RECURRENT LOW BIRTH-WEIGHT INFANTS

Although much progress has occurred throughout the nation in the past 10-20 years in the reduction of perinatal mortality and morbidity, problems still exist which result in less-than-optimal offspring. One of these is that of the low birth-weight infant from an obstetrical point of view.

Review of perinatal statistics at Denver General Hospital over the past decade shows (1) that perinatal mortality has dropped about 50% but (2) that the incidence of infants born weighing less than 2500 grams is still 14% which is far too high. 1971 data indicate that (1) a substantial number of mothers delivering truly premature or small-for-gestational-age infants are "normal" and without apparent cause for either premature labor or the low infant birth weight and (2) many "normal" multiparas who deliver one such infant go on to deliver another premature or S. G. A. child in the future.

In short, adequate prenatal care does not seem to be doing much for many apparently normal mothers who give birth to repeated low birth-weight infants.

Time and effort must be devoted to women who deliver one or more small infants to find and correct causes, many of which are not apparent, both during the interconceptional period and in the subsequent pregnancy.

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THE EFFECT OF 17, B-ESTRADIOL ON UTERINE BLOOD FLOW AND
DISTRIBUTION OF BLOOD FLOW BY THE RADIOACTIVE MICROSPHERE METHOD

It has been suggested that subnormal uterine blood flow (UBF) causes retarded fetal growth and development. The control of UBF is unknown at present, but past studies suggest that the partial pressures of the respiratory gases have no direct effect. The control of UBF may be hormonal. Exogenous estrogens have been shown to cause a rise in UBF in the nonpregnant ewe. Utilizing a new animal preparation which permits the infusion of estradiol into chronic, unstressed, nonpregnant, ovariectomized ewes, the distribution of blood flow and UBF were measured by means of electromagnetic flow probes and radioactive microspheres before and after IV infusion of 17, B-estradiol. The UBF increased as high as thirteenfold of the control values, or flows of 300-400 cc/min. Approximately 30% of the UBF after the administration of estradiol went to the uterine caruncles, or sites of possible implantation. The increase in UBF seen after estrogen administration in the standing, nonstressed animal was much greater, at least twofold, than that observed under conditions of surgical stress.

The ability of physiologic doses of estradiol to cause a rise in UBF to levels generally observed in the ewe at midpregnancy supports the hypothesis that estrogens play an important role in the control of UBF.

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Ritodrine HCl was given by intravenous infusion to 23 pregnancies to determine its effect on uterine motility, and on the maternal and fetal cardiovascular system.

In 12 term pregnancies an infusion of Ritodrine HCl (100 mcg/min) was begun during established labor (3-4 cm cervical dilation) and increased until uterine contractions were considerably reduced. The infusion was then maintained at that effective dose for one hour. Uterine motility and fetal heart rate were monitored by internal methods. There was a significant reduction in frequency of contractions for 90 min., amplitude for 150 min., and units of activity for 150 min. The fetal heart rate increased, however, this increase was significant only for the first 30 min. post infusion. There was a significant increase in maternal heart rate during and 1 hour post infusion; a significant decrease in mean diastolic pressure during the infusion but no significant increase in systolic pressure. There were no significant changes in fetal scalp or maternal venous pH, PO2, PCO2, or base deficits during or post infusion.

In 11 cases of premature labor Ritodrine HCl was infused either until labor stopped or until there was evidence for treatment failure. Uterine motility and fetal heart rate was monitored by external methods. Labor was successfully inhibited in 7 cases. Similar significant findings were observed for fetal and maternal heart rate and maternal diastolic pressure during the infusion. The infusion was maintained for approximately 12 hours after which an oral preparation of Ritodrine was given. In six cases labor was successfully prolonged on the oral preparation. In 4 infusion cases (2 marginal abruptions, 1 incompetent cervix, 1 normal) Ritodrine failed to control uterine motility.

These preliminary studies suggest that Ritodrine hydrochloride effectively inhibits uterine motility with relatively few maternal or fetal side effects. It may be useful in certain cases of premature labor.

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*DU-21220 Investigational Drug. Philips Roxane Laboratories, Inc., Columbus, Ohio
FETAL GLUCOSE AND O₂ UPTAKES IN FED AND STARVED SHEEP

It is known that severe and prolonged maternal undernutrition can reduce the birthweight of fetal lambs. Our studies were aimed at determining umbilical O₂ and glucose uptakes (\(\dot{Q}_O₂, \dot{Q}_G\)) and the placental clearance of glucose (\(C_G\)) in late gestation and to observe the effects of acute maternal starvation on these variables. \(C_G\) was estimated as the ratio of \(\dot{Q}_G\) over the glucose concentration difference between maternal and umbilical arteries. In chronic, unstressed sheep preparations, fetuses were studied repeatedly for up to 21 days. In each study, umbilical blood flows, glucose and O₂ contents in umbilical arterial and venous and maternal arterial blood were determined on 5-7 samples. In the fed group, \(\dot{Q}_O₂\) increased significantly with time (~2%/day), but there was no significant growth of \(\dot{Q}_G\) or \(C_G\). Hence, the glucose/oxygen quotient decreased from ~0.7 at 120 days to ~0.3 at 140 days gestation. The constancy of \(C_G\) with age is in contrast to the previously observed growth of urea and antipyrine clearances. In the starved group, the \(\dot{Q}_G\) per kg. of fetal body weight was lower than in the fed group (2.7 vs. 6.4 mg. / min·kg. respectively) and there was no appreciable growth of \(\dot{Q}_O₂\). The efficiency of placental glucose transfer, as measured by the glucose clearance, was not increased by starvation.

These studies provide the first demonstration that placental glucose transfer does not grow in proportion to fetal O₂ consumption and that maternal starvation over a comparatively short time span has a demonstrable effect upon both glucose and O₂ utilization by the fetus.

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Seventy-nine normotensive pregnant women undergoing cesarean section were divided into two groups to study the value of lower extremity support in reducing the need for vasopressor therapy of spinal hypotension. Physiologic means (i.e., preloading intravenous fluid administration, placement in a slight Trendelenburg position, further rapid infusion of fluids to treat hypotension, and LUD) were employed in both groups. The incidence of hypotension was similar in both groups with LUD proving to be the most effective way to reverse a decrease in blood pressure.

Our results failed to confirm that lower extremity support either lowers the incidence of post spinal hypotension or facilitates its treatment by other means. The use of elastic bandages or stockings cannot be recommended for this purpose.

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"BLOOD PATCH" FOR POST-LUMBAR PUNCTURE HEADACHE

The incidence of post-lumbar puncture headache ranges from 0.5 to 60 percent, averaging 18 percent in the post-partum patient. Leakage of cerebrospinal fluid through a rent in the dura which results in a decrease of CSF volume and traction on the lepto-meninges appears to be the cause of this type of headache.

Characteristics of post-lumbar puncture headache are:
1. Onset - when the patient is erect, one to several days after lumbar puncture.
2. Temporary Relief - when the patient is supine or by abdominal compression.
3. Duration - days (usually) to months (rarely).
4. Associated Symptoms - vertigo, nausea, vomiting and visual disturbances.

Treatment includes analgesics, abdominal binders, hydration and peridural injection of air or various solutions with varied success. The correction and/or prevention of the CSF hypovolemia is the key to effective therapy. Recently, the use of autologous blood injected into the peridural space has been suggested by Gormley; Ozdil and Powell, and is now being studied by Di Giovanni.

In our small series of twelve patients, we were able to completely relieve post-lumbar puncture headache by injection of 10 to 20 ml. of autologous blood into the peridural space with no discernible sequelae. We recommend this technique and encourage others to utilize it in selected patients to effectively decrease the stigma of post-lumbar puncture headache.

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This clinical study employed a standardized technique of performing epidural anesthesia for labor and delivery. Two different methods of dosing were selected, both using 2% lidocaine with epinephrine 1:200,000.

One method resulted in a large number of asymmetrical or unilateral blocks, requiring more frequent and larger doses of anesthetic to establish pain relief. The other method differed from the first in the route of administration of the drug and the position of the patient, and resulted in more symmetrical blocks, requiring smaller doses of drugs. The blocks obtained with this method were also more predictably adequate and required less supplementation to achieve good anesthesia.

Inadequate blocks were improved or corrected by changing the volume of drug used, the timing of the dose, the position of the catheter or the position of the patient. Radiopaque dye mixed with lidocaine was injected via epidural catheter in several patients and the distribution of the dye compared with the distribution of anesthesia as determined by sensitivity to pinprick.

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OBSTETRICAL USE OF ETHRANE

The new inhalational anesthetic Ethrane was employed for light general anesthesia for vaginal delivery in 50 patients. Clinical impressions were recorded as to effect of the anesthetic on uterine tone, estimated blood loss, and condition of the infant at birth. As more experience was gained, the agent was used to anesthetize mothers for the delivery of breech infants and twins.

Ethrane was administered by a non-rebreathing technique to patients in active labor who were continuously monitored by the intra-uterine pressure - fetal EKG monitor. Maternal arterial blood levels of Ethrane were obtained at various times during the anesthetic. Umbilical artery and umbilical vein Ethrane levels at birth were also obtained in several cases.

From this data it appears that Ethrane is a potent suppressor of uterine contractility at light anesthetic levels. As such, it may be useful in obstetrical situations requiring uterine relaxation, that is, version and extraction, difficult breech, shoulder dystocia, uterine tetany and uterine exploration. As with halothane, proper technique of administration and judicious use of pitocin is necessary to minimize blood loss after infant delivery.

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Ketamine was administered intravenously to 200 parturients for second stage of labor and vaginal delivery. The basis for administration of ketamine included inadequate regional anesthesia, sudden operative intervention, precipitous delivery, uncooperative and uncontrollable patient, patients requesting general anesthesia or unawareness of the event or outcome of the delivery. The ketamine was administered at an appropriate time just prior to delivery in doses of 12.5 to 25 mgm, with no patient receiving more than 75 mgm. The analgesia, following ketamine administration, was sufficient for vaginal delivery, was profound, and was associated with some retrograde amnesia. There were no associated complaints of moribund-type of hallucinations during the recovery phase. The incidence of neonatal depression was lower than that in a control group of patients delivering under other forms of anesthesia. The authors conclude that in carefully selected and indicated instances the use of ketamine can be safely administered to the parturient with little fetal or newborn effect.

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KETAMINE IN OBSTETRICS

Ketamine is being considered as an agent to be used in vaginal delivery. The purpose of our study was to evaluate the effects of low dosages of ketamine on both the mother and her baby.

Thirty relatively randomly selected mothers received ketamine. Patients excluded from this study were those in whom fetal distress had been demonstrated and those who had a systolic blood pressure of 150 mm. Hg or greater.

The mean dosage given to the mothers was 0.23 mg./pound with a range of 20 mg. to 60 mg. The anesthesia effect of the administered dosage was considered extremely adequate by all in the room. All mothers appeared asleep but did respond to direct commands. Of the thirty deliveries 26 were elective outlet forceps and four were spontaneous with fundal pressure. All mothers were awake and alert within one hour and no mother experienced any unpleasant dreams. In fact, all mothers awoke as if emerging from a "pleasant trip".

Based on the one minute apgar score thirty percent of the infants were depressed with the cry being the major factor. At five minutes ten percent of the infants were considered depressed. Delayed urinary excretion greater than 24 hours was noted in 3 of the babies and an inability to handle excess secretions in another three.

Ketamine while producing an ideal anesthetic situation in the mother is by no means innocuous to the infant. The neonatal effects appear to be closely related to dose and we are now in the process of attempting to lower dosages.

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Meperidine has been widely used as an obstetric analgesic agent. Many reports indicate that this drug should not be used in premature labor patients because of the frequency of the infants being depressed. Other reports have shown that a high incidence of depressed infants appear, whether premature or full term, when delivery is two to three hours after the administration of meperidine to the mother. Studies in our laboratory indicate that the in vivo metabolism of meperidine is closely related with infant depression. Patients included in this study had either full term or premature infants. None of the patients showed signs of biological or physical complications. All patients received 50 mg. of meperidine intravenously, and maternal blood samples were taken at specific time intervals during a six hour period after administration. A modification of the methyl orange method described by Burns et al. (J. Pharmacol. Exptl. Therap. 114, 289, 1955.) was used to assay for the presence of meperidine and certain of its metabolites. Three distinctive patterns of meperidine metabolism emerged. These patterns appear to be related to the rate of formation of metabolites of meperidine which are five to ten times more toxic than the parent compound. The pattern which showed the most rapid formation of metabolites was associated with the greatest percentage of depressed infants. In contrast the metabolic patterns which were slower in the formation of metabolite products were seldom associated with fetal narcosis. No infant, whether full term or premature, and regardless of the maternal serum pattern showed signs of depression when delivery was during the first hour following the administration of meperidine. However, when the time lapse between administration of meperidine and delivery exceeded one to two hours depressed infants were observed. The incidence of fetal depression was greatly increased in this time period if the maternal serum pattern resembled the more rapid type of meperidine metabolism. These metabolic decay curves are reproducible in the same individual many months apart and in the pregnant or nonpregnant state. These data support the proposal that infant depression, when meperidine analgesia is used, is directly related to two variables: 1) the length of time that the patient is in labor following the injection of the compound; and 2) the particular pattern of meperidine metabolites in the maternal serum. It is evident that prematurity has no effect on the number of depressed infants observed and it is conceivable that by using these assay procedures one might predict prior to delivery which patient would have rapid rates of meperidine metabolism and therefore would have an instant increase in depression.

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BLOOD LOSS FOLLOWING FLUROXENE ANESTHESIA  
FOR CESAREAN SECTION - A CLINICAL STUDY

The purpose of our study was to evaluate the halogenated inhalation agent, fluroxene, regarding blood loss during Cesarean Section. Samples of heparinized blood were drawn before and after a measured amount of Evans blue dye was injected into the mother. Dye studies were performed both immediately pre-op and post-op. Fluroxene anesthesia was begun immediately upon intubation of the patient and was continued throughout the entire case. The concentration of fluroxene before delivery was 2% with oxygen and nitrous oxide being 50-50 with a total flow of 10 liters per minute. After delivery fluroxene anesthesia was increased as needed to provide an adequate surgical field. Evans blue dye was selected as a means of measuring blood loss due to the fact that the dye is incorporated by the plasma volume and blood volume can then be calculated. The method is simple and involves no radioactive dosages to the patient or the fetus. For comparison, a group of patients were studied utilizing halothane or regional anesthesia. To date a total of 20 patients have been studied.

Mean blood loss following fluroxene anesthesia was 1088 ml. ±455 ml. Studies are now underway utilizing halothane and regional anesthesia but not enough patients have been studied in order to provide a valid statistical comparison. Preliminary results show that the blood loss following halothane or regional anesthesia will be the same as the blood loss following fluroxene anesthesia.

The apgar score of the neonate showed only 10% were depressed at one minute. All neonates had apgar scores of greater than seven at five minutes. These apgar scores compare favorably to the apgar score of infants born following N₂O/O₂ anesthesia for section as done for the past year. The operative field did not appear to be grossly bloody and in fact the surgeons were not impressed either pro or con regarding the use and had no knowledge of when either inhalation agent was being used.

Blood loss following fluroxene anesthesia, halothane anesthesia, or regional anesthesia appears to be the same. Apgar scores of neonates born after the three types of anesthesia appear to be not significantly different and compare favorably to our overall neonatal depression rate. Fluroxene is another inhalational anesthetic agent that can be used in Cesarean Section as well as halothane without undo concern regarding excessive blood loss.

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USE OF CONTINUOUS NITROUS OXIDE INHALATION DURING OBSTETRICAL DELIVER

INTRODUCTION

During the past several years there has been a resurgence of interest in nitrous oxide for dental procedures; however, the application of the anesthetic gas has been not as the supplementary or major anesthetic agent but for its mild analgesic and narcotic properties. The property most desired by the dentists using the agent has been mild euphoria, cooperation, and relaxation. For this, dentists have been using a concentration from 30% to 60% delivered via nasal mask with no attempt to avoid air dilution during oropharyngeal route of respiration. After observing several demonstrations of this technique and the easy rapport dentists have with the patient during the period of use which might extend for as long as four hours, in addition to ready reversibility and complete recovery, we decided to apply this technique to the obstetric scene.

REPORT

A small series of 20 patients was done in a preliminary study. These patients were unpremeditated and although having had a complicated obstetrical course, were to be delivered vaginally. In all instances these patients were prima gravida with most having had breech presentations. The nitrous oxide was delivered from a standard anesthesia machine via a standard face mask (not the nasal mask technique but this may be readily accepted by patients who object to a mask over their face.) The nitrous oxide flow was 3 liters and oxygen at 5 liters. This mixture was administered continuously after a period of a few minutes of denitrogenization with 100% oxygen at 10 liters per minute.

RESULTS

Patients cooperated much more fully in such procedures as bearing down. A little discomfort was present when the needle was being used for the pudendal block but the patients rested comfortably between contractions and were alert, responsive and knew when a contraction started and finished. No complications arose. The nitrous oxide was stopped several minutes before the delivery was completed. All of the neonates responded well and rapidly, and cord blood Hs were in the range that would have been anticipated with the difficulties that the babies were having. All babies prior to delivery were monitored with fetal EKG's and Doppler Ultrasonic. No change occurred in the fetal cardiovascular reactions associated with the anesthetic except in three instances, less prominent decrease in heart rate occurred with the contractions.

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HEMODYNAMIC EFFECTS OF ACUTE INFUSIONS OF THAM OR BICARBONATE IN NEWBORN LAMBS

Following the implantation of electromagnetic flow probe on the main pulmonary artery and ligation of the ductus arteriosus in 6 newborn lambs, the acute hemodynamic effects of rapid infusion on 0.6 m THAM or NaHCO₃, 0.9 m Eq/ml in quantities and rates used in the resuscitation of newborn infants were studied 24-96 hours later in the non-sedated, non-anesthetized lambs. Catheters were placed in the IVC for infusions and in femoral and pulmonary arteries for recording pressures and sampling of arterial blood for pH, PO₂ and PCO₂ determinations. Cardiac output was calculated from mean main pulmonary artery flow measurements. In non-acidotic lambs breathing room air, THAM infusion increased cardiac output (P<.05) and lowered calculated systemic resistance (P<.05), NaHCO₃ also produced similar changes on the 4 occasions studied in non-acidotic animals. Neither drug caused significant changes in aortic pressures or pulmonary arterial pressures. In lambs made acidotic by breathing 10% CO₂ in air, THAM infusion resulted in a marked increase in cardiac output (P<.005) with significant fall in aortic pressure (P.01) systemic resistance (P.01) and pulmonary resistance (P.02), while NaHCO₃ increased cardiac output (P.05) without changing pressures or resistances significantly. All changes were maximal 1-3 minutes following completion of the infusions. These effects of THAM on systemic circulation and pulmonary vascular resistance in acidotic newborn lambs should be considered in using acute infusions to correct acidosis in the newborn infant.

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FACTORS AFFECTING THE HEART RATE IN THE NEWBORN

During the first half hour of extrauterine life, the neonate is subjected to many procedures. Among these are oxygenation, nasal and oral suction, nasal and gastric catheterization, digital rectal examination, and prophylactic treatment of the eyes for gonococcal infection. The physiological significance of these procedures is little understood.

This study attempts to evaluate the effect of these manipulations on the heart rate of the neonate. The electrocardiographic signal was processed by a commercial fetal cardiotachometer, and the heart rate was written out by a strip-chart recorder.

Transient heart rate decelerations were observed following various stimuli including oxygenation, nasal and gastric catheterization, and routine eye care. Episodes of breathholding were also noted, especially when oxygen was blown over the infant's face.

Although this study was restricted to normal infants, an occasional baby showed marked bradycardia with a rate as low as 80 beats per minute for a few seconds.

In several instances in which mothers received anticholinergics during labor, the infant heart rates remained stable in the face of these various stimuli.

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POSTOPERATIVE END-EXPIRED PRESSURE ADMINISTRATION IN RDS NEONATES VIA A FACE MASK

Because of the complications occurring with endotracheal intubation, various techniques have been devised to permit use of constant positive end-expired pressure without intubation. These have included the use of the Air Shields negative-pressure ventilator and various types of head boxes which will hold a positive pressure and allow exchange of CO₂. Mask use has been described and was first tried in the Intermountain Neonatal Intensive Care Center approximately 1 1/2 years ago on five infants and abandoned because of the complication rate, the most serious being acute gastric distention and the second most common complication being aspiration of regurgitated gastric contents. We have tried it again during this last year, using an indwelling gastric feeding tube with considerable success.

We now have a series of 20 patients receiving constant positive end-expired respiration with pressures up to 10 cm. H₂O, and we have had no incidence of aspiration or of gastric distention. A major series is needed to learn the effectiveness of this technique in terms of altering the natural course of the disease but our preliminary data indicate that in many neonates this has prevented the need for ventilator therapy and endotracheal intubation and shortened the period we have needed it in others.

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PROSPECTIVE ANALYSIS OF INFANT RESUSCITATION

This study was designed to correlate the specific details of infant resuscitation with development in early infancy. Neonatology literature regarding controlled resuscitation details with outcome of infants is indeed sparse.

All severely depressed newborn infants (one minute Apgar 0-3, or five minute Apgar 0-6) delivered at Grady Memorial Hospital during a period of 6 months are included in this study.

The infant was placed in a radiant heat environment, on its side, and with its head extended. Only bulb syringe suctioning was utilized. Artificial ventilation was initiated if adequate spontaneous respiration did not begin by one minute of life. In all cases initial ventilation was with a bag and mask and intubation was utilized later only if adequate ventilation was difficult to achieve. (3/23 total cases). Sodium bicarbonate was administered if inadequate improvement was observed by 4 minutes of life.

Careful follow-up of neonatal survivors was performed except in cases where the infant was not brought back for clinic visits. Perinatal pathology data is included in the results so that we have documentation of the cause of death in non-survivors. The Denver development chart was utilized to plot the development of all follow-up cases over a period of 6 to 16 months.

We are very encouraged by the apparent normalcy of our surviving infants, and feel that this study makes an attempt to relate details of resuscitation with outcome.

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