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Carbon dioxide pneumoperitoneum induces fetal acidosis in a pregnant ewe model

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Abstract. The objective of this study was to evaluate the physiologic consequences of a pneumoperitoneum (pneumo) to the midterm fetus in a pregnant sheep model. The performance of laparoscopic cholecystectomy (LC) during pregnancy is controversial. The primary concern regarding the safety of LC during pregnancy is the physiologic consequences of the CO_2 pneumo to the fetus. Eight ewes with singlet pregnancies between 100 and 120 days of gestation were anesthetized and intubated. Carotid artery and internal jugular catheters were placed in the ewe and in the fetus. Two trocars were placed through the abdominal wall of the ewe and the abdomen was inflated with CO_2 or N_2O at 15 mmHg pressure for 90–120 min. Hemodynamic and blood gas data were obtained every 15 min before, during, and after the pneumo. In two ewes attempts were made to keep maternal Pco_2 constant with hyperventilation. In two other animals the pneumo was increased stepwise in five mmHg increments to 25 mmHg. One fetus succumbed during the CO_2 pneumo, but this animal appeared to be ill during the establishment of invasive monitoring. Fetal respiratory acidosis occurred, reproducibly, after establishment of CO_2 pneumo but did not occur before insufflation or under N_2O pneumo ($P < 0.0001$). Hemodynamic changes were minimal with all agents but it appeared that there a was greater prevalence of fetal tachycardia and hypertension during CO_2 pneumo than during N_2O pneumo. Alterations in ventilator settings based on maternal capnography resulted in late and incomplete correction of respiratory acidosis. Despite clinical reports of successful LC during pregnancy, significant respiratory acidosis may be induced in the fetus with CO_2 pneumo. Alternative gases (e.g., N_2O) or abdominal suspension devices may be preferable to CO_2 when performing laparoscopy in pregnant patients.

Key words: Carbon dioxide — Fetal acidosis — Pregnant ewe — Model

It is still unclear whether it is prudent to perform laparoscopic cholecystectomy in pregnant patients. Most small clinical series are free of obstetrical complications occurring during or after a laparoscopic procedure [2, 4, 6, 12, 14, 16, 17], yet concerns remain as to whether increased intraabdominal pressure, hypercarbia, or acidosis confers a significant risk to the developing fetus. Until now there have been few data describing fetal hemodynamic and acid–base responses to a therapeutic pneumoperitoneum [9]. An accurate description of fetal physiology in this setting requires invasive monitoring, and cannot be performed in human fetuses. The pregnant ewe has become the standard model with which to investigate fetal–maternal physiology [13, 15].

Our aim was to determine the effects on the fetus of a CO_2 and N_2O pneumoperitoneum over the time period necessary to perform a short (less than 2 h) laparoscopic procedure.

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Methods: experimental model

Eight mixed Western breed ewes with singlet pregnancies were transferred to the Oregon Health Sciences University Animal Care Unit and managed under the regulations of the animal care and use committee. Between d 100 and 120 of a 150-d gestational cycle, the

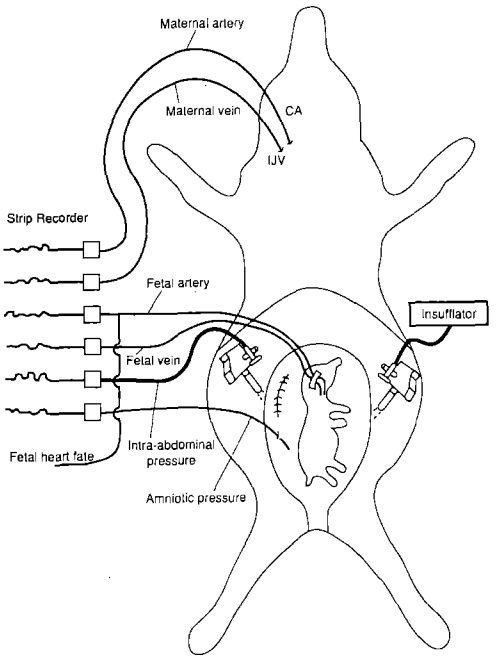


Fig. 1. Experimental setup: Six pressure-monitoring lines were placed, in the carotid artery and internal jugular vein of fetus and ewe, in the amniotic cavity, and in the abdominal cavity of the ewe. Fetal heart rate was determined from the arterial line. An insufflator was attached to a second trocar.

following experimental protocol was performed: Anesthesia was induced with diazepam and ketamine. After intubation, anesthesia was maintained with halothane 1%, nitrous oxide 48%, and oxygen 50%. Ventilation was initiated at a tidal volume of 10 ml/kg at 12–15 breaths/min, and adjusted slightly (TV ± 50 ml) if initial maternal Pco_2 was >37 mmHg or <33 mmHg. After reaching the desired maternal Pco_2 range the ventilator settings were not altered, except in part II (below).

A laparotomy and hysterotomy were performed. The head of the sheep fetus was exteriorized and two 1.3-mm polyvinyl chloride (PVC) catheters were placed, through a cut-down, into the carotid artery and internal jugular vein of the fetus. Each catheter was passed 8 cm, centrally. Similarly, two 1.7-mm PVC catheters were placed through a cut-down into the carotid artery and internal jugular vein of the ewe and passed 10 cm proximally. A fifth monitoring catheter was left in the amniotic cavity, and the uterus was closed with suture. Prior to closing the abdominal wall two 10-mm disposable trocars (Ethicon Endosurgery, Cincinnati, OH) were placed across the abdominal wall on either side of the incision. One trocar was connected to a pressure transducer through standard insufflator tubing and the other trocar was connected to a Solos high-flow insufflator (Birtcher, Inc., Irvine, CA). The abdominal wall was closed with a running Prolene suture. All six pressure-monitoring catheters were attached to Stratham-Gould pressure transducers (Gould, Inc., Oxnard, CA) which were attached to an eight-channel R612 Dynograph strip recorder (Beckman Instruments, Inc., Schiller Park IL). Fetal pulse rate was measured on a seventh channel (Fig. 1).

Experimental protocol

I. Control: no pneumoperitoneum

Control data were obtained in each sheep over a 30–120-min period, during which the intraabdominal pressure was zero. Fetal and maternal hemodynamics were recorded on the strip recorder as described above. Every 15 min, an arterial blood gas (ABG) sample was drawn from the fetus and ewe. Standard blood gas analysis was performed with an IL482 CO oximeter (Instrumentation Laboratories, Lexington, MA).

II. Intraabdominal pressure constant (six sheep)

After acquisition of control data, the peritoneum was insufflated with either nitrous oxide (two ewes) or carbon dioxide (three ewes) or carbon dioxide followed by nitrous oxide (one ewe) to 15 mmHg pressure. The ewe was positioned in 10° reverse Trendelenburg position. Over the next 90–120 min—the duration of a difficult laparoscopic cholecystectomy—hemodynamics were constantly measured and blood-gas determinations were made each 15 minutes. In one preparation, fetal metabolic acidosis and bradycardia were managed with intravenous $NaHCO_3$ and abdominal desufflation, respectively.

In the four ewes undergoing carbon dioxide pneumoperitoneum, end-tidal Pco_2 ($ETPco_2$) was followed with a capnograph (Novametrics model 1260, Wallingford, CT). In the first two ewes, tidal volume and respiratory rate were increased in an attempt to keep end-tidal CO_2 at the same level as before pneumoperitoneum. In the second two ewes $ETPco_2$ was recorded, but no ventilator adjustments were made.

III. Intraabdominal pressure varied (two sheep)

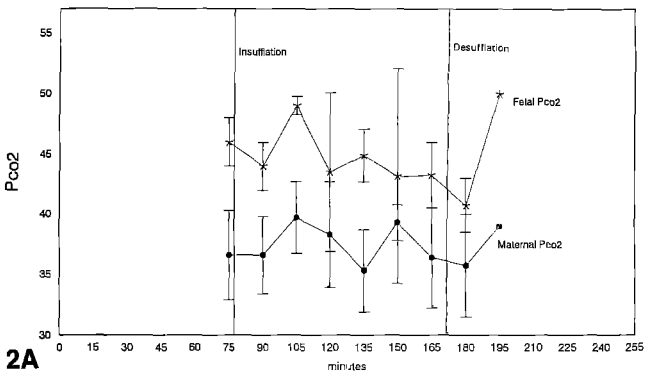
In the remaining two ewes a carbon dioxide pneumoperitoneum was induced in a stepwise fashion by increasing intraabdominal pressure 5 mmHg each 15 min until a pressure of 25 mmHg was reached. At each interval hemodynamic and blood-gas assessments were performed for fetus and ewe.

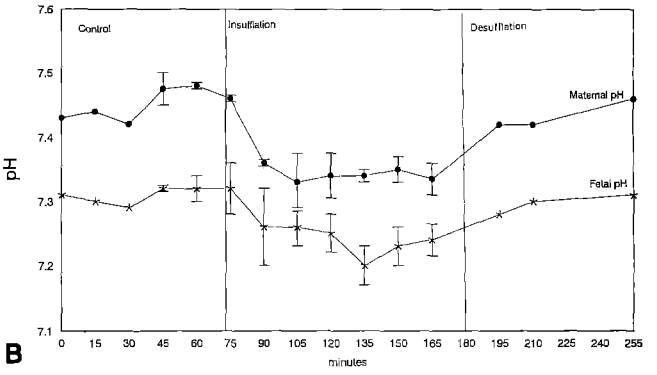
IV. Recovery

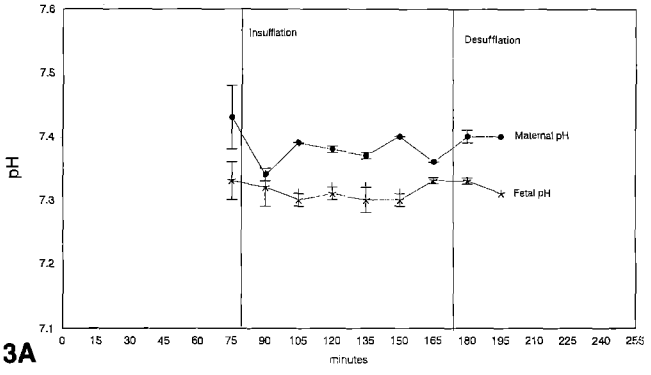
After the experimental data had been acquired, the pneumoperitoneum was released and ABGs were obtained until the pH and Pco_2 had nearly returned to baseline values. Euthanasia was achieved with Beuthanasia-D (Burns-Biotec, Omaha, NE).

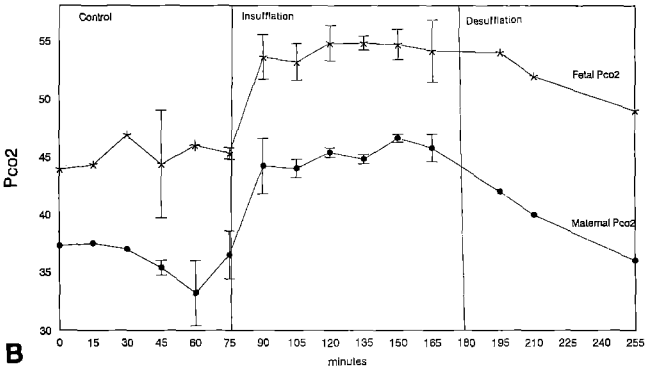
Data analysis

From 15 min after the onset of pneumoperitoneum (or control period) fetal arterial pH values were collected and recorded as the change from baseline pH; the differences were summed to arrive at the integrated change in pH. Change in fetal pH was compared between the control, N_2O, and CO_2 pneumoperitoneum groups with analysis of variance (ANOVA) using Epi-Info version 5 (USD Incorporated, Stone Mountain, GA).









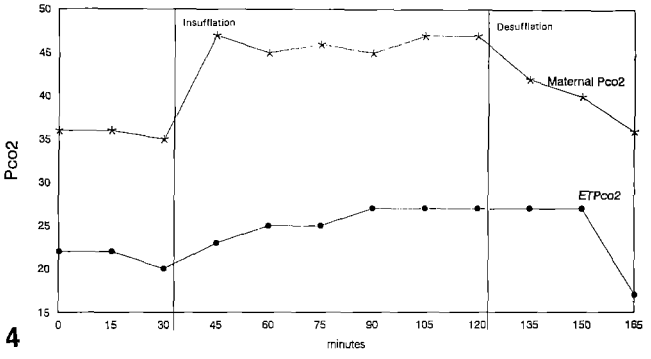


Fig. 2. **a** Mean arterial Pco_2 during N_2O pneumoperitoneum (n = 3). **b** Mean arterial Pco_2 during CO_2 pneumoperitoneum (n = 4).

Fig. 3. **a** Mean arterial pH during N_2O pneumoperitoneum (n = 3). **b** Mean arterial pH during CO_2 pneumoperitoneum (n = 4).

Fig. 4. Maternal end-tidal Pco_2 and arterial Pco_2 during CO_2 pneumoperitoneum (15 mmHg) without ventilator adjustment.

Results

Seven of the eight fetuses survived the 2-h pneumoperitoneum, and they had nearly returned to prepneumoperitoneum physiology at the end of the protocol. The fetus that died experienced severe metabolic acidosis and bradycardia. At the time of hysterotomy for central venous line placement, this fetus appeared mildly cyanotic and its fetal arterial blood gases revealed a metabolic acidosis. Sodium bicarbonate was administered, the uterus and abdomen were closed, and a CO_2 pneumoperitoneum was initiated. Eight minutes later the fetus became profoundly bradycardic (pulse—60/min). The pneumoperitoneum was released, and fetal pulse returned to 160/min. Five minutes later, shortly after reinsufflation, the fetus again became bradycardic, but the bradycardia was not reversed by desufflation and the fetus died 5 min later. Autopsy did not show a technical problem with experimental setup or intrauterine fetal position.

I. Control

There were no changes in maternal or fetal hemodynamics or acid–base balance during the control period (Figs. 2, 3). In one fetus, the heart rate declined 20% over 90 min, most likely signifying recovery from laparotomy and hysterotomy.

II. Intraabdominal pressure constant

a. Acid–base balance

After insufflation to 15 mmHg with carbon dioxide, there was a decline in maternal pH and rise in Pco_2 (Figs. 2, 3). Fetal arterial pH and Pco_2 followed maternal pH without time delay. On several occasions fetal pH, normally 7.33 ± 0.02 (mean ± standard deviation), fell below 7.2 while Pco_2, normally 44 ± 0.3 mmHg, rose above 55 mmHg. When nitrous oxide was used to create the pneumoperitoneum, there was no

Table 1. Decrease in fetal pH during 90-min pneumoperitoneum

	Control no pneumoperitoneum	N_2O pneumoperitoneum	CO_2 pneumoperitoneum
Mean	0.01	0.01	0.08*
Standard deviation	0.005	0.02	0.01

* $P < 0.0001$.

Table 2. Effects of increasing pneumoperitoneum pressure on fetal physiology and arterial blood gases ($n = 2$)

Intraabdominal pressure	Mean corrected fetal arterial pressure (mmHg)[a]	Mean fetal heart rate	pH	Mean fetal Pco_2 (mmHg)	Mean fetal arterial Po_2 (mmHg)
0	41	170	7.32	44	27
5	42	167	7.31	47	27
10	37	185	7.30	47	28
15	37	190	7.31	48	27
20	37	202	7.27	52	27
25	40	210	7.26	55	28

* Corrected fetal arterial pressure = mean fetal arterial pressure-amniotic pressure.

change in fetal or maternal pH or Pco_2 ($P < 0.0001$) (Table 1).

In the CO_2 pneumoperitoneum preparations, when $ETPco_2$ was recorded but the ventilator was not altered (two ewes), there was a 60 minute lag time between the plateau in maternal Pco_2 and $ETPco_2$ (Fig. 4). As well, $ETPco_2$ was 15 mmHg below arterial Pco_2 at a steady state and lagged further behind immediately after abdominal insufflation with CO_2. When respiratory rate and tidal volume were increased to offset this trend, acidosis was improved, but capnography exaggerated the improvement. The difference between arterial Pco_2 and $ETPco_2$ was increased under these circumstances. Thus, ventilator adjustments made in response to $ETPco_2$ lagged far behind the development of acidosis in fetus and ewe.

b. Hemodynamics

Tachycardia (fetal pulse >200) was seen in three of four fetuses and one of three fetuses during CO_2 and N_2O pneumoperitoneum, respectively. A mild decrease in pulse rate was seen in one fetus undergoing CO_2 pneumoperitoneum. There were few perceptible changes in maternal hemodynamics in any preparation. Amniotic fluid pressure and fetal central venous pressure responded directly with changes in intraabdominal pressure. Fetal arterial pressure increased by 10–15 mmHg during CO_2 pneumoperitoneum, but did not change with N_2O pneumoperitoneum.

c. Oxygen delivery

Except in the fetus which succumbed, fetal arterial Po_2 stayed within 4 mmHg of the starting Po_2 (range 21–31 mmHg) throughout the protocol.

III. Intraabdominal pressure varied

The stepwise increase in the CO_2 pneumoperitoneum pressure caused a stepwise increase in fetal arterial pressure, fetal heart rate, and fetal arterial Pco_2 and a commensurate decrease in fetal Pco_2 (Table 2). The most dramatic increase in Pco_2 and decrease in pH occurred with pneumoperitoneum pressures greater than 15 mmHg.

Discussion

Laparoscopic cholecystectomy has much appeal to the pregnant female with biliary colic. The pain of an open cholecystectomy in the middle of pregnancy might be greater than at other times, because of the increased abdominal wall tension associated with pregnancy and the desire to minimize the postoperative use of narcotics. The morbidity associated with shallow breathing, inability to cough, hypercoagulability, and inactivity might be avoided by performing laparoscopic cholecystectomy in this group of patients. Balanced against these advantages are the potential adverse effects of the pneumoperitoneum to the fetus.

The pneumoperitoneum affects the fetus in two ways—by directly increasing pressure on the uterus and by altering maternal hemodynamics and acid–base balance. In these experiments, we demonstrated no adverse fetal effects of increased intraabdominal pressure alone. When N_2O was used to create a pneumoperitoneum, the pressure transmitted through the uterus raised fetal CVP, did not change fetal blood pressure, and had no affect on fetal blood-gas values, suggesting that fetal cardiac output was not significantly changed. When CO_2 was used to create a pneumoperitoneum, fetal pulse rate and mean fetal blood pressure were elevated in three of the four prepara-

tions, paralleling the development of fetal acidosis. Because these effects were not seen with a N_2O pneumoperitoneum it is most likely that fetal tachycardia and hypertension were caused by hypercarbia and not by increased intraabdominal pressure.

The most dramatic change in fetal and maternal physiology we observed in this experiment was the development of respiratory acidosis during a pneumoperitoneum. Fetal pH decreased by 0.08 ± 0.02 in concert with similar changes in the ewe. These changes were only partially ameliorated by increasing ventilatory parameters to keep $ETPco_2$ constant. (See discussion below.) The sheep fetus is very similar to the human fetus in that a mild respiratory acidosis is normally (pH ~7.35, Pco_2 ~45 mmHg) [7]. Carbon dioxide produced by fetal metabolism is eliminated by passive elimination across the placenta, and the rate of diffusion is dependent on fetal cardiac output and maternal Pco_2. Under physiologic conditions, the pregnant sheep (and human) maintains a mild respiratory alkalosis (pH ~7.43, Pco_2 ~35 mmHg). The normal carbon dioxide and pH gradient across the placenta is 8–10 mmHg and 0.05–0.08, respectively. Maternal hyperventilation and alkalosis help minimize fetal acidosis. If maternal respiratory acidosis is allowed to occur, fetal acidosis worsens. One potential benefit of mild fetal acidosis is to improve tissue oxygen unloading by right-shifting the fetal hemoglobin dissociation curve. This might be particularly important given the extremely low normal fetal arterial Po_2 (25–30 mmHg). There was little change in fetal Po_2 during these experiments, suggesting that maternal oxygenation and maternal and fetal cardiac output were maintained despite the perturbations in acid–base balance.

The long-term effects of a short period of fetal acidosis (pH 7.25–7.33) for 90 min during the midtrimester of pregnancy are unknown. It is generally felt that fetal pH <7.25 is worrisome, and <7.20 is dangerous [7]. The long-term effects of a brief period of fetal hypercarbia are also unknown. It is well known that hypercarbia will cause tachycardia and mild hypertension in adults. In the sheep fetus, tachycardia and mild hypertension were frequently observed in association with hypercarbia, but tachycardia was also seen shortly after establishing invasive monitoring and once during a N_2O pneumoperitoneum.

Because of the expense and ethics of a large animal study, this study only involved eight ewes. While this limited our ability to make statistical inferences, we were still able to gain significant insight by making multiple observations on each animal. An additional limitation of the acute preparation was the inability to follow the ewes until delivery. A small clinical experience suggests that there is no increase in prematurity in women who have undergone laparoscopic cholecystectomy during the second trimester of pregnancy [2, 4, 6, 12, 16, 17].

Except in patients with chronic pulmonary disease, respiratory acidosis occurring during laparoscopic surgery is easily corrected by the anesthesiologist, who increases ventilator rate and tidal volume. Continuous end-tidal capnography provides the data to make immediate ventilator adjustments to correct the respiratory acidosis associated with a CO_2 pneumoperitoneum. From this protocol it is clear that there is a significant lag time between changes in maternal arterial CO_2 and end-tidal Pco_2. In this protocol, the steady-state difference in maternal $Pco_2$and $ETPco_2$ was 15 mmHg, but this difference rose to 25 mmHg immediately after the pneumoperitoneum was initiated and took nearly an hour to again reach a steady-state difference of 15 mmHg. While capnography is a good noninvasive method for determining the adequacy of ventilation, there are certain situations in which more immediate and accurate information is needed, requiring that an arterial line be placed. Pregnant patients and patients with cardiopulmonary diseases should have arterial lines placed during laparoscopic surgery.

The ventilator adjustments which will correct respiratory acidosis are to increase the respiratory rate and/or to increase the tidal volume. Increasing the ventilatory rate will decrease alveolar Pco_2, but at some cost. By diminishing the time for alveolar and inspired gas mixing, an increased ventilatory rate will increase dead space ventilation to a greater degree than it increases alveolar ventilation. As respiratory rate increases, the $ETPco_2$ becomes a less-accurate reflection of alveolar and arterial Pco_2. In other words, increasing ventilatory rate to keep $ETPco_2$ constant will not necessarily keep arterial Pco_2 constant. Increasing tidal volume, the other means of increasing ventilation, will increase ventilation perfusion (V/Q) mismatching. The additional airway pressure necessary to generate greater lung volumes will decrease capillary perfusion, resulting in lung segments with high V/Q ratios. By increasing alveolor dead space in this manner, $ETPco_2$ becomes less reflective of arterial Pco_2 [18].

One of eight fetuses died during this protocol. While it was apparent that preterminal bradycardia was potentiated by the pneumoperitoneum, it was equally apparent that the fetus was unhealthy from the moment its head was delivered through the hysterotomy. Any or all of the additional stresses imposed by this model on the unhealthy fetus, including CO_2 pneumoperitoneum, may have contributed to its demise.

Nitrous oxide pneumoperitoneum caused insignificant changes in fetal hemodynamics and acid–base balance in this protocol. For this reason, there might be some advantage to using this agent or an inert gas in pregnant patients. Reports of the combustion risk of N_2O are questionable at best [5]. Gynecologists at Emory University have used electrosurgical energy to create sparks in a nitrous oxide environment to perform tubal ligation procedures in over 1,500 patients without adverse event (Warshaw, Jeff, personal communication).

It has been suggested that abdominal wall suspension techniques should be used in the pregnant patient. Experience with these devices has been limited, but two shortcomings are immediately apparent. Exposure with the "lift" device is inferior to conventional pneumoperitoneum exposure, because it does not increase intraabdominal volume, allowing the bowel to

be displaced from the surgical field. In addition, the "lift" will cause standard retraction pain if placed under the right costal margin to allow exposure of the right upper quadrant.

Despite many missing answers to the questions about pneumoperitoneum safety and fetal physiology, laparoscopic cholecystectomy has been performed successfully and reported in 21 patients without a major obstetrical or fetal complication [2, 4, 6, 12, 14, 16, 17]. Most recommendations for "safe" laparoscopy in pregnant patients are borrowed from the literature on appendicitis and cholecystitis during pregnancy [1, 3, 8, 10, 11]: Indications for operation must be strict. Patients referred for cholecystectomy should have daily biliary colic and/or weight loss. Operation should occur during the second trimester but before the 23rd week of pregnancy to minimize the risk of preterm labor [10] and to maintain adequate intraabdominal working room [16]. Tocolytics are beneficial to arrest preterm labor [1], but their prophylactic use during and after laparoscopic cholecystectomy is debatable [16]. Fetal monitoring with standard transabdominal stethoscopes becomes difficult with the abdomen inflated, but transvaginal ultrasonography allows continuous monitoring of fetal pulse rate [6]. Abdominal access should be achieved with open laparoscopy (Hasson technique) to minimize the risk of injuring the uterus or pelvic veins. Cholangiography should be performed selectively, when suspicion of choledocholithiasis is high, and the lower abdomen should be protected with a lead shield. Most importantly, informed consent must offer our incomplete knowledge about the adverse effects of pneumoperitoneum to the fetus, and clearly offer open cholecystectomy as the conservative option.

General anesthetic management of the pregnant patient undergoing laparoscopic cholecystectomy requires a sound knowledge of the physiology of pregnancy. Mechanical ventilation must be adjusted to maintain a physiologic maternal alkalosis, and further adjustments must be made after the pneumoperitoneum is initiated. When a rapid ventilator rate or large tidal volumes are necessary to maintain desired ET-Pco_2 levels, the measured $ETPco_2$ will be a less accurate reflection of arterial Pco_2 than when more physiologic ventilation parameters are used. For this reason, it would seem prudent to place an arterial line in the pregnant patient undergoing laparoscopic surgery and frequently check arterial blood gases to insure that maternal respiratory alkalosis is maintained.

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Discussion

Dr. Apelgren: (East Lansing) I have one comment and one question.

In your presentation, I think you ought to avoid the use of the word "abort." You're talking about aborting the procedure, not the fetus.

The question I had was: Did you see any effects from pressure differentials? You said in the beginning that you took the pressure gradually up. But was there any difference between, say, ten millimeters and 20 millimeters?

Dr. Hunter: I didn't show those graphs because they are really quite boring, and they reproduced what we had seen in earlier studies in which a pneumoperitoneum up to 20 millimeters of mercury had no effect on the hemodynamics, and it was the same all the way up. The only thing that you see hemodynamically is that there is a direct transmission of the intraabdominal pressure to the amniotic cavity and to the fetal central venous pressure. The best we can say from the blood gas analysis is that it has no effect on cardiac output until you get up above 20, at which point it did start to have an effect.

Dr. Wolfe: (Sacramento) I'm fascinated by these studies and particularly by the exaggerated acidemia and hypercarbia that the fetus has showed. I would assume at a steady state that there should be a relative equilibrium in P_{CO_2} and pH between the fetus and the maternal circulation. If there is not, perhaps there is an impaired buffering capacity on the part of the fetus at this point in development, which would make the fetus more susceptible to hypercarbia and acidosis. I would agree that it's virtually impossible to know whether this is bad for a fetus or not. I'm particularly concerned with the bradycardia that these fetal hearts showed, because we think of hypercarbia as inducing a catechol release, which is at least the standard explanation for the mediation of tachycardia and increased vascular resistance that we've all seen when we've done studies with CO_2 pneumoperitoneum. A bradycardia is the reverse of that. Might it be hypoxemia or some immature catechol response in fetuses? I really don't know much about fetal physiology, but certainly it does seem concerning.

Dr. Hunter: The PO_2 in the fetus was remarkably well preserved. PO_2s run very low in the fetus at about 30 torr, and that was preserved throughout these experiments.

Now, I don't know what to make of the fetal pulse rate. Initially I thought that we were going to see tachycardia, and we did in a few of our early ones. But then we saw bradycardia in a couple and no change in another couple. And I wonder whether the effects of preparation, the surgery necessary to establish the preparation, the anesthetic agent and all those other factors such as stress factors on the fetus may have played as important or more important a role in fetal heart rate than the actual pneumoperitoneum. We did see a steady state, and I think that the slides I showed of the two graphs of carbon dioxide and pH as a function of time showed steady state levels reached about 30 minutes after initiation of pneumoperitoneum, and the pH in the fetus did not drop any below that.

Dr. Eubanks: (Durham) It's a very nice study and I applaud your efforts to add some scientific information to what is currently primarily anecdotal literature with laparoscopy in the pregnant patient.

Two questions: First of all, did you evaluate uterine blood flow with both normal and supranormal pneumoperitoneum; and then secondly, our greatest risk with open or laparoscopic procedures in the pregnant patient is that of fetal loss. In your study with the eight ewes, you only saw fetal loss in one situation which you felt was explained. Do you feel that with greater numbers, even though it's a laparoscopic approach, we're going to see fetal loss, and if so, what would the mechanism be? Is it CO_2 and acidosis, or is there another mechanism?

Dr. Hunter: I'm not sure we have the data to answer that. Anything would be pure conjecture as to whether there would be more fetal loss with more numbers. It's a fairly expensive set-up to run and time consuming, and I do apologize for small numbers. I'd like to have a series of 40 of them, but I just couldn't do that.

I think the only way to respond to the question is that with the exception of the one fetus that died, all the changes we saw were reversible, and by the time we quit our study about an hour after desufflating, the PCO_2s and pHs had returned to normal. So I think that in the healthy fetus, there is a fairly rapid recovery.

Dr. Roberts: (Sacramento) I have a question about the alternative gasses. I saw that you used nitrous oxide and had a very interesting result, that it didn't show a lot of the same hemodynamic effects as CO_2. That seems to be supported with other literature in pigs and laparoscopic cholecystectomy. I have a question about the inability of nitrous oxide to suppress combustion.

Dr. Hunter: There is some laboratory data and some clinical data, and I'll try to answer this quickly. The laboratory data we presented as a poster last year. We determined from chemistry textbooks that the environment at which nitrous is combustible requires a five percent concentration of methane or hydrogen. In our experimental protocol we took samples of gas from the peritoneum during stages of several different laparoscopic procedures and ran them on a mass spec. We found that there was no methane in any of the specimens, and that we saw parts per million of hydrogen. So our conclusion was that nitrous oxide may be safe. The clinical data comes from the Grady Hospital where for the last five years the gynecology service has been performing tubal ligations with large amounts of electrosurgical energy under local anesthetic with a nitrous pneumoperitoneum. There are two reports, one is from Sri Lanka and one is from Egypt, involving combustion, and they are very sketchy. So I think we'd have to re-look at this issue.

Dr. Traverso: (Seattle) John, you are to be congratulated for taking a repetitive problem that we have with laparoscopic surgery and for going to the lab and getting us some answers.

When I last reviewed it, the literature stated that with open cholecystectomy, the incidence of spontaneous abortion is less than that of spontaneous abortion in the general population, if you review all those studies. So the literature is confusing at best. So that's why this information is very helpful.

My question is: Why did you choose the end of the second trimester to evaluate this problem when there are really two times when laparoscopic cholecystectomy is bothersome to us to advocate that it should be done. One is when the uterus is so large, and the other is in the first trimester. I presume maybe you couldn't cannulate the fetus in the first trimester in sheep. But that's really where the questions are asked.

I'd also like to ask your recommendation, if a

woman in her first trimester has biliary colic, not acute cholecystitis, but biliary colic, what would your advice be with this information?

Dr. Hunter: To answer your first question, I agree that I pushed our physiologist as hard as I could to do early cases, because I wanted to get early in the second trimester or even in the first trimester. And the answer was that they just couldn't get the lines in. We used a 1.3 millimeter external diameter line as it was. With modern technology, it may be possible to cannulate and get this data at an earlier phase.

The second question was: What do you do with a first trimester patient with biliary colic? I don't think all the answers are in about anesthesia. I've heard a variety of answers. My clinical approach would be to do everything I could to get them into the second trimester and then do a laparoscopic cholecystectomy with close monitoring and informed consent about the unknowns of laparoscopic cholecystectomy in the pregnant patient.