27 MANNOSE BINDING LECTIN HAPLOTYPES ARE ASSOCIATED WITH CEREBRAL PALSY CATHERINE GIBSON[1], ALASTAIR MACLENNAN[1], PAUL GOLDWATER[2], ERIC HAAN[3], KEVIN PRIEST[4], GUSTAAF DEKKER[1], [1]University of Adelaide, Obstetrics & Gynaecology, Adelaide, South Australia, Australia, [2]Children, Youth & Women's Health Service, Microbiology and Infectious Diseases, Adelaide, South Australia, Australia, [3]Children, Youth & Women's Health Service, Genetic Medicine, Adelaide, South Australia, Australia, [4]Department of Health, Epidemiology Branch, Adelaide, South Australia, Australia

OBJECTIVE: To investigate associations between infection, polymorphisms in the mannose binding lectin gene (MBL) & cerebral palsy (CP) in a large Caucasian population-based study.

STUDY DESIGN: Case-control study using newborn screening card DNA of 443 CP cases & 883 controls to screen for 6 polymorphisms in the MBL gene (−550, −221, +4, exon-1 codons 52, 54, 57).These polymorphisms combine to create "haplotypes" of high (HYPA), intermediate (LYQA, LYPA), low (LXPA) & defective (HYPD, LYQC, LYPB) circulating MBL levels.

RESULTS: χ^2 analyses demonstrated significant differences in MBL haplotype between CP cases & controls (CP <37 wks gestational age (GA) χ^2 14.99, p=0.02; <32 wks GA χ^2 13.62, p=0.02). The table below demonstrates significant associations observed for specific haplotypes. Subanalysis on samples previously testing positive for exposure to viral infection demonstrated similar significance patterns, whilst analysis on samples negative for exposure to viral infection showed no positive associations between MBL haplotypes & CP.

CONCLUSION: Carriage of the LYPA or HYPD haplotypes is associated with an increased risk of CP in the presence of exposure to viral infection & appears to act as a susceptibility factor for CP.

Significant associations (p<0.05) between MBL haplotype, CP type, GA & exposure to infection

CP Type	MBL Haplotype	GA (wks)	Infection Status	Odds Ratio (95% CI)
All	LYPA	All	Not considered	1.57 (1.00–2.46)
		<37		2.43 (1.41–4.18)
		<32		2.54 (1.34–4.76)
Hemiplegia	LYPA	<37		2.77 (1.02–7.26)
		<32		4.48 (1.55–12.65)
Quadriplegia	HYPD	All		3.47 (1.41–8.31)
		<32		7.86 (1.67–29.48)
Hemiplegia	LYPA	<32	Positive	8.25 (1.08–52.76)
Quadriplegia	HYPD	All		5.24 (1.03–21.67)
		<32		18.33 (2.06–150.68)

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.031

28 COMBINING FIRST AND SECOND TRIMESTER DOWN SYNDROME SCREENING RESULTS: A SIMPLE, EFFECTIVE APPROXIMATION TODD ROSEN[1], HOWARD CUCKLE[1], FERGAL MALONE[2], FLINT PORTER[3], DAVID NYBERG[4], CHRISTINE COMSTOCK[5], RADEK BUKOWSKI[6], RICHARD BERKOWITZ[1], SUSAN J. GROSS[7], LORRAINE DUGOFF[8], SABRINA CRAIGO[9], ILAN E. TIMOR-TRITSCH[10], STEPHEN R. CARR[11], HONOR M. WOLFE[12], DIANA BIANCHI[9], MARY E. D'ALTON[1], [1]Columbia University Medical Center, New York, New York, [2]Royal College of Surgeons in Ireland. Rotunda hospital, , Ireland, [3]University of Utah, Salt Lake City, Utah, [4]Swedish Medical Center, Perinatal Medicine, Seattle, Washington, [5]William Beaumont Hospital, Royal Oak, Michigan, [6]University of Texas,Medical Branch, Galveston, Galveston, Texas, [7]Montefiore Medical Center, Bronx, New York, [8]University of Colorado Health Sciences Center, Ob/Gyn, Denver, Colorado, [9]Tufts University, Boston, Massachusetts, [10]NYU Medical Center, School of Medicine and Obstetrics & Gynecology, New York, New York, [11]Women and Infants Hospital, Department of Obstetrics and Gynecology, Providence, Rhode Island, [12]University of North Carolina at Chapel Hill, Department of Obstetrics and Gynecology, Chapel Hill, North Carolina

OBJECTIVE: The proper interpretation of a second trimester serum Quad test in a woman who has had a first trimester Combined test is to calculate risk from maternal age and all seven marker levels. However, software needed for risk calculation is not always available and a simple approximation is the composite likelihood ratio (CLR), defined as (first trimester Combined risk ÷ maternal age risk) * Quad risk. We assessed the discriminatory power of this approach.

STUDY DESIGN: Data collected from women in the FASTER trial were analyzed to calculate Down syndrome (DS) risk from ultrasound nuchal translucency measurement and maternal serum markers in the first and second trimester. 32,269 women carrying singleton pregnancies completed both first and second trimester screens; 86 women had Down syndrome fetuses. DS detection and false-positive rates (FPRs) for the CLR were compared against first trimester Combined (NT, free β-hCG and PAPP-A), second trimester Quad (AFP, hCG, uE3, and inhibin), and Integrated (first trimester NT and PAPP-A, and second trimester Quad) tests.

RESULTS: DS detection rates and FPRs with a 1 in 270 second trimester risk cut-off, and detection rates for a fixed 5% FPR are shown in the Table. CLR outperformed first trimester Combined, Quad, and Integrated tests. Properly calculating risk from all seven marker levels detected 92% of DS cases at a 4.9% FPR, and a detection rate of 92% (79/86) for a 5% FPR.

CONCLUSION: The CLR is an effective method of interpreting screening results, despite only calculating DS risk approximately. The CLR may be useful when first and second trimester screens are performed in different laboratories or a provider does not have access to software to perform the Integrated screen.

Performance of CLR compared with other methods

	First Combined	Quad	Integrated	CLR
Sensitivity	85% (73/86)	84% (72/86)	88% (76/86)	92% (79/86)
FPR	6.7%	9.3%	4.9%	5.3%
Sensitivity for 5% FPR	85% (73/86)	81% (70/86)	88% (76/86)	91% (78/86)

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.032

29 FOLIC ACID RESCUE OF CARDIOVASCULAR DYSFUNCTION AND INTRAUTERINE DEMISE INDUCED BY SINGLE PULSE DOSE OF HOMOCYSTEINE IN EARLY GESTATION MARIA SERRANO[1], JAMES HUHTA[1], MINGDA HAN[1], KERSTI LINASK*[1], [1]University of South Florida, Pediatrics, St. Petersburg, Florida

OBJECTIVE: Congenital heart defects are associated with elevated homocysteine (Hcy) concentrations. Our aim was to evaluate, using color directed pulsed-wave Doppler echocardiography (echo), the effect of one-time Hcy exposure in early pregnancy on mouse embryonic cardiovascular function and evaluate simultaneous folic acid (FA) rescue.

STUDY DESIGN: Fifteen pregnant mice (C57BL/6) received one intraperitoneal injection of 125 μL of 75μmol L-homocysteine thiolactone (Hcy) or 75 μmol of Hcy plus 75μg of Folic acid (Hcy+FA) on E6.75. On E15.5 the mice were anesthetized with isoflurane and embryonic echo was performed. Maternal heart rate was determined and pulsatility index calculated from blood velocity waveforms of the uterine artery, descending aorta, umbilical artery, and ductus venosus. From the inflow-outflow velocity waveforms the outflow velocity and the cardiac cycle time intervals including isovolemic contraction and relaxation times were measured; myocardial performance index was calculated. Semilunar (SL) or atrioventricular (AV) valve regurgitation (VR) was recorded. At sacrifice, after the echo exam, the number of embryo resorptions was determined and crown-rump length (CRL), body and placental weight were measured.

RESULTS: Fifty five Hcy and 21 Hcy+FA embryos were studied. None in the Hcy+FA group had VR, but 27 (49.1%) of the Hcy group had SL VR and 7 (12.7%) had AV VR. There were 36.4% (20) embryonic resorptions in the Hcy group compared to none in Hcy+FA. All Hcy embryos had lower body and placenta weight and shorter CRL in comparison to Hcy+FA.

CONCLUSION: Pulsed Hcy exposure in early embryonic life increased the risk of intrauterine demise or growth failure and was associated with cardiac VR. Simultaneous folic acid treatment prevents fetal demise and rescues valvular regurgitation.

Supported by AHA0555321B to KKL

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.033