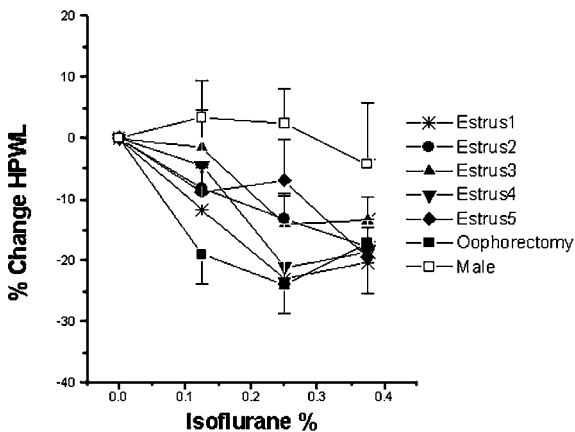


GERTIE MARX

GM-1

THE EFFECT OF OVARIAN HORMONES ON ISOFLURANE HYPERALGESIA Flood, P. Daniels, D. *Anesthesiology, Columbia University, New York, NY* Volatile anesthetics increase pain sensitivity at the low concentrations that are present on emergence in humans and animals [1-3]. Gender differences in pain sensitivity and in pharmacodynamic responses to drugs used to treat pain have been widely reported (reviewed by Berkley, 1997)[4]. To determine whether there was a gender difference in the hyperalgesic response to isoflurane, we measured hind paw withdrawal latency in male and female mice with and without isoflurane. Females had a more prominent hyperalgesic response to isoflurane than males (Figure 1). We tested female mice for HPWL in each stage of their estrus cycle, after oophorectomy and with exogenous estrogen replacement. Hyperalgesia was more prominent in stages 1 and 4 of the cycle (low estrogen and progesterone) and after oophorectomy. Estrogen replacement was not protective against isoflurane hyperalgesia. A combination of estrogen and progesterone may be required to mimic the isoflurane response found in estrus stages 2,3 and 5. Hyperalgesia from low isoflurane concentrations may be particularly problematic in females, but may not be a problem in pregnancy. 1. Zhang, Y, et al; *Inhaled anesthetics have hyperalgesic effects at 0.1 minimum alveolar concentration. Anesth Analg, 2000. 91:462-6.* 2. Dundee J and Moore J; *Alterations in response to somatic pain associated with anesthesia IV. The effect of sub-anesthetic concentrations of inbalational agents. British Journal of Anaesthesia, 1960. 32:453-9.* 3. Flood P et al; *Isoflurane hyperalgesia is modulated by nicotinic inhibition. Anesthesiology (in press).* 4. Berkley KJ; *On the dorsal columns: translating basic research hypotheses to the clinic. Pain, 1997.70:103-7.*



Females have more hyperalgesia from isoflurane than males. Hyperalgesia is pronounced at low estrogen, low progesterone stages of the estrus cycle and after oophorectomy.

GM-2

PEAK POINT CORRELATION DIMENSION: A NOVEL PREDICTOR OF ADVERSE HEMODYNAMIC RESPONSE TO SPINAL ANESTHESIA. Chamchad, D. Arkoosb, V.; Buxbaum, J.; Horrow, J.; Nakbambchik, L.; Kresb, J. *MCP Habnemann University, Philadelphia, PA*
Introduction: Cardiovascular instability often complicates spinal anesthesia (SPA) for Cesarean Section (C/S). Early detection of cardiovascular imbalance would enable prompt response or preemptive treatment. This study observed changes in point correlation dimension (PD2), an index of Heart Rate Variability (HRV), before and after SPA.
Methods: With IRB approval and consent 22 non-laboring parturients with a single fetus, scheduled for C/S under SPA, received spinal bupivacaine-morphine following intravenous prehydration. An adverse response was defined as hypotension (SBP \leq 75% baseline), nausea or vomiting. The ECG, obtained in LUD position before and 10 min after SPA, was stored in analog form. This was converted off-line (DataQ, Akron, OH) to digital RR intervals. Peak PD2(pPD2) analysis extracted the nonlinear parameters embedded in HRV.¹ Hemodynamic and pPD2 data were compared before and after SPA (paired Student's t-test). The median pPD2 value before SPA separated the 22 patients into two groups of 11 (LO,HI).
Results: pPD2 decreased after SPA [3.22(0.89)(mean(SD)) vs. before SPA 4.05(0.64) p=0.0003]. Median pPD2 measured 3.9 before SPA. Baseline heart rate was higher in the LO group [95/min (10.2)] vs. the HI group [81.4(9.6)]. No HI group patient pPD2 \geq 3.9 before SPA experienced an adverse response, whereas adverse responses occurred in all 11 LO group patients pre-SPA pPD2 $<$ 3.9 p=0.0000028, fig1. Groups LO and HI did not differ in age, height, weight, bupivacaine-morphine dose, initial BP or volume of IV prehydration.
Discussion: Because adverse responses to SPA are frequent (50% in our series), prior risk identification should advance patient safety and comfort. pPD2 successfully stratified patients undergoing C/S into risk cohorts. Additional studies are required to validate pPD2=3.9 as a risk discriminant and to investigate the use of this measurement to stratify patients for prophylaxis. 1. *Integ Physi & Beh Sc 1994; 29(3):217-35*

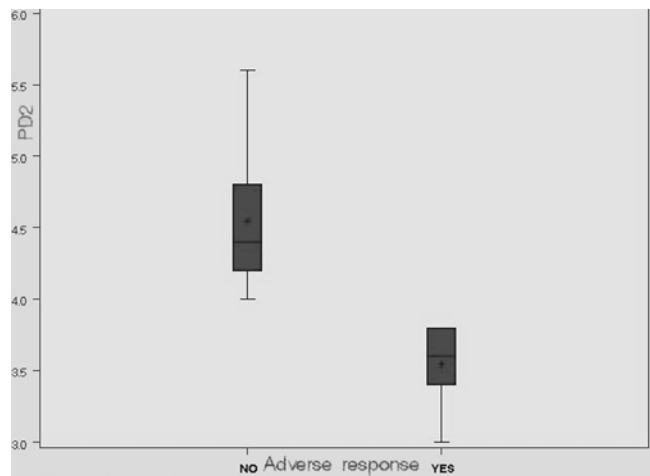


Figure 1: Boxplots of PD2 grouped by adverse response occurrence.

GM-3

EFFECT OF EPIDURAL TEST DOSE ON AMBULATION AFTER A COMBINED SPINAL EPIDURAL TECHNIQUE FOR LABOR ANALGESIA Calimaran, A.L., Strauss-Hoder, T.P.; McCarthy, R.J.; Wong, C.A.

Northwestern University, Chicago, IL Although the evidence suggests that ambulation during labor has no beneficial effect on the progress of labor (1,2), it remains popular amongst parturients and their health providers. Combined spinal epidural (CSE) analgesia using intrathecal bupivacaine and fentanyl without a local anesthetic epidural test dose provides satisfactory labor analgesia and successful ambulation (3). The purpose of this study is to determine the effect of a lidocaine-epinephrine epidural test dose on the parturient's motor strength and ability to perform simple ambulatory tests after CSE analgesia. Following written informed consent, 110 parturients were included in this randomized, double blinded study. CSE analgesia was initiated with intrathecal bupivacaine 2.5 mg and fentanyl 25 µg. Parturients were randomized to receive either 3-ml lidocaine (45 mg) with epinephrine (15 mg) (LE) or 3-ml 0.9% sodium chloride solution (NS) epidural test dose. Resistance to straight leg raise (SLR), modified Bromage score (MB), ability to step up and stand on a step-stool (ASS), perform a partial deep knee bend (PDKB), and the parturient(s) subjective ability to walk (SAW) were evaluated at 30 and 60-min. Data were compared between groups using a Chi-square test with P<0.05 significant (* in table). There were no differences between groups with respect to age, height, weight, parity, gestational age, and cervical dilatation at CSE analgesia. LE impaired the parturients ability to perform a PDKB and their SAW at 30-min, as well as the ability to ASS 30 and 60-min (Table). The important findings of this study are the impairment of the parturients ability to perform simple ambulatory tasks following an epidural test dose of lidocaine with epinephrine administered immediately after initiation of CSE analgesia. In addition the modified Bromage scale was not a sensitive indicator of the parturients ability to perform these ambulatory tasks. This data suggests that early ambulation be discouraged when the test dose is performed immediately after initiation of CSE analgesia, or the test dose should be avoided when early ambulation is desired. 1) *N Eng J Med* 1998; 339:76-9 2) *Anesthesiology* 2001; 95:857-61 3) *Int J Obstet Anesth* 1994; 3:75-81

	SALINE GROUP	LIDOCAINE-EPINEPHRINE GROUP
SLR 30 min, left %	96.4	88.9
SLR 30 min, right %	96.4	94.4
MB 30 min, left %	94.5	87.0
MB 30 min, right %	94.5	94.3
PDKB 30 min %	71.4	42.6*
PDKB 60 min %	91.1	79.6
ASS 30 min %	69.9	29.9*
ASS 60 min %	85.7	59.3*
SAW 30 min %	74.4	38.9*
SAW 60 min %	75.9	87.5

GM-4

PLATELET COUNT & PLATELET FUNCTION: AN IN VITRO MODEL FOR PRODUCING WHOLE BLOOD WITH LOW PLATELET COUNTS Patel, N.¹ Fernando, R.¹ Riddell, A.² Brown, S.²

1. Dept of Anesthesia, Royal Free Hospital, London, United Kingdom; 2. Katharine Dormandy Center for Hemophilia, Royal Free Hospital, London, United Kingdom The lowest platelet count considered safe for regional techniques has yet to be established in the normally hypercoagulable pregnant patient. This pilot study was conducted to produce an in vitro model to generate artificially low platelet counts in whole blood without disturbing hematocrit, clotting factors or the platelets themselves. This method will subsequently be used to identify the point at which a falling platelet count begins to interfere with platelet function in different pregnant subpopulations, as assessed by the Platelet Function Analyzer (PFA-100) measuring closure time (CT, s) and the Thromboelastograph (TEG)¹ measuring maximum amplitude (MA, mm). After IRB approval, 36ml of blood was withdrawn from male subjects¹ (n=4) and transferred into 3 x 10ml and 1 x 3ml buffered citrate, and 1 x 3ml EDTA collection tubes. Baseline hemoglobin (Hb), hematocrit (Hct), platelet count, coagulation tests (prothrombin time [PT], activated partial thromboplastin time [APTT] and fibrinogen), MA and CT were measured using citrated whole blood. The remaining citrated blood (30ml) was then divided: 20ml carefully centrifuged according to a protocol to prepare platelet depleted blood ("0% Platelets") and 10ml labelled as "100% Platelets" (count known and not centrifuged). Four test samples of varying platelet count were then reconstituted by mixing together different proportions of original whole blood containing "100% Platelets" with "0% Platelets" in predetermined ratios of 2:1, 1:1, 1:2 and 1:3. The above tests were then repeated on these reconstituted samples. Statistical analysis included repeated measures ANOVA (P<0.05). Whole blood with a range of low platelet counts, broadly comparable with the predetermined ratios, were generated without significantly altering Hb, Hct, coagulation (Table: data=mean,SD; *P<0.001) or platelet integrity. Within subjects, MA and CT showed significant differences with falling platelet count. Artificially low platelet counts created in whole blood using this in vitro model may potentially be used to study how variations in platelet numbers affect platelet function in different pregnant subpopulations. 1. *Gorton HJ, Warren ER, Simpson NAB, Lyon GR, Columb MO. Thromboelastography identifies sex-related differences in coagulation. Anesth Analg* 2000; 91: 1279-81.

	100%	2:1	1:1	1:2	1:3
Platelet range (x 10⁹ /L)	132-234	60-144	50-116	25-85	15-68
Hb (g/dL)	13.4(1.1)	13.4(1.3)	13.4(1.1)	13.4(1.1)	13.4(1.1)
PT (s)	13.7(0.9)	13.7(0.9)	13.7(1.0)	13.7(0.9)	13.7(1.0)
APTT (s)	36.1(5.9)	36.8(5.4)	36.6(6.3)	37.6(5.3)	36.6(6.0)
Fibrinogen (g/L)	2.4(0.2)	2.2(0.1)	2.4(0.2)	2.3(0.2)	2.4(0.2)
*MA (mm)	49.8(4.7)	39(4.2)	36(2.6)	32(8.5)	26.8(3.8)
*CT (s)	95(22)	148(8)	171(20)	248(74)	264(51)

GM-5

EARLY LABOR IS MORE PAINFUL IN PARTURIENTS WHO EVENTUALLY DELIVER BY CESAREAN SECTION FOR DYSTOCIA

Panni, M.K. Spiegel, J.; Segal, S. Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA Dystocia is characterized by abnormal progress of labor and is the most common contemporary indication for cesarean delivery in the United States. There has been considerable controversy as to whether epidural analgesia causes dysfunctional labor leading to cesarean delivery for dystocia. The minimum local anesthetic concentration (MLAC) is a clinical model used to determine the relative potencies of local anesthetics in the first stage of labor (1). In this paper we report a prospective study determining the MLAC of bupivacaine in early labor of nulliparous parturients who eventually deliver either vaginally or via cesarean section. An up-down sequential allocation technique was used to investigate the MLAC of bupivacaine in these parturients (2). In addition patients were assigned to groups who were or were not on intravenous oxytocin at the time of epidural catheter placement. In each arm of the study an additional criterion for rejecting a given patient was failure to deliver by that arm's randomly assigned mode. Parturients who later delivered vaginally had a 25% and 31% lower MLAC value (0.085% and 0.078% wt./vol. bupivacaine, receiving or not receiving intravenous oxytocin respectively) than those who later delivered by cesarean section (0.106% and 0.102% wt./vol. bupivacaine, receiving or not receiving intravenous oxytocin respectively). In addition it was seen that those parturients receiving intravenous oxytocin at the time of epidural catheter placement had slightly lower MLAC values (4% and 9% lower, delivering by vaginal or cesarean section respectively) than those not receiving oxytocin. Logistic regression showed both delivery mode ($p=0.0264$) and concentration ($p=0.0003$) to be highly significant independent predictors of response to bupivacaine. Our data do not establish cause or effect, but strongly suggest that a woman's need for labor analgesia is associated with intense pain related to labor dystocia. This relationship should be considered when studying the method of labor analgesia and its potential effects on the course of labor. Our observation that more intense pain is associated with difficult labor may also alert obstetricians that such pain is not caused by reduced pain threshold, but may also be a marker of intrinsically difficult and ultimately obstructed labor. 1. *Columb MO, Lyons G. Determination of the minimum local anesthetic concentrations of epidural bupivacaine and lidocaine in labor. Anesth Analg 1995; 81:833-837.* 2. *Dixon WJ, Massey FJ. Introduction to Statistical Analysis, 4th ed. New York, McGraw-Hill, 1983; 428-439.*

GM-6

THE IMPORTANCE OF METHODOLOGICAL VARIABLES IN THE STUDY OF HYPOTENSION AFTER SPINAL ANESTHESIA FOR CESAREAN SECTION: PENTASTARCH VS. NORMAL SALINE

Bach, P.S. Kamani, A.A.; Douglas, J.M.; Gunka, V.; Esler, M. Anesthesia, B.C. Women, Vancouver, BC, Canada Numerous studies have addressed the impact of fluid preloading on the incidence of hypotension after spinal for Cesarean section¹. The results have been highly variable and a number of methodological shortcomings have been identified¹ such as: Definition of hypotension used,^{1,2}; place where baseline BP was established (stress response in OR), crystalloid to colloid ratio³, failure to delineate preload-spinal interval³, prophylactic vasopressor use, reliance on single hypotensive BP readings, lack of standardized spinal dose and injection rate, and lack of adequate sample size¹. This study was designed to tightly control these variables and determine if the incidence of hypotension after spinal for C/S is as high as the literature suggests. After institutional ethics approval 160 healthy women were randomized in a controlled double blind fashion to receive pentastarch 10ml/kg or normal saline 30ml/kg prior to spinal for Cesarean section. Power analysis was based on a literature review¹. An average of 3 BPs were taken in the holding area to establish the baseline. Hypotension was defined as systolic BP<90mmHg or <70% of baseline or symptoms. Vasopressors were only given after two successive hypotensive readings or symptoms. Preload-to-spinal interval was <30 minutes. Spinal dose and injection rate were standardized. Interim analysis of 80 women enrolled to date indicates the incidence of hypotension is not statistically different between the groups (A=32.5% B=20.0% $p=0.155$). The groups are demographically similar. This is the first study that tightly controls all of the methodological variables discussed above. The incidence of hypotension in the two groups was similar and is less than in other studies that compare crystalloids to colloids¹. Close attention to these methodological variables may have reduced the observed incidence of hypotension in this study. 1. *Morgan PJ, et al. Anesth Analg 2001; 92: 997-1005.* 2. *Norris MC, Reg Anesth 1987; 12: 191-94.* 3. *Ueyama H, et al. Anesthesiology 1999; 91:1571-76.*