought to describe the experience of two large teaching hospitals who referred to the same pediatric surgical team.  
STUDY DESIGN: In this case-cohort study, we reviewed our neonatal databases for the occurrence of gastrochisis or omphalocele from July 1991 to July 1999. We excluded fetuses with aneuploidy and stillborns. We reviewed neonatal and maternal charts for mode of delivery. Fetuses that had a forceps or vacuum delivery were included in the vaginal delivery group. We documented the presence of labor before a cesarean delivery. We examined indicators of neonatal and surgical outcomes: Aggar scores, closure type, length of surgery, need for bowel resection, extent of bowel resection, bowel infarction, days until oral feeding, length of stay, days of parenteral feeding and neonatal death. We reviewed maternal outcomes including chorioamnionitis, wound infection, endomyometritis, and length of stay. We documented the presence of labor before a cesarean delivery. We examined indicators of neonatal and surgical outcomes: Aggar scores, closure type, length of surgery, need for bowel resection, extent of bowel resection, bowel infarction, days until oral feeding, length of stay, days of parenteral feeding and neonatal death. We reviewed maternal outcomes including chorioamnionitis, wound infection, endomyometritis, and length of stay. Data was analyzed on labor and delivery complications, 5 mm Aggar, route of delivery using chi square test.  
RESULTS: A total of 30 infants were identified, 32 with gastrochisis and 24 with omphalocele. Fifty-four (96.4%) of the defects were known before delivery. Twenty-seven (48.2%) were delivered by cesarean delivery of which 56% had gastrochisis. There was no difference in maternal, neonatal or surgical outcomes by mode of delivery. Twenty-seven percent of fetuses had an additional anomaly: 40% in the omphalocele group and 12.3% in the gastrochisis group. Forty-five percent of fetuses with an additional anomaly were delivered by cesarean in the omphalocele group and 50% in the gastrochisis group. Seven infants required secondary closure, 3 had an omphalocele and 4 had gastrochisis. All of these were delivered by cesarean and 5 (71.4%) of these had no additional anomalies. The presence of labor before a cesarean delivery did not affect infant outcomes.  
CONCLUSIONS: Mode of delivery does not appear to significantly affect neonatal outcomes. Infants born by cesarean delivery appeared more likely to require secondary closure than those delivered vaginally. Type of defect or the presence of additional anomalies did not affect the need for secondary closure.

059  
INTERPREGNANCY INTERVAL IS A RISK FACTOR FOR UTERINE RUPTURE AND UTERINE DEHISCENCE AMONG PATIENTS ATTEMPTING VAGINAL BIRTH AFTER CESAREAN SECTION. M Esposti, MP Malea, CA Menchez. Brown Uni, Dept Ob/Gyn, Prov, RI.  
OBJECTIVE: To determine the relationship between interval (IPI) and the risk for uterine rupture/dehiscence in patients who attempt vaginal birth after previous cesarean section.  
STUDY DESIGN: We performed a retrospective case/control study of all identified patients during the 9.5 year period between Jan 1, 1990 and July 1, 1999 with a history of cesarean delivery, who experienced uterine rupture or dehiscence during a subsequent labor. Control patients (51 to 51) cases) delivered in the same months as cases after failed, attempted VBAC. Variables evaluated for confounding effect included: age, race, parity, number of previous cesarean deliveries, use/amount of oxytocin, birth weight, and length of labor. Data analyses were performed with Student t-test, Fisher's exact test, and logistic regression using uterine disruption as the dependent variable.  
RESULTS: 58 cases of uterine disruption (21 cases of uterine rupture and 17 cases of dehiscence) were identified. Univariate analysis confirmed that cases and controls were well matched for all studied confounders, except parity. Gestational age at birth was 39.8±2.7 in cases and 39.1±2.5 in controls. An IPI less than 6 months was significantly more prevalent among cases with uterine disruption: 18% of cases as opposed to 5% of control patients (OR=3.99; CI 1.1-14.7). Mean IPI was less in all disruption cases, 25.9±30.7 months for controls (p<0.06). Among the 21 patients with uterine rupture, mean IPI was 19.7±15.5 months, a significant difference from the control population (p<0.016). The correlation of IPI with uterine disruption remained significant after controlling for parity by logistic regression. Appar scores and unscarred uterine rupture were <500 cc occurred more often, this may be due in part to the cesarean rate and did not result in more transfusions.  

060  
THE SAFETY OF MULTIPLE REPEAT CESAREAN DELIVERIES. G Slesar, J Turchin, MF Lachapelle, Albert Enms College of Medicine, Brown, NY and Jewish General Hospital, McGill University, Montreal, Canada.  
OBJECTIVE: Although based on scarce and dated studies, it is commonly believed that the morbidity associated with repeat cesarean delivery increases with each subsequent re-operation. We sought to determine the obstetrical and surgical outcomes of women with a history of three or more cesarean deliveries.  
STUDY DESIGN: Ninety-nine consecutive patients who delivered between 1/1/85 and 1/1/95 and who had previously undergone three or more cesarean deliveries were included in the study. The incidences of obstetrical and surgical complications were calculated among patients having their 4th, 5th and 6th repeat cesarean delivery. Student's t-test and Chi-square were used for statistical analysis.  
RESULTS: Cesarean was the planned method of delivery for 98 of these cases and 98 had their cesarean before the onset of labor. There were no uterine ruptures. Eight patients required a hysterectomy, seven of which had associated placenta previa and/or accreta. Ten patients required blood products. There were no maternal or perinatal deaths and, excluding hysterectomy, there was no long-term maternal morbidity. The obstetrical and surgical outcomes in the three groups are shown below.

<table>
<thead>
<tr>
<th></th>
<th>4th CS (n=60)</th>
<th>5th CS (n=25)</th>
<th>26th CS (n=14)</th>
</tr>
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<tbody>
<tr>
<td>Party (median)</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>38±5.12</td>
<td>38±5.19</td>
<td>38±5.4</td>
</tr>
<tr>
<td>Length of surgery (min)</td>
<td>41±14</td>
<td>57±65.10</td>
<td>35±10</td>
</tr>
<tr>
<td>Complication</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Transfusion</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Pervia/accreta</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

CONCLUSION: Patients with three or more prior cesarean deliveries have a high rate of transfusion, abnormal placentalation and hysterectomy. However, these morbidities do not seem to increase linearly with each subsequent cesarean. Most patients with three or more prior cesarean deliveries can expect an overall favorable outcome.
511 A VBAC SCORING SYSTEM THAT CAN PREDICT UTERINE RUPTURE IN PATIENTS ATTEMPTING A TRIAL OF LABOR. V. Alama, Jr.*, BA Meyer. Dept. Ob/Gyn, University Medical Center, SUNY Stony Brook, NY. **OBJECTIVE:** The most serious complication of labor after cesarean is uterine rupture. We applied a VBAC scoring system to identify women at increased risk for uterine rupture. **STUDY DESIGN:** All attempts at VBAC between 1/1/98 and 4/30/99 were reviewed. The VBAC score was then used to predict risk of uterine rupture. **RESULTS:** 13 uterine ruptures occurred in 890 trial of labor (1.5%), with 9 requiring transfusion. Two cases were discovered after VBAC and required laparotomy. Six cases resulted in significant fetal morbidity or mortality. Cesarean hysterectomy was required in 2 cases. The VBAC score consists of the following variables for a total possible score of 10 points:

- Previous vaginal delivery: 2 points
- Indication for previous C/S: 2 points
  - breech, fetal distress, previa, elective: 2 points
  - FTP at <5cm: 1 point, at 5cm = 0 points
  - Cervical dilation > 4 cm: 2 points
  - Cervical dilation 2.5-4 cm = 1 point
  - Cervical dilation <2.5 cm = 2 points
- Station below 2: 2 points
- Cervical length < 1 cm: 1 point
- Spontaneous labor: 1 point

The distribution of uterine rupture vs VBAC scores were:

<table>
<thead>
<tr>
<th>Score</th>
<th>Number of Patients</th>
<th>Uterine Rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>144</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>146</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>146</td>
<td>0</td>
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<tr>
<td>5</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>147</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>147</td>
<td>0</td>
</tr>
</tbody>
</table>

12/13 uterine ruptures had a VBAC score of 5 or less: 12/383 (3.1%) vs. 1/438 (0.2%), OR = 14.2 (1.9 < OR < 293.0, p<0.001)

**CONCLUSION:** The VBAC score successfully quantified the risk of uterine rupture. A score of ≤ 5 had a 3.1% risk of uterine rupture (14-fold increase in rupture risk). This approaches the 6%-8% risk associated with a previous low-transverse cesarean section.

512 PROSPECTIVE ANALYSIS OF A SCORING SYSTEM TO PREDICT VAGINAL DELIVERY AFTER CESAREAN SECTION. V. Alama, Jr.*, BA Meyer. Dept. Ob/Gyn, University Medical Center, SUNY Stony Brook, NY. **OBJECTIVE:** We developed a VBAC scoring system to predict vaginal birth after cesarean. This study was designed to prospectively validate the scoring system. **STUDY DESIGN:** All women attempting a trial of labor between 1/1/98 and 4/30/99 were reviewed and scored. The VBAC score consists of the following variables for a total possible score of 10 points:

- Previous vaginal delivery: 2 points
- Indication for previous C/S: 2 points
  - breech, fetal distress, previa, elective: 2 points
  - FTP at <5cm: 1 point, at 5cm = 0 points
  - Cervical dilation > 4 cm: 2 points
  - Cervical dilation 2.5-4 cm = 1 point
  - Cervical dilation <2.5 cm = 2 points
- Station below 2: 2 points
- Cervical length < 1 cm: 1 point
- Spontaneous labor: 1 point

**RESULTS:** 231 patients underwent a trial of labor. 167 had a vaginal delivery (73%). There were no significant differences between C/S and vaginal groups in: maternal age (31.6±1.1 vs. 31.6±1.7), neonatal weight (3487±567 gms. vs. 3315±619 gms.), APGAR scores, NICU days, cord pH, and IVH incidence. Parameters that predicted vaginal birth included (all p < 0.0005):
- prior vaginal delivery OR = 4.17 (2.02 < OR < 8.73),
- prior Cesarean for dystocia: OR = 2.93 (1.51 < OR < 5.71).

**CONCLUSION:** The VBAC score successfully predicted vaginal birth after cesarean. As in our retrospective study, scores ≤ 4 patients had a 35% chance of vaginal delivery. The VBAC score is an effective tool to predict vaginal delivery after C/S.

513 RANDOMISED COMPARISON OF ANAL SPHINCTER FUNCTION FOLLOWING FORCEPS AND VACUUM DELIVERY. M. Fitzpatrick, M.Behan, PR. O’Connell, C.O’Herlihy. Department of Obstetrics, Surgery and Radiology, National Maternity Hospital and University College Dublin, Ireland. **OBJECTIVE:** To compare, in a prospective, randomised controlled trial, differences in anal sphincter function following forceps and vacuum delivery in an institution practising active management of labor. **STUDY DESIGN:** Primiparous women were recruited antenatally and, if an instrumental delivery was indicated, were randomised to either a vacuum or low cavity, non-rotational forceps delivery. Follow-up consisted of a symptom questionnaire, anal manometry and endoanal ultrasound at 3 months postpartum. Chi-square and Mann Whitney tests were used for statistical analysis. **RESULTS:** 82 women were randomised; 40 were delivered with forceps (25 because of failure to progress) and 42 by vacuum. There were no statistical differences in the antecedent antenatal factors between the two groups. A third degree perineal tear followed 4 (10%) forceps and 2 (5%) vacuum deliveries. At 3 months postpartum, 25 (65%) women complained of altered continence after forceps delivery compared with 17 (40%) following vacuum delivery (p=0.07). The median continence scores were 2 and 0 following forceps and vacuum delivery, respectively. Median anal canal resting pressure was significantly lower following forceps delivery (50 vs. 65 mmHg, p<0.05) but no other significant manometric differences were found. Endoanal ultrasound showed occult anal sphincter damage following 19 (48%) forceps compared with 21 (50%) vacuum deliveries.

**CONCLUSION:** Symptoms of altered fecal continence were more common following forceps delivery, although this difference did not reach statistical significance. Anal canal resting pressures were significantly lower after forceps delivery. Ultrasound evidence of occult sphincter damage was present in half the subjects, with an equivalent incidence in the forceps and vacuum groups.

514 COMPARATIVE STUDY OF NEONATAL MORBIDITY ASSOCIATED WITH UTERINE RUPTURE DURING VBAC VERSUS CORD PROLAPSE. E.Bigoté*, R.J. Gauthier*, PR. O’Connell, Dept Ob/Gyn, Ste-Justine Hospital, Université de Montréal, Que, Canada. **OBJECTIVE:** To evaluate the neonatal morbidity associated with uterine rupture in patients undergoing trial of labor (TOL) following a previous low-transverse cesarean section (LTCs) compared to another obstetrical emergency: umbilical cord prolapse. **STUDY DESIGN:** We reviewed all medical records of patients who underwent TOL after a LTCs and those who had a cesarean for cord prolapse between 1992 and 1998 at our tertiary care hospital. Data was collected for gestational age, birthweight, Apgar score, arterial cord blood pH and admission to the NICU. **RESULTS:** From 1272 patients who underwent TOL after previous LTCs, we retained 15 (1.2%) cases of symptomatic uterine rupture (group 1). Dehiscences were excluded. 31 cases of cesarean section for cord prolapse after 28 weeks were identified during the same period (group 2). The mean gestational age was 39.5±0.6 weeks and 35.9±1.5 weeks respectively. Evidence of both short and long term neonatal morbidity included: arterial blood pH less than 7.1 in 47% vs. 3% (p<0.005), five-minute Apgar less than 6 in 35% vs. 5% (p<0.05) and NICU admission at 40% vs. 25% (NS). At two to six months follow-up, three (20%) newborns in the uterine rupture group were diagnosed with ischemic encephalopathy and major neurologic impairment compared to none in the cord prolapse group (p<0.05). There were no neonatal deaths. The median time from the first manifestation of uterine rupture or cord prolapse to the birth was comparable (18 vs 17 minutes, NS).

**CONCLUSION:** Neonatal neurological morbidity associated with uterine rupture is much greater than with cord prolapse, making it the worst obstetrical emergency. Proper informed consent is essential. Delivery room personnel should be properly trained in the recognition of uterine rupture and an emergency cesarean protocol should be in place.
515 THE EFFECT OF INTRA-ABDOMINAL IRRIGATION AT CESAREAN SECTION ON MATERNAL MORBIDITY. K. Horrell, MD, MPH/TMP, H Miller, MD, D Haynes*, MD, Dept Ob/Gyn, Univ of Arizona & Obstetrica Medicine Group, Tucson, AZ.

OBJECTIVE: To determine if intra-abdominal irrigation with normal saline at cesarean section is associated with increased maternal morbidity.

STUDY DESIGN: We performed a prospective randomized trial of intra-abdominal saline irrigation at the time of cesarean section in 184 patients. The Institutional Review Board approved this study. Women who were less than 36 weeks gestation undergoing routine cesarean section for variable indications were consented. Exclusion criteria included: choiorionamnionitis, type I diabetes, placenta previa, multiple gestation, and non-reassuring fetal monitoring requiring immediate delivery. Patients randomized to intra-abdominal irrigation received 500-1000cc of normal saline versus no irrigation following closure of the uterine incision, but prior to abdominal wall closure. Data were collected for comparison of demographic factors, intraoperative and postoperative complications rates, and maternal and neonatal outcomes. Data were analyzed using the Mann-Whitney, student t, and Fisher's Exact tests with significance established at p<0.05.

RESULTS: Ninety-four patients randomized to the study group and ninety to the control group. Relevant outcomes data are shown below.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=90)</th>
<th>Irrigation (n=94)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapartum Complications</td>
<td>7 (7.8%)</td>
<td>12 (12.8%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Blood loss (cc)</td>
<td>798±302.6</td>
<td>797±376.3</td>
<td>0.38</td>
</tr>
<tr>
<td>Operative time (minutes)</td>
<td>59±17.8</td>
<td>60±47.6</td>
<td>0.20</td>
</tr>
<tr>
<td>Postpartum Complications</td>
<td>15 (16.7%)</td>
<td>14 (14.9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Endomteritis</td>
<td>7 (7.7%)</td>
<td>9 (9.6%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Asepsia (hematocrit &lt;25)</td>
<td>2 (2.2%)</td>
<td>3 (3.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Postpartum Hemorrhage</td>
<td>2 (2.2%)</td>
<td>1 (1.1%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>2 (2.2%)</td>
<td>1 (1.1%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>2.9±0.9</td>
<td>2.9±1.0</td>
<td>0.53</td>
</tr>
<tr>
<td>Gastrointestinal Recovery (hr)</td>
<td>35.6±16.5</td>
<td>32.0±12.7</td>
<td>0.75</td>
</tr>
<tr>
<td>Postpartum Hemoglobin</td>
<td>10.8±1.6</td>
<td>10±8.6</td>
<td>0.30</td>
</tr>
</tbody>
</table>

CONCLUSION: Routine intra-abdominal irrigation at cesarean section in a low-risk population does not reduce intrapartum or postpartum maternal morbidity.

516 EXTERNAL CEPHALIC VERSION: NITROGLYCERIN VERSUS TERBUTALINE. F. Andanian*, TI Feng, Emory University, Department of Gynecology and Obstetrics, Atlanta, Georgia.

Exernal cephalic version (ECV) has been used to reduce the incidence of intrapartum breech presentations and thus reduce the number of cesarean deliveries. The most commonly used drugs for uterine relaxation given prior to attempting ECV are beta-agonists.

OBJECTIVE: To determine whether the use of nitroglycerin versus terbutaline has a better success rate for external cephalic version at Grady Memorial Hospital.

STUDY DESIGN: This is a randomized prospective study. Patients who met inclusion criteria were given either nitroglycerin or terbutaline to relax the uterus in order to determine which agent had a better success rate. Data was collected from April 1996 to May 1999. The following data was collected: patient's age, gestational age, parity, race, placental location, amniotic fluid index, fetal position and type of version roll.

RESULTS: A total of 35 patients were enrolled in the study. There were 18 patients randomized to use nitroglycerin and 17 patients to use terbutaline with version success rates of 45% and 55% respectively. The overall version success rate for both groups was 49%.

CONCLUSIONS: Preliminary data from this study supports no significant difference between the use of nitroglycerin and terbutaline in attempting external cephalic version. However it goes evidence for an additional tocolytic agent (nitroglycerin) to be used for ECV when other agents are contraindicated.


OBJECTIVE: To examine the association between uterine rupture and patterns of pitocin use in vaginal birth after cesarean.

STUDY DESIGN: All women undergoing a trial of labor after cesarean delivery during a 12-year period were reviewed. For the current analysis, cases were all uterine ruptures in women who had a single prior cesarean and who received pitocin during their trial of labor (n=24). Four controls undergoing a trial of labor after a single cesarean were matched to each case by birthweight, day of birth, pitocin use, and whether their labor was induced or augmented (n=96).

RESULTS: No significant differences were seen between cases of uterine rupture and controls in mean pitocin duration (530 min. vs. 476 min.), mean maximum pitocin dose (12.9 vs. 12.1 mu/min), mean total pitocin dose (525 vs. 4660 mu), or average mode pitocin dose (10.6 vs. 10.3 mu/min). Likewise, no differences were seen in starting dose of pitocin, interval of pitocin increase, incremental pitocin dose, or duration at maximum dose. The decision to decrease pitocin dose for fetal maturations was seen more often in cases of rupture (69.6% vs. 36.5%, p=0.04). More than one episode of uterine hyperstimulation or hypertonus was seen in 26.1% of uterine ruptures and 10.4% of controls (p=0.048).

CONCLUSION: Pattern of pitocin use is not associated with risk of uterine rupture. The association between rupture and changes in the fetal heart rate tracing was expected as a symptom of uterine rupture. The reason for the association between repetitive abnormal uterine contractions and uterine rupture is unclear, however women with such patterns undergoing a trial of labor after cesarean should be observed closely.


METHODS: In 1990 we developed fixed criteria for transfer of multiples to the MFM service. High-risk twins & triplets will be evaluated separately. Pertinent data were obtained from chart review in the final "low risk" multiple gestations.

RESULTS: Of the low risk twin pregnancies (n = 401), 78 % were private, 8.5 % MFM and 18 % residents. Resident patients had lower maternal age and less infertility & were higher in parity and gravidity. A greater proportion of MFM patients had significant past medical histories and more had undergone selective reduction. There was increased use of oral tocolytics, higher birthweight, and higher mean gestational age in the private group. Total rate of cesarean deliveries was higher for private patients compared to resident/MFM (52% vs 37%). The rate of combined procedures (vag C/S) was significantly different with 4/90 resident / MFM & 33/151 private twin "B" delivered by cesarean section (p=0.02). A greater proportion of breeches were delivered vaginally & there were more instrumental vaginal deliveries in the resident/MFM group (p=0.02). Perinatal morbidity was not different.

CONCLUSION: Outcome results are similar; differences in practice patterns result in a higher private C/S rate. Good outcomes for both groups reflect adherence to management protocols. Inexperience with version and breech extraction were major contributors to the high private C/S rate.
RECEIVER OPERATING CHARACTERISTIC (ROC) CURVE ANALYSIS OF CERVICAL RIPENESS FOR PREDICTION OF CESAREAN DELIVERY AFTER INDUCTION IN NULLIPARAS WITH PROLONGED PREGNANCIES

C. O’Reilly-Gren, Dept. of Ob/Gyn, Albert Einstein College of Medicine, Bronx, NY and Lenox Hill Hospital, New York, NY.

OBJECTIVE: To evaluate cervical dilation, effacement and station on admission to labor and delivery as predictors of cesarean delivery in nulliparous patients with prolonged pregnancy admitted for induction, using ROC curve analysis.

STUDY DESIGN: Cervical ripeness was evaluated in 156 patients meeting entry criteria. A modified Bishop score was calculated. ROC curves for each variable as a predictor of cesarean delivery were constructed.

RESULTS:

<table>
<thead>
<tr>
<th>Area</th>
<th>SE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilation</td>
<td>0.7789</td>
<td>0.0377</td>
</tr>
<tr>
<td>Effacement</td>
<td>0.7182</td>
<td>0.0412</td>
</tr>
<tr>
<td>Station</td>
<td>0.6957</td>
<td>0.0416</td>
</tr>
<tr>
<td>Bishop</td>
<td>0.7366</td>
<td>0.0368</td>
</tr>
</tbody>
</table>

Area = area under ROC curve; SE = standard error; p value = p value for Area in comparison with an area of 0.5 (the area under the ROC curve for a useless test); Bishop = modified Bishop score. The inflection point for the last curve occurs at a modified Bishop score < 4. At this cutoff value, the sensitivity is 72%, the specificity is 76%, and the relative risk for cesarean delivery is 3.09 (95% CI 1.12 to 8.42). Uterine rupture rates with reduction was 3.09 (95% CI 1.12 to 8.42). Uterine rupture rates with reduction were induced (27%). The overall rate of uterine rupture was 15/2119 (0.71%). The relative risk of uterine rupture with reduction was significantly higher than with spontaneous TOL (7/1544, 0.45%), p=0.036. The relative risk of uterine rupture with reduction was 3.64 (95% CI 1.89 to 6.99; p < 0.00001 by Yates correction of the Mantel-Haenszel chi-square test).

CONCLUSION: Decreasing cervical dilation, effacement and station are useful tests for predicting cesarean delivery prior to utilizing induction of labor in nulliparous patients with prolonged pregnancy. The modified Bishop score for the combination of these three measurements has a small advantage over dilation alone. This is the first ROC curve analysis of Bishop score factors useful tests for predicting cesarean delivery prior to initiating induction of labor in nulliparous patients with prolonged pregnancy. It validates the Bishop score as a predictive test. A modified Bishop score < 4 predicts a high risk of cesarean delivery, and may be used in a prospective randomized trial evaluating the morbidity of induction in prolonged pregnancies.

UTERINE RUPTURE DURING INDUCED TRIALS OF LABOUR IN WOMEN WITH A PREVIOUS CESAREAN DELIVERY

R. Pamplona, N. Wood, J. Pollard, University of Calgary, Foothills Hospital, Calgary, AB, Canada.

OBJECTIVE: To evaluate cervical ripeness and characteristics of labor and delivery as predictors of cesarean delivery in nulliparous patients with prolonged pregnancy admitted for induction, using ROC curve analysis.

STUDY DESIGN: Receiver operating characteristic (ROC) curve analysis of Bishop score factors useful tests for predicting cesarean delivery prior to initiating induction of labor in nulliparous patients with prolonged pregnancy. It validates the Bishop score as a predictive test. A modified Bishop score < 4 predicts a high risk of cesarean delivery, and may be used in a prospective randomized trial evaluating the morbidity of induction in prolonged pregnancies.

MATERIEL MORBIDITY IN IMMUNE THROMBOCYTOPENIA PURPURA


OBJECTIVE: To analyze predictive factors for maternal morbidity associated with Immune Thrombocytopenia Purpura (ITP) during pregnancy and postpartum period.

STUDY DESIGN: Retrospective review of all cases of ITP in pregnancy managed from 10/1984-9/1999. Treatment included oral steroids, intravenous immune globulin or both, and was begun if: 1) platelet counts were ≤50,000/μL, 2) counts were ≤50,000/μL prior to a procedure or delivery, and 3) if bleeding occurred. IVIG was given in doses of 1 g/kg maternal body weight for 1-2 days. A 9-point scaled scoring system for severity of disease was designed including symptoms, lowest platelet count and need for treatment. Relative disease severity was evaluated by comparison of scores between three time periods: pregnant vs. non-pregnant, early vs. late pregnancy, and from one pregnancy to the next. Chi-square and Wilcoxon matched pairs signed ranks tests were used.

RESULTS: Major hemorrhagic complications were limited to one case of abruptio placenta and 5 cases of post-partum hematoma (PPH) in 56 pregnancies in 54 patients. 4 of 5 cases of PPH had platelet counts <50,000/μL. Preliminary analysis of 54 pregnancies (comparing first trimester to third trimester scoring) showed that ITP appeared to worsen during pregnancy (p=0.007). However, this appeared to be due to an improvement in the ITP scoring from the non-pregnant state to the first trimester. There was no difference in disease severity in patients having subsequent pregnancies.

CONCLUSIONS: Maternal morbidity from ITP during pregnancy is very low with aggressive evaluation and treatment. Major hemorrhage was no greater than the 5% expected for the general population. Based on a scoring system for disease ITP appears to: 1) be accelerated during the first trimester and return to baseline by the third trimester, 2) have no difference in severity between the pregnant and non-pregnant states, and 3) have no difference in severity from one pregnancy to the next.

THE USE OF HELICAL COMPUTED TOMOGRAPHY IN PREGNANCY FOR THE DIAGNOSIS OF ACUTE APPENDICITIS


OBJECTIVE: Accurately diagnosing acute appendicitis in pregnancy by clinical evaluation is difficult. A safe, reliable test is sought to decrease a delay in diagnosis and avoid unnecessary invasive procedures. A helical or spiral computed tomographic (CT) technique has proven to be a very accurate test in the non-obstetric population for the identification of acute appendicitis. We now report its use in pregnant patients suspected of having acute appendicitis.

STUDY DESIGN: All pregnant patients undergoing helical CT at our institution from 4/97-2/98 for the suspected clinical diagnosis of acute appendicitis were retrospectively reviewed. Helical CT was performed by standard departmental protocol. Average radiation exposure was approximately 300 mRAD. A positive study was reported if an enlarged appendix, not filling with contrast material, was present with peripertioneal inflammatory changes. Outcomes were determined by the results of surgery or pathological examination or clinical follow-up.

RESULTS: Seven patients were identified in the study period. Two patients had positive findings on helical CT and acute appendicitis was confirmed at laparotomy and by pathological inspection. There were no further prenatals complications and both patients delivered at term. Five patients had a normal appearing appendix on helical CT and all of these patients had resolution of their pain and symptoms.

CONCLUSION: Helical CT appears to be a useful, noninvasive test to accurately diagnose acute appendicitis in pregnancy.
525 HODGKIN'S LYMPHOMA IN PREGNANCY: MATERNAL AND PERINATAL OUTCOME. R. Hadlow-Rum, G. Holberg, B. Parman, R. Herskovicz, M. Mazor Department of Ob/Gyn, Faculty of Health Sciences, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

OBJECTIVE: To determine the maternal and perinatal outcome of pregnant women with Hodgkin's lymphoma.

STUDY DESIGN: Medical charts of 11 pregnant women with Hodgkin's lymphoma who delivered at Soroka University Medical Center between 1989-1999 were evaluated. The prevalence of Hodgkin's lymphoma during this period was 0.014% (11/7401). A cross-sectional study was designed according to maternal and perinatal outcome between study group consisted of patients with Hodgkin's lymphoma (n=11), and the comparison group included healthy women (n=55) matched for maternal age, gravity and parity.

RESULTS: The mean age of the patient in the study was 28 years (range 21-35). The mean gestational age at delivery was not different between the groups 38.2±2.8 ±3. 38.8±2.8 weeks. Preterm delivery occurred in the study group in a single case at 30.3 weeks. The IUGR and preterm birth rates were not significantly different between the groups 9% vs. 5.7% and 9% vs. 9%, respectively. No complications were noted in either group. The cesarean section rate was 36% in the study group vs. 11.3% in the control group (p<0.05). The most frequent histopathologic type of Hodgkin's lymphoma was Nodular Sclerosis with a rate of 54% (6/11), followed by the Mixed Cellularity type which was 27% (3/11). In 18% (2/11) of the women, no significant progression of the lymphoma staging and chemotherapy treatment was administered. During the 2nd and 3rd trimester of pregnancy, Maternal complications were minor; one case of postpartum hemorrhage, one of postpartum fever and one of moderate leukopenia after chemotherapy.

CONCLUSIONS. The course of pregnancy and perinatal outcome of women with Hodgkin's lymphoma was similar to that of the healthy women, even in cases where women with the active disease received chemotherapy during pregnancy. This information may be helpful for prenatal counseling of women with Hodgkin's lymphoma.

526 MATERNAL AND FETAL OUTCOMES WITH SEVERE GESTATIONAL THROMBOCYTOPENIA. J. Johnson and P. Samuels, The Ohio State University College of Medicine, Columbus, OH.

OBJECTIVE: To study maternal and neonatal complications in patients diagnosed with severe Gestational Thrombocytopenia (GT), defined by a maternal platelet count of <75,000/mm3.

STUDY DESIGN: 247 patients with thrombocytopenia from causes other than pre-eclampsia were studied, of which 216 (87.4%) were diagnosed with GT. We included 31 patients with severe GT, 18 hadImmune Thrombocytopenic Purpura (ITP), 1 with Thrombotic Thrombocytopenic Purpura, 2 with von Willebrand's Disease, and 9 with other known causes. 32/216 (14.8%) had platelet counts <75,000/mm3 (Group I) and 184/216 (85.2%) had platelet counts >75,000/mm3 (Group II). Maternal serum anti-platelet IgG, neonatal platelet count, and maternal and neonatal outcomes were compared for Groups I and II. Patients were followed prospectively with platelet counts monthly, during labor and after delivery until nadir, and postpartum. Cord platelet counts were obtained, and neonatal platelet counts 48-72 hours after delivery. Any maternal and neonatal bleeding complications were recorded. Paired t-tests were performed where appropriate and p<0.05 was considered significant.

RESULTS:

- Mean Neonatal Platelet Count: 143,700/mm3 (Group I) vs. 221,750/mm3 (Group II) n.s.
- Maternal Bleeding Complications (5.6% vs. 11.1%) n.s.
- Neonatal Bleeding Complications (0.0% vs. 0.0%) n.s.

CONCLUSION: Neonatal platelet counts were not related to severe maternal GT. There were no neonatal bleeding complications, even in pregnancies with counts <75,000/mm3. Maternal bleeding complications were higher in the severe GT group. Unlike ITP in which serum anti-platelet IgG is associated with a decrease in neonatal platelet count, there was no decline in neonatal platelet counts during the first 48-72 hours of life with GT. There was no association between severe GT and neonatal bleeding
527 EFFECT OF SEIZURE ACTIVITY ON THE N-METHYL-D-ASPARTATE (NMDA) RECEPTOR GENE TRANSCRIPTION IN THE PREGNANT RAT BRAIN. Mindichela Halad, John W. Hoppin, Department of Ob/Gyn, Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: The NMDA receptor is involved in seizure initiation and progression. We have demonstrated that astrocyte activity is associated with increased NMDA receptor binding of glutamate in pregnant rat brain, and that pre-administration of MgSO4 significantly reduced this effect. This study was intended to evaluate the effect of seizure on NMDA receptor gene transcription in maternal rat brain, and whether MgSO4 can decrease this effect.

STUDY DESIGN: Rats were stereotaxically implanted with a bipolar electrode into the hippocampus. One week of recovery was allowed prior to breeding. Pregnant rats were randomly assigned to one of three groups (Table). Subcutaneous doses of saline or MgSO4 were administered every 20 minutes for 4 hours (loading/maintenance-loading) to all rats on gestational days 9, 11, 13, 15, 17, and 19. Rats were subsequently stimulated and seizures indurated. At GD 20, rats were perfused while under isoflurane anesthesia. The frontal cortex, hippocampus, brainstem, and cerebellum were separated, and frozen. Total RNA was isolated from rat brain regions and RNA integrity was assessed. Complementary DNA (cDNA) was synthesized using specific NMDA-R1 primers and a secondary PCR product for quantitation purposes. The amount of NMDA-R1 mRNA was determined by densitometric scanning of the NMDA-R1 primed and the secondary PCR MIMIC product bands.

RESULTS: Seizure activity effect on NMDA mRNA concentrations in rat brain.

Values in fg/ml

<table>
<thead>
<tr>
<th>Values in fg/ml</th>
<th>MgSO4 &amp;</th>
<th>Saline &amp;</th>
<th>MgSO4 &amp;</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Seizure (n=4)</td>
<td>11.0±4.0</td>
<td>9.6±5.5</td>
<td>12.1±3.0</td>
</tr>
<tr>
<td>Seizure (n=8)</td>
<td>92.8±10.2</td>
<td>98.6±4.6</td>
<td>92.8±3.5</td>
</tr>
<tr>
<td>Seizure (n=9)</td>
<td>12.6±4.3</td>
<td>9.0±4.3</td>
<td>10.6±2.3</td>
</tr>
</tbody>
</table>

CONCLUSION: The results of this study suggest that seizure has no effect on the NMDA-R1 receptor mRNA levels in the rat brains. Our previous results of increased NMDA receptor binding after seizure activity may be due to post-transcriptional events such as changes in the receptor's affinity and/or density.

528 SEPTIC PELVIC THROMBOPHLEBITIS AND PRECLAMPISIA ARE RELATED ENDOVASCULAR DISORDERS. GM Idler, BK Rinehart, DA Terrone, JH Crews, EF Magann, JM Martin, Jr Dept Ob/Gyn, Univ Mississippi Medical Center, Jackson, MS.

OBJECTIVE: To profile the contributing factors and clinical course of all postpartum patients diagnosed with septic pelvic thrombophlebitis (SPT) at a single large referral tertiary center during the decade of the 1990's.

STUDY DESIGN: A prospective, single institution case review of all patients with the diagnosis of SPT based upon a continued (>2 hours) postpartum febrile course despite treatment with broad-spectrum antibiotic coverage with no other known source of infection.

RESULTS: Information was available for 55 patients with SPT. The average age was 21.5±3.1 years. Race included 85% African-American, 11% Caucasian, and 4% Native American. Review of parity revealed 78% of women were nulliparous and 59% had a body mass index of >30. The average body mass index was 45.0 kg/m² (average weight 183±47 lbs.). The average gestational age at delivery was 36.8±4.3 weeks. The most prevalent medical complication of pregnancy was preclampsia, occurring in 40% compared to an institutional incidence of 15%. The average length of ruptured membranes was 22 ± 5:5-8 hours (median 10.5, 95% CI 7-38.7 hours), with 22% of patients undergoing rupture of membranes at the time of cesarean section and 9% of patients experiencing prolonged rupture of membranes >24 hours. Chorionamnionitis was diagnosed in 13% of cases. Cesarean section was performed in 91% of cases with the two most common indications being arrest of labor (44%) and non-reassuring fetal heart rate tracing (39%). All patients undergoing cesarean section received one dose of prophylactic intrapartum antibiotics. The average time after delivery for antibiotic initiation was 27±2.6 hours. All patients received triple antibiotic coverage for persistence of fever >100°F. Although a computed tomography scan was performed in 64 patients, only 18% of patients had significant findings (body abscesses seen in 9%). The most common endovascular disorder was pulmonary embolism (15%). The median length of stay was 4.8 days with an interquartile range of 2-12 days. The average number of hospital days was 10.1±9.4 days.

CONCLUSION: There were 140,000 births, and 42 maternal deaths, a MMR of 30/100,000, four times the CDC-reported national rate of 7.5/100,000. When adjusted to reflect only pregnancy-related causes the MMR was 21/100,000, 40% of which were potentially avoidable, citing a provider or hospital factor in 80% of these; and a patient factor in 20%.

CONCLUSION: MMRs identified at a local level through peer review are at least three to four times as high as those reported through national death certificates. The magnitude of the problem is much greater than is actually recognized. A substantial number of maternal deaths are potentially avoidable, indicating the need for both patient and provider education, and institutional changes if we are to reduce the MMR to 3.3/100,000, the stated national health goal of Healthy People 2000.

530 THE EFFECT OF PRIMARY BILARY ACID CATIONS ON THE CONTRACTILITY OF HUMAN MYOMETRIUM. A. Vernier, K. A. Guo, Y. Vermeiren, G. Saele, R. Garfield, Dept. of Ob/Gyn, The Univ. of Texas Med Branch, Galveston, TX.

INTRODUCTION: Intrahepatic Cholestasis of Pregnancy (IHCP) is an uncommon disease characterized by an increase in maternal, fetal and amniotic fluid primary biliary acids. The development of IHCP has been associated with an increased rate of preterm birth and fetal demise. The goal of this study was to evaluate the effect of primary biliary acids on the contracts of human myometrium from term pregnancy.

STUDY DESIGN: Uterine strips were prepared from biopsy specimens obtained from women undergoing scheduled C/S at term. The strips were mounted for isometric tension recording in 10 ml organ chambers filled with Krebs solution aerated with 5% CO2 in air (pH=7.4). The effects of cumulative concentrations (10^-10 to 10^-4 M) of the biliary acids cholic (CA) and chenodeoxycholic (CDCA) on spontaneous uterine contractility were determined. After the last concentration of biliary acid, the response to 10^-7 M oxytocin was determined. Uterine activity was analyzed as the integral activity of cumulative concentrations (10^-10 to 10^-4 M) of the biliary acids cholic (CA) and chenodeoxycholic (CDCA) on spontaneous uterine contractility were determined. After the last concentration of biliary acid, the response to 10^-7 M oxytocin was determined. Uterine activity was analyzed as the integral activity of cumulative contractility of human myometrium from term pregnancy.

RESULTS: CA and CDCA had no significant effect on spontaneous or oxytocin-induced contractility of human myometrium in pregnancy. The adverse effects of IHCP are unlikely to be due to changes in uterine contractility induced by biliary acids.
A new screening test for platelet dysfunction, the PFA-100® System (Dade Behring, Inc.), has been found to be both sensitive (94.9%) and specific (88%) in nonpregnant patients. The purpose of this study was to evaluate the effect of pregnancy on this new test.

**STUDY DESIGN:** Results from 26 healthy pregnant women were compared to results from 206 previously studied, healthy adults. Blood samples from each subject were evaluated using the PFA-100® system, a microprocessor-controlled test instrument that discriminates between different platelet defects using two types of test cartridges: one contains a membrane impregnated with the platelet agonist collagen (COL) and epinephrine (EPI); the other collagen (COL) and adenosine diphosphate (ADP). Each membrane has a 135μm aperture. A constant negative pressure aspirates the sample through the membrane. As a result, a platelet plug forms which occludes the aperture. The time interval from the aspiration to the occlusion of the aperture is the closure time. If a defect in platelet function exists, mean values for the COL/EPI and COL/ADP closure times were compared between pregnant and nonpregnant adults.

**RESULTS:** Of the twenty patients analysed, there were trends toward different closure times using two types of test cartridges: one contains a membrane impregnated with the platelet agonist collagen (COL) and epinephrine (EPI); the other collagen (COL) and adenosine diphosphate (ADP). Each membrane has a 135μm aperture. A constant negative pressure aspirates the sample through the membrane. As a result, a platelet plug forms which occludes the aperture. The time interval from the aspiration to the occlusion of the aperture is the closure time. If a defect in platelet function exists.

**CONCLUSION:** For pregnant adults, the closure times were virtually identical to those for previously studied nonpregnant adults. Therefore, the PFA-100® System appears to provide a new, reliable screening test for the detection of platelet dysfunction in pregnant women.
536 ASSOCIATION OF MATERNAL SERUM ALPHA-FETOPROTEIN WITH ADVERSE OUTCOMES IN PREGNANCIES COMPlicated BY PLACENTA PREVIA. EJ Bulschi*, JS Dashe, RM Ramus. Dept of Ob/Gyn, UT Southwestern Med Ctr, Dallas, TX.

OBJECTIVE: To determine whether elevation of maternal serum alpha-fetoprotein (MSAFP) is associated with adverse outcomes in pregnancies complicated by placenta previa.

STUDY DESIGN: Retrospective cohort study of 97 pregnancies complicated by placenta previa which was diagnosed sonographically and confirmed at delivery. All women underwent MSAFP screening at 15 to 29 weeks of gestation and delivered a liveborn infant without malformations between 1/1/90 and 6/1/93. Statistical analysis was performed using chi-square test.

RESULTS: Selected outcomes are presented using an MSAFP cutoff > 2 multiples of the median (MOM). This provided the best combination of sensitivity and specificity based on examination of receiver operator characteristic curves.

<table>
<thead>
<tr>
<th>AFP-2 MOM</th>
<th>AFP2 MOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=85</td>
<td>n=12</td>
</tr>
</tbody>
</table>

Hospitalization for bleeding
- ≤30 weeks: 9 (11) vs. 7 (58); P<0.001
- Preterm birth ≤34 weeks: 12 (14) vs. 6 (50); P=0.003
- Preterm birth ≥35 weeks: 4 (3) vs. 4 (35); P=0.001
- Preeclampsia ≤34 weeks: 0 vs. 2 (17); P=0.01
- Placental abruption: 4 (5) vs. 2 (17); P=0.11
- Placenta accreta: 11 (13) vs. 3 (23); P=0.27
- Cesarean hysterectomy: 20 (24) vs. 3 (35); P=0.46

Data expressed as n (%) and P value

CONCLUSIONS: Women with placenta previa who also have MSAFP elevation are at increased risk for bleeding in the early third trimester, as well as preterm birth. Women who required cesarean hysterectomies, including those with placenta accreta, did not consistently have an elevated MSAFP.

537 EFFECT OF ANTENATAL EXPOSURE TO ST. JOHN'S WORT (HYPERICUM) ON NEUROBEHAVIOR OF DEVELOPING MICE OFFSPRING. W. Ragan*, D. Christensens*, C. Gougeauxs*, Dept Obstet Gynecol, Univ Oklahoma, Okla City, OK and Dept Obstet Gynecol, Univ New Mexico, Albuquerque, NM

OBJECTIVE: To conduct, in a randomized placebo-controlled manner, behavioral testing on mice offspring exposed antenatally to the herbal antidepressant St. John's wort (Hypericum).

STUDY DESIGN: A daily dose of St. John's wort, (0.75 mg/gm of food consumed), equivalent to that in humans according to body surface, was given to pregnant dams from gestational day 7 to 20. After delivery, offspring were divided into 2 groups: the St. John's wort- and the placebo-exposed litters were reduced to 8 pups per litter. Behavioral testing consisted of two early developmental tasks of geodesia and homing, followed by motor, anxiety and depression assessments into adulthood.

RESULTS: Birth weights were less in the St. John's wort group than in the placebo group (1.65 g versus 1.74 g; p<.01). Offspring in both treatment groups spent more time in locomotor and exploratory activity throughout development. Performances on a depression test (forced swim) and on anxiety tasks (elevated plus maze as juvenile and adult) revealed no differences between treatment groups.

CONCLUSION: Antenatal exposure to a therapeutic dose of St. John's wort did not impact performances on select behavioral tasks by developing mice offspring.


OBJECTIVE: To examine lipopolysaccharide binding protein (LBP) levels in high-risk patients at increased risk for pulmonary injury.

STUDY DESIGN: 22 patients with pyelonephritis who had a history of respiratory problems were recruited. Blood was drawn before and after treatment. LBP levels were measured using an enzyme-linked immunosorbent assay (ELISA).

RESULTS: LBP levels were significantly higher in high-risk patients compared to low-risk patients. The increase in LBP levels was correlated with the severity of pulmonary injury.

CONCLUSION: LBP levels may be a useful biomarker for predicting pulmonary injury in patients with pyelonephritis.

535 PREVALENCE AND PERSISTENCE OF POSTPARTUM DEPRESSION IN AN INNER-CITY MATERNAL HEALTH CLINIC: A MULTINATIONAL, MULTI-VARIANT STUDY. KA Yonkers, SH Ramas, AL Rush*, S Harrell*, RL Lavin, Dept Psychiatry and Ob/Gyn, UT Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To estimate rate of depressive symptoms and syndrome of major depressive disorder (MDD) during pregnancy in a large cohort of African-American and Hispanic women, and to determine whether the onset and persistence of depressive symptoms or MDD could be predicted based upon readily available medical and demographic information.

STUDY DESIGN: Women at 4 inner-city clinics were assessed at 2 (T1), 3 (T2), and 4 weeks (T3) postpartum using demographic and medical history questionnaires, the Inventory for Depressive Symptomatology—Self Report (IDS-SR), the Edinburgh Postnatal Depression Scale (EPDS), and the Quality of Life in Depression Scale. A Structured Clinical Interview for the Diagnostic and Statistical Manual for Psychiatric Disorders, 4th edition DSM-IV and Social Adjustment Scale—Self Report were administered to those women who scored above threshold at T2.

RESULTS: 802 of 890 postpartum women approached agreed to participate. 75.8% were Hispanic-American, and 10.8% were African-American. At T1, 57% of cohort scored above threshold for EPDS or IDS-SR. At T2, 29% were evaluated and 28% continued to experience depressive symptoms. In the 71 women with continued depressive symptoms at T3, 61% were positive for the syndrome of MDD but in only 28 women was the onset postpartum. The point prevalence rate for postpartum depressive disorder was 10%. Women who breastfeed have 1/2 odds of having MDD at T3 (p=0.02). Each prior child resulted in a 32% increase in odds of having MDD at T3 (p=0.02). Women who live with their extended family (rather than a significant other or spouse) have 2 1/2 times odds of having MDD at T3 (p=0.02).

CONCLUSIONS: In this cohort of postpartum women, over 1/3 exhibited symptoms of depression. An estimate for the prevalence of postpartum MDD is 10%. The major predictors of MDD at one month postpartum are not breastfeeding, more births, and living with extended family.
540 A RANDOMIZED CONTROLLED TRIAL OF URSODEOXYCHOLIC ACID AND S-ADENOSYL-L-METHIONINE IN THE TREATMENT OF GESTATIONAL CHOLESTASIS. N Roncagl et al, A Ghidzzi, A Ghidzzi, A Ghidzzi, C Andreotti, G Okradar, S Gerardo, and Georgetown University Medical Center, Monza, Italy, and Washington, D.C.

OBJECTIVE: To compare the efficacies of S-adenosylmethionine (SAM) and ursodeoxycholic acid (UDCA) at improving pruritus and serum biochemical abnormalities in gestational cholestasis.

STUDY DESIGN: All patients at <36 weeks' gestation with severe gestational cholestasis were randomly assigned to receive oral SAM 500 mg twice daily or oral UDCA 300 mg twice daily until delivery. Pruritus score, serum levels of transaminases, bile acids, and bilirubin were compared between the two groups in patients treated for 2-10 days.

RESULTS: Of the 29 patients enrolled, the 7 delivery before 10 days and were excluded from analysis. Gestational age at enrollment and at delivery, duration of therapy, rate of relapse, pruritus score, and biochemical characteristics at enrollment were similar between the two groups. At the last evaluation before delivery, patients receiving UDCA (n=14) had significantly lower serum levels of bile acids (mean standard deviation: 5.2 ± 5.2 vs 25.7 ± 25.5 μM/L, p=0.02), bilirubin (0.5 ± 0.2 vs 0.9 ± 0.4 mg/dL, p=0.001), SCOT (44.7 ± 28.1 vs 125.5 ± 126.5 mg/dL, p=0.04) and SGPT (60 ± 61.0 vs 207.1 ± 202.6 mg/dL, p=0.05), but higher pruritus score (1.1 ± 0.5 vs 0.02) than those receiving SAM (n=8).

CONCLUSIONS: In patients with intrahepatic cholestasis of pregnancy, UDCA is more effective than SAM in improving hepatotoxic abnormalities but less effective at alleviating pruritus.

542 AN OBSERVATIONAL COHORT STUDY TO EVALUATE THE EFFECTS OF ASTHMA SEVERITY ON PERINATAL OUTCOME. Dombrudsch MP for the NICHD MFMU Network and NHLBI, Bethesda, MD.

OBJECTIVE: A major study reported a four-fold increase in the rate of preterm delivery (PTD) <32 weeks among asthmatics (AJOG 1992; 167:963). The objective of this large prospective study was to determine whether or not asthma is associated with adverse perinatal outcomes.

STUDY DESIGN: Prospective observational cohort study among 16 clinical centers of subjects with mild, moderate (mod), and severe asthma. All had singleton pregnancies, control subjects were matched by ethnicity and smoking status. The study was designed with 80% power to detect a 2.0-fold increase in PTD <32 weeks. The lost to follow up rate was 0.0%.

RESULTS: Outcomes stratified by asthma severity are listed below

<table>
<thead>
<tr>
<th>n</th>
<th>mod/severe</th>
<th>mild</th>
<th>control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTD &lt;32 weeks</td>
<td>3.0%</td>
<td>3.5%</td>
<td>3.3%</td>
<td>0.863</td>
</tr>
<tr>
<td>PTD &lt;37 weeks</td>
<td>15.9%</td>
<td>16.3%</td>
<td>15.8%</td>
<td>0.952</td>
</tr>
<tr>
<td>weight (g)</td>
<td>3146</td>
<td>3136</td>
<td>3160</td>
<td>0.270</td>
</tr>
<tr>
<td>PROM</td>
<td>11.6%</td>
<td>11%</td>
<td>11.2%</td>
<td>0.942</td>
</tr>
<tr>
<td>SGA</td>
<td>7.0%</td>
<td>7.5%</td>
<td>6.1%</td>
<td>0.619</td>
</tr>
<tr>
<td>perinatal mortality</td>
<td>1.3%</td>
<td>1.3%</td>
<td>1.0%</td>
<td>0.857</td>
</tr>
<tr>
<td>chronic lung Dz</td>
<td>0.9%</td>
<td>0.7%</td>
<td>0.2%</td>
<td>0.164</td>
</tr>
<tr>
<td>neonatal sepsis</td>
<td>1.7%</td>
<td>1.2%</td>
<td>0.8%</td>
<td>0.488</td>
</tr>
<tr>
<td>preeclampsia</td>
<td>4.3%</td>
<td>4.8%</td>
<td>4.1%</td>
<td>0.957</td>
</tr>
<tr>
<td>CS for fetal distress</td>
<td>3.9%</td>
<td>4.1%</td>
<td>4.0%</td>
<td>0.995</td>
</tr>
</tbody>
</table>

CONCLUSION: Except for an increased incidence of a discharge diagnosis of neonatal sepsis, asthma and its contemporary management were not associated with adverse perinatal outcome.
BETA-HCG DETERMINATION IN THE FLUID SAMPLE FROM THE DOUGLAS POUCHE: A NEW TOOL FOR A QUICK DIFFERENTIAL DIAGNOSIS OF ECTOPIC PREGNANCY. H. E. Yaziczolu*, Y. Gunay* Dept. Ob/Gyn Taksim Hospital, Istanbul, Turkey

OBJECTIVE: To test the hypothesis that in cases of ectopic pregnancy beta HCG values in the peritoneal fluid are significantly higher than the serum values.

STUDY DESIGN: Peripheral venous blood and peritoneal (Douglas Pouch) fluid samples were drawn simultaneously in a total of 46 patients suspected to have an ectopic pregnancy on the grounds of a positive pregnancy test, fluid in the Douglas Pouch and no conclusive ultrasonographic evidence of intrauterine pregnancy. Beta HCG determinations with the RadioimmunoAssay method were done immediately in all samples. All patients then underwent a classical approach consisting of clinical and laboratory observations, repeat sonograms and laparoscopy and D&C where indicated. The final diagnosis were based on histologic evidence in all cases. Then a retrospective analysis for the diagnostic efficiency of the ratio of the peritoneal fluid to venous blood beta HCG values were done. For the statistical analysis χ² and Student’s t test were done where appropriate.

RESULTS: Of the 46 patients 6 were found to have intrauterine abnormal, 2 intrauterine normal, 2 ovarian ectopic and 36 tubal ectopic pregnancy. Mean Douglas beta HCG values were significantly higher (p<0.001) than that of peripheral venous samples in the ectopic pregnancy group whereas no significant difference could be shown in intrauterine group. Further the ratio of peritoneal to peripheral beta HCG values was > 1 in all 38 cases of ectopic pregnancy whereas only one patient with an intrauterine pregnancy had this ratio to be greater than 1.

CONCLUSIONS: The ratio of peritoneal to venous blood sample beta HCG has a 100 % sensitivity for the diagnosis of early ectopic pregnancy and can be used as a screening test to exclude ectopic pregnancy in cases with a subthreshold value of serum beta HCG.
POSTER SESSION V

Saturday, February 5, 2000
10:00 am - 12:00 pm

Fontainebleau Ballroom A/B

CATEGORIES
Fetus
Genetics
Physiology/Endocrinology

Poster Numbers
544-668

Judges: Berry A. Campbell, MD
Washington C. Hill, MD
Tariq A. Siddiqi, MD
544 THE EFFECT OF MATERNAL HYPOXIA AND REOXYGENATION ON FETAL CEREBRAL AND MYOCARDIAL TRACE METALS. B. Pouret, E. Gurzenda, D. Maulik, Dept. Obstetrics-Gynecology, Winthrop University Hospital, Mineola, NY

OBJECTIVE: The purpose of this study was to determine if maternal hypoxia and reoxygenation affects fetal cerebral and myocardial pro- and antioxidant trace metals.

STUDY DESIGN: Dunkin-Hartley guinea pigs (45-60 days gestation) were exposed to 1 h hypoxia (7% O2/93% N2) followed by up to 4 h reoxygenation in room air. At various times the fetuses were removed via C-section, their brains and hearts harvested and analyzed for total organ content of copper, iron, magnesium and zinc using atomic absorption spectrophotometry.

RESULTS: Results are summarized in the following table.

<table>
<thead>
<tr>
<th>Trace Metal</th>
<th>Prehypoxic</th>
<th>Posthypoxic (PH)</th>
<th>1 h PH</th>
<th>4 h PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copper</td>
<td>8.7±1.3</td>
<td>11.3±0.8*</td>
<td>10.4±1.4</td>
<td>10.9±0.6</td>
</tr>
<tr>
<td>Iron</td>
<td>215±13</td>
<td>270±28*</td>
<td>260±14*</td>
<td>295±13</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1286±62</td>
<td>1095±37*</td>
<td>1229±56</td>
<td>1114±41</td>
</tr>
<tr>
<td>Zinc</td>
<td>77±4</td>
<td>85±3</td>
<td>85±4</td>
<td>70±1</td>
</tr>
</tbody>
</table>

Values are expressed as mg/g dry weight and are the mean ± SEM of 8 to 12 determinations. *P<0.05, compared with prehypoxic value.

CONCLUSIONS: These results indicate that the pro-oxidant metals, copper and iron, are increased in posthypoxic fetal heart and brain; and the protective metals, magnesium and zinc, are decreased in posthypoxic fetal brain during a time when these issues may be highly vulnerable to oxidative injury.

546 USE OF QUANTITATIVE PCR TO DETECT FETAL-MATERNAL TRANSFUSION FOLLOWING FETAL SURGERY. TM Greensleeths, BS. Walsh, TL Long, LJ. Howell, AW Flacke, NS Adzick, MP, Johnson, DW Bianchi, Center for Fetal Diagnosis and Treatment, Children’s Hosp. of Philadelphia and Tufts Univ. School of Medicine/New England Med. Center, Philadelphia, PA, and Boston, MA

OBJECTIVE: To determine the incidence and magnitude of fetal-maternal transfusion during fetal surgery using a sensitive quantitative PCR technique (qPCR). In addition, to determine if the amount of transfusion is related to the underlying diagnosis, presence of hydrops, or the type of surgical procedure.

STUDY DESIGN: Blood samples were obtained from 13 pregnant women pre- and post-fetal surgery. Two women underwent a second fetal procedure yielding 14 paired samples. Eleven of the women carried a male fetus, and one carried a female fetus. DNA was prepared from whole blood, and qPCR was performed using primers that amplify a Y chromosome-specific sequence. Results were expressed as male fetal cell equivalents per 8ml umbilical cord blood. Pre and post-surgery results were compared in the same woman.

RESULTS: Mean gestational age of the fetuses was 27.7 weeks (range 25-36). The indication for fetal surgery was diaphragmatic hernia=5, congenital cystic adenomatous malformation (CCAM) with hydrops=3, sacrococcygeal teratoma=1, myelomeningocele=4, and ex utero intrapartum treatment procedure (EXIT)=3. The number of male fetal cell equivalents per 8ml ranged from 0-10 preoperatively and 0-60 postoperatively in 12 samples (normal range 0-46). No male fetal cell equivalents were detected in the woman carrying a female fetus. In one case of CCAM with hydrops, higher numbers of fetal cells were detected at both the initial resection and the subsequent EXIT procedure. Equivalents of 86 and 178 were detected preoperatively, but there was no significant elevation post-surgery (115 and 221).

CONCLUSION: Fetal surgery does not cause significant fetal-maternal transfusion as determined by a very sensitive method for fetal cell quantitation in maternal blood. Hydrops may predispose to fetal-maternal transfusion, but without significant increase following fetal surgery. The risk of fetal-maternal transfusion in open fetal surgery is very low.

545 TRANSVAGINAL ULTRASONOGRAPHIC MEASUREMENTS OF THE FETAL FOURTH VENTRICLE. I. Goldstein, D. Nisman, A. Tannia, G. Eshcalante, J. Isgakvitz-Eldor, Department of Obstetrics and Gynecology, Ramuh Medical Center, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, and Department of Obstetrics, Hospital Dr Rafael A. Aggel Calderon Guardia, San Jose, Costa Rica

OBJECTIVE: To define the normal measurements of the fetal fourth ventricle in the early second trimester using transvaginal ultrasonography and to correlate it with standard biometric parameters.

STUDY DESIGN: A prospective study was carried out. Consecutive routine biometric measurements and fetal organ scan were obtained from patients undergoing fetal anatomical survey. Special focus was given to the posterior fossa of the fetal brain. The fourth ventricle was identified and measured. Data was statistically analyzed using Pearson correlation.

RESULTS: One hundred and four fetuses between 13.5 and 16.5 weeks gestation were scanned. The fourth ventricle was visualized as a hypoechogenic triangle below the level of the cerebellum. The mean values of the fourth ventricle were: length = 6.0 mm, height = 2.5 mm, area = 7.6 mm² and circumference = 13.8 mm. Fourth ventricle measurements were independent of gestational age. In addition, 5 cases of enlarged fourth ventricle were identified and all of them were spontaneously resolved after 18 weeks gestation.

CONCLUSIONS: Fetal fourth ventricle size is independent of gestational age throughout the early second trimester. The identification of its ultrasonographic characteristics is important to rule out posterior fossa malformations. Isolated large fourth ventricle found in the early second trimester should be followed up and no decisions should be made based on the finding.

547 CHORIONIC VILLUS SAMPLING PRIOR TO MULTIFETAL PREGNANCY REDUCTION. R. Eldad, J Stone, J Lynch, R. Berkowitz, Dept. Ob/Gyn, Mount Sinai Medical Center, New York NY

OBJECTIVE: To determine the technical feasibility and accuracy of chorionic villus sampling (CVS) prior to multifetal pregnancy reduction (MFR) and to determine if CVS increases the loss rate after MFR.

STUDY DESIGN: Between 1986 and 1999, 1117 patients underwent MFR at our institution. 120 fetuses were evaluated by CVS in 66 patients prior to undergoing MFR. Information on the technical success and accuracy of CVS, as well as pregnancy outcome was collected on all patients. Technical success was defined as obtaining a sample in all fetuses not being reduced and obtaining a result prior to the MFR procedure. An overall pregnancy loss rate after MFR of 6.1% previously reported from this institution was used for comparison of loss rates in patients undergoing CVS prior to MFR.

RESULTS: CVS was successfully completed in all 66 patients attempted. One to 3 fetuses were sampled in each patient, depending on the clinical situation and the desire of the patient. A total of 120 fetuses were sampled. None of the patients undergoing CVS prior to MFR have experienced a pregnancy loss greater than 43 of the patients have delivered. Average gestational age at delivery was 36.9 weeks. Two patients delivered between 24-28 weeks, 1 between 28-32 weeks, 6 between 32-36 weeks and 33 after 36 weeks. Of the 25 ongoing pregnancies, 10 are beyond 24 weeks. Therefore, 53 patients have either delivered or are beyond 24 weeks. Based on a loss rate after MFR at our institution of 6.1%, we would expect 3.2 losses prior to 24 weeks in a sample of 55 patients but found none. One karyotypic abnormality (trisomy 21) was identified and the fetus was reduced. Of the 89 inliers delivered who had been sampled prenatally by CVS, there were no phenotypic findings suggestive of aneuploidy and there were no reported cases of an unexpected discordance in fetal gender.

CONCLUSIONS: CVS prior to MFR appears to be technically feasible and accurate. Additionally, CVS prior to MFR does not appear to increase the rate of pregnancy loss after MFR, although a larger sample size is needed to substantiate this conclusion.
GESTATIONAL AGE CHANGES IN CORD BLOOD HEMATOPOIETIC PROGENITOR / STEM CELL ADHESION MOLECULE EXPRESSION. D.V.Synhoh, C. Steinmann$, M. Burk5, S. Hahn5, A. Tichelli5, W. Holzgreve, Departments of Obstetrics & Gynecology and Hematology, University of Basel, Switzerland

OBJECTIVE: To determine if expression of the cell adhesion molecules CD44 and CD34 in cord blood changes during gestation.

STUDY DESIGN: In a prospective observational study, three-color fluorescence-activated cell sorting was used to assess the level of expression of CD44 and CD34 in cord blood samples collected at delivery between 22 and 42 weeks of gestation.

RESULTS: The relative number of CD34+ cells decreases as gestational age increases (r=0.71, p<0.001). Conversely, we found a significant increase in cell adhesion molecule expression by CD34+ cells during gestation (LFA-1, r=0.47, p=0.001; VLA-4, r=0.35, p=0.031). Comparison of between-group samples of early preterm (week 22-32), late preterm (week 33-37), and term (week 38-42) gestation confirmed this correlation and revealed that the major increase occurs between early and late gestation.

CONCLUSION: These results suggest a role for cell adhesion molecule expression in the process of migration and homing of circulating stem cells to the fetal bone marrow toward the end of pregnancy. The findings might have implications for the use of preterm cord blood for hematopoietic stem cell transplantation as well as for prenatal gene therapy.

RISK FACTORS FOR LOSS AFTER MULTIFETAL PREGNANCY REDUCTION. J. Stone, R. Eddleman, S. Patel, I. Lynch, R. Berkowitz, Dept. Ob/Gyn, Mount Sinai Medical Center, New York

OBJECTIVE: To determine risk factors for subsequent pregnancy loss in women undergoing multifetal pregnancy reduction (MFR).

STUDY DESIGN: Between 1986 and 1998, 960 patients underwent transabdominal MFR at a single institution. Outcome data was available on 874 patients. 47 of 874 patients (5.4%) subsequently lost the pregnancy prior to 24 weeks, and complete data was available on 44 patients. These 44 patients were matched by starting and finishing number of fetuses to the next two consecutive patients who had undergone MFR but did not sustain a pregnancy loss. The two groups were compared for maternal age, parity, prior pregnancy history, presence of uterine abnormalities, mode of conception, and presence of bleeding within 2 weeks of the time of initial consultation. Chi-square analysis was used for categorical variables and a p-value <0.05 was considered statistically significant.

RESULTS: No differences were noted between cases and controls for mode of conception as seen in (ovarian stimulation with or without IVF and IVF without ovarian stimulation).

The table below shows results for other factors analyzed.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n=44)</th>
<th>Controls (n=88)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulliparity (R)</td>
<td>79.6%</td>
<td>79.5%</td>
<td>0.27</td>
</tr>
<tr>
<td>History of bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks or more</td>
<td>26%</td>
<td>26%</td>
<td>0.27</td>
</tr>
<tr>
<td>History of bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 days or less</td>
<td>31%</td>
<td>34%</td>
<td>0.38</td>
</tr>
<tr>
<td>History of bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>43%</td>
<td>40%</td>
<td>0.27</td>
</tr>
<tr>
<td>History of bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>43%</td>
<td>40%</td>
<td>0.27</td>
</tr>
<tr>
<td>Bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-7 days</td>
<td>38.6%</td>
<td>35.6%</td>
<td>0.16</td>
</tr>
<tr>
<td>Bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks or more</td>
<td>24%</td>
<td>24%</td>
<td>0.65</td>
</tr>
<tr>
<td>Bleeding (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>39%</td>
<td>39%</td>
<td>0.59</td>
</tr>
</tbody>
</table>

CONCLUSION: The only single risk factor for pregnancy loss following MFR is a history of bleeding within 2 weeks of the initial consultation. Bleeding had an OR=4.0, with 95% CI=1.74-9.17. A history of a prior full term delivery showed a trend toward a protective effect, with an OR=0.42, 95% CI=0.16-1.11.


OBJECTIVE: To assess the frequency of significant fetal-maternal hemorrhage during cesarean sections.

STUDY DESIGN: Prospective case control study in 63 patients who underwent cesarean section and 63 controls matched for age, parity, ethnic group and gestational age at delivery. The method for detection of fetal red blood cells in maternal blood is based on acid elution, which leaves only ghosts from the maternal cells, whereas the fetal cells remain intact. The values obtained from this test are in percentage of fetal from total red blood cells. The method was first described by and named after Kleihauer and Betke. On each occasion, blood from a newborn and blood from an adult Askenazi male were used as positive and negative controls, respectively.

RESULTS: The mean reading in non pregnant subjects was 0.2%. Cesarean section was not associated with higher rates of fetal-maternal hemorrhage. Mean newborns 0.2%. (95% CI 0.2% to 9.2%) and 0.2% (95% CI 0.2% to 9.2%) for cesarean vs. vaginal delivery, respectively.

CONCLUSION: These results seem to be no justification to double the dose of Anti-D in women who deliver by cesarean sections. Israeli nationwide rate of cesarean section is 17% and the fraction of Rh-negative women is 10%. Total annual deliveries are 125,000. Thus, about 20,000 doses of Anti-D would be saved annually from a change in the current policy.

OBJECTIVE: Next to procedure related fetal loss other adverse effects of invasive prenatal diagnosis have been reported. Lamb defects after chorionic villus sampling (CVS) or early amnioncentesis and respiratory distress or iogenus asisla after amnioncentesis (AC). Because minor abnormalities may be overlooked in routine follow-up we obtained long-term follow-up data after CVS and AC.

STUDY DESIGN: 1509 women with singleton pregnancy who had transcervical CVS were matched on age and season of conception with 1509 women with a singleton pregnancy who had AC. All procedures were performed during 1985-1992 for advanced maternal age >35 years. Data regarding congenital malformations (classified according ICD-10), neonatal and pediatric morbidity and complications of motor development, speech, hearing and visual function were obtained by questionnaire in 1993-1995.

RESULTS: Short-term outcome was known in all but 10 infants. Questionnaires were mailed to all women with a surviving infant (n=2808) ; 2434 were returned (87%). No difference was detected between infants after CVS compared to infants after AC regarding congenital malformations (6.7% vs 6.0%), neonatal mortality (15.0% vs 15.9%), pediatric mortality with clinical treatment (7.6% vs 6.3%) or outpatient treatment only (45.8% vs 40.2%) and evident function disturbance (9.0% vs 2.9%) or doubtful function disturbance (0.5% vs 6.7%). The number of infants with physical growth <10th centile for Dutch infants was equal (10.9% vs 10.8%) Sub-analysis for limb abnormalities or respiratory complications did not demonstrate differences between infants after CVS and AC. Only 10% of all congenital malformations was already known through routine post partum follow-up.

CONCLUSION: An extensive long-term survey could not demonstrate differences of health status between infants after prenatal diagnosis by transcervical CVS or by AC.

555 OUTCOMES OF SMALL, FOR GESTATIONAL AGE AND APPROPRIATE FOR GESTATIONAL AGE INFANTS LESS THAN 1500 GRAMS. M. Learia, CC Lin, R. Mitendorf, Dept. OB/GYN Univ. of Chicago, Chicago, IL.

OBJECTIVE: Our hypothesis is that, among the very low birthweight infants (VLBW, < 1500 gms), the outcomes of small for gestational age (SGA) infants are worse than appropriate age (AGA) infants of same gestational age (GA), but the outcomes of SGA infants are better than AGA infants of same birthweight (BW).

STUDY DESIGN: We compared 33 SGA and 161 AGA infants for neonatal mortality and morbidity (RDS, NE, NEC, sepsis, sepsis, retnopathy, PDA, Apgas < 7, cord pH < 7.20, and anomalies). We also compared 15 categories of maternal high risk factors and delivery data between the two groups. Statistical methods used were Fisher's exact test, odds ratio, and logistic regression analysis.

RESULTS: SGA infants had significantly less RDS (51% vs 75%, OR = 0.39, 95% CI 0.19-0.84), NEC (0% vs 15%, OR = 0, 95% CI 0.1-6.88), and sepsis (24% vs 46%, OR = 0.37, 95% CI 0.16-0.86). Other morbidity categories and neonatal mortality rate did not differ between the two groups. Using multiple logistic regression, only maternal hypertension was associated with a decreased risk of RDS in SGA, but no other maternal high risk factor was predictive of neonatal mortality. Mean BW were similar in both groups (SGA 1022 ± 570 gms, AGA 1063 ± 580 gms, p = 0.4), but mean GA was higher in SGA than AGA infants (SGA 31.4 ± 2.6 weeks vs AGA 28.3 ± 2.5 weeks, p < 0.001). When multiple logistic regression including GA was performed, SGA infants were not found to have better outcomes than AGA infants with respect to RDS, NEC, and sepsis.

CONCLUSION: VLBW SGA infants have significantly lower risks of RDS, NEC, and sepsis as compared to AGA infants of similar BW. However, VLBW SGA infants have no survival advantage over AGA infants of the same GA.
556 FETAL RAT BRAIN DAMAGE DUE TO MATERNAL SEIZURE ACTIVITY: MECHANISM AND PREVENTION. Mordecha Hallak, John W Horst*, Joshua B Evans*, Michael L Kruger*, Departments of Ob/Gyn, Ben Gurion University/Soroka Medical Center, Beer Sheva, Israel and Wayne State University School of Medicine, Detroit, Michigan

OBJECTIVE: Maternal rat seizure activity throughout pregnancy was associated with fetal histopathologic brain damage. The N-Methyl-D-Aspartate (NMDA) receptor is thought to be the final common pathway for brain injury. Prenatal exposure to magnesium sulfate (MgSO4) has been shown to protect against brain injury and NMDA neurodegeneration. This study was initiated to evaluate whether maternal seizure activity affects the NMDA receptor binding capacity in the fetal rat brain and whether MgSO4 can prevent this effect.

STUDY DESIGN: Bipolar electrodes were stereotaxically implanted into the hippocampus of non-pregnant rats 1 week prior to breeding. Pregnant rats were randomly assigned to 1 of 4 groups (Table). On gestational days (GD) 9, 11, 13, 15, 17, and 19, dosages of saline or MgSO4 were administered to all rats every 20 minutes for 4 hours (loading-maintenance-loading), followed by seizure induction. At GD 20, rats were perfused with saline and fetuses were delivered via cesarean section. Fetuses were perfused transcardially, the brains removed, and frozen. Cryostat sections were taken, labeled in-vitro by [3H]-Glutamate (NMDA recognition site agonist) for autoradiographic assay, and mounted on Hyperfilm-CH for 10 weeks. Optical density measurements of binding of 12 brain regions on each section were performed using an image analyzing system.

RESULTS: Maternal seizure activity was associated with increased NMDA receptor binding of glutamate in the fetal rat brain. Pre-administration of MgSO4 significantly reduced this seizure effect. (Hindbrain includes midbrain, cerebellum and brainstem; Mean ± SD; *p<0.05)

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Saline &amp; No Seizure (n=28)</th>
<th>MgsO4 &amp; No Seizure (n=25)</th>
<th>Saline &amp; Seizure (n=15)</th>
<th>MgsO4 &amp; Seizure (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Binding</td>
<td>31.0±19.1</td>
<td>32.5±15.1</td>
<td>35.0±19.5</td>
<td>30.6±11.1</td>
</tr>
<tr>
<td>Hind-brain</td>
<td>30.0±14.5</td>
<td>34.2±9.4</td>
<td>36.0±13.5</td>
<td>31.1±12.8</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The mechanism for fetal rat brain injury due to maternal seizure activity is, at least in part, associated with overexcitation of the NMDA receptor binding of glutamate in the fetal rat brain and may reduce resultant total brain damage.

557 FETAL RAT BRAIN DAMAGE DUE TO MATERNAL SEIZURE ACTIVITY: EFFECT ON N-METHYL-D-ASPARTATE-R1 RECEPTOR GENE TRANSCRIPTION. M Halik, JW Horst*, DM Sunaradich. Department of Ob/Gyn, Wayne State University School of Medicine, Detroit, Michigan

OBJECTIVE: Maternal rat seizure activity throughout pregnancy was found to be associated with fetal histopathologic brain damage and an increase in N-Methyl-D-Aspartate (NMDA) receptor binding capacity. These effects were decreased by magnesium sulfate (MgSO4). The objective of this study was to evaluate whether the increase in NMDA receptor binding in fetal rat brain was due to changes at the gene transcription level.

STUDY DESIGN: Bipolar electrodes were stereotaxically implanted into the hippocampus of non-pregnant rats 1 week prior to breeding. Pregnant rats were randomly assigned to 1 of 4 groups (Table). On gestational days (GD) 9, 11, 13, 15, 17, and 19, subcutaneous doses of saline or MgSO4 were administered to all rats every 20 minutes for 4 hours (loading-maintenance-loading), followed by seizure induction. At GD 20, rats were perfused with saline and fetuses were delivered via cesarean section. Fetuses were perfused transcardially, the brains removed, and frozen. Total RNA was isolated from pooled fetal rat brains and RNA integrity was assessed. cDNA was constructed by reverse transcription using an anti-sense NMDA-R1 receptor subunit primer. Quantitative reverse transcription polymerase chain reaction (QRT-PCR) was subsequently performed using specific NMDA-R1 amplifiers and a secondary PCR MIMIC(TM) for quantitation purposes. The PCR MIMIC(TM) is composed of a non-homologous DNA fragment of known concentration, which bears the same NMDA primer attachment sites. The amount of transcribed NMDA-R1 mRNA was determined by densitometric comparison of the PCR MIMIC(TM) products.RESULTS: Table. Effects of maternal seizure activity on NMDA-R1 mRNA concentrations in fetal rat brain. (Mean ± SD; values in fg/μL)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Forebrain</td>
<td>73±34.7</td>
<td>75±37.7</td>
<td>46±19.6</td>
<td>76±32.7</td>
</tr>
<tr>
<td>Hindbrain</td>
<td>71±24.9</td>
<td>74±34.2</td>
<td>40±15.9</td>
<td>70±24.4</td>
</tr>
</tbody>
</table>

Two way ANOVA revealed hypoxia effect on the Kainate and AMPA receptors, as well as magnesium effect (AMPA agonist) and interaction effect between hypoxia and magnesium (AMPA agonist & Kainate, p<0.05).

CONCLUSIONS: Severe hypoxia resulted in significant changes in binding of the EAAR (Kainate & AMPA) in the fetal rat brain. MgSO4 administration resulted in an attenuation of this hypoxic related effect to control levels (or at least significantly decrease neuronal damage).
560 RHEUS-D DIAGNOSIS FROM AMNIOTIC FLUID BY GENOTYPING

M. Kirschbaum, B. Rothe, G. Bern Dept. Ob/Gyn and Inst. of Clin. Immunology, Univ. of Giessen, Germany

OBJECTIVE: Polymerase chain reaction (PCR) is the well established method to determine Rhesus blood group antigens in very small cell samples, where serologic methods fail. Aim of the study was to show the reliability of the Rh-D genotyping by PCR from amniotic fluid cells as a tool in prenatal diagnosis.

STUDY DESIGN: In 119 samples of amniotic fluid (median 16th week of pregnancy) a Rh genotyping with two independent methods was performed: (1) Arce et al. Method 1 (Arce); (2) Bennett, Method 2 (Arce/Nurse). The Rh-D phenotype was determined from blood of the umbilical cord with monoclonal Anti-D Antiserum after delivery. The DNA preparation was performed with a standard DNA extraction kit.

RESULTS:

<table>
<thead>
<tr>
<th>Samples</th>
<th>Serology (post partum)</th>
<th>PCR (Arce) (amniotic fluid)</th>
<th>PCR (Bennett) (amniotic fluid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=130</td>
<td>96/130</td>
<td>96/130</td>
<td>96/130</td>
</tr>
<tr>
<td>Rhesus-D positive</td>
<td>17/150</td>
<td>12/150</td>
<td>14/130</td>
</tr>
<tr>
<td>Rhesus-D negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>false positive</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>false negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>results with only one of the techniques</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>no result with either technique</td>
<td>0</td>
<td>3</td>
<td>1/2</td>
</tr>
</tbody>
</table>

The table shows, that all Rh-D positive samples were recognized by all 3 applied techniques. There were no false negative results. From the 3 resp. 5 samples, which were false positive, 2 were contaminated with maternal Rh-D positive DNA. 3 samples with no result did not show any DNA at all. 8 samples showed results only with 1 method.

CONCLUSION: Prenatal Rh-D genotyping with allel specific PCR is a reliable method to type the fetal Rhesus factor in pregnancies with irregular antibodies against the D-antigen. This is a useful tool to evaluate the fetal risk without umbilical cord puncture. To prevent false results at least 2 different PCR-primers should be used. The determination is only reliable in case of coincidence of both results.

561 NEITHER CESAREAN SECTION NOR DELIVERY IN A TERTIARY CARE CENTER IMPROVES NEONATAL OUTCOME IN INFANTS WITH OMPHALOCELE. BK Rothen*, DA Terrone*, P. Hugl*, CM Isler, FS Barcellona*, WE Roberts, Dept. Ob/Gyn, Univ. Mississippi Medical Center, Jackson, MS

OBJECTIVE: To determine if neonatal outcome of infants with omphalocele is effected by the route of delivery or delivery in a tertiary care institution.

STUDY DESIGN: A computer search was conducted for all infants with omphalocele admitted to the University Medical Center between January 1994 and January 1999. Medical records from the obstetric, neonatal, and ultrasound units were reviewed for maternal demographic, diagnostic, and neonatal outcome variables. Statistical analysis was performed using the student's t-test, Kruskal-Wallis, Chi-square, and Fisher's exact test as appropriate. A p<0.05 was considered to be statistically significant.

RESULTS: Fifty-one cases of omphalocele were identified. Nine cases (18%) underwent pregnancy termination. Of the remaining 42 cases, 22 (52%) were delivered at the medical center and 30 were delivered at non-tertiary institutions. Nineteen (45%) were delivered vaginally. When appropriate a p<0.05 was considered to be statistically significant.

DECLINE OF CAESAREAN SECTION RATE AFTER INTRAUTERINE TRANSFUSIONS.

563 PLASMA ERYTHROPOIETIN AND IRON CONCENTRATIONS IN THE OVINE FETUS WITH IMMUNE-INDUCED HEMOLYTIC ANEMIA. RB Wolf, KJ Moise, JA Widness, RA Brace, Dept of Reproductive Medicine, Div of Perinatal Medicine, Univ of California at San Diego, La Jolla, CA, Dept of Ob-Gyn, Univ of North Carolina, Chapel Hill, NC, and Dept of Pediatric Research, Univ of Iowa, Iowa City, IA

OBJECTIVE: To determine changes in plasma erythropoietin (EPO) and iron concentrations in ovine fetuses treated with anti-red cell antibodies.

STUDY DESIGN: Seven chronically catheterized fetal sheep were infused daily with anti-red cell antibodies over a 10-day period. Fetal arterial blood was sampled daily prior to infusion for hemoglobin and hematocrit (hct), EPO and iron, and arterial blood gases (pH, pO2, pCO2). Indicator dilution studies were performed every other day to determine red cell mass (RCM). Results were then compared to seven age-matched control fetuses in which no antibodies were administered.

RESULTS: During the 10-day antibody infusion, RCM decreased 18.9±5.2% while it increased in the control group by 92±7.9% (p<0.001). During the same time, fetal EPO increased from a baseline of 532±20 to 519±572 mU/ml in the antibody infused fetuses while decreasing from 48±17 to 19±3 in the control fetuses (p=0.001). Increased EPO levels were significantly correlated with declining hct and lower A5 (p<0.0001) not with changes in pH or pO2. Although fetal plasma iron increased with time, there were no significant differences between the 2 groups (interaction, p>0.47).

CONCLUSIONS: Immunologically induced fetal anemia produces hypoxia and elevated EPO concentrations. Fetal plasma iron is not increased with red cell destruction, suggesting iron may be sequestered within the fetal reticuloendothelial system. We speculate that fetal supplementation with iron via intra-amniotic injection could enhance erythropoiesis in these anemic fetuses.
LONG TERM CLINICAL AND IMMUNOLOGICAL FOLLOW-UP AFTER INTRAPERITONEAL INTRAUTERINE TRANSFUSIONS (IUT). Henk E Veer1, Eric Hallensleben1, Humphrey HH Kanhai1, Arneke Brand2, Frans HJ Claas2. From the Department of Obstetrics1, and the Department of Immunohematology and Blood Bank2, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden.

OBJECTIVE: The purpose of these investigations was to perform a long term follow-up study of intraperitoneal, intrateroneal transfused patients.

STUDY DESIGN: Between 1966 and 1976, 75 fetuses received an intraperitoneal intrauterine transfusion (IUT) for severe hemolytic disease at our center. Twenty-four patients survived this condition and IUT treatment. All 21 individuals, who were still alive at the time of these investigations, participated in the long term follow-up study. They had a physical examination, routine laboratory testing and screening for the presence of autoantibodies performed and their medical history was taken. Seven female IUT recipients who received at least one transfusion from a male donor were analyzed for the persistence of donor lymphocytes using a polymerase chain reaction (PCR) for Y-chromosome specific sequences.

RESULTS: All patients were in good health at the time of the examination and routine laboratory testing revealed no abnormalities. Six female IUT recipients, who had never been pregnant, revealed Y-chromosome specific sequences in their peripheral blood.

CONCLUSION: The long term results of IUT are favorable. We did not observe any adverse effects of IUT treatment, but this therapy is associated with persisting microchimerism with donor cells.

ETIOLOGIC CAUSES FOR DISCORDANT TWINS FETAL GROWTH. D. Shah, H. Saker, A. Salvador, R. Redline. Department of Obstetrics & Gynecology, University MacDonald Women's Hospital, Case Western Reserve University, Cleveland, Ohio.

OBJECTIVE: To correlate placental pathologic findings with growth in twin gestations to define etiologic causes for discordancy.

STUDY DESIGN: All the twin gestations (n=249) delivered at the University MacDonald Women's Hospital between January 1996 and July 1998 were included in the study. A retrospective review of maternal and infant data was conducted. The results of dichotomy were based on postnatal birth weight data. Placental examination was performed in 218 cases and adequate data was available in 198 cases. There were 50 (30%) pairs of discordant twins (D) and 139 (70%) pairs of non-discordant twins (ND) out of 198. A perinatal pathologist blinded to the clinical data on fetal growth analyzed placental data. Placental findings were grouped into the following etiologic categories: 1) Chorionic villous abnormalities (CVA): chronic villitis, fetal vasculopathy and perivillous fibrin deposition 2) Maternal vasculopathy (MV): decidual arteropathy, placental infarctions and syncytial knotting, and 3) Implantation Abnormalities (IA): eccentric placental cord insertion, abnormal placental shape and chronic peripheral separation. Data on chorionicity and inter-twin vascular communication were also collected. Placental findings were then correlated with discordant and non-discordant twins and analyzed by chi square analysis or Fisher's exact test as appropriate.

RESULTS: High percentage of discordant twins in this data reflects tertiary referral nature of this data, allowing us to analyze for etiologic causes. The prevalence of placental findings in discordant vs. non-discordant twins were: CVA 15% vs. 9% (p=0.29), MV 13% vs. 11% (p=0.69), and IA 56% vs. 25% (p=0.001). Vascular anastomosis were evaluated infrequently (n=45), only in monochorionic placentae and revealed inter-twin vascular anastomosis 5% (D) vs. 3% (ND) (p=0.43).

CONCLUSION: Our results suggest that the most important etiologic factors for discordant twin growth are implantation abnormalities. These data have implications for sonographic evaluation & clinical management of twin gestations because these findings are sonographically diagnosable.

STRESS DURING DELIVERY INCREASES THE NUMBER OF UCLEATED CELLS AND HEMATOPOIETIC PROGENITOR CELLS IN UMBILICAL CORD BLOOD. Lisa F. Falenberg, J. Kanhai H., Schrey S. Department of Obstetrics, and Haematology, Leiden University Medical Center (LUMC), PO Box 9600, 2300 RC Lenden, The Netherlands.

OBJECTIVE: Study the relationship between antenatal stress variables and the quality of umbilical cord blood (UCB) for stem cell transplantation.

METHODS: Colony-forming unit-granulocyte, monocyte (CFU-GM) used to predict hematopoietic capacity of a stem cell transplant. Together with CD34+ cell content and the number of hematopoietic progenitor cells (HPC) this is used as a UCB quality measure. We studied the effects of labour parameters on CFU-GM, HPC (data not given) and number of CD34+ cells in 284 UCBs collected at our department after non complicated term pregnancies. Correlation coefficients (r) and p values are given.

RESULTS:

<table>
<thead>
<tr>
<th>variable</th>
<th>UCB</th>
<th>r</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ruptured membranes &gt;24h</td>
<td>CFU-GM*</td>
<td>0.304</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CD34+</td>
<td>0.223</td>
<td>0.003</td>
</tr>
<tr>
<td>duration first stage</td>
<td>CFU-GM</td>
<td>0.209</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CD34+</td>
<td>0.148</td>
<td>0.021</td>
</tr>
<tr>
<td>duration second stage</td>
<td>CFU-GM*</td>
<td>0.254</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CD34+</td>
<td>0.148</td>
<td>0.019</td>
</tr>
<tr>
<td>pH ven</td>
<td>CFU-GM</td>
<td>-0.386</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CD34+*</td>
<td>-0.277</td>
<td>0.000</td>
</tr>
<tr>
<td>Apgar 1</td>
<td>CFU-GM</td>
<td>-0.294</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CD34+</td>
<td>-0.153</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*these four variables explain 35% of the variance in CFU-GM
#these two variables explain 38% of the variance in CD34+ cells

CONCLUSIONS: A highly significant postive association was found between antenatal stress factors and parameters of UCB quality. This positive association may be explained by the process of delivery, possibly by cytokine induction. Although a longer duration of ruptured membranes did not influence UCB quality, we found a positive association between stress factors occurring during parturition. In addition, children with lower Apgar scores indicating acute stress have higher numbers of UCB parameters. UCB can be a rich source of hematopoietic stemcells, especially after stressfull delivery.


OBJECTIVE: We evaluated the association between fetal iron nutriture as assessed by cord serum ferritin (Ft) levels and psychomotor development of children at age five.

STUDY DESIGN: Psychomotor tests for full-scale IQ, language ability, fine and gross motor skills, attention, and tractability were given to 278 children (whose mothers participated in a study of fetal growth) at a mean age of 5.5 years. Umbilical cord Ft levels were measured by immunoradiometric assay. Psychomotor test scores were compared between the lowest, highest and two median quartiles of cord Ft values.

RESULTS: Children with low cord Ft levels at birth had significantly worse language ability, fine-motor skills and tractability than those with median cord Ft levels. Those in the lowest Ft quartile were 4.8-fold more likely to score poorly in fine-motor skills and 2.7-fold more likely to have poor tractability than those with median levels. Full scale IQ in the high cord Ft quartile was slightly lower (83 ± 12, SD) than the median quartiles (84 ± 12), but an odds ratio for having a score of less than 70 was 3.3 (95% C.I., 1.2-9.1) in the highest quartile.

CONCLUSION: Our data indicate that poor fetal iron nutriture (low Ft) may retard fetal brain development resulting in diminished performance in certain tests of psychomotor development. High Ft, reflecting either iron overload or an acute-phase reaction (i.e., infection) may adversely affect full-scale IQ.
568 EFFECT OF OLIGOHYDRAMNION ON FETAL SPINAL FLEXION


OBJECTIVE: Oligohydramnios (OH) is associated with fetal abnormalities including lung hypoplasia. A study in sheep has proposed that exaggerated flexion of the fetal trunk induced by OH might be a cause of fetal lung hypoplasia, but the relationship between OH and fetal spinal flexion has not been quantified in human pregnancy.

STUDY DESIGN: We compared the degree of spinal flexion in fetuses surrounded by normal and reduced volumes of amniotic fluid. Ultrasound images of the spine (sagittal view) of 10 fetuses (5 OH, 5 controls) were obtained at 20±1.5 weeks of gestation. The degree of spinal curvature was assessed as the mean of 5 evenly spaced radii measured between upper thoracic and lower lumbar levels; the mean radius was normalized with respect to spinal segment length.

RESULTS: In OH cases the amniotic fluid index was 3.9±1.03, compared to 14.5±3.31 in controls (p<0.05). The mean normalized spinal radius for OH fetuses was 0.57±0.03 which was significantly less than the value obtained for controls 0.96±0.12 (p<0.05).

CONCLUSION: OH is associated with exaggerated spinal flexion in the human fetus which could affect infant lung growth and development.


OBJECTIVE: To determine the relative risk of various peripartum and obstetrical complications associated with open fetal surgery for nonlethal complications.

STUDY DESIGN: A single-institution nonrandomized contemporary observational study comparing risks of antenatal repair of fetal myelomeningocele performed through a hysterotomy since 1997 to comparable controls receiving standard care since 1990.

RESULTS: The 29 study patients were older (31 ± 25 yrs, p < 0.001), with more multigravidas (96% vs 56%; p = 0.01) and greater parity (1 vs 0.5, p = 0.02) than the 32 controls, but no difference was detected in preexisting risk factors. The mean EGA at surgery was 26.8 (range 24.3-29.6) wks, mean operating time was 95 (range 67-131) mins, and mean intraoperative blood loss was 95 (range 25-500) ml. MgSO4 was administered postoperatively for a mean of 22 (range 0-360) hrs, and was discontinued in only 1 patient due to an adverse reaction. Only 2 patients developed pulmonary edema postoperatively, and neither required intubation or admission to an ICU, an additional 5 received laxis. Dosage of the terbutaline pump did not have to be changed in the operating room was 95 (range 67-131) mins, and mean intraoperative blood loss was 95 (range 25-500) ml. MgSO4 was administered postoperatively for a mean of 22 (range 0-360) hrs, and was discontinued in only 1 patient due to an adverse reaction. Only 2 patients developed pulmonary edema postoperatively, and neither required intubation or admission to an ICU, an additional 5 received laxis. Dosage of the terbutaline pump did not have to be changed in any patient due to side effects. The mean length of stay was 33 (range 3-7) d; no patient required a transfusion, or developed an infection, preterm labor, or fluid leakage postoperatively. After initial discharge, study patients were at greater risk for oligohydramnios (48% vs 5%; p < 0.001), preterm labor (43% vs 6%; p = 0.001), PPROM (34% vs 3%; p < 0.002), and readmission to the ICU (40% vs 9%; p < 0.001). The mean EGA at delivery was earlier among study patients (33.2 ± 37.1 wks; p < 0.001).

CONCLUSION: Perioperative complications of open fetal surgery for nonlethal malformations were few, although patients were at significant risk for subsequent oligohydramnios, PPROM, preterm labor and delivery.


OBJECTIVE: To identify factors present prior to performance of open fetal surgery for repair of spina bifida which may predict the need for ventriculoperitoneal shunt placement.

STUDY DESIGN: All infants > 6 mos old after intrauterine repair of spina bifida were studied. Potential determinants analyzed included preoperative ventricular measurements, anatomical level of the lesion, type of lesion, presence of talipes, and gestational age at repair.

RESULTS: Of 29 infants studied, 17 (59%) required shunts and 12 did not. Maternal age, race, gravidity and parity did not affect the need for shunt placement, neither did the type of lesion (myelomeningocele or myeloschisis) or the presence/absence of talipes in the fetus. The strongest predictor of shunt requirement was the upper level of the lesion: all 5 fetuses with lesions ≥ L2 required shunts, as did 13/14 (93%) with lesions ≥ L3; only 4/15 fetuses (27%) with lesions ≤ S1.4 required shunts. In those fetuses with lesions ≤ S1.4, size of the ventricles prior to repair was the strongest predictor: all those with ventricles ≥ 15.7 mm required shunts. EGA at the time of repair was not a significant independent predictor, but a trend toward a decreased need for shunts was noted with earlier repairs.

CONCLUSION: Fetuses with spina bifida lesions at L4 or below and mild ventriculomegaly are at low risk for ventriculoperitoneal shunt placement if the defect is repaired in utero. This combination of factors is more likely at earlier gestational ages.

571 FACTORS AFFECTING PERINATAL OUTCOME IN 134 SINGLETON PREGNANCIES FOLLOWING OVUM DONATION. G. Shaffer, D. Levan, J. Dor, S. Mashiach, M. Kupferminc, D. S. Seidman, L. Lie Maternity Hospital, Sourasky Medical Center, Tel Aviv 1, Dept. Ob/Gyn, Sheba Medical Center Tel-HaShomer 2; and Sackler school of Medicine, Tel Aviv University, Tel Aviv, Israel.

OBJECTIVE: The purpose of this study was to evaluate the interactions between perinatal outcome in ovum donation pregnancies and various factors (e.g. obstetric complications, personal characteristics).

STUDY DESIGN: The study comprised 134 women who conceived and delivered following ovum donation. Obstetric and perinatal data were collected retrospectively through personal interviews and medical files. Multiple stepwise logistic regression analyses were used to evaluate the association between perinatal outcomes and the following variables: women's age, parity, ovarian function, gestational hypertension (GHTN), gestational diabetes mellitus (GDM) and second trimester bleeding (STB).

RESULTS: The rates of the variables appear in the table. There was no perinatal mortality. The factors associated with preterm delivery (PD) (<37 of gestational weeks), low birth weight (LBW) (<2500 gr), babies born small for gestational age (SGA) (<10th percentile), the need for neonatal intensive care (NIC) and their odds ratios [and 95% confidence interval] are as follows:

<table>
<thead>
<tr>
<th>Factor (%)</th>
<th>OR (CI)</th>
<th>GHTN (%)</th>
<th>GDM (%)</th>
<th>STB (%)</th>
<th>Nulliparity (67.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW (14.9%)</td>
<td>4.55 [1.4, 13.9]</td>
<td>*</td>
<td>22.5 [2.6, 194]</td>
<td>*</td>
<td>8.3 [1.4, 49.2]</td>
</tr>
<tr>
<td>SGA (7.6%)</td>
<td>4.10 [1.2, 14.1]</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>NIC (11.9%)</td>
<td>4.10 [1.1, 15.1]</td>
<td>*</td>
<td>8.3 [1.4, 49.2]</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

*No statistically significant association found.

CONCLUSIONS: In singleton pregnancies following ovum donation, adverse perinatal outcomes were strongly associated with gestational hypertension, but not with age >45 and ovarian failure.
572 BENZODIAZEPINE AND METHADONE USE IS ASSOCIATED WITH LONGER NEONATAL WITHDRAWAL IN POLY-SUBSTANCE EXPOSED INFANTS. P. Wilson, V. Dorazio, W. Miller, L. Currer, Dept. of Psych. and Dept. of OB/GYN, Univ. of New Mexico, Albuquerque NM.

OBJECTIVE: We predicted that individual differences in neonatal withdrawal would be accounted for by social, medical and substance use characteristics of the mother. We hypothesized that factors from each domain would predict length of neonatal detoxification.

STUDY DESIGN: Charts of women and children participating in a comprehensive perinatal program for pregnant substance abusers were reviewed to collect information regarding medical, social and substance use variables. Stepwise, hierarchical multiple regression analysis was used to examine predictors of the length of neonatal withdrawal treatment. Neatons experiencing withdrawal were compared to poly-substance exposed infants who did not experience withdrawal.

RESULTS: Significant positive univariate correlations were found between the length of neonatal detoxification and maternal age (p<0.01), maternal history of rape (p<0.05), number of antenatal infections (p<0.025), percent of toxicologies positive for benzodiazepines (p<0.0005), cocaine (p<0.058), and opiate (p<0.005), as well as the number of drugs used during pregnancy (p<0.005) and infection with Hepatitis B (p<0.001) or Hepatitis C (p<0.005).

CONCLUSIONS: Older maternal age, maternal history of rape, multiple antenatal infections, benzodiazepine use, cocaine use, methadone use, poly-substance use, hepatitis infection and hepatitis carrier status were independent risk factors for extended neonatal withdrawal. Because of their independent contribution to increased neonatal withdrawal, decreased gestational age, benzodiazepine use and methadone use are likely to have causal relationships with extended neonatal withdrawal.


OBJECTIVE: To evaluate the association of birthweight with five-year growth and neurodevelopmental outcomes in twins

STUDY DESIGN: Forty-seven sets of twins were recruited prenatally for a longitudinal study of growth and neurologic development. Extensive maternal demographic, risk assessment, and antepartum data were compiled on each patient. Comprehensive anthropometric measurements were obtained on each infant at birth. Infants were followed for five years. Anthropometric measurements and neurodevelopmental tests (including tests for IQ, WISC Full Scale, Primary Scales of Intelligence-Revised, motor function, Pediatric Fine/Gross Motor Scales), and psycholinguistic ability (Test for Auditory Comprehension of Language-Revised) were obtained at the five-year assessment. Statistical analyses included the paired Student's t-test, McNemar's test, and linear regression analysis.

RESULTS: Of the initial 47 sets of twins identified, 37 sets completed follow-up testing thru 5 years. Average delivery gestational age (mean±SD) for the study cohort was 35.6±2.2 wks. Intra-twin birthweight difference was 322±288 g. No significant differences were noted between the co-twins with respect to Apgar scores, infant sex, or incidence of respiratory distress syndrome. For each twin set, the lower birthweight twin had a significantly lower IQ at five-years (Δ 3.4±7.7 points, p=0.05) as compared to the larger twin. In spite of this difference, however, no significant correlation was noted overall between the intra-twin birthweight difference (%: large-small twin/large twin birthweight x 100) and IQ at five years. A significant correlation, however, was noted between the intra-twin birthweight difference and weight (r=0.49, p=0.005) and height (r=0.34, p=0.05) at five years of age. Interestingly, comparison of the fetal growth restricted twin (FGR, defined as <15% for growth based on Alabama standard) with race, sex, and parity to the normal growth twin (AGA) in AGA:FGR twin pairs (n=17) revealed a significantly lower IQ (Δ 3±6 points, p=0.05) a reduction in fine motor skills (Δ 2±4 points, p=0.05) in the FGR twin at five years of age. These differences were more pronounced using a standard obstetric definition of discordance (25% intra-twin birthweight difference) where the small twin of discordant twin pairs (n=5) had a significantly lower IQ as compared to the larger co-twin (Δ 6±5 points, p=0.05).

CONCLUSION: Fetal growth restriction in twins appears to be associated with a reduction in IQ at five years of age.

574 PERINATAL OUTCOME OF THE CO-TWIN AFTER THE DEMISE OF THE FIRST TWIN IN PREGNANCIES COMPLICATED BY TWIN-TWIN TRANSFUSION SYNDROME. J. Delisi, G. Mars, International TTS Registry Group, Maternal Fetal Medicine, Yale University, New Haven, CT.

OBJECTIVE: To determine the perinatal outcome of monochorionic twin pregnancies complicated by twin-twin transfusion syndrome (TTTS) following the intrauterine demise of one twin.

STUDY DESIGN: Longitudinal follow-up study of 225 pregnancies diagnosed with TTTS prior to 28 weeks' gestation. Eighteen centers worldwide participated in the study. All patients were uniformly treated with serial therapeutic amnioreductions. Following the diagnosis of fetal death, the remaining pregnancies were allowed to continue until the spontaneous onset of labor or the development of fetal or maternal indications for induction of labor or delivery by cesarean section.

RESULTS: Sixty-eight pregnancies (30.5%) were complicated by intratranse death of at least one twin. In 52 pregnancies (14.5%) both twins died in utero. In 27 pregnancies (12%) the donor twin died in utero and the recipient was delivered alive; 18 of them survived at one month of age. Six of the 18 had major morbidity during their first month of birth (multisystemic encephalomalacia: n=1; intraventricular hemorrhage: n=1; renal failure: n=1; left foot amputation: n=1; mild ventriculomegaly: n=1). The remaining 12 infants did not have any complications. In nine pregnancies (4.0%) the recipient twin died in utero and the donor twin was born alive; eight of them survived at one month of age. One infant developed sepsis; a second twin developed unresponsive hemorrhagic, patent ductus arteriosus and broncho-pulmonary dysplasia. The other six infants were developing well at four weeks after birth. Overall, the intact survival rate at four weeks was 66.1% for the recipients (12/18) and 75.0% for the donors (6/8).

CONCLUSION: The intratranse demise of one twin in pregnancies complicated by TTTS is associated with a perinatal mortality and morbidity of the co-twin as high as 75.5%. Among the alive twins, 33.3% of the donor and 25% of the recipients were complicated by perinatal morbidity.

575 RISK FACTORS AND SURVIVAL RATE IN TWIN-TWIN TRANSFUSION SYNDROME. E. Kovancz, S.L. Ramsey, V. Dorato, S.M. Ramey, L.B. Curet. Dept. of Psych. and Peds., Univ. of Miami, Miami, FL.

OBJECTIVE: To predict the probability of survival at 4 weeks of age for fetuses with twin-twin transfusion syndrome (TTTS)

STUDY DESIGN: 225 pregnancies diagnosed with TTTS before 28 weeks' gestation were enrolled from 18 centers participated in this study. All patients were treated with aggressive amnioreduction. Logistic regression analysis was used to determine risk factors associated with perinatal mortality from 11 antenatal parameters (Table 1) and the survival rate at 4 weeks of age based on factors selected by the logistic regression were calculated.

RESULTS: After 4 weeks of age, both twins were alive in 48.4% of the pregnancies; at least one twin was alive in 70.8% of the pregnancies; the recipient twins were alive in 64.5% and the donor twins were alive in 54.7% of the pregnancies. The logistic regression selected the following risk factors: volume removed per week (VRPW), hydrops of recipient, absent of endocardial cushion defect (ECD), recipient twin died in utero and the donor twin was born alive; 18 of them survived at one month of age. Six of the 18 had major morbidity during their first month of birth (multisystemic encephalomalacia: n=1; intraventricular hemorrhage: n=1; renal failure: n=1; left foot amputation: n=1; mild ventriculomegaly: n=1). The remaining 12 infants did not have any complications. In nine pregnancies (4.0%) the recipient twin died in utero and the donor twin was born alive; eight of them survived at one month of age. One infant developed sepsis; a second twin developed unresponsive hemorrhagic, patent ductus arteriosus and broncho-pulmonary dysplasia. The other six infants were developing well at four weeks after birth. Overall, the intact survival rate at four weeks was 66.1% for the recipients (12/18) and 75.0% for the donors (6/8).

CONCLUSION: The intratranse demise of one twin in pregnancies complicated by TTTS is associated with a perinatal mortality and morbidity of the co-twin as high as 75.5%. Among the alive twins, 33.3% of the donor and 25% of the recipients were complicated by perinatal morbidity.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Both Twins</th>
<th>Recipient</th>
<th>Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.49</td>
<td>0.92</td>
<td>0.9</td>
</tr>
<tr>
<td>B</td>
<td>0.35</td>
<td>0.39</td>
<td>0.47</td>
</tr>
<tr>
<td>C</td>
<td>0.19</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>D</td>
<td>0.55</td>
<td>0.34</td>
<td>-</td>
</tr>
<tr>
<td>E</td>
<td>0.36</td>
<td>0.36</td>
<td>0.39</td>
</tr>
<tr>
<td>F</td>
<td>0.46</td>
<td>0.34</td>
<td>0.11</td>
</tr>
<tr>
<td>G</td>
<td>0.17</td>
<td>0.64</td>
<td>0.8</td>
</tr>
<tr>
<td>H</td>
<td>0.2</td>
<td>0.195</td>
<td>0.26</td>
</tr>
<tr>
<td>I</td>
<td>0.16</td>
<td>0.134</td>
<td>0.192</td>
</tr>
<tr>
<td>J</td>
<td>0.92</td>
<td>0.35</td>
<td>-</td>
</tr>
<tr>
<td>K</td>
<td>0.07</td>
<td>0.62</td>
<td>0.07</td>
</tr>
<tr>
<td>L</td>
<td>1.5</td>
<td>0.52</td>
<td>1.42</td>
</tr>
<tr>
<td>M</td>
<td>0.44</td>
<td>0.76</td>
<td>0.17</td>
</tr>
<tr>
<td>N</td>
<td>0.67</td>
<td>0.47</td>
<td>0.48</td>
</tr>
<tr>
<td>O</td>
<td>0.68</td>
<td>0.37</td>
<td>-</td>
</tr>
<tr>
<td>P</td>
<td>0.77</td>
<td>0.41</td>
<td>0.94</td>
</tr>
</tbody>
</table>

*Twenty-two weeks' gestations and 1100 cc of amniotic fluid removed per week were obtained using receiver operating characteristic curves.*

CONCLUSION: Outcome for fetuses with TTTS treated with amnioreduction depends on several antenatal variables which may help in counseling patients with pregnancies complicated by TTTS.
576 SEVERE PREECLAMPSIA LESS THAN 34 WEEKS: THE IMPACT OF FETAL GROWTH RESTRICTION ON RESPIRATORY DISTRESS SYNDROME. A Sharpe, L. Leduc. Dept. of Ob/Gyn, Ste Justine Hospital, Univ. of Montreal, Quebec, Canada.

OBJECTIVE: To evaluate the effects of fetal growth restriction on respiratory distress syndrome (RDS) in cases of severe preeclampsia ≤ 34 weeks who were managed expectantly.

STUDY DESIGN: A retrospective cohort design was used. All patients meeting criteria for severe preeclampsia at ≤ 34 weeks who were managed expectantly at our tertiary institution between 1994-99 were included. Patients with multiple gestation, prematurity rupture of membranes, known fetal anomalies, maternal medical disease or a contraindication to expectant management were excluded. Groups with and without fetal growth restriction (FGR) were compared and stratified by severity: ≤ 3rd percentile, 3rd-5th, 5-10th, >10th. Multiple logistic regression was used to adjust for birthweight, gestational age, maternal age and diastolic blood pressure. Corticosteroids, surfactants, mode of delivery, infant gender, maternal diabetes or proteinuria were not confounded.

RESULTS: 26 cases of severe preeclampsia < 34 weeks who were managed expectantly were identified, 13 with FGR and 13 without FGR. All comparisons were done to the subgroup with normal fetal growth (< 10th percentile). After multivariate analysis, RDS was significantly decreased for infants ≤ 5th percentile:

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3rd vs 10th</td>
<td>0.075</td>
<td>0.01-0.92</td>
</tr>
<tr>
<td>5-10th vs 10th</td>
<td>0.52</td>
<td>0.12-2.28</td>
</tr>
<tr>
<td>&lt;5th vs &gt;5</td>
<td>0.19</td>
<td>0.04-0.88</td>
</tr>
<tr>
<td>&lt;10th vs &gt;10th</td>
<td>0.65</td>
<td>0.17-2.40</td>
</tr>
</tbody>
</table>

CONCLUSION: Preliminary results suggest that after controlling for gestational age and birthweight, the presence of FGR ≤ 5th percentile significantly decreases the risk of RDS in cases of severe preecampsia less than 34 weeks managed expectantly. This should be taken into account when considering expectant management of these patients.

577 FETAL URINARY ALBUMIN: A MARKER OF RENAL DYSPLASIA IN LOWER URINARY TRACT OBSTRUCTION (LUTO). MP Johnson, S. Caddigan, P. F. Qureshi, B. Feldman, S. Kapera, M. King, M. Evans, Dept Ob/Gyn & Pathology, Wayne State University, Detroit, MI and Center for Fetal Diagnosis & Treatment, Children's Hospital of Philadelphia & University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Analysis of fetal urine using electrolyte and protein markers is predictive of renal damage in LUTO. Fetal proteinuria increases with severity of renal damage, and in contrast to electrolyte markers, may be more reflective of glomerular and proximal tubular damage. Protein electroelrophoresis has shown albumin to be a major component of proteinuria. We evaluate the use of urinary albumin as an indicator of fetal renal damage.

STUDY DESIGN: Amniotic fluid from 53 pregnancies with confirmed LUTO that underwent complete prenatal evaluation between 14-32 wks gestation from 1988-98 were reviewed. Values from the last of a series of at least 3 amniocenteses used as they have been shown to be most predictive of fetal renal function. Cases were categorized according to renal histology or nadir creatinine values at one year of age as - dysplasia (Cr>1.0mg/dl) or + dysplasia (Cr ≥1mg/dl). Specimens were analyzed for total protein (TP), albumin fraction from protein electrophoresis (PE-A) and microalbumin (m-A), and compared to standard markers (Na, Osm) for ability to predict absence of severe renal dysplasia. Screening thresholds for TP (<20mg/dl), Na (<110mEq/L), and Osm (<200mOsm/L) have been previously reported. Proposed thresholds for PE-A (<10mg/dl) and m-A (<90 µg/mgCr) were based on data distribution analysis in this study.

RESULTS:

<table>
<thead>
<tr>
<th>TP</th>
<th>m-A</th>
<th>PE-A</th>
<th>Na</th>
<th>Osm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens</td>
<td>0.92</td>
<td>0.85</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Spec</td>
<td>0.86</td>
<td>0.86</td>
<td>0.82</td>
<td>0.83</td>
</tr>
<tr>
<td>PPV</td>
<td>0.82</td>
<td>0.87</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>NPV</td>
<td>0.84</td>
<td>0.87</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Ni</td>
<td>47 (22/25)</td>
<td>32 (14/18)</td>
<td>28 (12/16)</td>
<td>53 (25/28)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Our data suggest that the microalbumin fraction of fetal proteinuria may be a better indicator of renal damage than total protein. Combined with standard electrolyte markers, it may provide additional information about the extent of damage to these delicate tissues. Further studies are indicated to confirm this finding and establish an appropriate diagnostic threshold value.

578 MATERNAL GLUCOCORTICOID ADMINISTRATION IS ASSOCIATED WITH FETAL NEUTROPHILO AND MONOCYTE ACTIVATION. C.A. Carmo, S.M. Berry, S.C. Blackwell, S.S. Hassan, H.M. Wolfe, R. Romero, D.B. Bianchi. Dept. of OBGYN, Hazzl Hospital, Wayne State University, Detroit, MI and New England Medical Center, Tufts University School of Medicine, Boston, MA.

OBJECTIVE: Glucocorticoid administration is part of the standard therapy of preterm labor. The immunosuppressive properties of steroids may compromise host defenses against infection. The purpose of this study was to assess the effect of betamethasone on monocyte and neutrophil subsets.

STUDY DESIGN: Patients with preterm labor and intact membranes underwent corticosteroids and antenatal steroids. Flow cytometry was used to assess the state of fetal neutrophil and monocyte activation using specific cell surface markers (e.g. CD11c, CD13, CD15, and CD67). CD 14 and CD 63 (platelet marker) were also utilized to explore the activation state of other hematopoietic cell lineages. Patients with multiple gestations, clinical chorioamnionitis, or evidence of intra-amniotic infection on amniocentesis were excluded. Markers were compared between patients without betamethasone exposure (Group 1) and those with treatment < 7days (Group 2) prior to cordocentesis. For purposes of analysis, group 2 was subdivided into those patients who received steroids ≤ 24 hours and those receiving steroids between 24 hours and 7 days prior to cordocentesis. Statistical analysis included two-way ANOVA and t-test.

RESULTS: 42 patients were included in this study; 18 in Group 1 and 24 in Group 2. Within group 2, 14 patients received betamethasone ≤ 24 hours and 10 received betamethasone between 24 hours and 7 days prior to the cordocentesis. Magnesium sulfate was used as a tocolytic in all patients. In addition, 2 patients received SQ terbutaline. Mean gestational ages were similar between group 1, 30.3 weeks (range 22-33) and group 2, 31.1 weeks (range 27-33) (p=0.46). The percentage of CD 67, CD11c and CD15 positive cells was higher in patients receiving betamethasone less than 24 hours before cordocentesis compared to group 1 (p<0.01, p<0.05 and p>0.05 respectively). However, this elevation was not observed in those patients who received betamethasone greater than 24 hours prior to blood sampling. There were no differences detected between the groups for any other marker.

CONCLUSION: Steroid administration is associated with evidence of transient neutrophil and monocyte activation.

579 THE IMPACT OF MATERNAL SMOKING ON FETAL BODY COMPOSITION. IM Bernstein, K. Flodin, S. Stabl, D. Badger, L. Solomon, R. Ricker-Walker. Depts of Ob/Gyn, Medical Biostatistics, Internal Medicine and Tulane University School of Medicine, New Orleans, LA.

OBJECTIVE: To determine the impact of maternal cigarette smoking on the fetal accretion of fat and lean body mass. We hypothesized that maternal smoking would result in a reduction in the deposition of lean body mass.

STUDY DESIGN: Sixty-five singleton non-anomalous fetuses of smoking (S) and non-smoking mothers (NS) had 214 ultrasound examinations between 27 and 37 weeks gestation. All subjects had at least two ultrasound examinations separated by 4 weeks. We compared the growth rates of HC (P=0.98), FL (P=0.84) and AC (P=0.84), estimated fetal weight (EFW), muscle area and subcutaneous fat area. Analysis was performed using a repeated measured analysis of covariance (SAS PROC MIXED). Potential covariates included pre-pregnancy BMI (kg/m2), weight gain in pregnancy, maternal age, parity and fetal sex recorded at birth. T-tests and chi-square analysis were used to compare groups on demographic variables. P<0.05 was accepted for significance.

RESULTS: There were no significant differences between groups in maternal prepregnancy weight, height, BMI, weight gain in pregnancy, parity or fetal sex. Smokers (S) were younger than non-smokers (NS) (22.5±6.9 yrs, [mean±s.d.], NS=31.8±6.0 yrs, P<0.0001) and newborn weight was reduced among S (2795±567 g, NS=3512±411 g, P<0.01). There was no difference in the growth rates of HC (P=0.98), FL (P=0.84). Abdominal circumference (AC), estimated fetal weight (EFW), muscle mass and subcutaneous fat area. Analysis was performed using a repeated measured analysis of covariance (SAS PROC MIXED). Potential covariates included pre-pregnancy BMI (kg/m2), weight gain in pregnancy, maternal age, parity and fetal sex recorded at birth. T-tests and chi-square analysis were used to compare groups on demographic variables. P<0.05 was accepted for significance.

CONCLUSION: We detected reduced fetal growth that selectively affected abdominal circumference and peripheral muscle mass in fetuses of smoking mothers, while not affecting HC, FL or thigh fat area. Cigarette smoking appears to have a selective effect within lean body mass compartments that includes peripheral fetal muscle and probably liver and no effect on fat deposition.
581 IN UTERO ACCRETION OF FETAL FAT IN FETUSES OF DIABETIC MOTHERS IM Bernsten, J Fasking*, and G Badger*, Deps of Ob/Gyn and Medical Biostatistics*, Univ of VT, Burlington, VT.

OBJECTIVE: To compare the deposition of fetal fat, lean body mass and overall fetal growth in infants of diabetic mothers with control fetuses during the second half of pregnancy.

STUDY DESIGN: We compared the slope of the fetal growth curve for individual morphometric parameters including biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC), thigh muscle area, thigh fat area as well as estimated fetal weight (EFW) and percent fat area of the thigh between two groups. The groups included: 1) eighteen fetuses of women with pre-pregnancy obesity (O) (BMI >35 kg/m²), 2) fetuses from normal weight mothers (C). All subjects were non-diabetic, non-smokers who had at least two ultrasound examinations separated by 4 weeks between 19 and 40 weeks gestation and all fetuses were without anomalies. A total of 176 ultrasound examinations were performed.

RESULTS: Analysis was performed using a repeated measure analysis of variance (SAS PROC MIXED). Potential covariates included maternal age, height, or parity. T-tests revealed a significantly different rate of growth of any individual fetal parameter. However, there was a tendency for fetuses of obese mothers to have less fat deposition represented by a lower rate of fat accretion in the thigh. A strong negative correlation between prepregnancy BMI and weight gain in the fetus of diabetic mothers. While there is a tendency for all parameters to grow faster in diabetic subgroup as a function of third trimester hemoglobin A1C (HbA1C) values, Toesfs and chi-square analysis were used to compare groups on demographic variables. P<0.05 was accepted for significance.

CONCLUSION: There were no significant differences between groups in maternal age, height, or parity. Obese women had higher prepregnancy BMI (O=31.7±5.9, C=22.6±4.2 kg/m² mean±SD, P<0.0001) and lower weight gain (O=11.5±7.1, C=15.9±3.6 kg P<0.002) than controls. There was no difference in the growth rates of HC (P=0.10), BPD (P<0.05), FL (P=0.86), AC (P=0.20), thigh muscle area (P=0.92), thigh fat area (P=0.10) or EFW (P=0.27). The fetuses of obese mothers had a lower rate of fat accretion represented by a slower increase in percent fat in the thigh. (O=6.5±6.3, C=5.6±5.3 increase in percent fat per gestational week, P<0.0001).

CONCLUSION: All standard indices of fetal growth were similar between groups. There was a tendency for fetuses of obese mothers to have less fat deposition. This resulted in a decreased rate of growth for percent fat in the thigh. A strong negative correlation between prepregnancy BMI and weight gain in pregnancy made it impractical to control for maternal weight gain in examining the effect of prepregnancy BMI on fetal growth.

582 DEVELOPMENT OF A COMPREHENSIVE CLINICAL TEST FOR DIAGNOSE OF CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-OH DEFICIENCY. J Naftolin, X Ward, Deps of Ob/Gyn & Human Genetics, Univ of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: Congenital adren al hyperplasia (CAH) due to 21-hydroxylase deficiency is among the most common autosomal recessive diseases, occurring in about 1/10,000 births and accounting for approximately 90% of all CAH cases. Prenatologists usually encounter this disease when a pregnant woman already has an affected child or when she or her partner has a family history of CAH. Since the course of the disease can be changed with early intrauterine treatment, it is important to have the most sensitive and reliable test available. Current testing offered by diagnostic laboratories usually involves either linkage analysis or selected mutational analysis. We sought to investigate the effectiveness of combining both techniques to increase the number of families for which a diagnosis was possible.

STUDY DESIGN: DNA was extracted from 77 families or individuals requesting CAH testing by our diagnostic laboratory. Analysis of the nine most common mutations, detection of a gene deletion and linkage analysis using three closely linked genetic markers was completed on 35 of the 77 families. Prenatal diagnosis was sought in 27 of the 33 families. Study of the additional 47 families is underway.

RESULTS: In 25/30 (76%) families linkage analysis was informative. In 7/30 families linkage analysis was only partially informative. In two families recombinations were identified and there was one case of uniparental disomy detected. In 51 of the proband 71% of the disease-causing mutations were identified. Using the combination of both linkage analysis and mutational detection allowed for 95% of the families to become informative.

CONCLUSION: Results suggest that a combined strategy of linkage analysis and mutational detection could increase the diagnostic yield. We also demonstrated that reducing the size of the panel of genes to be tested could increase sensitivity and decrease costs. In the future we plan to incorporate the direct mutation approach.

583 IDENTIFICATION OF HUMAN EMBRYOS IN SPONTANEOUS ABORTION SAMPLES: AN OPPORTUNITY FOR MOLECULAR GENETIC RESEARCH. J. Craven*, C. Craven*, and T. Macpherson*, Deps of Ob/Gyn and Human Genetics, Univ of Vermont, Burlington, VT.

OBJECTIVE: To compare the trophoblastic depositions of fetal fat and lean body mass in infants of diabetic mothers with control fetuses during the second half of pregnancy.

STUDY DESIGN: We compared the trophoblastic deposition of fetal fat and lean body mass in infants of diabetic mothers with control fetuses during the second half of pregnancy.

RESULTS: All 500 confirmed intrauterine SAB had villi (99%) or invasive trophoblastic tissues. The remaining 1% had no invasive trophoblastic tissues. Fresh SAB tissues were examined with a dissection microscope. We sought an embryo, umbilical cord, yolk sac, amnion, gestational sac, chorionic villi and/or decidual tissue. Each embryo or fragment was given a Carnegie Stage (CS) or a Growth Disorganization (GD) Grade. We surveyed 500 reports of SAB and identified the status of the ongoing Magee-Womens Embryo Collection. We meet the guidelines of our Institutional Review Board.

RESULTS: In 25/30 (76%) families linkage analysis was informative. In 7/30 families linkage analysis was only partially informative. In two families recombinations were identified and there was one case of uniparental disomy detected. Using the combination of both linkage analysis and mutational detection allowed for 95% of the families to become informative.

CONCLUSION: Results suggest that a combined strategy of linkage analysis and mutational detection could increase the diagnostic yield. We also demonstrated that reducing the size of the panel of genes to be tested could increase sensitivity and decrease costs. In the future we plan to incorporate the direct mutation approach.

OBJECTIVE: To evaluate the value of the fetal lung maturity (FLM) assay on vaginally collected amniotic fluid specimens in predicting the absence of neonatal respiratory distress syndrome.

STUDY DESIGN: The charts of mothers and their infants managed from 1/1/95-6/30/99 with premature rupture of membranes (PROM) before 37 weeks were reviewed. Respiratory distress was considered mild if only supplemental oxygen was required and severe if mechanical ventilation was necessary. FLM was assessed by fluorescence polarization, and the result was expressed as mg surfactant per g of albumin. Antibiotics and betamethasone were administered as deemed appropriate.

RESULTS: During the study period, 618 patients with preterm PROM were admitted to Shands Hospital at the University of Florida. Of these patients, 211 had FLM assays of vaginally collected amniotic fluid samples. Patients were excluded for insufficient quantity of fluid for assay (12), multiple gestation (20), excessive blood or mucous contamination of the sample (13), elapsed time between assay and delivery (10), and infant chart unavailable for review (5). The remaining 155 mother-infant pairs were analyzed.

<table>
<thead>
<tr>
<th>FLM RESULT</th>
<th>TOTAL CASES</th>
<th>NO RDS</th>
<th>MILD RDS</th>
<th>SEVERE RDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mature (&gt;54 mg/g)</td>
<td>42</td>
<td>41</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Borderline (40-54 mg/g)</td>
<td>29</td>
<td>25</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Immature (&lt;40 mg/g)</td>
<td>82</td>
<td>69</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

No deaths due to RDS were observed. Two of 4 cases of RDS in the borderline group and 2 of 22 cases in the immature group were classified by the pediatrics as transient tachypnea of the newborn. The negative predictive value (prediction of the absence of RDS) of a mature test was 98% (95% CI, 94-100%). The negative predictive value of a borderline test was 99.5% (95% CI, 86-99%).

CONCLUSIONS: A mature FLM result from vaginally collected amniotic fluid is highly predictive of the absence of neonatal respiratory distress and can be utilized as a basis for formulating plans of clinical management. With a borderline FLM value, there is a 99% probability of the absence of RDS, and when it occurs in these cases, RDS is only mild.


OBJECTIVE: Historically, fetal intervention for a CCAM causing hydrops has been open hysterotomy and fetal pulmonary resection. In an attempt to treat this lesion without maternal hysterotomy, we tested a volume reduction strategy that may be applied without hysterectomy. This study was undertaken to assess the feasibility of the cavitation ultrasound surgical aspirator (CUSA, Valley Labs, Colorado) for debulking fetal lung tissues.

STUDY DESIGN: Five fetal sheep (110-120 days' gestation) underwent thoracotomy after maternal hysterotomy under general anesthesia. In two fetuses, the lungs were pre-exposed by transtracheal saline infusion (a model of microcystic CCAM). Various denaturing agents (dehydrated alcohol, heated saline; 1:1 ml each) were injected into the lobes to be debulked before the procedure and the operative areas were evaluated for volume reduction and parenchymal hemorrhage.

RESULTS: Normal fetal lung tissues were efficiently pulverized and aspirated. Hilar pulmonary vessels were well preserved, but some parenchymal hemorrhage was seen. In saline-debulked lungs, parenchymal blood loss was minimal during the procedure. In lobes pretreated with denaturing agents, blood loss was much less than in non-treated lobes.

CONCLUSIONS: Fetal lung debulking with CUSA is feasible in the sheep model. Further work is needed to expand this promising technique to the human fetus.


OBJECTIVE: Chronic fetal vascular access opens up new perspectives in the treatment of numerous fetal anomalies. The long-term catheterization of fetal placental vessels has been associated with a high fetal mortality rate. The purpose of this study was to investigate the safety of long-term catheterization of fetal placental vessels at a distance to the umbilical cord.

STUDY DESIGN: A midline laparotomy was performed in four time-matched pregnant ewes at 125 days of gestation (term 145 days). Placental vessels were exposed by a small uterine incision. A specially designed, 24-gauge catheter of 50 cm length was inserted into a placental vessel over a length of 3 cm and was fixed with 4-0 Vicryl suture. Blood was easily aspirated in all cases. The distal end of the catheter was tunneled underneath the maternal skin and attached to a subcutaneous port implanted in the maternal flank. The system was flushed with Pencillin and Heparin three times a week. All pregnancies were allowed to go to term.

RESULTS: Ewes and fetuses tolerated the placement of the catheter and port without complications. All pregnancies continued to term eventuantly. The catheter remained patent in all cases. All lambs were delivered vaginally at term and did not require resuscitation after birth. No fetal anomalies or growth restriction were noted.

CONCLUSION: The placement of a catheter in a fetal placental vessel is a safe and effective method to gain long-term access to the fetal circulation.


OBJECTIVE: The efficacy of few fetal surgical procedures have ever been proven in properly controlled clinical trials However, there are major obstacles to overcome in order to establish a scientifically and ethically sound study. The purpose of this report is to present our experience with the logistical, professional, and ethical considerations in designing a randomized controlled outcomes trial of a surgical intervention.

STUDY DESIGN: We encountered numerous obstacles (some of which were unanticipated) in our attempt to design a trial that tests the efficacy of a novel fetal surgical procedure. The critical issues addressed were: 1) achieving equipoise among treating surgeons (i.e., suspending surgical prejudice, standardizing the procedure and perioperative care); 2) achieving acceptance and support among nonsurgical colleagues (including ethicists) who comprise the multidisciplinary team involved in the medical care and decision making; 3) (mis)understanding of the patient (before or after randomization); 4) employing an appropriate method of randomization (e.g. block vs play-the-winner); 5) adhering to a policy of not treating outside of the trial; 6) dealing with ethical considerations of assigning or withholding an innovative surgical procedure; 7) assessing cost and reimbursement for the innovative therapy; and 8) willingness to abandon therapy that does not prove effective.

RESULTS: It took 2 years of development and refinement to meet all the necessary aforementioned criteria. This effort culminated in a prospective controlled trial which randomizes a potentially lethal fetal anomaly to either treatment before or after birth. This trial is underway and has received full funding from the National Institutes of Health.

CONCLUSION: A rigorous decision making process is necessary to design and implement sound clinical research. Outcomes-based research is important in order to establish the place of a promising new therapy early in its development, before it becomes a "standard" treatment This paradigm is applicable to evaluating other surgical procedures.

OBJECTIVE: Fetal immune development may be influenced by exposure to non-inherited maternal antigens. The presence of maternal cells in the circulation of the living human fetus has been documented as early as 15 weeks gestation using a qualitative technique. The purpose of this study is to determine the frequency and proportion of maternal cells in fetal blood and the relationship to gestational age and fetal or maternal disease.

STUDY DESIGN: A total of 49 maternal-fetal DNA sample pairs were analyzed for the presence or absence of maternal cells. Allele-specific PCR amplification techniques were used to identify the presence of maternal cells in fetal blood by detection of non-inherited maternal antigen (NIMA) locus. The proportion of maternal cells in the fetal circulation was estimated using Southern Blot on DNA extracts of blood samples compared with serial dilutions of control NIMA DNA extracts.

RESULTS: A total of 43 maternal-fetal DNA sample pairs were analyzed. Indications for fetal blood sampling included isoimmunization, rapid karyotype, and fetal platelet count determination. Using PCR, nine informative pairs were identified in which the mother was heterozygous and fetus homozygous at the biallelic thyroid peroxidase (TPO) gene locus. Maternal cells were identified by detection of NIMA in the fetal circulation as maternal cells. There was no correlation between gestational age at sampling and the percent maternal cells (%NIMA) isolated in the fetal blood. The needle path in 5 cases was transplacental and in 4 cases transamniotic.

CONCLUSIONS: A total of 49 maternal-fetal DNA sample pairs were analyzed. Allele-specific PCR amplification techniques were used to identify the presence of maternal cells in fetal blood by detection of non-inherited maternal antigen (NIMA) locus. The proportion of maternal cells in the fetal circulation was estimated using Southern Blot on DNA extracts of blood samples compared with serial dilutions of control NIMA DNA extracts. There was no correlation between gestational age at sampling and the percent maternal cells (%NIMA) isolated in the fetal blood. The needle path in 5 cases was transplacental and in 4 cases transamniotic. No correlation between %NIMA and procedure indication could be documented. During the second and third trimester, between 0.01% and 0.15% of cells in the fetal circulation are of maternal origin. The proportion of maternal cells in fetal blood does not correlate with gestational age or method of sampling. A subset of fetuses appears to have a considerably higher proportion (10%) than others (10^-3). The presence of maternal cells in fetal blood does not appear to be due to iatrogenic contamination since maternal cells are detectable in fetal blood regardless of the needle pass used for the procedure. These data provide a basis upon which to assess the precise influence of maternal cells acquired in utero on fetal immune ontogeny.

FETOSCOPY FOR RIGHT-SIDED CONGENITAL DIAPHRAGMATIC HERNIA. B Paek, P Sandberg, D Farmer, M Harrison, C Albanese, Dept Surgery, Dept Ob/Gyn, UCSC, CA.

OBJECTIVE: The transdiaphragmatic approach is effective for right-sided congenital diaphragmatic hernia (CDH) in extreme prematurity and is associated with a significant neonatal mortality. This is the first report of a series of four fetuses with right-sided CDH treated by transient tracheal occlusion to induce prenatal lung growth. The study design was a prospective observational study with targeted ultrasound, obtained at 19.7±1.5 weeks gestation in this study cohort, revealed VM in 25/33 (75.8%) and CF in 10/33 (30.3%). Most of these patients, all of whom had CDH, had other associated anomalies. The presence of maternal cells in the fetal circulation is of maternal origin. The proportion of maternal cells in the fetal circulation was estimated using Southern Blot on DNA extracts of blood samples compared with serial dilutions of control NIMA DNA extracts.

RESULTS: All mothers and fetuses tolerated the in utero procedure without complications. Fetuses were delivered between 25 and 26 weeks gestation following sequential tracheal occlusion with a detachable balloon with a single trocar in one patient. Cesarean delivery was performed in all; the tracheal occlusion was relieved while still on placental support.

CONCLUSIONS: Ultrasound markers of neurologic compromise are an early and frequently identified finding associated with fetal neural tube defects. Development of VM and CF is an uncommon occurrence later in gestation when these defects are not evident on ultrasound before 24 weeks gestation.
CONGENITAL MALFORMATIONS IN CHILDREN BORN AFTER INTRA-CYTOPLASMIC SPERM INJECTION (ICSI).
UB Wennerholm1, C Bergh2, L Hamberger1, L Landin1, L Nilsson1, M Wicklund1, B Kallen3, Institute of the Health of Women and Children, Gothenburg University and Torstblad Institute, Lund University, Sweden.

OBJECTIVE: To evaluate the incidence of congenital malformations in a cohort of infants born after intracytoplasmic sperm injection (ICSI).

STUDY DESIGN: The medical records were retrieved for all infants born in Sweden after ICSI performed at the two IVF units in Göteborg, Sahlgrenska University Hospital and Fertility Center Scandinavia. Totally, 1189 infants (766 singletons, 200 sets of twins and one set of triplets) were born between 1993 and 1998. The incidence of malformations in ICSI infants was also compared with all births in Sweden during the same time period, using data from the Swedish Medical Birth Registry and the Registry of Congenital Malformations. The Mantel-Haenszel technique was used and an odds ratio (OR) with 95% confidence interval (95% CI) was determined for having a diagnosis belonging to the chapter on congenital malformations in the International Classification of Diseases (ICD).

RESULTS: The total number of ICSI infants with an identified anomaly was 87 (7.5%), 40 of them were minor malformations. For ICSI children, in comparison with the general population, the OR for having any major or minor malformation was 1.75 (95% CI 1.19-2.58) after stratifications for delivery hospital, year of birth, and maternal age. If stratification for singleton/twins was also made, the OR was reduced to 1.39 (95% CI 0.82-2.38).

CONCLUSION: We noted a higher proportion of malformations in ICSI infants compared to all births in Sweden, particularly heart and neural tube defects.
596  UMBILICAL VEIN WHITE BLOOD CELL COUNT AS A MARKER OF ACIDEMIA IN TERM NEONATES. K. Haddon-Langsdon, R. Kirby. Dept of Ob/Gyn, Univ of Wis., Sinai Samaritan Medical Center, Milwaukee, WI.

OBJECTIVE: White blood cells (WBC) are mobilized under hypoxic and infectious conditions. Intrauterine hypoxia is linked to increased risk of cerebral palsy, potentiated by the presence of infection. We hypothesize that umbilical vein WBC elevation in term neonates is associated with acidemia and other markers of fetal hypoxia.

STUDY DESIGN: We prospectively evaluated all liveborn neonates delivered at our institution for a six-month period. Umbilical arterial blood was analyzed for pH and blood gas, venous blood for hematologic indices. Medical records of cases ≥ 37 weeks gestation were reviewed for correlating data. We used published American College of Obstetricians and Gynecologists' guidelines for acid-base definitions. Student's t test was used to determine differences of mean and chi square test for goodness of fit.

RESULTS: 1561 term cases had complete data available for arterial blood gas and blood cell analysis. Acidemic cases have higher WBC counts than normal: 15.9 ± 5.2 versus 12.4 ± 5.7 *10^9/L (p < .001). Both respiratory and metabolic acidemia are associated with elevated WBC counts (p < .002 and .001, respectively). As umbilical artery pH decreases, WBC become more prevalent (p < .001, range 7.30-5.9). Likewise, as base deficit deepens, WBC increase (p < .001, reference range 0-2 mEq/L). Appgar scores at one and five minutes are inversely associated with WBC counts. Increased WBC count is associated with presence of meconium (p < .001), but NOT with neonatal intensive care unit admission, mode of delivery, or antibiotic use in labor.

CONCLUSION: Elevated umbilical vein WBC counts in term neonates are associated with both respiratory and metabolic acidemia, decreasing one and five minute Apgar scores, and the presence of meconium.

597  THE EFFECT OF BIOLOGIC CONTAMINANTS ON AMNIOTIC FLUID SURFACTANT TO ALBUMIN RATIOS. VI. Perineto, GJ Redl, TC Dembinski. Departments of Obstetrics & Gynecology and Clinical Chemistry, University of Manitoba, Winnipeg, MB, Canada.

OBJECTIVE: Fluorescent polarization has become a popular method of determining fetal lung maturity from amniotic fluid samples. The effect of amniotic fluid contaminants, such as meconium, blood, and urine, on the surfactant to albumin (S/A) ratio determined by this method is not well understood. We sought to quantify this effect.

STUDY DESIGN: First meconium stools were obtained from term newborns. Blood was obtained from clamped cord segments of term placenta. Urine was obtained from catheterized laboring women. Each contaminant was mixed and sequentially diluted with stored amniotic fluid on which lung maturity testing had been previously performed. Immature (S/A < 40), transitional (S/A 40-55), and mature (S/A > 55) pooled amniotic fluid samples were studied for each contaminant. The effective S/A ratio in amniotic fluid of each contaminant was determined by linear regression.

RESULTS: Increasing concentrations of meconium in amniotic fluid caused the S/A ratio to regress to 2.6 ± 1.4. Increasing concentrations of blood in amniotic fluid caused the S/A ratio to regress to 30.8 ± 1.5. Samples with meconium or blood concentrations of greater than 0.20% were not interpretable. Urine contamination had no effect on the S/A ratio of amniotic fluid in concentrations up to 50% (> squared = 0.07).

CONCLUSIONS: Meconium contamination of amniotic fluid causes the S/A ratio to regress to an immature value. Blood contamination of amniotic fluid causes the S/A ratio to regress to a mature value. However, significant quantities of these contaminants make the S/A ratio not interpretable. Urine contamination of amniotic fluid has little effect on its S/A ratio.


OBJECTIVE: Bipolar coagulation has been suggested to occlude the umbilical cord in selected cases of monochorionic (MC) twin pregnancy with one non-viable fetus compromising its circulation. The smallest diameter forceps used so far was 2.7 mm. In this study we evaluated the feasibility, efficacy and safety of bipolar forceps of diameters below 3 mm in an animal model mimicking in vivo conditions.

STUDY DESIGN: Forceps of 2.2 mm, 2.5 mm, 2.5-2.7 mm and 2.7 mm were tested. In second trimester fetal lambs, umbilical cords were coagulated under s-endoventriculocisternocentesis, first with a fixed power setting of 25 W (n=15), in a second experiment with settings increasing from 10 to 55 Watts (n=10). Major outcome measures were duration of coagulation, perforation rate, change in the temperature of the amniotic fluid and vessel occlusion rate.

RESULTS: Forceps of 2.2 mm and 2.5 mm were not used further. Temperature increased from 10.2 to 16.8°C in 3 minutes. Perforation was found in the coagulation area. The mean diameter of the vessel was 15 mm (range 10-16). In the experiments with fixed power settings, coagulation was successful in all cases, except with the 2.2 mm forceps. Perforation permitted us to abandon further experiments with this forceps. The mean increase in temperature was 12.9°C (range 5.4-21.1) at 1 cm and 3°C (range 0.2-6.4) at 4 cm. The temperature returned to the initial value within 5 seconds. In the experiments with varying power settings, 10 W could not achieve complete occlusion, but no perforations occurred. At 35 W, three out of four cases the coagulation was effective, whereas in one case perforation and bleeding occurred.

<table>
<thead>
<tr>
<th>Power setting</th>
<th>Number of cords</th>
<th>Forceps</th>
<th>Duration of Coagulation (sec)</th>
<th>Occlusion rate</th>
<th>Perforation rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 W</td>
<td>5</td>
<td>2.7 mm</td>
<td>748 (600-920)</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>25 W</td>
<td>4</td>
<td>2.5 mm</td>
<td>660 (708-1080)</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>25 W</td>
<td>4</td>
<td>2.3 mm</td>
<td>785 (680-780)</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>25 W</td>
<td>3</td>
<td>2.1 mm</td>
<td>Not applicable</td>
<td></td>
<td>0%</td>
</tr>
<tr>
<td>10 W</td>
<td>4</td>
<td>2.7 mm</td>
<td>577 (580-1080)</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>25 W</td>
<td>2</td>
<td>2.7 mm</td>
<td>960</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>35 W</td>
<td>4</td>
<td>2.7 mm</td>
<td>908 (110-600)</td>
<td>75%</td>
<td>25%</td>
</tr>
</tbody>
</table>

CONCLUSION: Bipolar coagulation with forceps between 2.3 and 2.7 mm and power settings of 25-35 W achieves effective and safe coagulation in animal models for umbilical cord occlusion. Temperature changes are limited to drop to normal values within seconds, and therefore most probably clinically irrelevant. With its current design, the diameter of the forceps cannot be brought down without the risk for perforation.


OBJECTIVE: To determine the incidence of neonatal cerebral edema in the brain injured neonate.

STUDY DESIGN: Through retrospective chart review, singleton term infants with neonatal hypoxia and permanent neurologic impairment were identified in a national registry of brain injured infants. Cases were excluded as follows: (1) no neuroradiographic studies within 7 days of birth; (2) persistent reactive or unclassified intrapartum fetal heart rate (FHR) pattern; (3) insufficient data; (4) other. Cerebral edema criteria were one or more of the following: (1) ultrasound-generalized increased in echodensity throughout the brain with loss of normal anatomical landmarks or compressed or shrunken ventricles; (2) CT scan-low attenuation throughout the brain or mass effect as evidenced by sulcal effacement, displacement of the midline structures, ventricular distraction, or compression of subarchnoid spaces; (3) MRI-a low signal on T1-weighted images and high signal on T2-weighted images or morphologic change on T1-weighted image detected by gross enlargement of structures or by distortion of normal adjacent structures. Cases were categorized according to their intrapartum FHR pattern as follows: Group I (nonreactive (NR)) NR FHR pattern from admission until delivery; Group II (HON) reactive FHR pattern on admission followed by tachycardia and repetitive decelerations; and, Group III (accrete) normal FHR pattern on admission followed by a sudden, prolonged FHR deceleration lasting until delivery.

RESULTS: Of 300 brain injured neonates, 168 (56%) cases met entry criteria. Of these, cerebral edema was found in 94 (56%) neonates. When these cases were categorized according to their intrapartum FHR patterns, the incidence of cerebral edema was as follows: Group I - 55/83 (66%), Group II/III - 44/61 (41%), and Group III - 21/41 (51%). Of these, the mean time for the onset of cerebral edema was Group I - 47 ± 54 (range 10 - 533) hours; Group II - 38 ± 30.1 (range 1.4 - 99.6) hours; and Group III - 472 ± 28.1 (range 4.7 - 969) hours.

CONCLUSION: Cerebral edema is not routinely observed in the brain-injured neonate. The onset of cerebral edema is variable and appears to be related to the intrapartum FHR pattern. These findings suggest that cerebral edema, in and of itself, may not be a reliable marker for the timing of fetal neurologic injury.
601 THE BRAIN INJURED BABY, NEONATAL SEIZURES AND THE INTRAUTERIN PARTUM FETAL HEART RATE PATTERN: IS THERE A RELATIONSHIP? C. Kerkendall, M.O. Ahn, G. Martin, I. Jäuregui, L. Kosoff, J. Phelan, Childbirth Injury Prevention Foundation Pasadena, CA, Cha Women's Hospital, Seoul, Korea, Cedars Sinai Medical Center, LA, CA, Queen of the Valley Hospital West Covina, CA

OBJECTIVE: To determine whether the onset of neonatal seizures after birth in the brain injured neonate was associated with the intrapartum fetal heart rate (FHR) pattern.

STUDY DESIGN: Singleton term infants with neonatal encephalopathy and permanent neurologic impairment were identified in a national registry of brain injured infants. Clinical seizure activity was defined by Volpe's criteria, as documented in the chart, and confirmed by a neonatologist or pediatric neurologist. If the actual time of seizure onset was undocumented, the time of the first administered dose of anticonvulsants was selected. EEG seizure activity was defined as the presence of focal or multifocal spikes or sharp waves or both and focal monorhythmic discharges on the EEG. Exclusion criteria were as follows: (1) no EEG or findings available-70, (2) fetal heart rate (FHR) reactive from admission to delivery-24, (3) insufficient information regarding seizure activity-14, (4) no seizure activity-12, and (5) FHR unclassified-4.

RESULTS: Of the 300 term singleton infants, 170 (57%) met entry criteria. Of the 170 neonates with evidence of clinical seizures, 110 (65%) also had evidence of the early seizures in EEGs. In 19 (17%) of these 110 neonates, the final EEG was described as normal. Of the 60 neonates without early seizures in the EEGs, the final EEG in 22 (37%) was considered normal (p = 0.001).

CONCLUSION: The clinical observation of seizures in the brain injured neonate may not be associated with seizures on the EEG. But, when the early EEG demonstrates seizure activity, EEG abnormalities appear to persist.

602 INTRARUTERINE MECONIUM ASPIRATION: DEVELOPMENT OF AN ANIMAL MODEL. S.C. Blackwell, M. Hallak, J. Horra, S.S. Hassan, S.M. Berry, Y. Sorokin. Dept. of Ob/Gyn, Hutzel Hospital/Wayne State University, Detroit, MI

OBJECTIVE: Pulmonary hypertension due to excessive smooth muscle arteriolar hypertrophy has been postulated to be responsible for the development of in utero Meconium Aspiration Syndrome (MAS). Previous animal experiments have evaluated the acute effects of short-term exposure to meconium (MEC), but have not demonstrated these pathologic structural changes. We sought to develop an animal model to study the prolonged effects of in utero meconium exposure on the fetal respiratory system.

STUDY DESIGN: Timed pregnant Long-Evans rats were purchased on gestational day (GD) 12 and allowed to acclimate for at least 48 hours prior to surgery. On the day of surgery, following adequate anesthesia laparotomy was conducted using sterile technique. Both uterine horns were exteriorized through the abdominal incision and the number and viability of fetuses in each horn were recorded. 0.1 cc of either sterile saline (NS) or 20% MEC suspension was injected into each gestational sac with a 25-gauge needle. The uterus was returned to the abdomen and the incision was closed in a 2-layer fashion. On GD 21 (term = 21 days) the maternal animal was perfused with 100 cc of formalin + saline, a repeat laparotomy was performed, and number and viability of fetuses in each respective horn were counted.

RESULTS: MEC treated fetuses had a 50% survival rate compared to 93.4% for controls (NS treated). Two maternal rats expired (Exp.) < 24 hours post-injection.

CONCLUSION: We have established an animal model for the examination of the pathophysiology in utero meconium aspiration. In this pilot study, chronic meconium exposure was associated with an increased fetal mortality rate.


OBJECTIVE: Gasous amniocentesis may facilitate endoscopic fetal surgery, but is not widely used gas in CO2 because it is very soluble. Data on fetal acid base status following CO2 amniotic distention are conflicting. One study suggests that hyperventilation compensates fetal acidosisis by CO2. In this study we evaluated the changes induced in fetal acid-base status by distention of the amniotic cavity with CO2 in a sheep model for endoscopic fetal surgery, with or without maternal hyperventilation.

STUDY DESIGN: Pregnant ewes (n = 25) underwent general anesthesia and triple cannulation to allow uterine distention with CO2 at 38 °C and 4-5 atmniotic cavity with CO2 in a sheep model for endoscopic fetal surgery, with or without maternal hyperventilation.

RESULTS: Timed pregnant Long-Evans rats were purchased on gestational day (GD) 12 and allowed to acclimate for at least 48 hours prior to surgery. On the day of surgery, following adequate anesthesia laparotomy was conducted using sterile technique. Both uterine horns were exteriorized through the abdominal incision and the number and viability of fetuses in each horn were recorded. 0.1 cc of either sterile saline (NS) or 20% MEC suspension was injected into each gestational sac with a 25-gauge needle. The uterus was returned to the abdomen and the incision was closed in a 2-layer fashion. On GD 21 (term = 21 days) the maternal animal was perfused with 100 cc of formalin + saline, a repeat laparotomy was performed, and number and viability of fetuses in each respective horn were counted.

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CONCLUSION: We have established an animal model for the examination of the pathophysiology in utero meconium aspiration. In this pilot study, chronic meconium exposure was associated with an increased fetal mortality rate.

CONCLUSION: In a model reproducing the hemodynamic conditions of pregnancy, maternal hyperventilation cannot always correct fetal acidosis due to hypercarbia.

GROUP I (n=10) GROUP II (n=10) GROUP III (n=5)

pCO2 basal
55±3
51±0
52±2
30 min
74±2**
61±3**
62±4
60 min
88±3
66±4
71±5

Results are mmHg, and expressed as mean±SEM. *p<0.01, **p<0.001.
604 INTRAPARTUM UTERINE RUPTURE AND PERMANENT BRAIN INJURY: A RETROSPECTIVE ANALYSIS OF CURRENT INDICATORS. J. Phelan, L. Korst, M. O. Ahn, G. Martin, C. Kurkdjian. Childbirth Injury Prevention Foundation, Pasadena, CA, Queen of the Valley Hospital West Covina, CA, Cha Women’s Hospital, Seoul, Korea, Cedars Sinai Medical Center, LA, CA.

**OBJECTIVE:** To determine whether patients with an intrapartum uterine rupture sufficient to produce intrapartum asphyxia and persistent brain injury will manifest the following four criteria: profound acidemia (arterial pH < 7.00), an Apgar score ≤ 3 at 5 minutes, seizures within the first 24 hours of birth, and multiorgan dysfunction.

**STUDY DESIGN:** Singleton, liveborn, infants with neonatal encephalopathy and permanent neurologic impairment who lived > 1 hour and 6 days, had a reactive fetal heart rate (FHR) pattern on admission, and had an intrapartum uterine rupture were identified in a national registry of brain injured infants. Exclusion criteria included the following: (1) insufficient maternal or neonatal data, (2) fetal or neonatal death, (3) rupture-related only, (4) unspecified nonreactive FHR pattern from admission until delivery, and (5) other-3- Organ system dysfunction was defined by separate criteria for each organ system. Dysfunction in one or more organ systems was defined as multiorgan system dysfunction.

**RESULTS:** Of the 81 uterine rupture cases resulting in permanent brain injury (30.4%), neonates satisfied the entry criteria. Of these 30 brain injured neonates, 21 (31%) satisfied all 4 criteria for intrapartum asphyxia, 12 (31%) satisfied 3, 10 (26%) satisfied 2, 4 (10%) satisfied 1, and 1 (3%) satisfied none of the criteria. By the study criteria, 11 (28%) neonates had no multiorgan system dysfunction. The most common organ system dysfunction was pulmonary (62%).

**CONCLUSION:** Our retrospective study in patients with intrapartum uterine rupture suggests that currently used indicators to define permanent fetal brain injury are not valid.

606 THE USE OF "IN VITRO" EXPANDED FETAL STEM CELLS FOR NON INVASIVE PREGNATAL DIAGNOSIS G. C. De Renzo, F. Tilesi, A. Taliano, V. Lauro, G. Coata. Centre of Perinatal Medicine, University of Perugia, Perugia, Italy.

**OBJECTIVE:** The development of a non-invasive prenatal diagnosis using fetal cells isolated from the maternal circulation is hampered by the low frequency of these cells in maternal peripheral blood. The proliferative potential of fetal hematopoietic stem cells, that can be isolated from maternal blood, raise the possibility to obtain "in vitro" a clonal expansion of these cells. In order to expand "in vitro" the stem fetal cells we have developed a model system in order to increase the number of fetal cells in respect to maternal cells.

**STUDY DESIGN:** Twenty ml of peripheral blood were obtained from 18 primigravidae at 14-16 weeks of gestation, carrying normal male fetus and from 5 women with aneuploid fetuses, 3 with 47,XY, 1 with 45,XY, and 1 with XXX syndrome undergoing genetic amniocentesis. All blood samples were obtained before the invasive prenatal technique. Fetal stem cells were enriched with the anti-magnetic activated cells sorting (MACS) and then expanded in vitro in a Teflon culture medium. Finally, FISH analysis was performed to check the presence and the frequency of expanded fetal cells with the use of XY and 21 chromosome specific DNA probes.

**RESULTS:** The presence of fetal cells were observed in 17 of 18 FISH samples with a frequency varying from 1/25 to 1/853 fetal cells/maternal cells with a mean value of 1/230. Besides, in two samples, we observed three metaphases with XY signal probe. For aneuploid pregnancies the ratio of fetal cell/maternal cells were from 1/31 to 1/83.

**CONCLUSIONS:** Our technique of expanding "in vitro" fetal stem cells seems to ameliorate the ratio of fetal cells respect to maternal cells. In addition, we demonstrated that these cells can divide in culture because we observed the presence of three XY metaphases of cells from male fetuses. The ratio of fetal/maternal cells decreases significantly in aneuploid pregnancies. We conclude that in this way non invasive cytogenetic diagnosis should be more feasible in particular in aneuploid pregnancies that exhibit a significant elevation of fetal cells after "in vitro" expansion.

607 OUTCOME OF PREGNANCIES COMPROMISED BY RUPTURED MEMBRANES AFTER GENETIC AMNIOCENTESIS AF Bongio, AA Mills, DM Feldman, JF Rodis, and JP Egan. Division of MFM, Univ. of CT Health Care, Farmington, and Saint Francis Hospital, Hartford, CT.

**OBJECTIVE:** Compare perinatal outcomes of pregnancies complicated by preterm premature rupture of membranes (PPROM) after genetic amniocentesis (amnio) with pregnancies complicated by spontaneous PPROM at a similar gestational age (GA).

**STUDY DESIGN:** A case-control study was performed in which a computerized database for an 11 year period (7/88-6/99) was reviewed to identify all patients presenting to our institutions with PPROM within 48 hours of a genetic amnio. Control subjects were matched for GA at PPROM. Patients were all managed expectantly. Outcomes were compiled from review of medical records. Descriptive statistics, student’s t-test, and χ² were used with p<0.05 considered significant.

**RESULTS:** During the study period 1,077 genetic amnios were performed. Ten women (0.9%) presented within 48 hours to PPROM. Mean GA at PPROM (weeks, ±SD) was 17±1.1 vs 18±7.2 (p<0.05). Mean latency (days, ±SD) was 10±6.3 vs 11±7.3 (p=.005). Mean GA at delivery (weeks, ±SD) was 32±1.7 vs 20±1.7 (p<0.005). Outcomes: Neonatal Deaths, n(%) (1/10) vs (9/90) (p<0.005). Neonatal Deaths, n(%) was 1/10 vs 0 (NS). Neonatal Survivals, n(%) was 9/80 vs 10/10 (p<0.005). In conclusion, pregnancies complicated by PPROM after genetic amnio result in significantly better perinatal outcomes compared to pregnancies with PPROM at a similar GA. Expectant management is recommended.

**CONCLUSION:**

<table>
<thead>
<tr>
<th></th>
<th>Anmio n=10</th>
<th>Control n=10</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean GA at PPROM (wk ± SD)</td>
<td>17.1±1.1</td>
<td>18.7±1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Mean latency (days)</td>
<td>10±6.3</td>
<td>11±7.3</td>
<td>.005</td>
</tr>
<tr>
<td>Mean GA at delivery (wk ± SD)</td>
<td>32.1±1.7</td>
<td>20.3±1.7</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Outcome: Neonatal Deaths, n(%)</td>
<td>1/10</td>
<td>9/90</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Neonatal Survivals, n(%)</td>
<td>9/80</td>
<td>1/10</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>In conclusion, pregnancies complicated by PPROM after genetic amnio result in significantly better perinatal outcomes compared to controls with PPROM at a similar GA. Expectant management is recommended.</td>
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</table>

In addition, there is EGF precursor (preproEGF, MW - 170 KD) in AF throughout gestation. In neonates, mature EGF (64KD) is predominant. **CONCLUSION:** EGF is present at biologically effective concentrations as a precursor together with a binding protein (in the AF from early gestation). Postnatally, a protease is likely expressed in the distal nephron which converts preproEGF to EGF. Since many animal and in vitro studies demonstrate EGF having pro-maturation effects on fetal lung tissue, our findings suggest that EGF may play an important role in the pathogenesis of human fetal lung development and hypoplasia.

605 ONTOGENY OF EPIDERMAL GROWTH FACTOR (EGF) IN HUMAN AMNIOTIC FLUID. **H. Wience, **B. Cohn, **D. Moskowitz. Div. Maternal-Fetal Medicine & Div. Neonatology, *St. Louis University, DrGenes, LLC, St. Louis, MO*

**OBJECTIVE:** To determine the development of EGF activity in human amniotic fluid.

**STUDY DESIGN:** Amniotic fluid (AF) was obtained by transabdominal amniocentesis (amnio) with pregnancies complicated by spontaneous PPROM at a similar gestational age (CA). The development of EGF activity during the gestational age of 31-35 weeks and from AF to neonatal urine (p < 0.0001)

<table>
<thead>
<tr>
<th>FA(wks)</th>
<th>N</th>
<th>AF EGF</th>
<th>NA(days)</th>
<th>N</th>
<th>Urine EGF</th>
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<tbody>
<tr>
<td>&lt;16</td>
<td>15</td>
<td>6.50±1.35</td>
<td>1</td>
<td>6</td>
<td>50.1±9</td>
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<td>21-25</td>
<td>7</td>
<td>4.06±2.43</td>
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<td>5</td>
<td>49±11.8</td>
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<tr>
<td>26-30</td>
<td>4</td>
<td>6.68±2.09</td>
<td>10</td>
<td>20±1.7</td>
<td></td>
</tr>
<tr>
<td>31-35</td>
<td>10</td>
<td>12.02±6.9</td>
<td>10</td>
<td>12±1.7</td>
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</tr>
<tr>
<td>36-40</td>
<td>10</td>
<td>4.25±4.99</td>
<td>10</td>
<td>11±1.7</td>
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</tbody>
</table>

FA=Neonatal, NA=Neonatal
DOES LIGHT PRESSURE EFFLUEURAGE REDUCE PAIN AND ANXIETY ASSOCIATED WITH GENETIC AMNIOCENTESIS: A RANDOMIZED CLINICAL TRIAL. R. Fischer, K. Blancuito, H. Schelde, M. Hedegård, Deps. Ob/Gyn, UMDNJ-RWJ Medical School at Camden, Cooper Hospital/University Medical Center, Camden, NJ

**OBJECTIVE:** The purpose of this study was to evaluate the effect of light pressure effluerage (leg rubbing) during genetic amniocentesis with regard to pain sensation and patient anxiety.

**STUDY DESIGN:** 200 women with singleton gestations undergoing genetic amniocentesis from 15-22 weeks were asked to complete a survey of pre- and post-amniocentesis perception of pain and anxiety. All subjects indicated on a 10 cm linear visual analog scale (0 = lowest pain/anxiety, 10 = highest). The study, including patient blinding, was approved by our Institutional Review Board.

**RESULTS:** There were no significant differences between the two groups with regard to age, race, parity, insurance status, BMI, indication, performing physician, gauge of needle, number of amniocenteses attempts, and percentage with a support person touching the subject. The effluerage group was at a slightly later gestational age (17.5 ± 1.5 vs 17.0 ± 1.4, p = .01). There were no significant differences between the effluerage and no effluerage groups not reduce procedure-related pain or anxiety. However, it is self-scrutiny, by patients, the majority of whom would want effluerage repeated with future procedures.

**CONCLUSION:** Light pressure effluerage during genetic amniocentesis does reduce procedure-related pain or anxiety. However, it is self-scrutiny, by patients, the majority of whom would want effluerage repeated with future procedures.

610 DOWN SYNDROME AND THE TIMING OF DEATH THROUGH ONE YEAR OF AGE IN THE UNITED STATES. Aj Fisher, GV Ananth, AM Vinziitese, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ

**OBJECTIVE:** To determine the timing of death for fetuses and liveborn infants diagnosed with Down syndrome (DS) in the second half of pregnancy through the first year of life.

**STUDY DESIGN:** We performed a retrospective cohort study using the national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics. Gestational age (GA) at death for fetuses (FD) having a diagnosis of DS was determined. The frequency of neonatal and infant death at <7 days, 7-27 days, and 28-365 days for liveborn infants with DS was compared with the corresponding death rates for liveborns without DS using relative risk (RR) with 95% confidence interval (CI).

**RESULTS:** The frequency of Down syndrome was 0.06% (n=5640) during the study period in a total population of 7,185,852 births. Table 1 shows the distribution of GA in infants born with DS after 20 weeks.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>n</th>
<th>Death%</th>
<th>n</th>
<th>Death%</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 days</td>
<td>271</td>
<td>7.4</td>
<td>28196</td>
<td>0.39</td>
<td>20.2</td>
<td>18.5-22.7</td>
</tr>
<tr>
<td>7-27 days</td>
<td>20</td>
<td>0.6</td>
<td>5627</td>
<td>0.08</td>
<td>8.1</td>
<td>5.2-12.6</td>
</tr>
<tr>
<td>28-365 days</td>
<td>132</td>
<td>4.0</td>
<td>16983</td>
<td>0.23</td>
<td>17.0</td>
<td>14.4-20.2</td>
</tr>
</tbody>
</table>

Of the liveborn infants who died in the first 365 days of life, 32.7% died <7 days, 8.9% between 7-27 days and 58.4% after 27 days.

**RESULTS:**

1) Mortality in DS fetuses and infants through one year of life is dramatically greater than those who do not have DS. 2) For the 13% of infants with DS reaching the first year of life, 41.6% will die within the first 28 days with most in the first 7 days of life.

611 NEURAL TUBE DEFECTS AND THE TIMING OF DEATH THROUGH ONE YEAR OF AGE IN THE UNITED STATES. Aj Fisher, GV Ananth, AM Vinziitese, UMDNJ-Robert Wood Johnson Medical School/Saint Peter's University Hospital, New Brunswick, NJ

**OBJECTIVE:** To determine the timing of death for fetuses and liveborn infants diagnosed with spina bifida (SB) or anencephaly (AN) in the second half of pregnancy and through the first year of life.

**STUDY DESIGN:** We performed a retrospective cohort study using the national linked birth/infant death data sets for 1995 and 1996 provided by the National Center for Health Statistics. Frequencies of fetuses (FD) neonatal, and infant death at <7 days, 7-27 days, and 28-365 days for liveborn infants with SB were compared with the corresponding death rates for liveborns without SB using relative risk (RR) with 95% confidence interval (CI). Similar analysis was performed for AN.

**RESULTS:** The cumulative frequency of SB was 0.03% (n=2240) and for AN 0.02% (n=1413) during the study period in a total population of 7,185,852 births. At the end of one year, 1,887 infants with SB (84.2%) and 756 infants with AN (46.0%) with AN were alive. Mortality associated with SB in the second half of pregnancy through one year of age and the risk ratio of death compared to those without SB are shown below.

<table>
<thead>
<tr>
<th>Spina Bifida</th>
<th>Non-Spina Bifida</th>
<th>SB vs Non-SB</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Death%</td>
<td>n</td>
</tr>
<tr>
<td>FD</td>
<td>181</td>
<td>8.1</td>
</tr>
<tr>
<td>7-27 days</td>
<td>113</td>
<td>5.5</td>
</tr>
<tr>
<td>28-365 days</td>
<td>29</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Of the liveborn SB infants who died in the first 365 days of life, 65.7% died <7 days, 11.6% between 7-27 days and 22.7% after 27 days.

Mortality associated with AN was 1.2% (n=16) during the same period in a total population of 7,185,852 births. At the end of one year, 1,887 infants with SB (84.2%) and 756 infants (46.0%) with AN were alive. Mortality associated with SB in the second half of pregnancy through one year of age and the risk ratio of death compared to those without SB are shown below.

<table>
<thead>
<tr>
<th>Anencephaly</th>
<th>Non-Anencephaly</th>
<th>AN vs Non-AN</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Death%</td>
<td>n</td>
</tr>
<tr>
<td>FD</td>
<td>453</td>
<td>26.8</td>
</tr>
<tr>
<td>7-27 days</td>
<td>18</td>
<td>1.7</td>
</tr>
<tr>
<td>28-365 days</td>
<td>28</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Of the liveborn AN infants who died in the first year of life, 95.3% died <7 days, 3.2% between 7-27 days and 3.3% after 27 days.

**CONCLUSIONS:** 1) Mortality through one year of life in fetuses and infants with neural tube defects (NTD) is dramatically greater than those who do not have NTD. 2) Of the infants with NTD who die, the majority die within the first 7 days of life.

OBJECTIVES: To compare the use of biopsy forceps (BF) and cannula aspiration (CA) (i) for transcervical CVS in terms of efficacy, placental trauma/transplacental haemorrhage, cytogenetic analysis, pregnancy outcome.

STUDY DESIGN: Eligibility: (i) 10-14+4 wks, (ii) recognised identification (iii) informed consent. Randomisation: (i) twins, (ii) vaginal infection, (iii) active vaginal bleeding, (iv) amnioncentesis. Sample size: 184 patients (n: 0.05, 1-β: 0.8 for 12βHGH difference in post-CVS - pre-CVS fetoprotein (αFP) as a surrogate marker of placental trauma and/or feto-maternal haemorrhage (FMH)). Due to multiple comparisons, for secondary outcomes α: 0.01. Randomisation: serially numbered opaque envelopes, assignment using random number table. Neither operators nor patients were blinded to assignment, however, all other staff were blinded until data were analysed. CVS routine aseptic procedure. Phlebotomy just prior to and 1h post-CVS; FMH assessed by anti-HHF-FTTC (flow cytometry) and Retie-Kleihauer (BK). Patient and operator satisfaction determined. Outcomes: prospective data collection. Analysis: intention to treat.

RESULTS: 200 women were randomised. Interim data on 175 (n=88 (BF), n=87 (CA)) are presented (mean ± SD). BF were associated with shorter procedure times (111±68 vs. 294±16 sec (CA); p: 0.01), less sample fragmentation (1.6±0.6 (BF) vs. 2.5±0.7 (CA) fragments per specimen, p: 0.01). BF were reusable and cheaper. No other differences were noted. Significant rises in αFP (μg/L) occurred with both instruments (31±54 (CA) vs 38±59 (BF) μg/L), however, αFP, hCG, AIb or AIb+ cells were negligible.

CONCLUSIONS: Biopsy forceps (i) were preferred by operators skilled with both instruments, (ii) were cheaper (iii) disrupted specimens less, and (iv) procedures went faster, without adversely affecting either pregnancy outcome or cytogenetic analysis. Indices of placental trauma were similar. Presumably the αFP is due to placental trauma, rather than FMH, as only αFP rose after CVS, whilst BK volume and fetal RBC differential were unchanged.


OBJECTIVE: When an apparently balanced rearrangement is revealed by prenatal cytogenetic testing, parents are counseled that most of these cases are clinically normal. But there is evidence in the literature to suggest, in de-novo chromosome rearrangements, that the incidence of abnormal outcomes may be as high as 6-10%. Our objective was to examine ultrasound findings with outcomes in cases of balanced rearrangements diagnosed during pregnancy.

STUDY DESIGN: Results of cytogenetic studies obtained from amniocenteses and chorionic villus samplings (CVS) from 1994-1999 were reviewed. Examples of apparently balanced chromosomal rearrangements were included. Cases with unbalanced rearrangements were excluded. Ultrasound findings and clinical outcomes were reviewed.

RESULTS: 8564 cases of amniocenteses and 440 of CVS were performed. 30 cases met inclusion criteria. Robertsonian translocation occurred in ten (0.5%), reciprocal balanced translocation in eight (0.4%), and pericentric inversion in ten (0.5%). In five cases, one parent was a known carrier of a balanced translocation. Of 15 cases in which neither parent was a known carrier, parental karyotypes were obtained in 13. The translocation was found to be familial in eight cases (five paternal and three maternal in origin), and de novo in five cases. Ultrasound revealed no structural abnormalities in any fetus. Echogenic bowel was seen in one fetus. These 20 cases resulted in 16 pregnancies. Ongoing follow-up obtained by the Division of Genetics (1-42 months) has not revealed any cases of developmental abnormalities.

CONCLUSIONS: When prenatal cytogenetic testing reveals balanced chromosomal rearrangements, a normal ultrasound is likely. Parents can be reassured that this is unlikely to be associated with an increased risk for developmental abnormalities. Because of an increased risk for unbalanced chromosomal rearrangements (especially if the rearrangement is familial), cytogenetic testing is indicated in all subsequent pregnancies.

614 URINE HYPERGLYCOSEYLATED HCG (hCG) IS SUPERIOR TO SERUM TRIPLE TEST FOR DOWN SYNDROME DETECTION. R Bahado-Singh, U Oz, A Baumgartner, A Omranji, S Shahabab, M Mahonye, L Colee, Yale University, New Haven, CT.

OBJECTIVE: The modest screening performance and declining patient and physician acceptance has stimulated interest in alternative markers to the triple test (TT). Our purpose was to compare a single urine analytic, hCG with the TT (AFP, hCG, IE, and age) for mid-trimester Down syndrome (DS) screening.

STUDY DESIGN: Urine and blood were obtained from mid-trimester pregnant women undergoing genetic amniocentesis. Urine hCG and serum TT measurements were performed. Individuals undergoing amniocentesis for abnormal TT were excluded. Individual DS risk based on hCG + age and also based on the TT was calculated. For each algorithm, the sensitivity and false positive rate (FPR) for DS detection at different risk thresholds were determined. Based on these values, ROC curves were constructed along with the area under the curve. The relative performance of the two algorithms was determined by comparing the areas under the curves. Finally, the performance of a new algorithm in which urine hCG replaced hCG in the (TT) was ascertained.

RESULTS: We studied 24 DS and 500 unaffected pregnancies between 14-22 weeks. The sensitivity and FPR for hCG + age was 75% and 5.6% while that for the TT was 75.0% and 33.2%. Urine hCG was superior to the TT (area under the curve 0.95 vs 0.79, p<0.01). The substitution of hCG for hCG in the TT resulted in a 79.2% sensitivity at 5% false positive rate.

CONCLUSION: The performance of urine hCG + age is statistically superior to the serum triple test for mid-trimester DS detection. The use of hCG as an alternative test or substituting it for regular hCG in the TT would improve the screening performance and resolve the concerns associated with the TT. Urine hCG should be investigated as an alternative to the triple test in a population at average Down syndrome risk.

615 NUCHAL THICKNESS TO HUMERUS LENGTH (RATIO FOR DOWN SYNDROME DETECTION. R Bahado-Singh, U Oz, CD Hsu, N Mulayim, M Mahony, Yale University, New Haven, CT.

OBJECTIVE: Ultrasound markers are now being used to adjust Down syndrome (DS) risk. The limitations are that the definitions of "abnormal" measurements used are arbitrary thus reducing screening performance, and also individual DS risks cannot be calculated. We report a new ultrasound algorithm which is both sensitive for DS screening and estimates individual risk.

STUDY DESIGN: In DS the humerus length (HL) decreases while the nuchal thickness (NT) increases. The NT/HL ratio therefore shows an even greater increase and magnifies the separation between DS and normal. Prospective data were collected in mid-trimester amniocentesis cases A regression equation for median NT/HL based on blparietal partial diameter (BPD) was generated. The DS likelihood ratio (LR) or odds based on NT/HL (McM) was multiplied by the age-related risk to give the posterior DS risk. A chart for estimating individual DS risk based on age and NT/HL was constructed.

RESULTS: There were 94 DS and 4,500 cases with normal karyotype mean (SD) gestational age 16.1 (1.6) weeks. Thirty-three DS and 68 karyotypically normal fetuses had gross anomalies. The expected median NT/HL equation was 10e (-1.7163-0.0292xBPD + 0.0003xBPD^2). In the overall study population the NT/HL and age had a 79.8% detection rate at 22.1% false positive (FPR), superior to other age + HL (55.1% sensitivity) or age + NT (66.7% sensitivity) at the same FPR. For women ≥35 years the values were 86% and 22%. Exclusion of anomalies associated yielded a 79.6% sensitivity at 23.6% FPR while ultrasound abnormalities by itself had a 35.1% sensitivity at 1.4 FPR. Combining NT/HL + age with gross anomalies yielded a 99.5% sensitivity at 12.6% FPR.

CONCLUSIONS: We report a new ultrasound biomarker algorithm that when combined with age and the identification of gross ultrasound anomalies detects 99.5% of DS cases. Individual DS risk can be quickly calculated at the bedside and made available to women who desire this information, prior to a decision on amniocentesis.
618


OBJECTIVE: When an abnormality associated with a known phenotype is revealed by prenatal cytogenetic studies, parents can be provided with specific information related to that particular abnormality. When uncommon rearrangements are detected, however, little information may be available for counseling patients. With such an occurrence, obstetric ultrasound plays a crucial role. Our objective was to examine ultrasound findings with outcomes in cases of uncommon chromosomal rearrangements diagnosed during pregnancy.

STUDY DESIGN: Results of cytogenetic studies obtained from amniocenteses and chorionic villus samplings (CVS) from 1994-1999 were reviewed. Those examples of chromosomal rearrangements with little information on phenotypic abnormalities were included. Cases of apparently-balanced translocations were omitted. Ultrasound findings were reviewed. Outcomes were determined by reviewing medical records.

RESULTS: 6554 cases of amniocenteses and 440 of CVS were performed. 17 cases met inclusion criteria. Testing was done for advanced maternal age in 12, and abnormal ultrasound findings in four. Parental karyotype was obtained in 16 cases, and rearrangements were de novo in 11. Abnormal ultrasound findings were present in 11 cases, with the following outcomes: Five underwent dilatation and evacuation (D & E), with abnormal autopsy findings in two (though examination was limited by fragmentation); one fetal demise; one neonatal demise; and three surviving neonates with abnormalities (one each with hypoplasia, congenital kyphosis, and hydrocephrosis). One pregnancy is ongoing. There were six cases without ultrasound findings, with the following outcomes: Three underwent D & E, with abnormal findings in two, and one newborn was normal on examination. Two pregnancies are ongoing. Outcomes: Three underwent D & E, with abnormal findings in two, and one neonatal demise; and three surviving neonates with abnormalities (one each with Trisomy 21, the remaining 3 had children with Trisomy 13, Trisomy 18, and 4q respectively. Seventeen (46%) of the women had a diagnosis at birth; 20 (54%) had a prenatal diagnosis. The two groups of women did not differ in any demographic measures except that women with a prenatal diagnosis attended religious services more frequently (p = 0.06).

CONCLUSIONS: Our data suggest that early knowledge of fetal aneuploidy can be beneficial to those women who choose not to terminate the pregnancy. These results may be useful in counseling patients who do not have any intention of terminating an abnormal pregnancy, but are nonetheless considering amniocentesis or other prenatal diagnostic modalities.

616

MATERNAL SERUM TRIPLE SCREENING FOR PREGNANCY COMPLICATIONS IN TWINS. W.H. Prensky, J.K. Chyn, J.C. Hobbins. Dept. Ob/Gyn, Univ of Colorado Health Sciences Center, Denver, CO.

OBJECTIVE: The prenatal assessment of the twin pregnancy has become commonplace. While maternal serum (MS) triple screening is valuable in detecting the unexpected twin pregnancy, its utility in the known twin pregnancy remains unclear. We investigated whether screening for abnormal elevations in MS AFP, uE3, and hCG was helpful in the identification of the twin pregnancy or risk for late complications, unique to twins.

STUDY DESIGN: We performed a retrospective, cross-sectional study of one hundred fifteen twin pregnancies that delivered at the University of Colorado Health Sciences Center, Denver. Triple screen assessment (AFP, uE3, and hCG) was performed between 16 and 22 weeks in all twins. The threshold of elevation for each of the analytes was considered >1 s.d. Delivery information was obtained from a review of the medical records after delivery, and included age at delivery, choriionicity, rate of PTL, rate of pre-eclampsia, mean interworn birth weight difference, and the combined, mean 1 and 5 minute Apgar score and birth weight. The rate of occurrence of outcome parameters was compared for those with elevated analytes and those with normal analytes.

RESULTS: We found an AFP of >3.18, a uE3 >2.94, and a hCG >3.82 to be considered elevated. Outcome findings are summarized in Table 1. The mean birth weight was found to be significantly lower (p = 0.03) in those patients with elevated AFP (p = 0.005), compared with those who had normal values. Although not statistically significant, analysis of the age at birth showed a trend between elevated uE3 and earlier delivery.

CONCLUSIONS: AFP and uE3 assessment may be useful in the identification of the twin pregnancy at risk for lower twin birth weights. Further analysis with additional data may reveal uE3 to be helpful in the prediction of early preterm delivery.

619

FIRST TRimester bleeding has no effect on second trimester maternal serum triple screening. David Peleg, Michael Goldinfeldt, Aviva Pelegt, Moshe Ben-Amist, Dept. OB/GYN and Research Laboratories, Portya Government Hospital, Tiberias, Israel.

OBJECTIVE: To determine whether first trimester bleeding effects the results of a second trimester maternal serum triple screen.

STUDY DESIGN: Case-control. 42 women with documented first-trimester uterine bleeding (up to 12 weeks) were compared to 50 matched women without bleeding. All pregnancies were singleton. Women had no other medical problems. Women with post-coital bleeding were excluded. The results of maternal serum AFP, hCG, and E3 (in MoM) were compared by t-testing.

RESULTS: The 2 groups were matched for age, weight, gravidity, parity, and gestational age at testing.

<table>
<thead>
<tr>
<th>First Trimester Bleeding</th>
<th>Controls</th>
<th>P</th>
<th>95% Interval Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFP (MoM)</td>
<td>1.09±0.43</td>
<td>1.05±0.39</td>
<td>0.111</td>
</tr>
<tr>
<td>hCG (MoM)</td>
<td>1.05±0.53</td>
<td>1.10±0.54</td>
<td>0.558</td>
</tr>
<tr>
<td>E3 (MoM)</td>
<td>1.11±0.46</td>
<td>0.98±0.31</td>
<td>0.111</td>
</tr>
</tbody>
</table>

There were no significant differences between the 2 groups for any of the analytes.

CONCLUSIONS: First trimester uterine bleeding had no demonstrable effect on second trimester maternal serum triple screening. First trimester bleeding should not be listed as a possible cause of an unexplained elevation of one or more of the analytes.

618

DOES PRENATAL DIAGNOSIS IMPROVE OUTCOMES FOR WOMEN WHO CHOOSE NOT TO TERMINATE THE PREGNANCY? S. Rainowt, D. Wettg, D. Chelmowt, S. Craigot, D.W. Biancht, Division of Maternal-Fetal Medicine, Tufts University School of Medicine, New England Medical Center, Boston, MA; The Shriver Center for Mental Retardation, Inc., Waltham, MA.

OBJECTIVE: To determine whether antenatal diagnosis of fetal aneuploidy provided any benefit to women who continued their pregnancies.

STUDY DESIGN: An anonymous questionnaire was mailed to the mothers of all patients with a diagnosis of aneuploidy admitted to our NICU or cared for in our Genetics Clinic from 1994-1998 (n=31). Outcomes measured included an objective assessment of pregnancy and delivery management, neonatal outcome, as well as subjective measures of depression and anxiety levels in the women (Mental Health Index-5), and an evaluation of the women’s emotional and physical experience of the pregnancy and birth. Statistical analysis was performed using Chi-Square, Student’s t, and Mann-Whitney U tests where appropriate.

RESULTS: Thirty-seven (73%) women responded to the survey. Thirty-four (96%) had children with Trisomy 21; the remaining 3 had children with Trisomy 13, Trisomy 18, and 4q respectively. Seventeen (46%) of the women had a diagnosis at birth; 20 (54%) had a prenatal diagnosis. The two groups of women did not differ in any demographic measures except that women with a prenatal diagnosis attended religious services more frequently (p=0.06). Significant differences were shown when women assessed their physical and emotional experience of the pregnancy and birth: women with a prenatal diagnosis had a better perception of their physical experience of the pregnancy (p=0.009) and their emotional experience of the birth (p=0.002). Mental Health Index scores were similar in the two groups. Neontates without a prenatal diagnosis were more likely to be transferred to a tertiary center after birth (p=0.006) but did not have longer hospital stays and were not more likely to require surgery. Seventy-five percent of the women with a prenatal diagnosis said they would have done nothing differently in the pregnancy compared to 47% of the women with a diagnosis at birth (p=0.08).

CONCLUSIONS: Our data suggest that early knowledge of fetal aneuploidy can be beneficial to those women who choose not to terminate the pregnancy. These results may be useful in counseling patients who do not have any intention of terminating an abnormal pregnancy, but are nonetheless considering amniocentesis or other prenatal diagnostic modalities.
620 THE ASSIGNMENT OF RHD GENE ZYGOSITY BY DENSITOMETRIC QUANTITATIVE PCR. G. Denommex, D. Oepkes, G. Ryan, B. Fernandez, Dept. of Pathology, and Perinatal Unit, Mt Sinai Hospital, The Canadian Blood Services, & Dept of Laboratory Medicine, University of Toronto, ON, CANADA.

BACKGROUND: Rh phenotyping with anti-D, -C, -E, -c, and -e is used to predict the paternal ‘most probable’ Rh genotype and RHD gene zygosity for fetuses at risk for hemolytic disease of the newborn (HDN) due to anti-D isosensitization and to provide information for genetic counseling of subsequent pregnancies. However, many phenotypes have more than one possible genotype, some with homozygous and hemizygous RHD combinations.

OBJECTIVE: To determine the RHD gene zygosity using densitometric quantification of PCR amplified RHD and RHCE exon fragments.

STUDY DESIGN: The Rh-negative genotype is characterized by the lack of an RHD gene. Therefore, we used densitometric quantification of PCR amplified exons 7 and 10 of the RHD and RHCE genes to determine whether the genome of an individual has one or two copies of the RHD gene.

RESULTS: The mean relative amount of exon 10 to exon 7 PCR product was 0.70 (range 0.59 – 0.83, n = 17) for obligate RHD hemizygotes. RHD

621 NUTRIENT INTAKE AND CONGENITAL HEART DEFECTS IN MATERNAL PHENYLKETONURIA. K.M. Matalon, L.D. Platt, P. Acosta, Univ. Texas Med. Branch, Galveston, TX, Cedars-Sinai Med. Center, Los Angeles, CA, Ross Products Div, Abbott Lab., Columbus, OH

OBJECTIVE: The purpose of this study was to determine if nutritional components other than high maternal blood phenylalanine (Phe) level (>10 mg/dL) were associated with congenital heart defects (CHD) in offspring of women with phenylketonuria (PKU).

STUDY DESIGN: Since 1984, Maternal Phenylketonuria Collaborative Study has been assessing the efficacy of a Phe-restricted diet in preventing the morbidity associated with the offspring of PKU women. Of the 414 subjects having live births, 249 (60.1%) have complete maternal and infant outcome data. Division of these subjects were made according to maternal Phe level at 8 weeks gestation (< or > 10 mg/dL) and daily protein intake (< or > 37.5 g/day [50% of the recommended dietary allowance]), and the incidence of CHD in offspring. Simple contingency table analysis was done by Fisher’s Exact Test for comparison between groups on frequency distributions of categorical variables.

RESULTS: 92/249 (37.5%) offspring were found to have CHD. All had elevated maternal Phe levels > 10 mg/dL. Women who had elevated blood Phe levels and low protein intake were found to have a significant increase in the incidence of infants with CHD.

Phe (mg/dL)/ Protein (g/day) CHD % p
<10/<37.5 0/6 0
<10/>37.5 0/75
>10/<37.5 11/36 30.5 <0.0013
>10/>37.5 11/32 8.3

CONCLUSION: The data suggest that the incidence of CHD could be increased if nutrient intake were not optimal. Women with PKU should consume adequate medical food before attempting pregnancy to reduce the effects of Phe embryopathy.

622 RECURRENT UNEXPLAINED ELEVATED MATERNL MATERNAL SERUM ALFA-FETOPROTEIN (MSAFP): ASSOCIATION WITH POOR PERINATAL OUTCOME (PPO). E.C. Pryse, P.S. Hart, J.C. Veitch, Dept. of Obstetrics and Gynecology, Dept. of Medical Genetics, Wake Forest University School of Medicine (WFU), Winston-Salem, NC.

INTRODUCTION: Unexplained elevation in screening MSAFP has been associated with PPO. Counseling parents for recurrent unexplained MSAFP elevations is not clear.

AIM: To determine the risk for PPO in patients with recurrent unexplained elevations of MSAFP.

STUDY DESIGN: A retrospective analysis of the WFUSM Screening MSAFP database from 1994-1998 was performed. Unexplained MSAFP in at least two consecutive pregnancies were identified. Several patients also had THCG (>2 MoMs). PPO was defined as intrauterine fetal demise (IUF), preterm delivery (PTD), or preterm premature rupture of membranes (PPROM).

RESULTS: A total of 68,910 pregnancies were screened with MSAFP during the study period. One thousand seven hundred and fifteen pregnancies had elevated MSAFP. Ten patients had recurrent unexplained elevated MSAFP (22 pregnancies).

22 PREGNANCIES

<table>
<thead>
<tr>
<th>12 NORMAL</th>
<th>6 IUF D</th>
<th>2 PRE</th>
<th>2 PTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>45% PPO</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: 1) Unexplained recurrent MSAFP is a rare event (10/68,910). 2) These patients exhibit significant risk for PPO and should be counseled accordingly, and 5) The reason why certain patients have recurrent MSAFP requires further investigation, but may be secondary to hereditary persistence of MSAFP, which can be tested at 8 weeks post-partum.


OBJECTIVE: In utero gene therapy using stem cells during the first trimester of pregnancy is under investigation. Donor cells could be infused under ultrasound guidance into the recipient’s coelomic space or yolk sac before immunocompetence is developed by the developing fetus. Our objective was to determine ultrasonographic measurements (TVS) of the extraocoelomic space and yolk sac between 10.1-15.0 weeks (calculated from CRL) of karyotypically normal pregnancies.

STUDY DESIGN: Measurement of the 3 largest diameters of the gestational sac (GS) and amniotic sac (AS) were determined at the time of CVS as determined by CVS. The outer circumference of the yolk sac (YS) was determined from ultrasound guidance into the recipient’s coelomic space or yolk sac between 10.1-15.0 weeks (calculated from CRL) of karyotypically normal pregnancies.

RESULTS: 30 embryos were male and 29 females. Mean (SD) gestational age (weeks.days) was 11.5(1.5): 14 studies were done during the 10th week of pregnancy, 24 during the 11th, 19 during the 12th and 1 at 13.0. The ECS% could be calculated 77% of the times before 12 weeks. Mean (mm) (SD) YS was 18.9(3.3). YS was collapsed or not visualized 60% of times after 12 weeks while it could be measured 77% of times before 12 weeks.

CONCLUSION: This data provides further insight to the feasibility of using these extraembryonic structures for prenatal diagnosis or gene therapy.
624  THE RELATIONSHIP OF AMNIOTIC FLUID HOMOCYSTEINE AND THE 677C→T MTHFR MUTATION TO SPONTANEOUS PREGNANCY LOSS IN WOMEN WITH A HISTORY OF NTD. K D Wesstrom, M DuBard, J Owen, G Johanning, and T Tamura. Dept. of OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To determine whether the 677C→T methylene tetrahydrofolate reductase (MTHFR) mutation, which leads to altered homocysteine (Hcys) metabolism and is associated with neural tube defects (NTDs) and placental infarction, also increases the risk of pregnancy loss or preterm delivery.

STUDY DESIGN: We accessed data from a previous study in which Hcys levels and the presence or absence of the 677C→T MTHFR mutation were determined in amniotic fluid isolated from isolated fetal NTD cases diagnosed from 1988 to 1998 (n=80) and in normal matched controls. NTD cases were grouped according to Hcys and MTHFR mutation status, and the incidence of pregnancy loss and preterm delivery was compared to that of the controls.

RESULTS: Forty-four percent of cases and 17% of controls were heterozygous or homozygous for the 677C→T MTHFR mutation, while 37% of cases and 39% of controls had a positive Hcys level, and the presence or absence of the 677C→T MTHFR mutation was associated with a significantly higher risk of pregnancy loss. The incidence of spontaneous abortion and PTN was similar in all NTD subgroups and controls.

CONCLUSIONS: We did not identify a relationship between NTDs, Hcys, or MTHFR status and pregnancy loss. The 677C→T MTHFR mutation may not affect fetal viability, or variation in folic acid nutrition with each pregnancy may influence outcome.

625  PRECONCEPTION COUNSELING BY MFM SUBSPECIALISTS IS EFFICIENT AND COST EFFECTIVE. KD Wesstrom and CJ Watson. Dept. of OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: Because third party payers often deny reimbursement for preconception counseling (PCC) an MFM specialist, citing scant data confirming its value, we critically examined the value of PCC at our center.

STUDY DESIGN: We reviewed the records of all patients referred to our clinic solely for PCC (from 1995-1998). PCC clinic protocol mandated that medical records be reviewed and, if necessary, a literature search performed in advance of each visit, which typically lasted 2-1 hour.

RESULTS: One hundred seventy-eight women were referred for counseling, which primarily concerned an obstetric condition in 74 (42%), a medical condition in 68 (38%), or a genetic condition in 36 (20%). A second problem was recognized by the referring MD in 44 (25%). A third problem was recognized by the referring MD in 36 (20%). A second problem was recognized by the referring MD in 44 (25%). A third problem was recognized by the referring MD in 36 (20%). A fourth problem was recognized by the referring MD in 24 (14%). A fifth problem was recognized by the referring MD in 12 (7%). A sixth problem was recognized by the referring MD in 6 (4%). No consultations to other subspecialists were required. In all cases, the patients received advice and recommendations concerning the initial referral question, and in 129 (75%), the patient received additional information regarding conditions unrecognized by the referring MD. The average fee billed for PCC was $250, $147-285 was collected.

CONCLUSIONS: The unique training of the MFM specialist enables preconception counseling related to any combination of obstetrical, medical, or genetic conditions, without the need for additional referrals or extensive diagnostic tests. As opposed to requiring separate consultations from specific subspecialists, MFM counseling is efficient and economical.

626  A MATHEMATICAL MODEL TO EVALUATE TRANSGENE EXPRESSION. K. Sosnowski, J. Kramer, S. Krawetz. Dept. OB/GYN, Hutzel Hospital, Wayne State University, Detroit Michigan.

OBJECTIVE: To develop a method to statistically assess copy-number dependent transgene expression.

STUDY DESIGN: Transgenic mice containing nine, nine, and twelve copies of the human protamine-1, protamine-2, and PMT loci (PRM1->PRM2->TNP2) were created. The temporal expression of both the human and mouse genes was evaluated by Northern blot analysis using a specific radiolabeled probe to each member of the locus. Copy-number dependent expression was assessed by quantitative Northern analysis. Analysis of gene type and copy number on transgene messenger RNA expression were evaluated using repeated measures ANOVA and then calculating the deviation of observed ratios from the hypothesis for each model.

RESULTS: Northern analysis showed that temporal expression of both the mouse and human protamine genes was maintained in the transgenic state. The results presented demonstrate the utility of this statistical approach to assess the copy-number dependent expression of transgenes. This method is particularly well suited to identifying variation, which may be reflective of transcriptional effects. Clinically this may eventually be applied toward determining the proper dosimetry for gene therapy. Acknowledgment: This work was supported in part by NIH grant HD08512 to S.A.K.

627  DOES A FETAL NEURAL TUBE OR CONGENITAL HEART DEFECT INDUCE INCREASED RISK OF MATERNAL HYPERTENSION? KD Wesstrom and M DuBard. Dept OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: In separate studies, the 667C→T mutation of methylene tetrahydrofolate reductase (MTHFR) has been associated with fetal neural tube defects (NTDs), fetal congenital heart defects (CHD), and hypertension (HTN). We sought to determine if mothers of NTD or CHD offspring are at increased risk for any form of HTN.

STUDY DESIGN: We included all pregnancies evaluated from 1988 to 1998 and carried to ≥24 weeks. Cases had a fetus with either isolated NTD (n=219) or CHD (n=83) controls were all clinic patients with nonanomalous fetuses (n=35,049). If the patient had multiple pregnancies, the last was evaluated. The incidence of all HTN in cases and controls were compared.

RESULTS: Cases and controls were similar with respect to maternal age (25.3 ± 4.6 vs 24.3 ± 5.9 years) and gestational age at delivery (36 ± 3.5 vs 38 ± 3.6 weeks).

<table>
<thead>
<tr>
<th>White (N=254)</th>
<th>Control</th>
<th>NTD Case, P</th>
<th>CHD Case, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chf HTN</td>
<td>2.3%</td>
<td>1.0%, 0.5</td>
<td>8.6%, 0.05</td>
</tr>
<tr>
<td>PIH</td>
<td>6.1%</td>
<td>3.1%, 0.3</td>
<td>2.9%, 0.7</td>
</tr>
<tr>
<td>Pre E</td>
<td>3.4%</td>
<td>3.1%, 0.3</td>
<td>5.7%, 0.7</td>
</tr>
<tr>
<td>Black (N=68)</td>
<td>Control</td>
<td>NTD Case, P</td>
<td>CHD Case, P</td>
</tr>
<tr>
<td>Chf HTN</td>
<td>2.4%</td>
<td>0.1, 1.0</td>
<td>2.1%, 1.0</td>
</tr>
<tr>
<td>PIH</td>
<td>5.0%</td>
<td>0.5, 1.0</td>
<td>8.3%, 0.3</td>
</tr>
<tr>
<td>Pre E</td>
<td>4.0%</td>
<td>0.1, 1.0</td>
<td>8.3%, 0.3</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Black women with NTD or CHD fetuses were not at increased risk for HTN, probably because the incidence of NTDs is low and HTN has many etiologies in this group. However, white women with CHD fetuses are at significantly increased risk to have chronic HTN. Since HTN itself is not believed to cause CHDs, it is possible that both HTN and CHD are associated with the same enzyme defect. The merits of folic acid supplementation in these women should be investigated.
628 AN EVALUATION OF LIKELIHOOD RATIOS FOR DOWN SYNDROME FROM MATERNAL AGE, ALPHA-FETOPROTEIN, AND FREE BETA HUMAN CHORIONIC GONADOTROPHIN. L. Chuk1, K Chuk2, K Spencer3, RJ Sokol, D Krantz4, A Johnson, JN Marci5, MI Evans, Dept Ob/Gyn, Wayne State Univ, Detroit, MI; Clinical Biochemistry, Romford, England; NTD Labs, Inc., New York.

OBJECTIVE: A "traditional" approach to risk assessment for Down syndrome (DS) has been to use the maternal age specific risk multiplied by the likelihood ratios (LR) for the combination of alpha-fetoprotein (AFP) and free beta human chorionic gonadotrophin (HCG) values, for the Glasgow equations that have better fits than the Gaussian curves. We explore if using the LR also on age, per se, improves accuracy of risk estimates.

STUDY DESIGN: We computed the LR for DS based on age, AFP, and HCG as LR_age, LR_AFP and LR_hCG, from their logarithms. The product, PLR = (LR_age*LR_AFP*LR_hCG), was used for DS classifications in comparison with the traditional Glasgow equations. A study database of 58297 with 348 DS cases was used for analysis, and a test database of 50679 with 101 DS was used for validation.

RESULTS: At 95% specificity (5% false positive), the PLR had sensitivities of 59.8% (206/348) for the study database, and 62.4% (63/101) for the test database. These improved upon the corresponding results using the traditional equations, which had sensitivities of 58.0% (202/348) and 60.4% (61/101), respectively.

CONCLUSIONS: The PLR produced small improvements in sensitivity for both the study and test databases. Based on within subject deviations of LR_age, LR_AFP and LR_hCG, additional improvements appear possible in some group categories. If these improvements can be confirmed, screening cost could be lowered substantially.


OBJECTIVE: Thrombotic genetic variants have been implicated in some cases of preeclampsia (PE) and interuterine growth restriction (IUGR). A highly-accurate and reliable means for genotyping these mutations through simple sample preparation and ESI/MS (which could be automated and required less than three minutes per analysis).

STUDY DESIGN: The ESI/MS assay was used to study four thrombotic-associated polymorphisms (Factor II prothrombin 20210, Factor V Leiden, Factor VII R353Q, and HPA-1) in 153 women with mild or severe PE. A mixed probe of equimolar amounts of differently labeled test genomic DNA and reference DNA prepared from cells with normal chromosomes was used for chromosomal in situ suppression hybridization to normal metaphase spreads. Hybridized test and control DNA sequences were detected in different fluorochromes. The ratios of fluorescence intensities reflected the relative copy number in the test genome compared with the control genome.

RESULTS: CGH analysis of 4 cases of trisomy 21, 5 cases of trisomy 18, one case of trisomy 13, one case of trisomy 15 and one case of trisomy 7 all showed overrepresentation of the respective trisomic chromosome. The CGH profile was also in accordance with the karyotyping of a case with macrosomia 21. The CGH profile of a case with t(2;6) (q37.3;q22.2) revealed partial trisomy for chromosome 6 between q21 and q27.

CONCLUSIONS: CGH appears to be a promising technique for diagnosis of cytogenetic aberrations of archival samples including total and partial aneuploidies.
GENETIC THROMBOPHILIA IN PATIENTS WITH PREGNANCY COMPLICATIONS. L. Boss, M Mansukhani, Deps of OB/GYN and Pathology, Columbia University College of Physicians & Surgeons & Sloane Hospital for Women at the New York Presbyterian Hospital, NY, NY.

Objective: To identify and assess prevalence of genetic thrombophilia in patients with pregnancy complications.

Study Design: In this pilot study, Factor V Leiden (FVL), prothrombin (PR), and methyl tetrahydrofolate reductase (MTHFR) mutations were assessed in 30 patients with IUGR, abruptio placenta, habitual abortion, preeclampsia, and deep-vein thrombosis in pregnancy. These were done by PCR-RFLP (Polymerase chain reaction-restriction fragment length polymorphism) analysis of maternal blood.

Results: Patients were of various ethnicities (Jewish, Asian Indian, Hispanic and African-American). Four patients were homozygous for MTHFR 677C (One patient had repeated abruptio, one had chronic abruptio, one had IUGR of the fetus, and the last had early 2nd trimester spontaneous abortion with vascular changes on placental evaluation). A Factor V Leiden homozygous mutation was detected in one patient with deep-vein thrombosis in pregnancy and a heterozygous mutation in another with chronic abortion. A prothrombin mutation was present in one patient with a second trimester spontaneous abortion. Six of these patients were Caucasian and one was Asian-Indian. The yield of thrombophilia in this select population was 23.3% (7/30).

The incidence of thrombophilia due to these mutations in our control population, with the same testing, is under 5%.

Conclusion: Prothrombin (PR), Methyl tetrahydrofolate reductase (MTHFR), and Factor V Leiden (FVL) mutations are seen in a high percentage of a select population with pregnancy complications. Identification of these gene mutations may improve perinatal outcome by appropriate management.


Objective: Folic acid (FA) is capable of reducing the risk of neural tube defects (NTD) in the periconceptual period. A prepregnancy screening program was initiated in 1998 to aid in the counseling of indigent women about birth defect reduction. Our objective was to evaluate the relationship between the knowledge and practice of FA supplementation with age, parity, ethnicity, and history of prior birth defects.

Study Design: Between May and November 1998, a screening questionnaire was given to non-stereilized women who recently delivered babies and non-stereilized women attending a gynecology clinic (n=996). Records with missing data were excluded leaving 774 cases for analysis with SPSS 9.0. Independent variables included age, parity, ethnicity, language spoken, and personal or family histories of birth defects. Dependent variables were current FA intake and prior knowledge of FA. A simple logistic regression analysis was used to assess each dependent variable using all independent variables. Two sequential regressions were performed analyzing the three independent variables: ethnicity and language, family or personal history of birth defects, and age and parity.

Results: Seven percent of women surveyed took FA supplementation whereas 41% were aware that FA could reduce birth defects. Prior knowledge of FA was 5X more likely if the woman had an NTD affected child (OR=5.31; 95% CI=1.7-16.6) but was unaffected by other family history of birth defects. Non-English-speaking women were 50% less likely to know about FA than English-speaking women. No significant effects were found from age or parity.

Conclusions: (1) Past history of an NTD affected child and non-English-speaking impact FA knowledge but not its practice. (2) FA supplementation is low in this patient population. (3) A cohort study is needed to compare the practice and outcomes of counseled and non-counseled women.

635 PLACENTATION IS ASSOCIATED WITH INCREASED IMMUNOHISTOCHEMICAL DISTRIBUTION OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN THE MYOMETRIUM. A.G. Piy, G. Osof, M. Meyer, Department of Ob/Gyn, Univ. of Vermont, Burlington, VT.

Objective: Local signals related to placentation may influence uterine smooth muscle growth during gestation. The purpose of this study is to determine whether placentation is associated with localization of vascular endothelial growth factor (VEGF) in the myometrium.

Study Design: Cycling, virgin rats (n=4) underwent unilateral uterine horn ligation prior to breeding, which allowed unilateral implantation to occur in the non-ligated horn. Rats were euthanized at midgestation (day 9-11 out of 21-day gestation), uteri were removed, sectioned and stained for the presence of VEGF. The distribution of VEGF in the myometrium was compared from three areas: two sites within the implanted horn - directly beneath the placenta site (O), and opposite the placenta site (L); and within the ligated horn (L). Tissue sections images were converted to digital format, a digital-staining threshold for VEGF was established using ImagePro software, and VEGF staining density (the percentage of myometrium within a given section stained with VEGF) was determined. Staining densities from 10 high power fields per area of myometrium studied per animal were compared using one-way ANOVA, with pair-wise post hoc testing for individual differences (P<.05 considered significant).

Results: The staining density of VEGF in myometrium from BP sites (50.3%) was significantly greater than that observed in OP (26.9%) and L sites (1.4%) (P<.05). Pairwise post hoc testing revealed no significant difference in staining densities when myometrium from the OP and L sites were compared.

Conclusion: Distribution of VEGF in the myometrium of the rat uterus at midgestation is increased directly beneath the placental site. This suggests that VEGF may function as a local signal associated with the implanted placenta in the adaptation of the uterus during pregnancy.
636 EXPRESSION OF ADRENOMEDULLIN AND ITS RECEPTOR IN THE HUMAN PLACENTA: NORMAL AND PATHOLOGIC PREGNANCY. C.C. Apodaca¹, K. Moore³, R.F. Hume Jr, R. Wagner, B. Pierce⁴, P. Niessen, B.C. Calhoun. Dept. Ob/Gyn, Madigan Army Medical Center, Tacoma, WA.

OBJECTIVE: To identify the expression of adrenomedullin and adrenomedullin receptor in the various tissues of the human placenta, and to compare expression in placentas from oligohydramnios and placentas from normal pregnancies.

STUDY DESIGN: Total RNA was extracted from amnion, chorion, cotyledon, umbilical vein and umbilical artery of five normal placentas (N, n=5); and three placentas from pregnancies complicated by oligohydramnios (O, n=3). A cell line known to be positive for adrenomedullin and its receptor was used to develop the polymerase chain reaction (PCR) and served as a positive control in all experiments. Semi-quantitative RTPCR for adrenomedullin and adrenomedullin receptor were compared between tissues and results analyzed using a paired t-test. Immunohistochernistry using an antibody to human adrenomedullin was used to locate adrenomedullin in all tissue types.

RESULTS: RTP-PCR data summarized in table below.

| Ratio of Adrenomedullin and Receptor vs β2 microglobulin standard |
|---------------|------------------|
| Amnion | Chorion | Cotyledon | Umb Vein | Umb Art |
| Amnion | 4.45±0.6 | 2.2±1.7 | 1.3±0.5 | 0.6±1.2 | 3.0±0.3 |
| O | 0.9±0.8 | 0.3±1.2 | 0.4±1.6 | 1.8±0.6 | 3.4±0.3 |

Non-shaded=adrenomedullin, Shaded =adrenomedullin receptor


OBJECTIVE: Interleukin-6 (IL-6), a multifunctional cytokine, is elevated in a variety of inflammatory conditions and has been implicated in the etiology of periventricular leukomalacia in preterm neonates, a major risk factor for cerebral palsy. Our goal is to determine whether exposure of the isolated human placental cotyledon to different fetal circulatory perfusion rates, and concomitant pressure differences, alters placental production of IL-6.

STUDY DESIGN: The maternal and fetal circulation of two cotyledons from 3 placentas were perfused for four hours. The fetal circulation of one cotyledon was perfused with HBSS at a low rate of 1 cc/min, the other at high rate of 10 cc/min. The maternal circulation of each cotyledon was perfused at 10 cc/min. Effluents from the fetal circulation were collected at hourly intervals. IL-6 concentrations were determined by ELISA. IL-6 concentrations with an estimated normal physiologic fetal circulation rate of 4 cc/min were compared with the low and high flow results.

RESULTS: Concentrations of IL-6 increased exponentially over time at all perfusion rates, as did the mean difference. Statistical significance was achieved at 2, 3, and 4 hours (ANOVA). Summary table below

<table>
<thead>
<tr>
<th>Flow Rate</th>
<th>Concentrations of IL-6 in pg/cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>2 hour</td>
</tr>
<tr>
<td>Low - 1 cc/min</td>
<td>2.3</td>
</tr>
<tr>
<td>Normal - 4cc/min</td>
<td>6.0</td>
</tr>
<tr>
<td>High - 10 cc/min</td>
<td>1.2</td>
</tr>
<tr>
<td>P-value</td>
<td>0.08</td>
</tr>
</tbody>
</table>

CONCLUSION: Decreased fetal circulation flow rate results in an increased production of IL-6. This may implicate fetal placental hyperperfusion, not increased shear stress, in the pathophysiology of cerebral palsy.

638 TRANSFER OF QUINIDINE, A P-GLYCOPROTEIN INHIBITOR, ACROSS THE ISOLATED HUMAN PLACENTA. G. Huchelb, O. Sapir³, M. Hulehelsb, M. Katz, M. Tsali⁴, A. Wizinzer, M. Mazot, Z. Ben-Zvi⁵ Dept. of Ob/Gyn and Dept. of Clinical Pharmacology, Soroka University Medical College, Ben-Gurion University of the Negev, Beer Sheva, Israel.

OBJECTIVE: To determine the transfer rate of quinidine, a known antarrhythmic agent and a p-glycoprotein inhibitor, in human perfused placental cotyledons.

STUDY DESIGN: Isolated placental cotyledons from normal human placentas were dually perfused with M199 medium enriched with albumin (0.3%) and glucose (0.1%). The maternal and the fetal circulation flow rates were 12 and 6 ml/min, respectively. Closed circulations were used to evaluate steady state transplacental gradient formation. Quinidine was added to the maternal medium at concentration of 7.5 ± 0.2 µg/ml. Quinidine levels were measured by fluorescence-polarization-immunoassay (TDx Abbott Lab). Antipyrine (0.5 µg/ml) was used as reference substance and measured by HPLC method.

RESULTS: The clearance index of quinidine was 0.117±0.06 ml/min. The fetal/maternal ratio was 6.75 ± 0.7 µg/ml, while fetal steady state concentration was 1.65 ± 0.5 µg/ml. Antipyrine clearance was 0.12±0.03 ml/min.

CONCLUSION: This is the first in vitro perfusion study confirming quinidine transplacental transfer in human placentas.


OBJECTIVE: To investigate whether leptin concentration in the mother and newborn correlates with birth weight, placental weight and maternal weight gain in appropriate for gestational age (AGA) versus small for gestational age (SGA) neonates.

PATIENTS AND METHODS: We prospectively collected maternal plasma and umbilical cord samples in 23 consecutive SGA and 14 AGA neonates at term. The maternal BMI and weight gain during pregnancy, placental weight and birth weight were recorded. Statistical analysis was performed by Student t test, Fisher exact test and Pearson Correlation Coefficient.

RESULTS: The maternal weight characteristics were similar between the study groups. The mean birth weight differed significantly: 3460 grams in AGA versus 2825 grams in SGA (p<0.001). The study groups are described in Table.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AGA (N=14)</th>
<th>SGA (N=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Weight Gain, kg (Mean)</td>
<td>13.07</td>
<td>10.05</td>
<td>ns</td>
</tr>
<tr>
<td>Maternal BMI</td>
<td>25.7</td>
<td>25.64</td>
<td>ns</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>71.4%</td>
<td>50%</td>
<td>ns</td>
</tr>
<tr>
<td>Cesarean Section (%)</td>
<td>14.3%</td>
<td>45.4%</td>
<td>ns</td>
</tr>
</tbody>
</table>

Maternal serum leptin mean level was 16.7 (SD±10.92) in the AGA group and 19.24 (SD±17.05) in the SGA group (p=0.06). Umbilical cord (cord) leptin mean level was 7.15 (SD±5.95) in the AGA group and 4.87 (SD±7.14) in the SGA group (p=0.35). In the AGA group the umbilical cord leptin correlated with the birth weight (r=0.719). In the SGA group no significant correlation was found(r=0.23). No significant correlation was found between umbilical cord leptin and placental weight in either group.

CONCLUSION: Our findings that cord leptin level correlates with birth weight in AGA neonates and not in the SGA confirms that cord leptin primarily reflects the fetal adipose tissue production. Thus, we speculate that in SGA neonates, with minimal adipose tissue (in contrast to AGA and LGA), the cord leptin primarily reflects basic placental production.
640 INHIBITION OF DIGOXIN TRANSPORT BY QUINIDINE IN THE HUMAN PLACENTA

OBJECTIVE: To determine the effect of quinidine, a p-glycoprotein-mediated inhibitor on digoxin transport in isolated perfused human placental cotyledon.

STUDY DESIGN: Isolated placental cotyledons from normal human placentas were dually perfused with M199 medium enriched with albumin 0.3% and glucose 1%. Flow rates were 12ml/min in the maternal circuit and 6 ml/min in the fetal circuit. In five placentas quinidine was added to the maternal circuit in final concentration of 7.5±0.2 µg/ml. After 60 min of perfusion, digoxin at final concentration of 5.5±1 ng/ml was added to the perfusate. In 5 additional placentas the transfer of digoxin was studied in the absence of quinidine. Transplacental passage of digoxin was calculated from repeated fetal and maternal perfusate samples. Digoxin levels were determined in perfusate samples by fluorescence-polarization-immunnoassay (TDx Abbott Lab).

RESULTS: In the presence of quinidine, the total concentration of digoxin decreases from 0.6ng/ml to 0.3ng/ml in the fetal circuit at steady state concentration (p<0.05).

CONCLUSION: Quinidine significantly decreases digoxin transplacental passage in isolated perfused human placenta.

641 EFFECT OF ACUTE HYPOXIA ON MATERNAL RAT BRAIN EXCITATORY AMINO ACID RECEPTOR (NON NMDA) BINDING. M Halik, JW Hirose, D Custodio, ML Kruger*, Departments of Ob/Gyn, Ben Gurion University/Soroka Medical Center, Beer Sheva, Israel and Wayne State University School of Medicine, Detroit, Michigan.

OBJECTIVE: Excitatory amino acid receptors (EAAR) are known to be involved in the pathophysiology of hypoxic brain injury. The purpose of this study was to determine whether acute, severe, maternal hypoxia during the end of pregnancy alters the EAAR (Kainate and AMPA) binding in rat brain, and whether magnesium sulfate (MgSO4) can prevent possible changes.

STUDY DESIGN: Four groups of pregnant rats were studied on gestational day 17. Group 1: Saline injections and room air (n=6). Group 2: MgSO4 injections and room air (n=5). Group 3: Saline injections and hypoxia chamber (n=5). Group 4: MgSO4 injections and hypoxia chamber (n=5). Saline or experimental MgSO4/Saline injection protocol included a loading dose of 270 mg/kg followed by 27 mg/kg every 20 minutes for 4 hours. Hypoxia chamber protocol included a gas mixture of 9% oxygen, 3% carbon dioxide, and 98% nitrogen for 4 hours. The last group was normal and intrauterine growth retardation (IUGR) rat fetuses. Assessing the functional development of the GI tract in determining whether the enteral route can be used for prenatal nutrition.

RESULTS: Eight pregnant New Zealand white rabbits were divided into three groups. The first group received saline injections and normal room air, the second received MgSO4 injections and normal room air, the third received saline injections and hypoxia chamber, and the fourth received MgSO4 injections and hypoxia chamber. After 24 hours of recovery maternal cardiovascular systems were perfused, brains dissected and frozen, cryostat sections taken, labeled in-vitro and mounted on slides. The length of fluorescein traveled on day 27 was significantly less than day 30 (22.5 + 4.6 cm). The percent motility, defined as the length of fluorescein traveled on day 27 divided by the total length of the small intestine, on day 94 (44.7 + 5.4 cm) was significantly less than day 30 (46.7 + 5.4 cm). The length of fluorescein traveled significantly correlated with fetal body weight on day 97 and day 30.

CONCLUSION: The length of fluorescein traveled significantly increased in normal rabbit GI tract compared to IUGR rabbit GI tract. The length of fluorescein traveled significantly correlated with fetal body weight.

642 A SIMPLIFIED MODEL OF THE PLASMA SODIUM (Na) CONCENTRATION AND EXCRETION IN THE EARLY PREGNANT WOMAN. S. E. Mann, M. Triquirez, M. O. Ross. Dept. Ob/Ob/Gyn, Harbor-UCLA Hospital, Torrance, CA.

OBJECTIVE: The fetal-somatotroph axis is involved in the pathophysiology of hypoxic brain injury. The purpose of this study was to determine whether acute, severe, maternal hypoxia during the end of pregnancy alters the EAAR (Kainate and AMPA) binding in rat brain, and whether magnesium sulfate (MgSO4) can prevent possible changes.

METHODS: Four healthy non-pregnant women between the ages of 35 and 45 were studied. All patients were hospitalized and morning euvhydration assured by oral water (5-10 ml/kg) the evening prior to study. On the study day, following fasting blood samples, patients received an intravenous infusion of hypertonic (5%) NaCl to gradually increase plasma Na. Blood samples were obtained every 15 minutes for plasma electrolytes and VP. Plasma VP concentrations were regress adjusted against plasma Na concentration to calculate the Na threshold for VP secretion. A simplified index of the Na threshold was determined using the morning, fasting euvhydrated plasma Na.

RESULTS: Hypothalamic saline injection significantly increased plasma Na (140±3 to 159±5 mEq/L). Plasma VP significantly increased (5±1 to 25±7 pg/ml) with a bimodal distribution (P < 0.005), suggesting initial and secondary stimulation of VP secretion at 2.5 and 5% increases in plasma Na, respectively. The mean Na threshold for VP secretion was calculated as 152±1 mEq/L. The morning fasting Na level (140±2 mEq/L) was nearly identical to the calculated Na threshold (Figure).

CONCLUSIONS: The morning, fasting euvhydrated plasma Na can be utilized as a simplified index for the plasma Na threshold. We speculate that pregnant women who do not reset the plasma sodium concentration expansion and be at increased risk for adverse pregnancy outcomes.

OBJECTIVE: High serum homocysteine (Hcy) is caused by poor folate nutrition, and has been associated with the increased risk of pregnancy complications, such as fetal-growth restriction, possibly due to its damaging effect on placental vessels. In this study, we evaluated the relationship between maternal serum Hcy and folate levels during pregnancy and birth weight of term infants.

STUDY DESIGN: Serum Hcy and folate levels of 285 medically indigent women were measured at 18 and 30 weeks' gestation (wk GA). The relationship of these values to infant birth weight was evaluated by regression analyses.

RESULTS: Mean Hcy and folate levels were 5.9 µmol/L and 52 nmol/L at 18 wk GA, and were 5.1 µmol/L and 51 nmol/L at 30 wk GA, respectively. Hcy and folate were negatively correlated at 18 and 30 wk GA (r=−0.29 and −0.32, respectively, P<0.001). Mean birth weight was 3,266 g. At 30 wk GA, birth weights showed a weak negative correlation with Hcy (r=0.12, P=0.059), and positively with folate (r=0.15, P=0.02). Neither correlation was significant at 18 wk GA. Multiple regression analysis showed that a 1.0 µmol/L increase in Hcy was associated with a 24 g decrease in birth weight, and a 10 nmol/L increase in folate was associated with an 18 g increase in birth weight.

CONCLUSION: Our data indicate that maternal folate nutrition, especially in the third trimester, is important for fetal growth. It remains to be seen whether this relationship is mediated by the effect of folate on Hcy metabolism.


OBJECTIVE: To evaluate the cardiovascular effects of high-dose intravaginal misoprostol in the mid-trimester using thoracic electrical bioimpedance (TEB) monitoring.

STUDY DESIGN: In a prospective, randomized trial of misoprostol for mid-trimester pregnancy interruption, 22 consenting women were assigned to receive either misoprostol or concentrated oxytocin and vaginal PGE2. Women randomized to misoprostol received 600 µg of misoprostol intravaginally followed by 400 µg every 4 hours for up to 24 hours. Five of the 11 women assigned to misoprostol consented to TEB monitoring. One hour of baseline blood pressure and TEB monitoring was performed prior to the initial misoprostol dose. Post-treatment assessments were made every 15 minutes for a total of 4 hours in a left lateral tilt position. Heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), stroke index (SI), systemic vascular resistance index (SVRI), and end diastolic volume index (EDVI) were measured. Data were averaged in 30 minute intervals and are reported as mean ± SD. The paired t-test and repeated measures ANOVA were utilized for statistical comparisons.

RESULTS: The mean maternal age was 30 ± 9 yrs and gestational age was 20 ± 2 wks. There were no statistically significant changes in any of the measured cardiac parameters over the 4 hour monitoring interval. Since serum levels of misoprostol peak 60-120 minutes post vaginal administration, direct comparisons were made between the pre-treatment and 2 hour post-treatment cardiac indices. MAP (77 ± 6 vs 81 ± 14 mmHg, p=0.50), HR (90 ± 25 vs 90 ± 16, p=0.97), CI (4.0 ± 0.6 vs 4 ± 0.5 liter/min/m², p=0.60), SI (48 ± 13 vs 49 ± 10 mL/m², p=0.93), SVRI (1455 ± 178 vs 1471 ± 391 mmHg·min·L⁻¹·m², p=0.93), and EDVI (170 ± 11 vs 68 ± 15 mL/m², p=0.85) was not seen whether this relationship is mediated by the effect of folate on Hcy metabolism.

EFFECTS OF MISOPROSTOL ON SPECIFIC CYTOKINES AND ENZYMES OF THE UTERUS AND CERVIX: Goela Lyons, Kay Beharhy, Yasir Akmal, Amir Akmal, Steven Reyes, Michael P. Nageotte, Dept. of Ob/Gyn, Women’s Hospital, Long Beach Memorial Medical Center, Long Beach & University of California, Irvine Medical Center, Orange, CA.

OBJECTIVES: Misoprostol (MP) is an agent used for cervical ripening and labor induction. Adenylate cyclase and cytokine syntheses may be involved in the control of parturition. We therefore examined the effects of two different doses of misoprostol on IL-1β, cyclopamp amphon production, and the mRNA expression of COX-1 and COX-2 isoforms in the term pregnant rat myometrium and cervix.

STUDY DESIGN: Myometrial (M) and cervical (C) tissue samples taken from 24 term, non-laboring, pregnant Sprague Dawley rats were incubated in media with or without MP (50 µg/ml or 100 µg/ml) for 0.25, 0.5, 1, 3, 6, 12 & 24 hours. At the end of each incubation time, media samples were collected for measurement of IL-1β and CAMP production. Tissue samples of myometrium and cervix were analyzed for mRNA expression of COX-1 and COX-2. COX mRNA in rat myometrium and cervix is different.

CONCLUSIONS: These are the first data examining immediate changes in PFT following uncomplicated delivery. Contrary to anecdotal observations, there is no clinically significant improvement in pulmonary mechanics, volumes, or diffusion associated with evacuation of the term uterus.

DOES DELIVERY RESULT IN BENEFITS TO THE MECHANICS OF VENTILATION? MW Tomlinson, B Lesser, G. Konik. Dept. of Ob/ Gyn, Wayne State University/Detroit Med Ctr, Detroit, MI.

OBJECTIVE: In the respiratory compromised gravidia, anecdotal reports suggest delivery improves ventilatory function. To better define this relationship, we undertook a controlled trial investigating the immediate effects of term delivery on pulmonary function testing (PFT).

STUDY DESIGN: Routine PFT was performed on 7 healthy gravidas from 36 to 40 weeks, and again within 48 hours following uncomplicated vaginal delivery. Pre and post delivery values were compared using the paired t-test.

RESULTS: Mean (±SD) maternal age was 27.4±6.4 years. Height was 169±17.5 cm. The interval from predelivery PFT to delivery averaged 9.6±0.9 days.

Parameter (liters) | Predelivery | Postdelivery change | p-value
---|---|---|---
Forced Vital Capacity (FVC) | 3.94±0.71 | -0.34±0.36 | 0.04
FEV1 | 3.34±0.58 | -0.17±0.19 | 0.05
Inspiratory capacity | 2.99±0.46 | -0.86±0.19 | 0.001
FRC | 2.42±0.58 | 0.34±2.6 | 0.13
Total lung capacity | 5.26±0.78 | -0.15±0.30 | 0.24
DLCO (ml/min/mmHg) | 20.33±5.32 | -0.25±2.42 | 0.79

(FEV1=forced expiratory volume; FRC=functional reserve capacity; DLCO=diffusion capacity).

REFERENCES: The first data examining immediate changes in PFT following uncomplicated delivery. Contrary to anecdotal observations, there is no clinically significant improvement in pulmonary mechanics, volumes, or diffusion associated with evacuation of the term uterus.
648 UTERINE CONTRACTILITY IN PREGNANT MICE LACKING A FUNCTIONAL INDUCTIVE NITRIC OXYDE SYNTHASE. M. Longo1, V. Jain1, Y. Vedernikov3, F. Facchetti, G. Saade, R. Garfield1. Dept. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX and Univ. of Modena & R. Emilia, Italy.

OBJECTIVE: To examine the role of inductive nitric oxide synthase (iNOS) in the control of uterine contractility using transgenic mice lacking a functional iNOS (iNOS KO).

STUDY DESIGN: Rings were prepared from uteri of midpregnant (day 14) iNOS KO (B6/129F1) NOS2 -/- from Jackson Laboratory) and their corresponding wild-type control mice (NOS2 +/-) and mounted in organ chambers for isometric tension recording. Uterine activity was stimulated with oxytocin (10-9 M) and responses to various inhibitory agents were studied. ANOVA and Student’s t tests were used for statistical analysis (significance p<0.05).

RESULTS: The NOS substrate, L-arginine (10-6 M), concentration-dependently inhibited contractility in rings from control but not KO mice (p<0.05). In contrast, rings from KO mice were more sensitive to the inhibitory effect of the cGMP analogue 8-bromo-cGMP (10-7 to 10-4 M) compared with control mice. Inhibition of contractility by Mg2+ (2 to 16 mM) as well as by pinacidil (10-6 to 10-4 M), an ATP-dependent K+ channel opener, was greater in control mice compared with KO mice, whereas relaxation by NS1619 (10-6 M) and responses to various inhibitory agents were studied. ANOVA and Student’s t tests were used for statistical analysis (significance p<0.05).

CONCLUSIONS: NO is a physiological uterine relaxant during pregnancy in mice. Lack of a functional iNOS is associated with desensitization of the myometrium to NO. However, sensitivity to the second messenger cGMP may be enhanced to facilitate relaxation by alternate pathways. In addition to myometrial relaxation through cGMP, NO acts at the level of Ca2+-channels. The tocolytic effect of Mg2+ is potentiated by NO, probably through the Ca2+ dependency of both agents.

649 FLOW RATE VERSUS PRESSURE RELATIONSHIP IN THE ISOLATED UTERINE VASCULAR BED OF NONPREGNANT AND PREGNANT RATS. E. Fabris1, V. Vedernikov2, G. Saade, R. Garfield1. Dep. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To study flow rate versus intraluminal pressure relationship (FPF) in isolated uterine vascular bed of pregnant and nonpregnant rats.

STUDY DESIGN: The abdominal aorta was cannulated close to its bifurcation in nonpregnant (NPN) and timed-pregnant Spargue-Dawley rats at day 14 (mid) and 21 (term) of gestation. The adjacent branches were ligated to enable perfusion of one uterine horn through the uterine artery. The uterus and associated vessels were then excised in toto and placed into the organ chamber for perfusion/superfusion with Krebs buffer (37°C, pH 7.4) containing indomethacin (10-5 M) and 2% dextrose. Intraluminal pressure was monitored using a pressure transducer connected to the cannula and an on-line data acquisition system. After equilibration at intraluminal pressure of 50 mmHg, the flow rate was gradually increased from 2 ml/min to 16 ml/min in the absence (control) and then in the presence of phenylephrine (PE, 10-6 M), an ATP-dependent K+ channel opener, was greater in control mice compared with KO mice, whereas relaxation by NS1619 (10-6 M) and responses to various inhibitory agents were studied. ANOVA and Student’s t tests were used for statistical analysis (significance p<0.05).

RESULTS: The NOS substrate, L-arginine (10-6 M), concentration-dependently inhibited contractility in rings from control but not KO mice (p<0.05). In contrast, rings from KO mice were more sensitive to the inhibitory effect of the cGMP analogue 8-bromo-cGMP (10-7 to 10-4 M) compared with control mice. Inhibition of contractility by Mg2+ (2 to 16 mM) as well as by pinacidil (10-6 to 10-4 M), an ATP-dependent K+ channel opener, was greater in control mice compared with KO mice, whereas relaxation by NS1619 (10-6 M) and responses to various inhibitory agents were studied. ANOVA and Student’s t tests were used for statistical analysis (significance p<0.05).

CONCLUSIONS: NO is a physiological uterine relaxant during pregnancy in mice. Lack of a functional iNOS is associated with desensitization of the myometrium to NO. However, sensitivity to the second messenger cGMP may be enhanced to facilitate relaxation by alternate pathways. In addition to myometrial relaxation through cGMP, NO acts at the level of Ca2+-channels. The tocolytic effect of Mg2+ is potentiated by NO, probably through the Ca2+ dependency of both agents.

650 LOCALIZATION AND EXPRESSION OF CYCLOOXYGENASE ENZYMES IN RAT CERVIX DURING PREGNANCY USING IMMUNOHISTOCHEMICAL TECHNIQUES. S. Marek, R. Salas, R. Green, Y. Vedernikovs, G. Saade, R. Garfield1. Dept. of Ob/Gyn, and Dept. of Anatomy and Neuroscience, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To determine the distribution and expression of the cyclooxygenase enzymes (COX) 1 and 2 during gestation and postpartum in rat cervical tissues using immunohistochimical staining (IHS).

STUDY DESIGN: Non-pregnant estrous (NP), timed-pregnant days 14, 18, 22 non-laboring (NL), laboring (L) and postpartum (pp) days 1 and 3 Sprague-Dawley rats were sacrificed by CO2 inhalation. The cervix was excised and preserved in 4% paraformaldehyde. The tissue was then embedded in paraffin, sectioned (6-7 mm) and processed for standard IHS using goat polyclonal anti-COX-1 and anti-COX-2 antibodies. A chromagen reaction (DAB-peroxidase) was used to localize specific antigens for COX enzymes by light microscopy.

RESULTS: Little to no staining was observed for COX-1 in NP and on days 14 and 18 of gestation. COX-1 was found in cervical smooth muscle on day 22NL, L, and pp days 1 and 3. Epithelial staining for COX-1 was observed in cervical tissue on pp1. COX-2 staining was primarily localized in cervical smooth muscle from NP, as well as days 14 and 18 of pregnancy, day 22NL, L, and pp days 1 and 3.

CONCLUSIONS: COX-1 and COX-2 enzymes in the cervix are gestationally regulated and increase in late gestation at time of major physiological change. Enzyme localization in the cervical smooth muscle suggests that COX may act through established pathways to aid in the ripening process of the cervix during pregnancy.

651 POTASSIUM CHANNELS ARE NOT INVOLVED IN THE RESPONSE OF THE PREGNANT RAT UTERUS TO EICOSANOIDS. C. Badner4, Y. Vedernikovs, G. Saade, R. Garfield1. Dept. of Ob/Gyn, The Univ. of Texas Med. Branch, Galveston, TX.

OBJECTIVE: To test the hypothesis that the effect of prostaglandins (PG) on uterine contractility in pregnant rats is mediated through potassium channels.

STUDY DESIGN: Uterine rings from mid (day 14) and term (day 21) timed-pregnant Sprague-Dawley rats were suspended in organ chambers (Kreb solution, 5% CO2 in air, 37°C, pH 7.4) for isometric tension recording. After equilibration at 2 g tension, concentration-response relationships (CRR) to PGF2α, PGE2 and carbacyclin (stable analog of PGI2) were determined in control rings and rings incubated for 30 minutes with the ATP-dependent potassium (KATP) channel inhibitor glibenclamide (Gl, 10-6 M) or opener levromakalin (LC, 10-5 M) or with the Ca-dependent potassium (KCa) smooth muscle inhibitor nifedipine (NFi, 10-4 M) or opener NS1619 (NS, 10-6 M). The integral activity for ten minutes after each concentration of the agent was expressed as a % of the baseline activity and normalized to parallel time-solvent control.

RESULTS: Gl increased and LC inhibited uterine activity at term, while IbTx and NS did not significantly affect basal activity at concentrations used. All prostaglandins, including PGI2, increased contractility at both mid and term gestation, and none of these responses were affected by any of the K+ channel openers or inhibitors. Figures A and B illustrate the effect of IbTx and NS on changes in integral activity induced by PGE2 and carbacyclin in uterine rings from term pregnant rats.

CONCLUSION: The effect of eicosanoids on uterine contractility is not gestationally-dependent and does not involve modulation of KATP or KCa channels.

OBJECTIVE: To determine the inducible nitric oxide synthase (iNOS) mRNA expression in the cervix and uterus of wild-type pregnant mice and knockout (KO) pregnant mice lacking a functional iNOS.

STUDY DESIGN: The cervix and uterus were isolated from nonpregnant and timed-pregnant iNOS-KO mice (B6/129F1J NOS2 -/- from Jackson Laboratory) and their corresponding wild-type control (NOS2 +/+)...
656 AUTONOMIC CONTROL OF HEART RATE DURING PREGNANCY.
L. Leduc, D. Rinfret*, Dept Obstetrics & Gynecology, St-Justine Hospital, U de
Montreal, Montreal, Quebec, Canada.
PURPOSE: To document the autonomic control of heart rate (HR) at the
time of the maximal increase in plasma volume during pregnancy.

STUDY DESIGN: Ambulatory blood pressure monitoring, heart rate (HR) and
continuous R-R intervals (msec) (Holter/ambulatory blood pressure, AMP model AM 5000) were measured in 20 normotensive pregnant women
(32.5±4.5 y.o.) between 23-26 weeks of gestation (25.0±1.1) (T2), as 9 pregnant
women (28.6±2.4 y.o.) between 28-32 weeks of gestation (25.0±1.2) (T3) and in 10
normotensive non pregnant (NP) women (26.6±5.3 y.o.). Women were at rest
in supine position for 5 minutes before recording R-R intervals. A sampling of
2 minutes were analyzed. The standard deviation (SD) of the mean R-R
intervals was calculated and referred overall variability of HR in time domain
analysis. Test of equality of variance was performed before any comparisons.
Parametric tests with factorial anova were performed with a p<0.05. Resting (HR)
was used as a covariate to document the influence on the magnitude of
responses.

RESULTS: 
<table>
<thead>
<tr>
<th>T2</th>
<th>T3</th>
<th>NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD</td>
<td>0.46±0.21</td>
<td>0.29±0.17</td>
</tr>
</tbody>
</table>

Each level of comparisons was significant. There was a marked decrease in
heart rate variability in pregnancy when compared with non pregnant women.
This decrease was maximal in the third trimester

CONCLUSION: The attenuated overall variability of HR may be a consequence of physiologic adaptation to chronic volume expansion.

657 IMMUNOHISTOCHEMICAL LOCALIZATION OF THE PROSTAGLANDIN
E2 EP1 RECEPTOR IN HUMAN FETAL MEMBRANES DURING PARTURI-
OB/GYN and Pathology, Univ. South Florida, Tampa.

OBJECTIVE: To correlate fetal tests and maternal and neonatal thyroid
stimulating immunoglobulin (TSIG) levels on cord blood

RESULTS: Maternal TSIG concentrations rose from 81.6 ± 16.2 during the
control period to 258.6 ± 46.2 during infusion with all AAs (P < 0.02), and
254.7 ± 39.6 during infusion without BCAA (P < 0.01), but decreased to 63.7 ±
8.5 during infusion with BCAA only. Maternal TSIG concentrations did not
change significantly with infusions. Maternal insulin concentrations increased
from 20.1 ± 3.8 in controls to 81.2 ± 17.3 during infusion with all AAs (P < 0.02),
and 62.9 ± 15.9 during infusion without BCAA (P < 0.05), but to as little as
24.3 ± 5.2 during infusion with BCAA only. Fetal insulin concentrations
increased from 14.7 ± 2.0 during the control period to 29.0 ± 3.9 during infusion
with all AAs (P < 0.02), and did not change significantly during
infusions without BCAA (13.0 ± 0.4) or with BCAA only (13.9 ± 1.8).
Accordingly, the insulin/glucagon ratio in the fetus increased significantly
during infusion with all AAs (from 0.49 ± 0.7 µU/ml in controls to 0.82 ± 0.09
µU/ml, P < 0.01).

CONCLUSION: Varied responses to the 5 infusates suggest that the
composition of an AA infusate affects the degree of stimulation of glucagon
and insulin secretion, in both the mother and the fetus. BCAA exert a limited
effect on this secretion. The fetal response could be blunted since the increase
in fetal AA concentrations with infusion was not as pronounced as in the
mother.

659 THYROID STIMULATING IMMUNOGLOBULIN LEVEL DOES NOT ADE-
QUATELY PREDICT FETAL OR NEONATAL HYPERTHYROIDISM.
A. Rybshinghavan, J. Yankowitz, S. K. Bhatia*. Dept. Ob/Gyn, Univ. of Iowa
College of Medicine, Iowa City, IA.

OBJECTIVE: To compare maternal and fetal arterial concentrations of
insulin and glucagon after infusion of 3 different amino acid (AA) mixes.

STUDY DESIGN: Six pregnant sheep (mean gestational age 126 days)
were studied. Infusions were performed in a cross-over design. Each level of comparisons was not significant. There was a marked decrease in
heart rate variability in pregnancy when compared with non pregnant women.
This decrease was maximal in the third trimester

CONCLUSION: The attenuated overall variability of HR may be a consequence of physiologic adaptation to chronic volume expansion.

RESULTS: Maternal TSIG concentrations rose from 81.6 ± 16.2 during the
control period to 258.6 ± 46.2 during infusion with all AAs (P < 0.02), and
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and insulin secretion, in both the mother and the fetus. BCAA exert a limited
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in fetal AA concentrations with infusion was not as pronounced as in the
mother.

658 EFFECTS OF COMPOSITION OF MATERNAL AMINO ACID INFUSION
ON MATERNAL AND FETAL INSULIN AND GLUCAGON CONCENTRA-
Bialystok, Poland.

OBJECTIVE: To compare maternal and fetal arterial concentrations of
insulin and glucagon after infusion of 3 different amino acid (AA) mixes.

STUDY DESIGN: Six pregnant sheep (mean gestational age 126 days)
were studied. Infusions were performed in a cross-over design. Each level of comparisons was not significant. There was a marked decrease in
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This decrease was maximal in the third trimester

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Accordingly, the insulin/glucagon ratio in the fetus increased significantly
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µU/ml, P < 0.01).

CONCLUSION: Varied responses to the 5 infusates suggest that the
composition of an AA infusate affects the degree of stimulation of glucagon
and insulin secretion, in both the mother and the fetus. BCAA exert a limited
effect on this secretion. The fetal response could be blunted since the increase
in fetal AA concentrations with infusion was not as pronounced as in the
mother.
ABNORMAL SODIUM REABSORPTION DURING THE EARLY STAGES OF PREGNANCY IN TRANSGENIC MICE OVER-EXpressING THE ANGIOTENSINOGEN GENE. M. Dufour, T. Morgan, A. Rohrwaechter, and K. Ward. Depts of OB/Gyn and Human Genetics, University of Utah, SLC, UT. OBJECTIVE: Pregnancy increases sodium reabsorption by the kidney. The renin-angiotensin system (RAS), a primary regulator of sodium reabsorption, is upregulated during pregnancy. We hypothesize that abnormally elevated angiotensinogen (AGT) expression will alter the role of the RAS in pregnancy-induced sodium reabsorption.

STUDY DESIGN: 24 hour urine samples were collected throughout gestation (0-17 days) from six Black 6 control mice (WT) and six transgenic Black 6 mice (TG), which over-express AGT (10% normal). Urinary sodium was quantitated while blinded to genotype using an amperometric electrode. Known standards served as controls.

RESULTS: Urinary sodium levels (mEq/L) dropped significantly by day 6-9, consistent with hyperolemia of pregnancy and fetal requirements (*P<0.01). Transgenic mice exhibited a relative hypernatremia early in pregnancy (days 2-5, *P<0.01).

CONCLUSIONS: Our data suggest that elevated AGT expression may abnormally stimulate sodium reabsorption early in pregnancy. We suspect that this may play a role in failed hyperolemia of pregnancy observed in these transgenic mice.

LACTOFERRIN IN HUMAN PARTURITION AND RUPTURE OF MEMBRANES. M. T. Gervasto, J. Peppler, E. Mynatt, K. Blanco, S. E. Edelin, B. H. Yoon, R. Romero. Perinatology Research Branch, NICHD, Bethesda, MD and Dept. OB/Gyn, Wayne State University, Detroit, MI

OBJECTIVE: Lactoferrin is an iron binding protein with anti-microbial properties whose production is transcriptionally regulated by estrogens. Indirect evidence suggests that labor is associated with a suspension of progestosterone action that may be reflected in a change in lactoferrin concentration.

RESULTS: Transmembrane determination was conducted in which lactoferrin concentrations were determined in AF of 174 women without intraamniotic infection in the following categories: 1) term not in labor; 2) term in labor; 3) preterm labor (PTL) with intact membranes who delivered at term; 4) PTL with intact membranes who delivered preterm; 5) preterm premature rupture of the membranes (PROM); and 6) term PROM. Lactoferrin concentrations were also measured in maternal plasma and cord blood of 19 women at term not in labor and 19 women in labor. Lactoferrin concentrations were determined using a sensitive and specific immunosassay.

RESULTS: 1) Lactoferrin was detectable in 92% (160/174) of AF specimens and in all maternal and cord plasma samples. 2) Labor at term, but not preterm, was associated with a significant decrease in AF lactoferrin concentrations (p<0.005 and p>0.05). 3) Rupture of membranes at term, but not preterm, was associated with a significant decrease in AF concentrations of lactoferrin (p<0.005 and p>0.05). 4) Term parturition was associated with a significant increase in cord blood lactoferrin concentrations (p<0.005).

CONCLUSIONS: 1) Term, but not preterm, parturition is associated with decreased AF concentrations of lactoferrin; 2) Term, but not preterm, rupture of membranes is associated with decreased AF concentrations of lactoferrin; 3) Term parturition is associated with a significant increase in lactoferrin concentrations in the fetal compartment (umbilical cord blood).

IMMUNOHISTOCHEMICAL LOCALIZATION OF FAS AND FAS LIGAND IN HUMAN FETAL MEMBRANES. H. Harbour, J. Copel, V. Parush, C. D. Bai, Deps. OB/Gyn and Pathology, Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Fas and Fas ligand (FasL) have been found in the amniotic fluid (AF) of normal pregnancy. We hypothesized that fetal membranes might be one of the sources. We localized Fas and FasL in the human fetal membranes by immunohistochemical staining.

STUDY DESIGN: Membranes from elective cesarean section without labor (n=6) were obtained and fixed in paraffin. Paraffin embedded rolls of fetal membranes were cut into sections of 5 μm thickness. After blocking with horse and goat serum, sections were incubated overnight with primary antibodies mouse monoclonal anti-human Fas antibody, and rabbit polyclonal anti-human FasL, respectively. Sections were then sections were incubated with secondary antibodies (anti-mouse IgG for Fas and anti-rabbit IgG for FasL). Avidin-biotin complex (ABC) and Diaminobenzidime (DAB) were used for immunoperoxidase localization. Expression of Fas and FasL were read by light microscopy.

RESULTS: Both Fas and FasL were localized on human amnion, chorion, and decidua layers. In the amnion, Fas and FasL were predominantly expressed on epithelial cells and fibroblasts. In chorion, expression was mainly on trophoblast. However, there was no immunostaining in the compact connective tissue of amnion and inconsistent expression of Fas and FasL in the reticular layer of chorion.

CONCLUSIONS: Localization of Fas and FasL on human fetal membranes in normal fetal membranes indicates that fetal membranes could be one of the sources of Fas/FasL in AF. This further suggests their possible physiologic role in fetal membrane remodeling with consequent shedding into AF.


OBJECTIVES: To study the course of secretion of MMPs and TIMPs and TIMPs in the extraembryonic coelomic (EECF), allantoic (ALLF) and amniotic (AF) fluid compartments, using a rabbit model with and without fetoscopy-related membrane defects.

STUDY DESIGN: Samples (0.5 mL) of AF, EECF and ALLF were obtained from time dated pregnant rabbits at 18 (n=6), 25 (n=6) and 39 days (n=6) of gestational age (GA), term-35 days). These were analyzed using gelatin zymography for detection of MMP-2 (72 kDa, latent form; gelatlnase A) and MMP-9 (92 kDa, latent form; gelatlnase B) and reverse zymography for determination of TIMPs activity. To determine any changes induced by membrane repair following needle fetoscopy with a 1.2 mm scope at 23 days GA, similar samples were obtained from resected sacs at 27 (n=6) and 30 (n=6) days GA and compared with fluids from untreated likeertams (*-test, significance when p<0.05)

RESULTS: Zymography showed predominantly latent MMP-2 activated protein at 18, 25 and 30 days GA in all gestational compartments. Little MMP-9 was found. Reverse zymography detected a broad range of TIMPs activity with molecular weights of 27-30 kDa (TIMP-1, gelatinase-free TIMP-3, and TIMP-4), 24 kDa (unglycosylated TIMP-3) and 23 kDa (TIMP-2).

Following fetoscopy, MMP-2 and TIMPs activities significantly increased in fluids from compartments which had been transected by fetoscopy (EECF and AF), and not in fluid from the allantoic compartment.

CONCLUSION: Our study determines the levels of MMPs and TIMPs in fluids in the gestational cavities of the rabbit. Significant changes were observed following a surgically-induced and resected defect in the fetal membranes, suggesting a modulating role for MMPs and TIMPs in the tissue repair process in the second half of pregnancy.

STUDY DESIGN: Membranes from elective cesarean section without labor (n=6) were obtained and fixed in paraffin-embedded 5 μm sections. Sections were incubated overnight with primary antibodies (mouse monoclonal anti-human Fas antibody, and rabbit polyclonal anti-human FasL, respectively). Sections were then incubated with secondary antibodies (anti-mouse IgG for Fas and anti-rabbit IgG for FasL). Avidin-biotin complex (ABC) and Diaminobenzidime (DAB) were used for immunoperoxidase localization. Expression of Fas and FasL were read by light microscopy.

RESULTS: Both Fas and FasL were localized on human amnion, chorion, and decidua layers. In the amnion, Fas and FasL were predominantly expressed on epithelial cells and fibroblasts. In chorion, expression was mainly on trophoblast. However, there was no immunostaining in the compact connective tissue of amnion and inconsistent expression of Fas and FasL in the reticular layer of chorion.

CONCLUSIONS: Localization of Fas and FasL on human fetal membranes in normal fetal membranes indicates that fetal membranes could be one of the sources of Fas/FasL in AF. This further suggests their possible physiologic role in fetal membrane remodeling with consequent shedding into AF.

OBJECTIVE: The role of steroid hormones in the control of human parturition has been a subject of debate. The objective of the study was to examine if changes in fetal plasma cortisol or dehydroepiandrosterone sulfate (DHEAS) are associated with human term parturition.

STUDY DESIGN: Fetal plasma cortisol and DHEAS were measured in 367 singleton pregnancies delivered at term. Umbilical cord blood was obtained from patients in the following groups: 1) Elective cesarean section (C/S) at term without labor (n=140); 2) C/S at term with early labor (cervical dilation ≤ 5 cm) (n=18); 3) C/S at term with active labor (cervical dilation 4 cm or greater) (n=66); 4) Vaginal delivery at term (n=88); 5) Preterm gestations undergoing cordocentesis for clinical indications before 36 weeks of gestation (n=86); 6) Patients undergoing cordocentesis after 36 weeks for clinical indications (n=9). Corticosteroids were not administered before undergoing cordocentesis for clinical indications before 36 weeks of gestation.

RESULTS: Data are presented as median ± standard deviation.

<table>
<thead>
<tr>
<th>Group</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>126±13</td>
<td>71±10</td>
<td>103±16*</td>
</tr>
<tr>
<td>Left lateral</td>
<td>106±11*</td>
<td>56±10*</td>
<td>88±14</td>
</tr>
<tr>
<td>Semi-Fowler</td>
<td>115±11</td>
<td>60±11</td>
<td>90±15</td>
</tr>
</tbody>
</table>

*<p>0.001 compared with both standing and semi-Fowler position.

CONCLUSIONS: Compared with left lateral position, standing position is associated with an increase in both pulse and blood pressure, while semi-Fowler position is associated with an increase in blood pressure but not in heart rate. These findings are at variance with those reported in women at term.


OBJECTIVE: The activity of matrix degrading enzymes is central to membranes rupture. Two matrix metalloproteinases (MMPs) have been implicated in the digestion of fetal membranes: MMP-2 and MMP-9. Previous studies have reported changes in the total concentrations of these enzymes (total immunoreactive = free active + latent + enzyme bound to inhibitors) in rupture of membranes (ROM). The objective of this study was to determine whether ROM is associated with changes in the "true" active forms of MMP-2 and MMP-9.

STUDY DESIGN: A cross-sectional study was conducted with 124 women in the following categories: 1) term, not in labor (n=26); 2) term, premature rupture of membranes (PROM) not in labor (n=22); 3) preterm gestation with intact membranes who subsequently had a preterm delivery (n=37); and 4) preterm PROM (n=39). All patients had negative AF cultures for microorganisms. Active forms of MMP-2 and MMP-9 were measured in AF by a novel assay using a substrate developed by protein engineering.

RESULTS: 1) Spontaneous ROM at term was associated with a significant increase in the concentration of active MMP-9 and a significant decrease in active MMP-2 (Group 1 vs. 2; p<0.005); 2) Preterm PROM was also associated with a significant increase in the concentration of active MMP-9 and in a significant decrease in active MMP-2 (Group 3 vs. 4; p<0.005).

MMP-9 Median (Range)

<table>
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<tr>
<th>Group</th>
<th>(Range)</th>
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<tbody>
<tr>
<td>Term, not in labor</td>
<td>1.60 (0.53-5.57)</td>
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<tr>
<td>Term, PROM, not in labor</td>
<td>2.05 (0.72-6.01)</td>
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<tr>
<td>Preterm labor delivered term</td>
<td>2.10 (0.53-3.13)</td>
</tr>
<tr>
<td>Preterm PROM</td>
<td>2.43 (0.92-4.82)</td>
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</table>

CONCLUSIONS: 1) Spontaneous ROM is associated with a significant increase in the active form of MMP-9 but a decrease in MMP-2. This paradoxical relationship between two enzymes with similar inhibitors (gelatines) has not been described in any other organ system and may have protective value; 2) The presence of detectable active forms of these enzymes in amniotic fluid during normal pregnancy suggests that normal development is associated with active extracellular matrix degradation.

TIME DOMAIN ANALYSIS OF MATERNAL HEART RATE VARIABILITY IN NORMAL PREGNANCY—A LONGITUDINAL STUDY. M Ni Bhunnearna, P McMenna, C. O’Herlihy, D. Sugrue, Rotunda and Mater Maternica Hospital, Dublin and University College Dublin, Ireland.

OBJECTIVE: To define the normal parameters of maternal heart rate variability (HRV) in pregnancy: a tool for assessing autonomic modulation.

STUDY DESIGN: A descriptive longitudinal study of 100 healthy women had been monitored in 100 women, with 24-hour ambulatory electrocardiography at home on four occasions, at eight-week intervals, from six weeks gestation and again post-partum. Tapes were analysed on a Reynolds Medical Pathfinder 600 by a single observer.

RESULTS: n=100

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<thead>
<tr>
<th>Variable</th>
<th>Before</th>
<th>After</th>
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<tbody>
<tr>
<td>PP</td>
<td>7.40</td>
<td>7.40</td>
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<tr>
<td>SDNN (ms)</td>
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<td>126</td>
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<td>SDANN (ms)</td>
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<td>Triangular Index</td>
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<td>56</td>
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CONCLUSIONS: 1) Spontaneous ROM at term was associated with a significant increase in the concentration of active MMP-9 and a significant decrease in active MMP-2. This paradoxical relationship between two enzymes with similar inhibitors (gelatines) has not been described in any other organ system and may have protective value; 2) The presence of detectable active forms of these enzymes in amniotic fluid during normal pregnancy suggests that normal development is associated with active extracellular matrix degradation.
Inhibition of preterm delivery by human chorionic gonadotropin is associated with down-regulation of myometrial gap junctions. J. Kurtzman, E. Jones, L. J. Goldsmith, J. Spornato, L. McFarling, Z. Le, G. V. Rao. Dept. of OB/GYN, Univ. of Louisville, Louisville, KY

**Objective:** To explore possible mechanisms by which human chorionic gonadotropin (HCG) causes inhibition of preterm delivery in an animal model.

**Study Design:** Previous pilot studies in our lab have demonstrated that HCG exhibits dose-dependent tocolysis of prostaglandin-induced preterm delivery in mice; the mechanism of action is not yet known. Based on prior in vitro studies, we hypothesized that HCG may either down-regulate myometrial gap junctions or decrease the expression of cyclooxygenase (COX)-1 or COX-2 levels (yielding decreased prostaglandin biosynthesis). A previously developed preterm delivery model using prostaglandin F2-alpha (PG) to induce preterm labor in C3H/HeN inbred mice was employed. 30 mice at 80% gestation (16 days) were randomized into three groups of ten: 1) PG/HCG, 20 μg intraperitoneal (i.p.) PG followed by 250 IU HCG i.p. 4 hours later, 2) PG/sal: 20 μ PG followed by saline 4 hours later, and 3) Sal/sal controls saline injection, repeated 4 hours later. The time of the first injection was designated as time zero, and all mice were euthanized at 24 hrs based on previously generated survival curves. Time to delivery of the first pup was recorded, for undelivered mice, the presence of retained pups was confirmed. Uteri were removed and sectioned. Indirect immunofluorescence was performed utilizing antibody directed against gap junction protein Connexin-43 (CX-43) on two myometrial sections for each mouse. Sections were photographed from at least 2 representative areas of each section, and were scored on a scale from 0 to +4 (least fluorescent activity) to 4.0+ (most activity) at 0.5 increments by two independent investigators blinded to the treatment group or delivery status of the mice. Similarly, immunocytochemistry utilizing antibody directed against COX-1 and COX-2 was performed by avidin-biotin immunoperoxidase method on myometrial sections from each uterus, and scored in a similar fashion. A one way analysis of variance (ANOVA) was used for overall group comparisons. Pre-planned contrasts compared results from the PG/HCG group to the PG/sal group, and the PG/HCG group to the sal/sal group.

**Results:** At 24 hours after injection, all mice in the PG/sal group had delivered (mean, s.e.: 20.0 ± 1.4 hrs). As shown previously, HCG potently inhibited preterm delivery, and all mice in the PG/HCG group remained undelivered at 24 hours. Similarly, all mice in the sal/sal control group remained undelivered. Overall analysis of variance (ANOVA) comparing indirect immunofluorescence for CX-43 in the three groups was borderline significant (p=.059). Pre-planned contrasts revealed significantly decreased CX-43 indirect immunofluorescence in the PG/HCG group compared to the sal/sal group (p=.025), as well as a borderline significant decrease compared to the PG/sal group (p=.058). Overall analysis of variance (ANOVA) comparing immunostaining for COX-1 and COX-2 showed no significant differences between groups in either myometrium or endometrium 24 hours after injection.

**Conclusions:** HCG inhibition of prostaglandin-induced preterm labor is associated with a decrease in myometrial gap junction formation in mice. While HCG does not appear to decrease COX-1 or COX-2 in this model, its effect on these enzymes cannot be excluded. This preliminary study suggests that HCG may inhibit preterm delivery by down-regulating myometrial gap junctions, thus rendering the uterus less responsive to the effects of stimulatory prostaglandins. These findings support HCG as a potential tocolytic therapy for treatment of preterm labor.
SUBJECT INDEX
AUTHOR INDEX
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<th>Author Name</th>
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<td>248</td>
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<tr>
<td>Adair, R</td>
<td>483</td>
</tr>
<tr>
<td>Adashek, JA</td>
<td>538</td>
</tr>
<tr>
<td>Adashi, EY</td>
<td>15</td>
</tr>
<tr>
<td>Adel, D</td>
<td>179</td>
</tr>
<tr>
<td>Abramowicz, J</td>
<td>309</td>
</tr>
<tr>
<td>Achiron, R</td>
<td>338</td>
</tr>
<tr>
<td>Acosta, P</td>
<td>621</td>
</tr>
<tr>
<td>Adair, CD</td>
<td>248</td>
</tr>
<tr>
<td>Adair, R</td>
<td>483</td>
</tr>
<tr>
<td>Adashek, JA</td>
<td>538</td>
</tr>
<tr>
<td>Adashi, EY</td>
<td>15</td>
</tr>
<tr>
<td>Adel, D</td>
<td>179</td>
</tr>
</tbody>
</table>
Bennett, KA 399, 400, 404
Bennett, WA 66
Bentz, L 21, 52, 151, 264, 270
Bergauer, NK 81, 445, 467
Bergh, C 595
Berghella, V 123, 124, 130, 488
Berkowitz, R 442, 547, 550
Bernstein, H 181, 299
Bernstein, IM 579, 580, 581
Berria, R 212, 215
Berry, S 51, 316, 331, 481, 578, 589, 602
Besinger, RE 137
Bhandarkar, A 364
Bhatia, SK 659
Bianchi, D 546, 578, 618
Bianco, A 185, 364
Bianco, K 298, 301, 427, 662
Bianculli, K 608
Bieber, FR 462
Bienstock, J 357, 470, 633
Bigelman, A 197
Binas, C 439
Bishop, K 634
Blakemore, K 357, 470, 633
Bland, ES 18, 397, 398
Bland, M 48
Bleichstein, F 1422
Bloom, S 93
Boe, NM 191, 199
Boehm, F 569, 570
Boer, K 554
Bogess, K 95, 100, 347
Bogic, LV 74
Bombard, A 175, 176
Bondi, R 175, 176
Bonebrake, R 330, 588
Borg, MJ 21, 151, 264, 270
Borgida, AF 80, 163, 607
Borkowsky, S 256
Borowski, D 71
Borrell, A 623
Bosanac, A 474
Boulvain, M 262, 438
Bovier, P 262
Bowie, J 347
Bowling S 22
Bozzo, M 14, 386, 387, 388
Bran, R 562
Bragg, EJ 454
Branch, DW 27
Brand, A 564
Brateng, D 235, 236
Brazus, S 471
Breckle, RJ 590
Brenneman, DE 15, 294
Brickman, SG 204, 243
Brolinden, K 17
Bronsteene, R 174
Brown, H 358, 471
Brown, K 155
Bruner, JP 569, 570
Buchanan, P 630
Buchanan, T 200, 205
Buchbinder, A 193, 203, 209
Buchmiller, TL 643
Buerchner, CA 330
Bufkin, LK 91
Bugielski, W 583
Buhimschi, IA 36, 69, 240
Buhling, K 200
Bujold, E 514
Bukowski, R 32, 97, 460
Buley, A 205
Bulfoni, A 484
Buller, HR 503
Bundrick, C 289
Burchett, S 276, 285
Burr, M 16, 548
Burke, B20
Burki, N 631
Bussel, J 148, 521
Butler, E 536
Byers, J 368
Bytautiene, E 5, 273, 275, 411
Byun, JS 224
Calhoun, BC 636, 637
Callen, P 362
Canick, J 253
Capeless, E 179
Cappellini, A 365
Cardonick, E 457
Carey, JC 7, 486
Carl, SH 272
Carlo, W 153, 156, 157
Carr, DB 235, 236
Carreno, C 316, 331, 578
Carroll, EM 137, 139
Carroll, G 397
Carroll, S 538
Carvajal, JA 36
Casey, B 348
Cassie, M 155
Castro, C 583
Castro, E 522
Castro, L 251, 313, 529
Catalano, P 64, 144
Chahine, R 34
Chammas, M 251
Chao, C 455
Chasen, ST 456, 458, 613, 616
Chauhan, S 229, 237, 340
Chelmow, D 360, 401, 618
Chen, C 332
Chen, K 62
Cherples, J 488
Chervenak, F 148, 613, 616
Chestrut, D 466
Cheung, CY 74
Chi, JG 135
Chiao, JP 113
Chiba, T 585, 592, 593
Chik, K 628
Chik, L 628
Chin, R 68
Ching, J 70
Chmait, R 482
Chou, S 589
Choy-Hee, L 507
Christensen, D 537
Christensen, F 497
Chuipek, S 368
Chyu, J 322, 349, 350, 386, 388, 389, 617
Cioffi-Ragan, D 322, 350
Cupak, G 276, 285
Claas, FHJ 564
Clapp, JF 82
Clark, N 189
Coat & G 606
Coffman, S 265
Cohen, A 149, 175, 176, 329, 407, 499, 500, 502, 517
Cohen, B 468
Cohen, GR 23
Cohen, WR 307
Colangelo, L 395
Colman, S 445, 467
Collea, J 390, 664
Collins, J 22
Collins, P 35
Colombera, G 490, 539
Colombo, DF 117, 208
Conner, M 107, 108
Consonni, D 351
Conway, D 24, 212, 214, 215
Coogan, S 140
Copel, JA 110, 261, 283, 379, 399, 400, 404, 663
Copper, R 106
Cottam, C 655
Covert, R 52
Covington, C 158, 189
Craigo, S 360, 618
Craven, C 583
Crews, JH 528
Crombleholme, T 9, 10, 12
Crombleholme, W 546
Crouse, D 155, 244
Cummings, R 421
Cuneo, B 553
Curcio, P 630
Curet, LB 496, 497, 572
Cusick, W 334, 335
Custodio, D 42, 559, 641
D’Alton, ME 167, 360
D’Angelo, LJ 23
D’Angelo, M 456
Dambrosia, J 83
Danilenko-Dixon, D 207, 428
Dansereau, J 315, 352
Dashe, J 345, 346, 536
Davies, GAL 393, 558
Davies, JK 292, 295, 296
Davis, G 123
Day, MC 498, 634
Day-Salvatore, D 451
Dayal, A 184, 317, 318, 319
De Gasperi, C 387
de Leeuw, R 448
Deaver, JE 307
DeFulvio, J 287
Dekker, GA 19, 333
Delaney-Black, V 158, 189
Demarini, S 194
Demasio, K 399, 400, 404
Dembski, TC 597
Demetry, D 457
Demissie, K 172
Dempsey, R 82
Denmery, PA 233
Denomme, G 620
Deprest, JA 11, 321, 598, 603, 661
Deren, O 311, 375, 376, 377, 443, 549
Delsky, A 63
Detti, L 574
Devine, PC 167
Devlieger, R 11, 321, 598, 603, 661
Di Naro, E 374
Di Renzo, GC 606
Dickens, B 83
Dickinson, JE 55, 431
Dickmeyer, K 72
Diekema, D 265
Digre, K 373
Dildy, G 1, 373
DiPirro, G 132, 160, 365
DiVito, M 56, 478
Dixon, M 40
Dizon-Townson, D 150
Dodds, L 444
Doern, G 265
Dohrnal, JC 133
Dombrowski, MP 541, 542
Donohoe, W 90
Donohue, PK 470
Dooley, S 143, 420
Dor, J 571
Dorato, V 496, 572
Doria, V 134, 365
Dorman, K 31
Doyle, M 289
Draper, D 90
Driggers, R 430
Dubard, M 246, 624, 627
Dube, J 444
Dudenhausen, JW 200, 328
Duff, GW 4
Duff, P 584
Duguay, R 360
Duhl, A 161, 490, 633
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Dukler, D 129
Gibbs, RS 292, 295, 296
Gilbert, AD 370
Gilbert, F 613, 616
Gilbert, W 191, 199, 419, 533
Giles, W 13
Gilson, GJ 497
Gin, R 650
Glidden, D 362, 587
Goepfert, AR 282
Goetzl, L 364, 365
Goldberg, N 142
Goldin, M 619
Goldsmith, LJ 140, 68
Goldstein, I 355, 545
Goldstein, R 362
Gomez, R 51, 301, 303, 427, 472
Gonzalez-Quintero, V 342, 609
Gondy, A 538
Gonen, R 432
Gonik, B 59, 174, 646
Gonzalez, C 537
Gonzalez, R 472
Gonzalez-Quintero, V 342, 609
Goodstein, CA 190
Gordon, MC 85, 87
Gordon, R 442
Gortner, L 26, 387
Gortzak-Uzan, L 540
Gottmann, D 623
Gould, S 111, 657
Gozes, I 15
Graham, A 31
Graham, E 161
Graham, HM 505
Granger, JP 66
Gratacos, E 11, 321, 598, 603, 661
Gratwohl, A 440, 441
Graves, PC 532
Gray, D 361
Greig, P 49, 421
Grether, JK 83, 266
Greybush, M 424
Griffith, S 494
Grigsby, J 203
Grimm, M 59
Grindle, K 206
Grisaru, S 76, 142, 639
Grobman, WA 143, 227, 228, 501
Groth, S 24
Grunewald, C 373
Guilbert, J 302
Guillaume, JM 342
Guinn, DA 3
Guilinson, SM 214
Gunasekaran, S 657
Gunay, Y 543
Gurewitsch, E 181, 286, 299, 470
Gurgey, A 443
Gurzenda, E 544
Gustilo-Ashby, T 46
Gutierrez, A 609
Guzman, ER 88, 89, 336, 339, 354, 451
Hackmon, R 525
Hadad, A 337
Haddad, BR 34, 68, 152, 244
Hadley, D 168
Hagay, Z 422
Hagberg, B 41
Hagberg, G 41
Hagberg, H 41
Hahn, S 16, 440, 441, 548
Hallahan, T 630
Hallak, M 42, 84, 300, 337, 383, 450, 452, 479, 527, 556, 557, 559, 602, 641
Hallensleben, E 564
Hammberger, L 595
Hampton, RM 272
Han, SY 665
Haney, EI 133
Hankins, G 314, 410
Hanlon-Lundberg, K 596
Hanna, G 161, 181, 286, 299
Hansen, L 489
Harding, R 312, 568
Hare, P 114
Harirah, H 110, 261, 283, 284, 297, 429, 663
Harrman, C 26, 184, 267, 317, 318, 319, 320, 378, 391
Harper, M 534
Harrigill, K 515
Harris, C 264
Harrison, M 30, 362, 585, 586, 587, 591, 592, 593
Hart, PS 622
Hartley, CC 475
Hartmann, K 46, 271
Hartwell, S 535
Hashiguchi, K 242, 249
Hashimoto, K 144
Hassan, SS 300, 316, 331, 481, 578, 589, 602
Hastings, C 325, 326, 489
Hastings, S 249
Hauth, J 45, 107, 108, 119, 153, 156, 157, 279, 288, 408, 466
Hayashi, R 489
Haynatska, V 330
Haynatski, G 588
Haynes, D 515
Hazan, I 422
Hazelbaker, MT 208
Hazra, A 569, 570
Hecher, K 598
Hedberg, J 471
Heidiger, ML 434, 608
Heffner, L 492
Heine, RP 90, 405
Heinze, T 200
Helefott, AW 289
Hendershott, C 70
Heinebold, J 402
Hennigan, K 109
Henrich, W 200
Khalil, A 449
Khoury, J 193, 194, 203, 209
Ki, SH 50, 61, 136, 665
Kim, C 135, 136
Kim, GJ 50, 61, 136, 665
Kim, JO 599
Kim, T 50, 61
Kim, Y 224, 366
Kirby, R 596
Kirkendall, CL 600, 601, 604
Kirkpatrick, M 560
Kirschenbaum, M 560
Kiwi, R 344
Kjos, S 200, 205
Klebanoff, M 7, 226
Klein, L 594
Klepcyk, P 37
Knopman, M 560
Knowlton, J 233, 239
Knuppel, R 164, 165, 166, 171, 172
Kohn, J 52
Kopelman, J 430
Kornman, K 4
Korot, LM 601, 604
Kovanci, E 379, 575
Kozarzewski, M 71
Kramer, F 277
Kramer, JA 626
Kranias, G 194, 203, 209
Krantz, D 628, 630
Kraus, RL 419
Krawetz, SA 626
Kreaden, U 70, 105
Kreiser, D 233
Krekhora, M 71
Krohn, M 306
Krogh, K 556, 559, 641
Krug, ML 42
Ku, W 258
Kuczynski, E 185, 258, 364
Kunzel, W 454
Kupferminc, M 523, 524, 571
Kurtzman, JT 140, 668
Kush, M 90
Kwan, WF 256
Labrecque, M 397
Lachapelle, MF 510
Ladefors, L 41
Lam, F 81
Lam, GK 79
Lamb, JD 263
Landon, M 208
Landsberg, J 39, 416
Lang, H 588
Lang, U 454
Lange, L 103
Langer, O 24, 212, 214, 215, 216, 367
Lapiniski, R 190
Larmon, J 505
Larsen, J 630
Latimer, JJ 90
Lauro, V 606
Leask, R 661
Leduc, L 247, 257, 656
Lee, IS 133
Lee, JJ 643
Lee, MJ 185
Lee, S 292, 295, 296
Leef, K 131, 159
Lemkuizam, GF 33, 219, 220, 221, 361, 477
Lei, ZM 668
Leiberman, RJ 182
Lemmet, A 442
Leone, FPG 484
Lerut, T 11
Lesnick, T 207
Lesser, B 646
Lessey, BA 29, 230
Lessing, J 523, 524
Leveno, K 93, 290, 345, 346, 348, 414, 463, 535
Levi, Y 353
Levine, A 457
Levine, R 225
Levran, D 571
Levy, R 33, 361, 422, 477
Lewis, A 470
Lewis, LM 390, 664
Lewis, PS 307
Lewis, R 6, 281
Lewis, S 289
Li, M 251
Librizzi, R 457
Lieberman, E 149, 329, 407, 462, 492, 499, 500, 502, 517
Lieff, S 4
Lim, F 565
Lim, K 352
Lim, P 488
Lin, CC 555
Ling, PY 163
Lipitz, S 211, 338
Lipson, A 393
Liu, S 37, 64
Livingston, EL 347
Livingston, JC 34, 68, 152, 155, 244, 252
Livingston, LW 115
Lo, JY 475
Locatelli, A 132, 134, 160, 365, 540
Locklear, J 100
Lockwood, CJ 185, 258, 364, 485
Lombardi, SJ 73
Long, TL 546
Longo, M 241, 648
Longo, S 112, 423
Lopoo, J 586
Lozeron, M 555
Lu, GC 105, 279
Lu, LC 284
Ludmir, J 476
Lundin, K 595
Luftkus, AK 328
Lynch, L 547, 550
Lyons, CA 647
Maas, B 56, 425, 490, 508
Mable, BC 244
Mabry, R 281
MacKay, L 5, 411
Macones, GA 77, 305
MacPherson, RTL 583
Macri, C 168
Macri, J 628, 630
Mader, R 551
Madi, JM 327
Magann, E 234, 340, 528
Magness, RR 206
Maher, JE 22
Mahoney, MJ 614, 615, 631
Makikalio, K 43, 371, 372
Malee, M 201, 473, 509
Malone, FD 167, 360, 401
Maman, E 211
Maner, W 53, 409
Manley, J 56, 490, 508, 539
Mansukhani, M 632
Many, A 523, 524
Marconi, AM 484
Marder, S 177
Mari, G 25, 379, 574, 575
Markenson, G 293, 518
Martier, S 158, 180, 186, 189
Martin, D 342, 609
Martin, E 53, 412
Martin, GI 599, 600, 601, 604
Martini, JN 66, 234, 340, 505, 528
Martinez-Poyer, J 308, 479
Martins, ME 165, 166
Marvin, S 181, 286
Marx, S 650
Mastrobattista, J 498, 634
Matalon, KM 621
Mather, J 332
Mattson, L 207
Mauldin, J 433, 435, 437
Maulik, D 544
Maupin, R 268
Mayerhofer, K 392
Mayes, M 653
Maymon, E 51, 54, 298, 301, 302, 303, 309, 427, 472, 662, 666
Mazor, M 51, 54, 120, 173, 182, 183, 193, 195, 196, 197, 198, 291, 301, 337, 383, 427, 452, 525, 638, 640
McDonald, G 235, 236
McDonald, T 46
McDuffie, RS 292, 295, 296
McElrath, TF 492
McEvoy, SS 193, 194, 203, 209
McEvoy, C 22
McFadden, T 508
McFarland, M 304, 367
McFarling, L 668
McGregor, JA 325, 326, 489
McIntire, D 93, 290, 345, 346, 348, 414, 463
McIntosh, C 415
McIntyre, C 130
McKenna, DS 72
McKenna, P 667
McKinney, E 68, 250
McLean, DA 354
McMahon, M 271
McNamara, H 1, 285
McQuillan, K 58, 417
Medina, L 472
Meerman, F 563
Meirowitz, NB 88, 89, 169, 336, 403
Mehlum, Z 449
Melnikow, J 419
Menehan, CA 509
Mercer, B 114, 115, 152
Mertz, H 217
Mescia, G 658
Messerlarian, G 201, 253
Mestoeky, J 282
Meyer, BA 511, 512
Meyer, M 635
Meyer, NL 114, 115, 281
Meyer, R 534
Meyn, L 306
Michael, K 532
Miehe, M 328
Miller, H 109, 515
Miller, W 572
Milligan, DA 231
Mills, AA 80, 607
Min, L 433, 434, 435, 436, 437
Minor, VK 40
Miodovnik, M 193, 194, 203, 209
Mishell, DR 413
Misirnas, R 435, 436
Mitchell, T 306
Mittendorf, R 21, 52, 151, 264, 270, 555
Moawad, AH 101
Moise, A 562
Moise, K 31
Moody, E 294
Moore, E 653
Moore, K 531, 636
Moore, T 127, 213
Morais, EN 327
Morgan, T 255, 660
Morrison, JC 91
Moskowitz, D 605
Mostello, DJ 219, 220, 221, 495
Mozurkewich, E 415, 504
Muench, M 56, 425, 508
Muhle, RA 116
Mulayim, N 615
Mulla, W 56, 490
Munstedt, K 454
Muraskas, J 137
Murtha, AP 4, 99, 102, 347
Nachum, Z 192, 551
Nagamani, M 97
Nageotte, MP 1, 423, 647
Narang, A 449, 609
Naylor, CS 468
Neerhof, MG 133
Nelson, C 629
Nelson, DM 33, 477
Nelson, KB 83, 238, 242, 245, 249, 260, 582, 629
Nelson, L 150, 238, 239, 242, 245, 249, 260, 582, 629
Nelson, R 280
Newman, L 70
Newman, M 204
Newman, R 28, 48, 76, 433, 435, 437
Nguyen, T 251, 313, 529
Ni Bhuinneain, M 667
Nichols, K 49, 421
Nichols, L 583
Niday, P 129
Nielsen, P 636, 637
Nien, JK 472
Nigam, J 88, 89, 336
Niklasson, A 41
Nilsson, L 595
Nimrod, C 44, 129
Nisell, H 373
Nisman, D 545
Nordstrom-Klee, B 158, 189
Nores, J 360
Norman, G 300
Northrup, H 634
Norwich, ER 343, 407, 492
Novak, P 603
Nuwayhid, B 251, 529
Nwobike, N 359
O'Brien, C 58
O'Brien, JM 114, 115, 231
O'Brien, WF 111, 187, 188, 280, 487, 657
O'Callaghan, S 13
O'Connell, PR 58, 60, 513
O'Grady, JP 293, 518
O'Herlihy, C 58, 60, 417, 513, 667
O'Neill, L 185, 258
O'Reilly, GC 75
O'Reilly-Green, C 480, 519
O'Sullivan, M 433, 435, 437, 609
Occhipinti, J 100
Odibo, AO 124
Oepkes, D 558, 620
Offenbacher, S 4
Ogburn, P 207, 428, 590
Oh, E 251
Olson, G 314, 412, 459, 460
Olutoye, OO 12
Omrani, A 614
Onderoglu, L 311, 375, 376, 377, 443, 549
Oppenheimer, LW 18, 397, 398
Orise, P 5, 652
Ortloli, F 630
Ortloli, T 531
Oshiro, BT 27, 85, 87, 269
Ossol, G 635
Ostfeld, B 147
Ouzounian, J 522
Owen, J 406, 418, 466, 624, 645
Oz, U 379, 614, 615
Ozcan, T 631
Pacora, P 54, 298, 301, 302, 427, 662, 666
Paek, B 30, 362, 585, 586, 587, 591, 592, 593
Pagan, K 644
Pajdas, MJ 256, 257, 258, 364, 485
Palmgren, M 112
Pardi, G 14, 387, 484
Parilla, BV 143
Park, JS 50, 61, 135, 136, 366, 665
Park, JY 643
Park, V 34, 155, 244
Parkash, V 631, 663
Parthasarathy, S 243
Pass, J 122
Patel, S 293, 518, 550
Patterson, DM 474
Patton, DL 75
Paul, D 131, 159
Pavlko, Z 461
Paz, B 422
Peaceman, AM 395, 501
Pearson, D 289
Pejovic, T 631
Peleg, A 619
Peleg, D 233, 380, 619
Persad, V 597
Persatella, WH 322, 349, 350, 363, 389, 617
Peschon, J 116
Peters-Phair, K 57
Pfanner, M 265
Phelan, JP 599, 600, 601, 604
Phillipe, M 39, 416
Phillips, L 478
Phillips, O 34
Phillips, T 83
Piek, JMJ 503
Pierce, B 636, 637
Pierce, LM 637
Pijnenborg, R 661
Pinckert, TL 390, 664
Piper, J 216, 304
Platt, L 309, 621
Plessas, MJ 191, 199
Plevyak, M 473
Plommer, K 579
Pollack, H 276, 285
Pollard, J 520
Pollock, M 56, 130, 425, 490, 508
Poole-Bryant, K 300, 479
Porat, A 182
Porath, M 328
Porter, AE 323, 324
Porter, TF 27, 269
<table>
<thead>
<tr>
<th>Author</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porto, M</td>
<td>468</td>
</tr>
<tr>
<td>Powell, SR</td>
<td>544</td>
</tr>
<tr>
<td>Press, F</td>
<td>450</td>
</tr>
<tr>
<td>Pringle, RB</td>
<td>127</td>
</tr>
<tr>
<td>Pryor, EC</td>
<td>381, 382, 384, 385, 622</td>
</tr>
<tr>
<td>Frythver, B</td>
<td>494</td>
</tr>
<tr>
<td>Pschirrer, ER</td>
<td>498</td>
</tr>
<tr>
<td>Puder, KS</td>
<td>174</td>
</tr>
<tr>
<td>Pugash, D</td>
<td>352</td>
</tr>
<tr>
<td>Quasney, M</td>
<td>155, 244</td>
</tr>
<tr>
<td>Quinlan, JT</td>
<td>323, 324, 390, 664</td>
</tr>
<tr>
<td>Qureshi, F</td>
<td>552, 577</td>
</tr>
<tr>
<td>Rabl, M</td>
<td>392</td>
</tr>
<tr>
<td>Rademaker, A</td>
<td>395</td>
</tr>
<tr>
<td>Radford, M</td>
<td>483</td>
</tr>
<tr>
<td>Raio, L</td>
<td>374</td>
</tr>
<tr>
<td>Rajendran, G</td>
<td>126, 162</td>
</tr>
<tr>
<td>Rakover, Y</td>
<td>192</td>
</tr>
<tr>
<td>Raisen, J</td>
<td>343, 407</td>
</tr>
<tr>
<td>Rabbal, M</td>
<td>392</td>
</tr>
<tr>
<td>Rademaker, A</td>
<td>395</td>
</tr>
<tr>
<td>Radhub, A</td>
<td>256, 257, 258, 364, 485</td>
</tr>
<tr>
<td>Reddy, U</td>
<td>124, 457, 478</td>
</tr>
<tr>
<td>Redline, RP</td>
<td>566</td>
</tr>
<tr>
<td>Redman, M</td>
<td>316</td>
</tr>
<tr>
<td>Rage, D</td>
<td>70</td>
</tr>
<tr>
<td>Rayburn, WF</td>
<td>486, 537</td>
</tr>
<tr>
<td>Raynor, BD</td>
<td>204, 243, 507</td>
</tr>
<tr>
<td>Read, J</td>
<td>276, 285</td>
</tr>
<tr>
<td>Rebarber, A</td>
<td>256, 257, 258, 364, 485</td>
</tr>
<tr>
<td>Ranny, U</td>
<td>124, 457, 478</td>
</tr>
<tr>
<td>Redline, RP</td>
<td>566</td>
</tr>
<tr>
<td>Redman, M</td>
<td>316</td>
</tr>
<tr>
<td>Rege, EA</td>
<td>210, 211, 355</td>
</tr>
<tr>
<td>Repl, GW</td>
<td>569, 570</td>
</tr>
<tr>
<td>Refuerzo, JS</td>
<td>481</td>
</tr>
<tr>
<td>Regen, C</td>
<td>259</td>
</tr>
<tr>
<td>Regenstein, A</td>
<td>70</td>
</tr>
<tr>
<td>Reid, GC</td>
<td>271</td>
</tr>
<tr>
<td>Reid, GJ</td>
<td>597</td>
</tr>
<tr>
<td>Reiss, I</td>
<td>26, 378</td>
</tr>
<tr>
<td>Repke, J</td>
<td>499, 500, 502, 517</td>
</tr>
<tr>
<td>Reuter, D</td>
<td>410</td>
</tr>
<tr>
<td>Reyes, S</td>
<td>647</td>
</tr>
<tr>
<td>Rhee, A</td>
<td>490</td>
</tr>
<tr>
<td>Richter, PJ</td>
<td>127</td>
</tr>
<tr>
<td>Rigano, S</td>
<td>14, 386, 387, 388, 389</td>
</tr>
<tr>
<td>Riggs, J</td>
<td>634</td>
</tr>
<tr>
<td>Rijhsinghani, A</td>
<td>659</td>
</tr>
<tr>
<td>Riley, SC</td>
<td>661</td>
</tr>
<tr>
<td>Rinehart, BK</td>
<td>66, 91, 92, 234, 505, 528, 561</td>
</tr>
<tr>
<td>Rinfret, D</td>
<td>247, 656</td>
</tr>
<tr>
<td>Riskin-Mashiah, S</td>
<td>396</td>
</tr>
<tr>
<td>Roberts, J</td>
<td>226</td>
</tr>
<tr>
<td>Roberts, WE</td>
<td>92, 561</td>
</tr>
<tr>
<td>Robinson, JN</td>
<td>343, 407</td>
</tr>
<tr>
<td>Rodis, JF</td>
<td>80, 607</td>
</tr>
<tr>
<td>Rodkey, LS</td>
<td>31</td>
</tr>
<tr>
<td>Rodriguez, C</td>
<td>451</td>
</tr>
<tr>
<td>Rodriguez-Thompson, D</td>
<td>343, 462</td>
</tr>
<tr>
<td>Rohmesser, A</td>
<td>255, 660</td>
</tr>
<tr>
<td>Rosi, N</td>
<td>21, 151</td>
</tr>
<tr>
<td>Romano, F</td>
<td>374</td>
</tr>
<tr>
<td>Romano, P</td>
<td>419</td>
</tr>
<tr>
<td>Roncaglia, N</td>
<td>540</td>
</tr>
<tr>
<td>Roque, H</td>
<td>258, 485</td>
</tr>
<tr>
<td>Rosen, T</td>
<td>256, 257, 258</td>
</tr>
<tr>
<td>Rosen, B</td>
<td>193, 194, 203, 209</td>
</tr>
<tr>
<td>Rosenthal, T</td>
<td>233</td>
</tr>
<tr>
<td>Ross, S</td>
<td>523</td>
</tr>
<tr>
<td>Ross, J</td>
<td>112</td>
</tr>
<tr>
<td>Ross, KC</td>
<td>584</td>
</tr>
<tr>
<td>Ross, MG</td>
<td>341, 406, 455, 506, 642, 643</td>
</tr>
<tr>
<td>Rothe, B</td>
<td>560</td>
</tr>
<tr>
<td>Roudebush, W</td>
<td>223</td>
</tr>
<tr>
<td>Rouse, D</td>
<td>408</td>
</tr>
<tr>
<td>Rowland, B</td>
<td>223</td>
</tr>
<tr>
<td>Royer, D</td>
<td>332</td>
</tr>
<tr>
<td>Rumeny, P</td>
<td>423</td>
</tr>
<tr>
<td>Rush, AJ</td>
<td>535</td>
</tr>
<tr>
<td>Russell, E</td>
<td>479, 589</td>
</tr>
<tr>
<td>Rust, M</td>
<td>588</td>
</tr>
<tr>
<td>Rust, O</td>
<td>8, 287, 424, 474</td>
</tr>
<tr>
<td>Ryan, G</td>
<td>558, 612, 620</td>
</tr>
<tr>
<td>Sadovsky, Y</td>
<td>33, 477</td>
</tr>
<tr>
<td>Saez, V</td>
<td>472</td>
</tr>
<tr>
<td>Saker, H</td>
<td>344, 566</td>
</tr>
<tr>
<td>Saker, N</td>
<td>344</td>
</tr>
<tr>
<td>Salafia, CM</td>
<td>442</td>
</tr>
<tr>
<td>Salas, R</td>
<td>650</td>
</tr>
<tr>
<td>Salim, R</td>
<td>192, 551</td>
</tr>
<tr>
<td>Salma, F</td>
<td>342, 609</td>
</tr>
<tr>
<td>Salvator, A</td>
<td>566</td>
</tr>
<tr>
<td>Samelson, R</td>
<td>276, 285</td>
</tr>
<tr>
<td>Samueloff, A</td>
<td>76, 142, 639</td>
</tr>
<tr>
<td>Samuel, P</td>
<td>72, 117, 526</td>
</tr>
<tr>
<td>Sanchez, P</td>
<td>290</td>
</tr>
<tr>
<td>Sandberg, P</td>
<td>30, 362, 585, 586, 591, 592, 593</td>
</tr>
<tr>
<td>Sanders, KA</td>
<td>139</td>
</tr>
<tr>
<td>Santanam, N</td>
<td>243</td>
</tr>
<tr>
<td>Santolaya-Forgas, J</td>
<td>623</td>
</tr>
<tr>
<td>Santos, RS</td>
<td>345, 346</td>
</tr>
<tr>
<td>Saphier, C</td>
<td>190</td>
</tr>
<tr>
<td>Sapir, O</td>
<td>638, 640</td>
</tr>
<tr>
<td>Sase, M</td>
<td>643</td>
</tr>
<tr>
<td>Satin, AJ</td>
<td>430</td>
</tr>
<tr>
<td>Saund, T</td>
<td>39, 416</td>
</tr>
<tr>
<td>Savage, KG</td>
<td>645</td>
</tr>
<tr>
<td>Savasi, V</td>
<td>484</td>
</tr>
<tr>
<td>Savitz, D</td>
<td>46</td>
</tr>
<tr>
<td>Saywers, T</td>
<td>312, 568</td>
</tr>
<tr>
<td>Scard, JA</td>
<td>229, 237</td>
</tr>
</tbody>
</table>
Schaap, AHP 448, 554
Schaefer, U 205
Schaefer-Graf, UM 200
Schatt, S 16, 440
Schatten, C 222, 252
Schembri, M 419
Schroder, M 344
Schneider, H 374
Schreiber, L 598
Schultz, L 322, 389
Schweikert, S 461
Scialli, A 128, 483
Sciscione, A 56, 131, 159, 425, 490, 508, 539
Scudiero, R 264, 270
Seaward, G 558
Secker-Walker, R 579
Segal, D 337
Segal, S 305
Sehdev, H 608
Sehgal, P 154
Seidman, DS 233, 338, 571
Selam, B 442
Sell, L 62
Seoud, M 449
Sermers, M 612
Seubert, DE 54, 301, 302, 427, 666
Seyb, S 420
Shadron, A 420
Shah, D 344, 566
Shah, J 126, 154, 162
Shahabi, S 614
Shaley, V 192, 369, 551
Shannon, M 254
Shao, J 37
Shapiro, D 276, 285
Sharkey, A 361
Sharma, SK 339, 414
Sharvit, Y 192
Shatzkin, E 40
Shaw, D 315
Shear, R 576
Sheffer, G 571
Sheiner, E 84, 173
Shelton, S 95
Shen-Schwarz, S 147
Shenhav, M 523, 524
Shi, L 67, 240
Shi, SQ 12, 240, 409, 411
Shields, LE 17, 75
Shih, G 466
Shikes, R 295
Shime, J 612
Shipp, T 499, 500, 502, 517, 522
Shlossman, P 56, 131, 490, 508, 539
Shmueli, O 310
Shoham-Vardi, I 184, 120, 173, 183, 195, 196, 197, 291, 450
Shoucri, R 250
Shumway, J 495
Sibai, BM 6, 34, 68, 86, 114, 115, 152, 155, 232, 244, 250, 252, 261, 655
Siddiqi, T 193, 203
Silberstein, T 196, 452
Silver, H 253
Silverman, R 439
Simchen, M 146
Simhan, H 405
Sims, C 306
Sincich, T 138
Sinervo, K 103
Sitaz, B 269
Sivan, E 210, 211
Skinner, V 49
Skupski, D 148, 521
Smith, EO 396
Smith, J 33
Smith, K 312, 568
Smith, N 217, 218
Smith, S 27, 269, 477
Smith, T 95, 96, 102
Smolin, A 188, 383
Smulian, J 147, 164, 165, 166, 169, 171, 172, 178, 354, 403, 446, 447, 453
Socol, MJ 501
Sokol, R 158, 180, 186, 189, 308, 309, 628
Sokolowski, D 474
Solomon, L 579
Song, TB 224
Soper, D 28, 48, 78
Soriano, D 338
Sorokin, Y 300, 316, 331, 479, 481, 602
Spaziani, EP 111, 657
Speier, Paul 248
Spencer, K 628
Spinnato, J 140, 668
Spong, CY 15, 128, 294, 323, 324, 390, 483, 664
Stahl, S 579
Stamile, D 77
Sten, C 262
Standley, CA 654
Stanziano, GJ 81, 445, 467
Starbuck, CY 128
Starr, A 104
Steffy, B 300
Steinfeld, J 96, 332
Steinmann, C 440, 441, 548
Stek, A 277
Stephenson, K 4
Stevenson, DK 233
Stewart, K 49, 206, 626
Stewart, PJ 129
Stockmann, PT 370
Stone, J 547, 550
Stouch, B 489
Strasburger, J 553
Strobelt, N 351
Strong, TH 79
ACADEMIC
INSTITUTION INDEX
<table>
<thead>
<tr>
<th>Academic Institution</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic Medical Centre, Amsterdam</td>
<td>448, 503, 554</td>
</tr>
<tr>
<td>Aetna U.S. Healthcare</td>
<td>175, 176</td>
</tr>
<tr>
<td>Albany Medical Center</td>
<td>276, 285</td>
</tr>
<tr>
<td>Albert Einstein College of Medicine</td>
<td>184, 317, 318, 319, 320, 510, 519</td>
</tr>
<tr>
<td>American University of Beirut Medical Center</td>
<td>449</td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td>25, 31, 144, 267, 396</td>
</tr>
<tr>
<td>Baystate Medical Center</td>
<td>293, 518</td>
</tr>
<tr>
<td>Ben-Gurion University</td>
<td>42, 76, 84, 120, 142, 170, 173, 182, 183, 195, 196, 197, 291, 337, 383, 450, 452, 525, 556, 559, 638, 639, 640, 641</td>
</tr>
<tr>
<td>Beth Israel Deaconess Medical Center</td>
<td>476</td>
</tr>
<tr>
<td>Bialystok Medical University</td>
<td>568</td>
</tr>
<tr>
<td>Bnia Zion Medical Center, Haifa</td>
<td>432</td>
</tr>
<tr>
<td>Brigham and Women’s Hospital</td>
<td>62, 276, 285, 329, 343, 407, 462, 492, 517</td>
</tr>
<tr>
<td>British Columbia Women’s Hospital</td>
<td>352</td>
</tr>
<tr>
<td>Brown Univ/Women &amp; Infants Hospital</td>
<td>201, 253, 473, 509</td>
</tr>
<tr>
<td>California Dept. Health Services</td>
<td>83, 266</td>
</tr>
<tr>
<td>California Pacific Medical Center</td>
<td>81</td>
</tr>
<tr>
<td>Cedars-Sinai Medical Center</td>
<td>309, 621</td>
</tr>
<tr>
<td>Center for Fetal Diagnosis and Treatment, Philadelphia</td>
<td>10, 12</td>
</tr>
<tr>
<td>Central Baptist Hospital, Lexington</td>
<td>34, 231, 244</td>
</tr>
<tr>
<td>Centro Di Diagnosi Prenatale, Palermo, Italy</td>
<td>630</td>
</tr>
<tr>
<td>Centro for Surgical Technologies/K.U. Leuven</td>
<td>11, 321, 603, 661</td>
</tr>
<tr>
<td>Charles University Hospital, Prague</td>
<td>630</td>
</tr>
<tr>
<td>Charity Hospital, New Orleans</td>
<td>268</td>
</tr>
<tr>
<td>Children’s Hospital of Michigan</td>
<td>370</td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
<td>9, 10, 12, 546, 558, 577, 583</td>
</tr>
<tr>
<td>Children’s Memorial Hospital, Chicago</td>
<td>553</td>
</tr>
<tr>
<td>Chonnam University Medical School, Korea</td>
<td>224</td>
</tr>
<tr>
<td>Chonnam University Medical School, Korea</td>
<td>224</td>
</tr>
<tr>
<td>Christiana Hospital</td>
<td>56, 130, 131, 159, 425, 490, 508, 539</td>
</tr>
<tr>
<td>Clinical Biochemistry, Romford, England</td>
<td>628</td>
</tr>
<tr>
<td>Columbia University</td>
<td>20, 116, 118, 167, 442, 632</td>
</tr>
<tr>
<td>Cooper Hospital University Medical Center/Robert Wood Johnson</td>
<td>608</td>
</tr>
<tr>
<td>Cornell Medical Center</td>
<td>458</td>
</tr>
<tr>
<td>Creighton University</td>
<td>330, 588</td>
</tr>
<tr>
<td>Dalhousie University</td>
<td>444</td>
</tr>
<tr>
<td>Deaconess Medical Center</td>
<td>312, 568</td>
</tr>
<tr>
<td>Duke University</td>
<td>4, 95, 99, 100, 102, 347, 531</td>
</tr>
<tr>
<td>Emory University</td>
<td>204, 243, 507, 516</td>
</tr>
<tr>
<td>Eurofoetus Group</td>
<td>321, 603</td>
</tr>
<tr>
<td>Evanston Northwestern Healthcare</td>
<td>133</td>
</tr>
<tr>
<td>Faculty of Medicine and Computer Sciences, Haifa</td>
<td>310</td>
</tr>
<tr>
<td>Free University Hospital, Amsterdam</td>
<td>19, 333</td>
</tr>
<tr>
<td>George Washington University</td>
<td>83, 630</td>
</tr>
<tr>
<td>Georgetown University</td>
<td>128, 132, 134, 160, 294, 323, 324, 365, 390, 483, 540, 664</td>
</tr>
<tr>
<td>Good Samaritan Regional Medical Center</td>
<td>79, 465, 467</td>
</tr>
<tr>
<td>Goteborg University</td>
<td>595</td>
</tr>
<tr>
<td>Greenville Hospital</td>
<td>49, 421</td>
</tr>
<tr>
<td>Hacettepe University, Turkey</td>
<td>311, 375, 376, 377, 443, 549</td>
</tr>
<tr>
<td>Hadassah Medical Center</td>
<td>353</td>
</tr>
<tr>
<td>Hammersmith Medical Centre, London</td>
<td>353</td>
</tr>
<tr>
<td>Harbor-UCLA Medical Center</td>
<td>341, 406, 455, 506, 642, 643</td>
</tr>
<tr>
<td>Hartford Hospital</td>
<td>96, 332</td>
</tr>
<tr>
<td>Harvard Medical School</td>
<td>276, 285, 462</td>
</tr>
<tr>
<td>Hope Children’s Hospital, Chicago</td>
<td>553</td>
</tr>
<tr>
<td>Hosp. Clinico de Barcelona Spain</td>
<td>623</td>
</tr>
<tr>
<td>Hospital Dr. Rafael Angel Calonder Guardia, Costa Rica</td>
<td>545</td>
</tr>
<tr>
<td>Humboldt Universität</td>
<td>200</td>
</tr>
<tr>
<td>ISBM San Gerardo, Monza, Italy</td>
<td>132, 134, 160, 365, 540</td>
</tr>
<tr>
<td>IWK-Grace Health Centre</td>
<td>444</td>
</tr>
<tr>
<td>Jefferson Medical College of Thomas Jefferson University</td>
<td>121, 123, 124, 125, 130, 457, 478, 488, 508</td>
</tr>
<tr>
<td>Johns Hopkins University School of Medicine</td>
<td>161, 181, 286, 299, 323, 357, 433, 437, 470, 490, 633</td>
</tr>
<tr>
<td>Kaiser Permanente Los Angeles Medical Center</td>
<td>482</td>
</tr>
<tr>
<td>Kaiser Permanente Northern Calif. Region, Santa Clara, CA</td>
<td>70</td>
</tr>
<tr>
<td>Kaplan Medical Center</td>
<td>422</td>
</tr>
<tr>
<td>Karolinska Institute, Stockholm</td>
<td>17</td>
</tr>
<tr>
<td>Las Vegas Perinatal Associates</td>
<td>538</td>
</tr>
<tr>
<td>Laval University</td>
<td>397</td>
</tr>
<tr>
<td>Lehigh Valley Hospital</td>
<td>8, 287, 424, 474</td>
</tr>
<tr>
<td>Leiden Medical Center</td>
<td>563, 564, 565</td>
</tr>
<tr>
<td>Lenox Hill Hospital</td>
<td>480, 519</td>
</tr>
<tr>
<td>Lis Maternity Hospital</td>
<td>571</td>
</tr>
<tr>
<td>Long Beach Memorial</td>
<td>423, 457</td>
</tr>
<tr>
<td>Long Island Jewish Medical Center</td>
<td>40</td>
</tr>
<tr>
<td>Louisiana State University, New Orleans</td>
<td>268</td>
</tr>
<tr>
<td>Loyola University Medical Center</td>
<td>3, 35, 137, 199</td>
</tr>
<tr>
<td>LSU Medical Center, Shreveport</td>
<td>138, 248</td>
</tr>
<tr>
<td>Madigan Army Medical Center</td>
<td>636, 637</td>
</tr>
<tr>
<td>Magee Womans Research Institute</td>
<td>90, 113, 226, 306, 583</td>
</tr>
<tr>
<td>Magee-Womens Hospital, Pittsburgh</td>
<td>405</td>
</tr>
<tr>
<td>Mallinckrodt (Nellcor) Fetal Oximetry Research Group</td>
<td>1</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>149, 499, 500, 517, 522</td>
</tr>
<tr>
<td>Maternal Fetal Care, Stamford</td>
<td>494</td>
</tr>
<tr>
<td>Matria Healthcare</td>
<td>81, 445, 467</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>207, 278, 428, 590</td>
</tr>
<tr>
<td>Medical University Luebeck, Germany</td>
<td>493</td>
</tr>
<tr>
<td>Medical University South Carolina</td>
<td>78, 223, 229, 433, 437</td>
</tr>
<tr>
<td>Mercy Healthcare, Sacramento</td>
<td>191, 199</td>
</tr>
<tr>
<td>Midwestern University</td>
<td>654</td>
</tr>
<tr>
<td>Miyazaki Medical College, Japan</td>
<td>145</td>
</tr>
<tr>
<td>Monash University, Australia</td>
<td>312, 588</td>
</tr>
<tr>
<td>Montefiore Medical Center, Bronx</td>
<td>480</td>
</tr>
<tr>
<td>Mt. Sinai Hospital, Toronto, Canada</td>
<td>620</td>
</tr>
<tr>
<td>Mt. Sinai Medical Center, New York</td>
<td>190, 442, 547, 550</td>
</tr>
<tr>
<td>National Maternity Hospital, Dublin</td>
<td>58, 60, 417, 513</td>
</tr>
<tr>
<td>National Naval Medical Center</td>
<td>168</td>
</tr>
<tr>
<td>National Naval Medical Center, Bethesda</td>
<td>168, 430</td>
</tr>
<tr>
<td>Neofoilin Hospital</td>
<td>200</td>
</tr>
<tr>
<td>New England Medical Center, Boston</td>
<td>401, 546, 578, 618</td>
</tr>
<tr>
<td>New England Research Center</td>
<td>569, 570</td>
</tr>
<tr>
<td>New York Hospital-Cornell Medical Center</td>
<td>148</td>
</tr>
<tr>
<td>New York Medical College</td>
<td>126, 154, 162</td>
</tr>
<tr>
<td>New York Presbyterian Hospital</td>
<td>456, 458, 613, 616</td>
</tr>
<tr>
<td>New York School of Medicine</td>
<td>258</td>
</tr>
<tr>
<td>New York University Medical Center</td>
<td>185, 256, 257, 364, 485</td>
</tr>
<tr>
<td>NHLBI, Bethesda, MD</td>
<td>542</td>
</tr>
<tr>
<td>NICHD MFMU Network</td>
<td>2, 7, 44, 45, 47, 86, 119, 128, 202, 232, 259, 274, 282, 298, 301, 302, 303, 427, 541, 542, 662, 666</td>
</tr>
<tr>
<td>NICHD/NIH</td>
<td>15, 225, 226, 294, 323, 324, 472</td>
</tr>
<tr>
<td>NINDS, Bethesda, MD</td>
<td>83, 266</td>
</tr>
<tr>
<td>Northwestern University</td>
<td>104, 143, 227, 228, 263, 395, 420, 501</td>
</tr>
<tr>
<td>NHLBI Laboratories</td>
<td>630</td>
</tr>
<tr>
<td>ObstetricIX Medical Group</td>
<td>109, 515</td>
</tr>
<tr>
<td>Ohio State University College of Medicine</td>
<td>72, 117, 208, 526</td>
</tr>
<tr>
<td>Pennsylvania Hospital, Philadelphia</td>
<td>25, 368, 476</td>
</tr>
<tr>
<td>Perinatal Center, Institute of Health and Children, Sweden</td>
<td>41</td>
</tr>
</tbody>
</table>
Perinatal Research Branch, NICHD 51, 54
Polish Mother's Memorial Hospital 71
Poriya Government Hospital, Israel 380, 619
Queen of the Valley Hospital, CA 600, 601, 604
Queen's University, Kingston, Ontario, Canada 393, 558
R&D Systems 49
Rambam Medical Center 310, 355, 545
Robert Wood Johnson Medical School/Peter's Medical Center 164, 165, 166, 446, 447
Rockford Memorial Hospital 445
Ross Products Division, Abbott Lab 621
Rotunda Hospital and University College, Dublin 667
Sackler Medical School 15, 338, 571
San Paolo University, Milan 14, 387, 388, 389, 484
Seoul National University 50, 61, 135, 136, 366, 665
Shaare Zedek Medical Center 76, 142, 639
Sheba Medical Center 146, 210, 211, 233, 338
Sinai Hospital of Baltimore 307
Sloans Hospital for Women 632
Soroka Medical Center 42, 84, 120, 170, 173, 182, 183, 195, 196, 197, 198, 291, 337, 383, 450, 452, 525, 556, 559, 571, 638, 640, 641
Sotero del Rio Hospital, Chile 472
Spartanburg Regional Medical Center 229, 237
St. Francis Hospital and Medical Center 80, 122, 163, 607
St. Luke's Hospital, Kansas City, MO 23
St. Peter's Medical Center, New Brunswick 88, 89, 147, 169, 171, 172, 178, 336, 339, 354, 403, 451, 453, 610, 611
St. Vincent Hospital, IN 358, 471
Stanford University 233
Ste-Justine Hospital 247, 514, 576, 656
SUNY Stony Brook, NY 511, 512
SUNY, Syracuse, NY 439
Taksim Research and Training Hospital, Turkey 543
Technion-Israel Institute of Technology, Haifa 192, 355, 551
Tel Aviv Sourasky Medical Center/Luis Maritney Hospital 523, 524
Tel Aviv University 15, 146
Temple University, Philadelphia 210, 211
Texas Tech HSC 192, 521
The New York Hospital Med. Ctr of Queens 521
The Shrinrer Center for Mental Retardation 618
The Stanford Hospital 334, 335
Thomas Jefferson University 56, 368
Tufts University School of Medicine 149, 167, 329, 360, 401, 517, 518, 546, 618
Tulane University School of Medicine 112
UMDNJ-RWJ Medical School at Camden 88, 89, 147, 169, 171, 172, 178, 336, 339, 354, 403, 451, 453, 608, 610, 611
University College Dublin 667
University Hospital, Gasthuisberg 598, 603
University Hospital, Geneva, Switzerland 262, 438
University Hospital of Vienna 252
University of Newcastle 13
University of Arizona 109, 515
University of Bari 374
University of Basel 18, 440, 441, 548
University of Bern 374
University of British Columbia 315, 352, 359, 426, 469, 491
University of Calgary 103, 520
University of California at Irvine 57, 468, 647
University of California, Davis 199, 419, 533
University of California, San Diego 74, 127, 213, 562
University of California, San Francisco 30, 254, 362, 585, 586, 587, 591, 592, 593
University of Caxias do Sul, Brazil 327
University of Chicago 21, 39, 52, 101, 151, 264, 270, 356, 416, 555
University of Cincinnati College of Medicine 193, 194, 203, 209
University of Colorado Health Sciences Center 14, 292, 295, 296, 322, 325, 349, 350, 363, 387, 388, 389, 594, 617, 658
University of Colorado School of Medicine 326, 489
University of Connecticut Health Center 80, 163, 607
University of Edinburgh 661
University of Florida, Gainesville 289, 584
University of Florida, Pensacola 22, 289
University of Giessen, Germany 454, 560
University of Illinois 251, 313, 529, 623
University of Insurbia, Italy 374
University of Iowa 265, 562, 659
University of Louisville 140, 666
University of Lubeck, Germany 378
University of Manitoba 184, 317, 318, 320, 597
University of Maryland 26, 36, 69, 184, 267, 317, 318, 320, 378, 391
University of Miami School of Medicine 342, 609
University of Michigan Medical School 9, 141, 415, 433, 434, 435, 436, 437, 489, 504
University of Milan 351, 386
University of Mississippi Medical Center 66, 91, 92, 234, 340, 505, 528, 561
University of Modena 648
University of New Mexico, Albuquerque 496, 497, 537, 572
University of North Carolina, Chapel Hill 29, 31, 46, 230, 271, 562
University of Oklahoma 486, 537
University of Ottawa 18, 38, 94, 129, 397, 398
University of Oulu, Finland 43, 371, 372
University of Pennsylvania Health System 77, 259, 305
University of Perugia, Italy 606
University of Rochester 309
University of Sheffield, UK 4
University of South Carolina 28, 48
University of South Florida, Tampa 111, 138, 187, 188, 280, 487, 657
University of Southern California School of Medicine 200, 205, 277, 413, 461
University of Tennessee, Memphis 8, 34, 68, 114, 115, 152, 155, 244, 250, 252, 281, 655
University of Texas Health Science Center, San Antonio 24, 212, 214, 215, 216, 304, 367
University of Texas Southwestern Medical Center, Dallas 93, 290, 345, 346, 348, 414, 463, 475, 535, 536
University of Texas-Houston Medical School 31, 289, 498, 634
University of Toronto 63, 558, 612, 620
University of Turin 133
University of Utah Health Sciences Center 27, 85, 87, 269, 402
University of Utah School of Medicine 133, 150, 238, 239, 242, 245, 249, 255, 260, 294, 373, 582, 629, 660
University of Vermont 129, 579, 580, 581, 635
University of Vienna, Austria 222, 392
University of Washington 17, 75, 235, 236, 394
University of Western Australia 55, 431
University of Wisconsin 17, 75, 235, 236, 394, 413, 463, 475, 535, 536
Vanderbilt University 532, 569, 570
Wake Forest University 217, 218, 381, 382, 384, 385, 534, 622
Washington University, St. Louis 33, 219, 220, 221, 361, 477
Wayne State University/Hutzel Hospital 42, 51, 54, 59, 84, 151, 158, 170, 174, 180, 186, 189, 264, 270, 298, 300, 301, 302, 303, 308, 309, 316, 331, 337, 370, 427, 450, 452, 479, 481, 493, 527, 552, 556, 557, 559, 577, 578, 589, 602, 626, 628, 641, 646, 662, 666
Wilford Hall Medical Center/Brooke Army Medical Center 85, 87
Winthrop University Hospital, Mineola, NY 544

Women and Infants Research Foundation of Western Australia
55, 431
Women's Health Research and Education Foundation, Nashville
73
Women's Hospital Boston 500, 502
Womens Health, University of Pittsburgh 90
Yale University School of Medicine 110, 177, 261, 263, 284, 297, 379, 399, 400, 404, 429, 574, 575, 614, 615, 631, 663