non-Hispanic white, as well as those who had induction or augmentation of labor, gestational diabetes, or epidural analgesia were more likely to have delayed pushing. Delayed pushing was more common when the second stage began during daytime hours or in hospitals with dedicated 24-hour obstetrical anesthesia. It occurred less commonly in hospitals with a 24-hour in-house attending obstetrician or neonatologist. After adjusting for differences in baseline characteristics, women in the delayed group had longer adjusted mean durations of the second stage (192 vs. 84 min, $p<0.001$) and of active pushing (86 vs. 76 min, $p<0.001$). Delayed pushing also was associated with a greater odds of cesarean delivery (11.2% vs 5.1%, $p<0.001$), operative vaginal delivery (16.2% vs 11.2%, $p<0.001$) and NICU admission (8.8% vs 6.8%, $p<0.001$), without an increase in risk of major perineal laceration, compared with early pushing (Table).

CONCLUSION: In this large birth cohort, delayed pushing was associated with a longer duration of pushing, increased odds of cesarean delivery and NICU admission.

Table: Delivery outcomes associated with delayed pushing

Outcome	Delayed pushing (N=3870)	Early pushing (N=17164)	aOR or difference between adjusted means (95% CI)*
Mean duration of second stage (minutes)	191.9 (1.61)	84.1 (1.36)	107.7 (105.6-109.8)
Mean duration of active pushing (minutes)	86.1 (1.47)	75.7 (1.24)	10.4 (8.5-12.3)
Cesarean delivery	432 (11.2%)	878 (5.1%)	1.86 (1.64-2.12)
Operative vaginal delivery	627 (16.2%)	1923 (11.2%)	1.33 (1.20-1.47)
Episiotomy	763 (19.7%)	2867 (16.7%)	1.07 (0.98-1.18)
3rd or 4th degree perineal laceration	340 (8.8%)	1198 (7.0%)	1.09 (0.96-1.24)
NICU admission	340 (8.8%)	1172 (6.8%)	1.19 (1.04-1.36)

aOR, adjusted odds ratio; NICU, neonatal intensive care unit
Data present as N(%) or adjusted mean(SE)
* Adjusted for maternal age, gestational age, BMI, race/ethnicity, insurance, gestational diabetes, labor augmentation/induction, neuraxial analgesia/anesthesia, birth weight, and chorioamnionitis

201 Human cervical smooth muscle stretch increases matrix metalloproteinase secretion: a new mechanism to explain premature cervical remodeling

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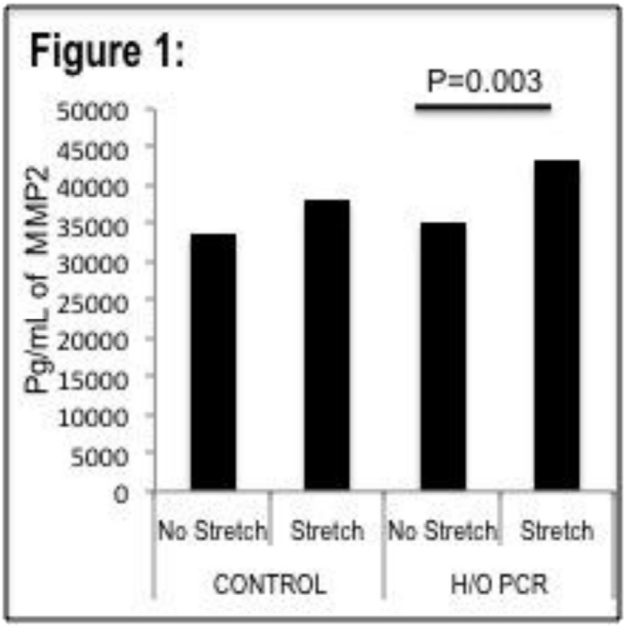
OBJECTIVE: We sought to define the role of cervical smooth muscle cells (CSMC) in normal and premature cervical remodeling (PCR). Specifically, we asked 1) if primary human CSMC secrete matrix metalloproteinases (MMPs; collagen remodeling enzymes), 2) if CSMC stretch induces MMP secretion, and 3) if CSMC stretch triggers increased MMP secretion in women with a history of PCR.

STUDY DESIGN: Using IRB approved protocols, CSMC were isolated from cervical tissue obtained prior to cerclage from 4 pregnant women (14-16wks) with a history of PCR resulting in preterm birth (PTB) <28 wks and 4 gestational-age matched controls (CTL) undergoing pregnancy termination. Immunocytochemistry for alpha-SMA, SM22 and desmin was used to identify smooth muscle cells (SMC). Cyclical stretch was applied (-13kpa, 15% elongation, 45s stretch, 15s release) for 24h using a Flexcell system and then MMP1, 2, 7, 9 and 10 concentrations in the basal media were determined by Luminex. Experiments were run in duplicate and statistical analyses included logistic regression, generalized estimated equation, ANOVA and Student's t-test.

RESULTS: SMC markers were evident before and after 24h of cyclical stretch. At baseline, CSMC secrete MMPs, predominantly MMP1 and 2 with lower levels of MMP9 and 10 and cyclic stretch significantly increased MMP2 secretion in women with a history of PCR vs CTL ($p=0.003$, Figure 1).

CONCLUSION: Primary human CSMC secrete MMPs, which are thought to be critical for cervical remodeling. CSMC from pregnant women with a history of PCR secrete higher levels of MMP2 in response to stretch than CTL. This abnormal CSMC stretch response, characterized by increased MMP2 secretion, may elucidate a potential mechanism in the pathophysiology of PCR and PTB.



202 Human myometrial in vitro effects of pharmacological agents used in the clinical management of postpartum hemorrhage

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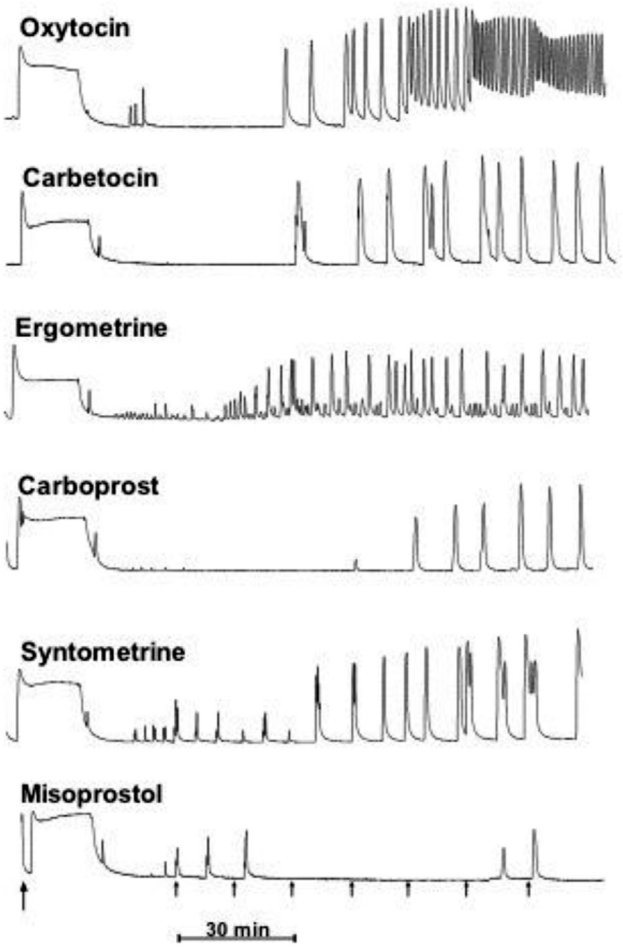
OBJECTIVE: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality in the developed and under-developed world, and uterine atony is the major contributing factor. Clinical guidelines for drug treatment of PPH vary internationally, and there are minimal comparative pharmacological data for the various uterotonic compounds used. The aim of this study was to evaluate a range of contractile parameters in human pregnant myometrium, for the uterotonic agents used clinically in the management of atonic PPH.

STUDY DESIGN: Myometrial biopsies were obtained from 19 patient donors undergoing elective cesarean delivery at term. The effects of the uterotonic agents oxytocin, carbetocin, ergometrine, carboprost, syntometrine and misoprostol were investigated in 146 myometrial strips. The potency (expressed as pEC50) and maximal response values were obtained, and compared, using both maximal amplitude and mean contractile force as indices of contraction. Single EC50 concentrations of the agents were administered and both force and contraction peak parameters were compared during a 15 minute exposure.

RESULTS: The most important difference between the agents was in their ability to increase the mean contractile force, with oxytocin superior to all agents except syntometrine. In single dose experiments mean contractile force was the parameter that separated the

agents. Oxytocin was not statistically different from carboprost or syntometrine but was superior to all other agents. There was a wide difference in potencies using both measures of contractility, with oxytocin and carbetocin being most potent. There were no significant differences in the peak amplitude of response between agents, except for misoprostol, which was inactive.

CONCLUSION: Consideration of the pharmacological effects of these compounds in vitro indicates that oxytocin is the most efficient of all compounds in achieving sustained uterine contractility, followed closely by syntometrine and carboprost. These findings question the potential clinical efficacy of misoprostol in the management of postpartum hemorrhage.



203 Maternal body mass index and spontaneous contractile activity of pregnant human myometrium in vitro

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OBJECTIVE: Dysfunctional labor and the need for cesarean delivery are more common among obese mothers. However there is controversy as to whether maternal body mass index (BMI) influences the contractility of human myometrium in pregnancy. The aim of this study was to examine spontaneous contractile activity of human myometrium in vitro, with respect to maternal BMI.

STUDY DESIGN: Myometrial tissue specimens were obtained at cesarean delivery from 74 women with BMI values ranging from 19 to 50.1kg/m2. By recording in vitro from eight strips per donor (590 strips in total) several parameters of spontaneous contractile activity were monitored. The relationship between BMI and uterine contractility was evaluated using linear regression analysis.

RESULTS: No significant correlation was observed with BMI, over the range studied, for maximal amplitude of spontaneous contraction, mean contractile force, time to maximal amplitude, maximum rate of rise or occurrence of simple and complex (biphasic and multiphasic) contractions. The mean maximum amplitude value for spontaneous contractions was 36 ± 3 mN, the mean contractile force for spontaneous contractions was 3 ± 0.3 mN, the average frequency of contractions was 6.5 ± 0.5 per hour and the average time to the first spontaneous contraction was 11 ± 1 minute.

CONCLUSION: These results indicate there is no significant functional impairment of spontaneous uterine contractility, with advancing BMI up to 50kg/m2. These findings do not support the concept that there may be a biological basis for dysfunctional labor or increased cesarean delivery rates in obese parturients.

Spontaneous contractility values for human pregnant myometrium and their relationship with maternal BMI.

Parameter	Mean value	r^2	P
BMI	25.7 ± 0.6 kg/m^2		
Average maximal amplitude	36 ± 3 mN	0.014	0.31
Average mean contractile force	3 ± 0.3 mN	0.019	0.24
Time to first spontaneous contraction	11 ± 1 min	0.039	0.09
Time to MAMP of spontaneous contractions	510 ± 4 min	0.020	0.22
Maximum rate of rise of spontaneous contractions	5.1 ± 0.2 mN/s	0.000	0.98
Maximum rate of relaxation of spontaneous contractions	−2.7 ± 0.2 mN/s	0.001	0.76
Contractions that were biphasic	13 ± 2 %	0.003	0.64
Contractions that were multiphasic	8 ± 1 %	0.000	0.90
Average frequency of contractions	6.5 ± 0.5 per h	0.000	0.98
Number of strips developing spontaneous activity[a]	6.8 ± 0.2 (85%)	0.03	0.16

Values are arithmetic means ± SEM from the averages of 8 strips taken from 74 independent donor biopsies except where there is only a single value from each biopsy. The r^2 and P values were obtained when the relationship between the average parameters and maternal BMI was investigated by linear regression.

204 Cell-free DNA and parturition: placental DNA stimulation of an innate immune response

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OBJECTIVE: It has been proposed that cell-free fetal DNA (derived from the placenta) stimulates TLR9 thereby activating an innate immune response within the pregnant uterus, thus triggering spontaneous parturition. Vertebrate DNA is normally a poor agonist for TLR9; however, removal of telomere sequences, as occurs during cellular apoptosis, reverses this negative effect. These studies sought