Using angiocardiology we studied twelve premature lambs of 130–145 days gestation (2.3–4.0 kg) obtained at caesarian section and maintained in a filtered and thermoregulated bath of synthetic amniotic fluid. By selectively varying the oxygen concentration in the gas compartment of the membrane lung we were able to control the level of blood oxygen tension independent of pH, PCO₂, and placental flow. Within 20 min after raising fetal umbilical pO₂ from 13–20 to 40–60 mm Hg there was almost total conversion of the fetal circulatory pattern to that of the newborn. The I.D. of the ductus arteriosus constricted from 4.1 mm to less than 1.0 mm; pulmonary circulation time decreased from more than 18.4 to 2.4 sec. These findings were not affected by metabolic or respiratory acidosis. Inferior vena cava injections illustrated complete closure of the foramen ovale; no opacification of the left atrium occurring at pO₂ from 40–60 mm Hg with a constricted ductus arteriosus. Oxygen consumption of fetuses paralyzed with succinylcholine measured continuously by spirometry averaged 6–7 ½ cm³/kg/min while carbon dioxide production was measured continuously by infrared analysis of effluent gas at 7–8.5 cm³/kg/min. Respiratory quotients consistently greater than one were observed with blood glucose levels above 100 mg%. Four fetuses were delivered following angiocardiological study; two are long-term survivors.

- 139 *Effects of Compression of the Umbilical Cord on the Unanesthetized Fetal Goat.* MOLLY E. TOWELL and HERMINIA S. SALVADOR, Dept. of Obstet. and Gynaecol., Univ. of British Columbia, Vancouver, B.C. (introduced by Sydney Segal).

Compression of the umbilical cord has previously been studied under acute experimental conditions but it is not known to what extent the effects are modified by anesthesia or the operative procedure. The purpose of these experiments was to investigate the effects of umbilical cord compression under relatively undisturbed conditions *in utero*. Seven fetal goats were prepared with intravascular catheters, subcutaneous electrodes and a device for compressing the umbilical cord with an inflatable balloon, by an operative procedure under halothane anesthesia. The fetus was replaced in the uterine cavity and the mother permitted to recover. Observations were made on heart rate (FHR), arterial pressure (FAP) and respiration of the fetus during and after cord compression. Arterial blood samples were analyzed at intervals for pH, PCO₂, PO₂ and O₂ saturation. During anesthesia and in the first few hours post-operatively, compression of the cord led to persistent bradycardia and elevation of FAP. After recovery from anesthesia cord compression was associated with a rise in FHR following bradycardia. Continued compression of the cord for more than 5 min led to a gradual fall in both FHR and FAP and severe fetal acidosis (arterial pH < 7.1). Respiratory movements *in utero* were induced by partial or total compression of the cord and were also seen during the recovery phase for as long as 60 min after release of the cord. It is concluded that halothane anesthesia may alter the response of the FHR to cord compression and that fetal respiration can occur *in utero* not only during intrauterine asphyxia but in the recovery phase as well.

- 140 *Glucose Oxygen Uptakes Across Umbilical and Cerebral Circulations of the Fetus.* NICHOLAS G. TSoulos, JAMES R. COLWILL, JACK M. SCHNEIDER, EDGAR L. MAKOWSKI, GIACOMO MESCHIA and

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Glucose has been considered the principal metabolic fuel of the mammalian fetus, but sound experimental evidence is lacking. In this study, the relative contribution of glucose to aerobic metabolism across the umbilical and cerebral circulations of fetal lambs was evaluated. The fetal vessels catheterized were: femoral artery and vein, umbilical vein, subclavian artery and periorbital vein. The arteriovenous differences in glucose and oxygen contents (Δ glucose and Δ oxygen) were determined from simultaneous samples across both circulations. The Δ glucose was expressed as the O₂ stoichiometrically required to metabolize glucose to CO₂ and H₂O. In six chronic, unstressed, unanesthetized animals, the Δ glucose/ Δ oxygen ratio across the umbilical circulation during control periods was 0.47 ± 0.04 (mean $\pm$ s.e.m.). Fetal infusions of porcine insulin increased the ratio by 90%.

We have attempted to compare metabolism in a single organ of the fetus, the brain, with that of the whole fetus (i.e. umbilical circulation) in acute experiments in seven fetuses. The ratio across the cerebral circulation was 1.5 ± 0.03 and across the umbilical circulation was 0.38 ± 0.03 . These data indicate that (a) under normal conditions, glucose supplies a maximum of 50% of the metabolic fuel of the fetal lamb, (b) exogenous insulin does affect fetal glucose uptake, and (c) in the acute preparation, the fetal brain utilizes more glucose than can be accounted for by aerobic metabolism.

- 141 *Inhibition of Mixed-function Oxidations by Pregnanolone: A Possible Basis for Impaired Drug Metabolism During Infancy.* LESTER F. SOYKA and LASZLO GYERMEK, Stanford Univ. Sch. of Med.

The presence of inhibitor(s) to explain impaired drug metabolizing capacity in the newborn remains an attractive, but unproven hypothesis. In the rat, by 3 days after birth, the endoplasmic reticulum assumes a mature appearance, but drug metabolism remains depressed until after weaning. Studies to date have failed to identify a particularly depressed component of the mixed-function oxidase system during the neonatal period. Progestational steroids are reasonable candidates for the role of physiologic inhibitors since their high levels late in pregnancy coincide with decreased drug metabolism of the mother and absent activity in the fetal liver. Moreover, inhibition of glucuronide conjugation reactions of liver microsomes by several steroids including progesterone, pregnanediol, and pregnanolone, has been reported. Pregnanolone (3 α -ol 5 β -pregnane-20-one) has been found in the human fetus after progesterone infusion and in the serum of newborn infants. Pregnanolone was a potent, non-competitive inhibitor of aniline hydroxylation and p-nitroanisole demethylation, typical reactions of the mixed-function oxidase system in rat microsomes. At saturating concentrations of substrate, inhibition by pregnanolone (5×10^{-4} M) was 20–40%. Duration of hypnosis in rats after hexobarbital and pentobarbital administration was prolonged by pretreatment with a non-hypnotic dose of pregnanolone. These results permit speculation on a possible role for pregnanolone and/or related steroids in the well-established decreased ability of newborns of many species to metabolize drugs. (Supported in part by USPHS Grant HD-03063.)