Research Summaries

Dr. Robert B. Bushnell, *Presiding*

Applications for Use of Chronically Instrumented Bovine Fetuses in Abortion Pathogenesis Studies

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Introduction

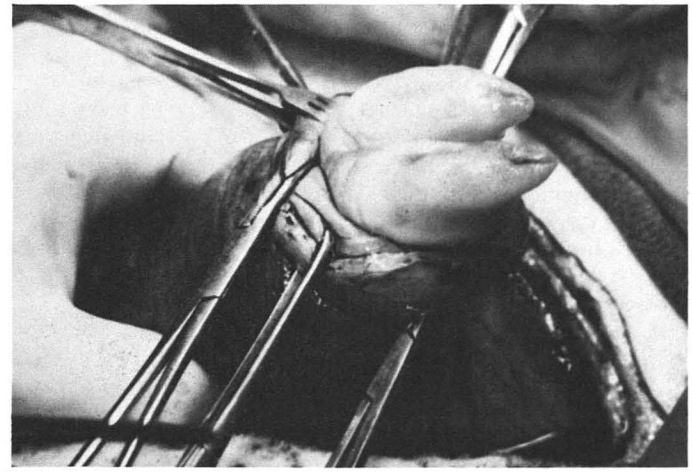
Our understanding of events leading to abortion in domestic animals is based on information from field cases or from experimental pathogenesis studies in which fetuses are collected by cesarean section or after euthanasia of dams. Because the fetus and placenta are relatively inaccessible, direct perturbation and/or sequential evaluation of the course of *in utero* events are difficult and have not been extensively utilized. The purpose of this communication is to transmit our initial experience with chronically catheterized bovine fetuses in abortion pathophysiology studies.

Methods

Twenty bovine fetuses between days 180 to 230 of gestation have undergone surgical placement of vascular catheters and other instrumentation *in utero*. Surgical procedures are conducted using halothane anesthesia of the dams. Surgical approaches have included paralumbar fossa, ventral abdominal midline, and paramedian approaches. Fetal vessels catheterized include tibial artery and vein, carotid artery and jugular vein, and umbilical artery and umbilical veins (Figures 1 and 2). Amniotic and/or allantoic catheters are also routinely placed. Catheters are maintained either by continuous infusion or by "loading" catheters with heparinized saline. In some animals, electromyographic (EMG) wires are sutured into the myometrium at different positions on the uterine wall.

The usefullness and potential applications of the chronically catheterized fetal preparations in research on pathogenetic mechanisms that lead to abortion are demonstrated in four pilot studies we have conducted: 1) clearance of particulate material from the fetal vascular system,[1] 2) predilection sites for fetal mycotic infection, 3) effect of short term occlusion of the maternal uterine blood supply on fetal oxygenation,[3] and 4) changes in fetal and maternal bovine placental lactogen during periods of fetal distress.[2]

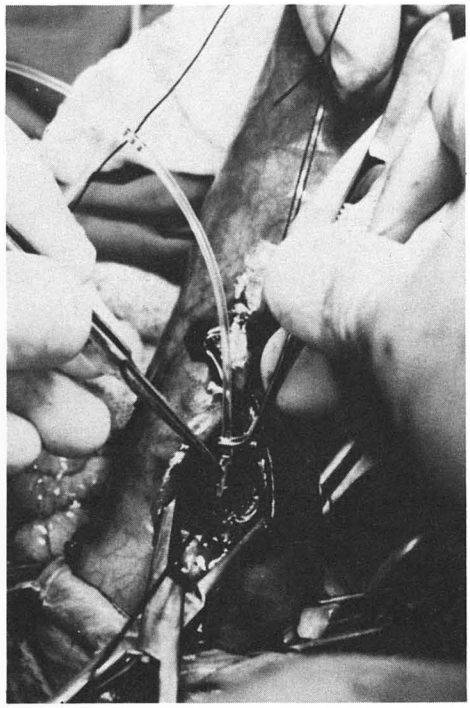
FIGURE 1. Surgical field showing hoof of fetal calf exteriorized through ventral midline abdominal incision. The placenta (chorioallantois and amnion) have been clamped to the uterine wall to prevent loss of allantoic fluids.



Results

1. *Clearance of particulate material (colloidal carbon) from the fetal vascular system.* Tissues from three fetuses injected with 20 mls of a colloidal carbon suspension via fetal vascular catheters (fetal aorta or fetal placental vein) were examined histologically for labeled phagocytic cells. Labeled cells were found in greatest concentration in fetal liver, spleen and adrenal cortex. Surprisingly very little circulating carbon was removed by cells in the fetal placenta.
2. *Predilection sites of mycotic infection in bovine fetuses.* Three bovine fetuses given intravascular injections of fungi were necropsied and fetal tissues examined histologically using Gomori's methenamine silver stain. Fungi established infection in the placentas of each fetus

FIGURE 2. Placement of vascular catheter into the tibial artery. The catheter is passed retrograde to position the tip in the caudal aorta. Potency was maintained over a period of 41 days in this fetus during which time daily fetal blood samples were collected.



but only a few small lesions were found in any other fetal tissue.

3. *Effects of occlusion of uterine blood supply on fetal oxygenation.* Fetal oxygen levels were monitored in instrumented fetuses before, during, and after periods of maternal uterine artery occlusion per rectum. Reduction in blood flow to the uterus for periods of 3 to 6 minutes caused fetal blood oxygen concentration to drop 2.7 to 6 mm Hg or on the average about 20% below baseline levels.
4. *Fetal and Maternal Bovine Placental Lactogen.* Fetal distress was reflected in changes in bovine placental lactogen (bPL) levels. Placental lactogen is a hormone produced by placental tissue in most mammalians and in some has been used as an indicator of fetal well-being. Preliminary studies of the potential application of bPL as a test of placental function and fetal health in cattle have been done. We have measured bPL in plasma from cows and their instrumented fetuses during surgery and for up to several weeks before premature delivery or abortion. Maternal bPL levels rose during surgery 130 to 300% of baseline values. Fetal bPL rose in one fetus twofold following acute reduction of uterine blood flow. Maternal and fetal bPL declined before abortion, occurring as early as 8 days before fetal death in one cow.

Conclusions

These preliminary experiments have demonstrated the usefulness of the chronically instrumented fetal calf both in understanding normal fetal-placental biology and for studying mechanisms involved in fetal losses. The examples presented deal with four different pathophysiological aspects of bovine abortion: 1) fetal defense mechanisms, 2) factors predisposing bovine fetuses to *in utero* infections, 3) effects of placental compromise on the fetus, and 4) fetal endocrine response to fetal distress.

Phagocytic cells responsible for clearing particulate maternal from the fetal vascular system were labeled by intravenous infusion of colloidal carbon. Tissues varies greatly in the concentration of labeled cells. A marked predilection for fungi to establish infection in the fetal placenta was demonstrated. A simple model of reduction of uterine blood flow has been described and effect on fetal oxygenation noted. Lastly, the usefulness of the chronically instrumented fetal calf in studying functional fetal placental biology in health and disease was demonstrated by monitoring fetal and maternal bovine placental lactogen changes during periods of fetal distress.

We feel that the chronically instrumented fetal calf has many applications in studies of fetal-placental pathophysiology and as such will become a valuable research tool in future studies of abortion pathogenesis.

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