A Discussion on Reproductive Failure in Cattle*

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Introduction

The terminology used in this discussion will coincide with that recommended by the Committee on Bovine Nomenclature (Hubbert). Early embryonic death refers to deaths occurring from the day of conception until about 42 days of gestation, which coincides with the end of the stage of differentiation. Embryos lost during this period may be either absorbed or aborted. Fetuses discharged from day 42 until approximately 260 days are generally called abortions and from day 260 unit term, premature deliveries.

Pathogenesis of Bovine Abortion

The magnitude of reproductive loss has been calculated by David et al. to be approximately 27 percent of all first breedings where healthy cows and fertile bulls are used. The majority of the losses occur in the first 45 days. Fourteen to 20 of the ova are not fertilized and 20 die by 45 days (Roche et al.). Four to six percent of pregnancies are presented as stillbirths, and of these seven to 28 percent have congential abnormalities (that is 0.5 to one percent of all calves), 84 percent die because of neonatal asphyxia, and 9.1 percent have evidence of infection (Leipold).

Genetic Factors

As for the causes of the losses early in gestation, failure of fertilization may be associated with blighted ova, abnormal ova, failure of sperm transport or survival, but in general causes are not well-defined (Diskin & Sreenan; Roche et al.). Of the remaining losses up to 90 days, a large proportion are probably of genetic origin and may be associated with errors of fertilization (eg. trisomy), mutations arising in gametogenic cells or hereditary factors. Bishop has termed these early losses "the elimination of faulty genetic experiments at low biological cost." Losses associated with genetic factors are beyond "routine diagonstic capability" except for those which occur near term and have some recognized phenotypic abnormality, for example "congenital osteopetrosis" which is inherited as a simple autosomal recessive in Angus calves (Leipole et al. 1971). Losses due to genetic factors are most completely recorded in human pregnancies. Of 100 human pregnancies 17 spontaneous abortions were observed, seven of these 17 had an abnormal chromosomal constitution. Approximately 0.4 percent are born with a chromosome abnormality (Carr).

Environmental Factors

Environmental factors may be used as a general term to include the effects of nutrition, season, exogenous hormones and toxic compounds

Nutritional factors such as phosphorus deficiency are more commonly associated with infertility and delayed puberty rather than abortion in cattle (Morror). Iodine deficiency however may result in the birth of weak, or dead, hairless and goitrous calves (Hidiraglou). A correlation between vitamin E/selenium deficiency and abortion in cattle has not been documented experimentally however lesions typical of vitamin E and selenium deficiency are not uncommon in aborted bovine fetuses (Hidiraglou; Miller and Quinn). Vitamin E and selenium deficiency is associated with the birth of weak and dead lambs (Hartley and Dodd). Selenium and/or vitamin E supplementation of deficient diets is thought to increase fertilization of bovine ova and decrease the incidence of retained placenta (Segerson et al). Vitamin A deficiency is associated with defective bone growth, birth of weak calves and/or abortion (Moustgaard, Thomas). In experiments conducted by Somerville et al. the effects of the plane of nutrition during lactation on the reproductive performance of beef cows was determined. It was found that the reproductive performance of cows on high and medium planes of nutrition was satisfactory but 18 percent of cows on a low plane of energy failed to conceive during a 100 day mating period. The authors concluded that a low plane of nutrition during lactation reduces the fertility of beef cows. Waldhalm et al. found that in feeding two levels of protein to pregnant beef cows that there was an increased calf mortality in the low protein group. This was associated with either dystocia or prematurity. They concluded that protein malnutrition in late pregnancy may be a factor contributing to neonatal mortality in beef calves.

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There is a genetically determined weight for heifers when breeding will result in a high pregnancy rate. Undernutrition can delay the age at which this target weight will be reached (Lamond). A low plane of nutrition is unlikely to produce abortion except perhaps terminally in starvation.

The age of the dam may be important in infertility and abortion. Heifers two years old have a five percent lower calving rate after first inseminations than cows three to four years, and about equal to cows of nine years. The decreased rate in primiparous animals appears to be related to problems in parturition and post-parturient period. When animals with no problems in this period were compared there was no difference (DeKruif). In moderate or cold climates fertility is lower in winter months but in warm climates, high termperatures may be associated with fertilization failure and abortion (Vincent). There is also some evidence to suggest that pregnant cows exposed to sudden rises in temperature may abort, however this manifestation is probably rare. Experimentally, extreme maternal hyperthermia gives profound fetal hypotension, hypoxia and acidosis. The fetal temperature is higher than the maternal (Morishima et al.).

Certain plants and toxic chemicals are capable of causing abortion. Abortion associated with eating the needles of Pinus ponderosa occurs in cattle during the last trimester and is characterized by weak parturition contractions, excessive uterine hemorrhage, incomplete dilatation of the cervix and usually retained placenta and metritis. Cows may become very sick and die (Stevenson et al.). Several chemicals capable of causing the abortion have been isolated. Experiments in mice show that fungi present on pine needles may produce a mycotoxin which induces reproductive failure (Chow et al.). A heat-stable factor probably composed of diterpene resin acid also exists in the pine needle which is toxic (Anderson and Lozano; Kibik and Jackson). In addition Adams et al. found they could induce *Listeria monocytogenes* infection in mice fed a diet of Pinus ponderosa needles. Diagnosis in cattle, until the toxin has been clearly identified, will be presumptive and associated with animals consuming pine needles. Nitrate or nitrites are commonly incriminated as a cause of abortion but experimental results have been equivocal (Davison et al.). Coumarin is a constituent of some clovers and is converted to dicoumarol by certain fungi. Warfarin, a constituent of rat baits, has three to ten times the potency of dicoumarin and has been observed naturally and experimentally to cause abortion in pregnant cattle (Pugh, 1967). Warfarin interferes with the reduction of vitamin K epoxide to the active form of the vitamin. Vitamin K is necessary for the incorporation of the amino acid, alpha carboxyglutamic acid into plasma proteins active in the coagulation mechanism (Pugh, 1980). These function in calcium binding (Gallap et al.). Early in pregnancy warfarin probably has teratogenic effects (Warkany).

Locoism is a disease produced by toxic varieties of plants in the genera Oxytrops or Astragalis. The effects of lathyrogens may be closely related (James et al.). Poisoning by locoweeds occurs particularly in western United States and Canada and is most prevalent when pastures are poor, as in winter feeding. The toxic principle can cause abortion or fetal abnormalities and may act through the placental and fetal vascular system (James). Many tissues are affected including the corpus luteum, chorioallantois and neurons resulting in lesions resembling mannosidosis, a hereditary storage disease which occurs in Angus calves (Jolly and Hartley). Lupins are capable of causing syringomyelia, cleft palate, microophthalmia and crooked legs in calves (Shupe et al.). The toxic substance is an alkaloid called anagyrine and acts in a limited time period from 40 to 60 days (Keeler). Use of sodium iodide intravenously in pregnant cattle has been customarily avoided because of the threat of abortion, however in a recent trial to test this premise, ten clinically normal pregnant cows were given a single intravenous dose of 50 grams of sodium iodide and no adverse effects on pregnancy were noted (Miller and Drost).

Five general principles suggested by Wilson apply to the effects of toxic chemicals or agents on the developing fetus:

> He stated; "1. The susceptibility of an embryo depends upon the developmental stage at which an agent is applied; 2. Each teratogenic agent acts in a specific way on a particular aspect of cellular metabolism; 3. The genotype influences to a greater or lesser degree an animal's reaction to a teratogenic agent; 4. An agent capable of causing malformations also causes an increase in embryonic mortality; 5. A teratogenic agent need not be deleterious to the maternal organism.

Infectious Causes of Abortion

The last category of abortion is associated with infectious causes. The proportion which occur in this group is not known, however of those abortions in which the cause is determined, approximately 90 percent are due to infection (Hubbert et al.).

We will now discuss generally the pathogenesis of abortion and in particular those associated with an infectious cause.

Several factors within the cow may result in abortion. The general causes of fever as already mentioned under thermal effects may result in abortion as the fetal temperature is above that of the mother. Therefore any cause of high fever, such as mastitis or pneumonia, may result in abortion. Maternal hypoxia may result in fetal hypoxia and subsequent abortion. This may be associated with circulatory failure as in traumatic pericarditis, or in severe maternal respiratory disease. Increased hemoconcentration as occurs in grain overload and also the concurrent acidosis, may contribute to fetal hypoxia and acidosis with subsequent abortion. Circulating endotoxin from any maternal Gram negative infection either in the feet, udder, throat, or intestine may result in endotoxemia. Endotoxemia may produce abortion by evoking a

generalized synthesis of F-prostaglandins (Skarnes and Harper) or indirectly by substances such as serotonin which may be released by endotoxin (Parant and Chedid; Hinshaw). In addition, endotoxin may induce intravascular coagulation and result in fetal hypoxia by disturbing placental circulation (Morrison and Ulevitch). Maternal endotoxemia has also been shown to produce central nervous system anomalies. This has been produced experimentally in rats and occurs naturally in women associated with renal infections early in pregnancy (Niswasnder and Gordon; Ornoy and Altshuler).

Organisms in the environment may enter the cow by a variety of routes. For example, infectous bovine rhinotracheitis (IBR) virus may enter by the conjunctiva or the nasal passages, Leptospira may enter by the mouth, conjunctiva or through the softened, unbroken surface of the coronet. The viruses of paranifluenza-3 (PI-3) and bovine virus diarrhea (BVD) may enter through the nasal passages. *Brucella abortus* and Salmonella spp. most likely enter through the mouth. The natural portal of entry of mycotic infections resulting in abortion is not established. The vagina may serve as a route of infection for such agents as *Campylobacter fetus, Haemophilus somnus, Corynebacterium pyogenes* and Ureaplasma. Once in the body the organism may travel to the uterus through the circulation (as with IBR virus), advance from the vagina to the uterus, as the influence changes from estrogen to progesterone, for example in *Campylobacter fetus* infections (Vandeplassche et al.). It is also speculated an organism such as *Corynebacterium pyogenes* may reside in the uterus in macrophages during the open period and emerge and disrupt the pregnancy as the influence changes as above from estrogen to progesterone. The most likely time for the disruption of pregnancy by this latter mechanism would probably be around the period of attachment from 20 to 30 days (King et al.).

When a bacterium reaches the placenta various factors in the placenta may contribute to its survival at that site. The oxygen tension in the placenta is lower than that in the dam and may contriubute to the growth of organisms preferring this atmosphere (Kirachbaum and DeHaven). Various nutrients supplied in the placenta are unique and may stimulate the growth of certain organisms. Brucella thrives in the presence of erythritol found in high quantities in placenta and fetal fluids (Pearce et al.). The growth of some fungi is stimulated by placental extracts, however these substances have not as yet been identified (Corbeil and Eades; White and Smith). The growth of Salmonella organisms in mice may be stimulated by extracts from the placenta. This effect did not occur in vitro (Wray and Corbel). Immature fetal immune development also favours colonization of placenta. Cellular defense mechanisms are incompletely developed (Schwartz and Osburn), and there is a lack of humoral immunity in the bovine fetus as compared to the mother (Brambell). When the organism reaches the placenta, depending upon the type and virulence of the organism and the stage of gestation, it may penetrate directly to the fetus or reside there, producing little visible lesion, or in contrast a placentitis. A mild placentitis may cause little disruption in the life of the fetus and normal parturition may eventually ensue with retained placenta occurring in the mother. If the organism is more virulent or has more time to bring about its manifestations a moderate placentitis may result. The lesions may be severe in parts of the placenta but be limited in extent and only slowly progressive. This slowly developing lesion produces stress in the fetus resulting in increased production of ACTH from fetal pituitary (Osburn et al., 1969). This acts on the fetal adrenal resulting in increased fetal cortisol concentration is followed by rising maternal levels of prostaglandins F_2 alpha, probably produced by the cow's uterus, rising levels of estrogen and declining levels of progesterone in the maternal circulation. The main source of progesterone in the cow is the ovary and estrogen is formed by the placenta and by the maternal adrenal (Wagner et al.). With increased estrogens and decreased progesterone levels in the maternal circulation, pressure on the cervix activates the release of oxytocin from the posterior pituitary. Increased prostaglandin F_2 alpha has a direct action on the myometrium and sensitizes uterine muscle to oxytocin (Comline et al.; Fitzpatrick). The end result is that the fetus attains its own delivery. It may be born alive, premature, perhaps small and weak and eventually dies (Osborn et al., 1969).

If the organism is virulent or has a prolonged time to act, a severe placentitis may develop. This may in turn result in retained placenta, premature delivery, abortion, meconium staining or the birth of a sick calf. When fetal hypoxia becomes severe, meconium staining may occur. There is a redistribution of blood flow from non-essential areas, such as gut, to essential areas such as the brain. Blood flow to the brain may increase as much as 275 percent (Johnson et al.). In the infant, where this is best described, decreased oxygenation in the fetal intestine results in increased peristalsis, anal relaxation and expulsion of meconium into the amniotic fluid and hence staining of the fetus. The fetus is now in a state of "compensated fetal distress" with well oxygenated vital organs and peripheral hypoxia (Abramovich et al.). Weak respiratory movements normally exhibited by the *in utero* fetus now become strong inhalatory movements, and meconium, and anything else in amniotic fluid, is inhaled into the lung resulting in fetal pneumonia. This is followed terminally by violent jerking of the legs as the fetus dies (Hems). Other causes of fetal hypoxia besides placentitis may give the same result: hypoxia in the maternal circulation because of circulatory failure or pneumonia; disturbances in oxygen exchange due to placental insufficiency or placental separation; impaired delivery of oxygen from the placenta to the fetus as occurs with cord compression; umbilical vessel abnormalities, eg. single umbilical artery; or fetal cardiovascular problems. Decreased circulation to the placenta may also follow contraction of the uterus as occurs in parturition

(Persianinov). When parturition is prolonged as in dystocia, fetal hypoxia may develop and aspiration of meconium and other amniotic fluid contents such as bacteria may precipitate neonatal pneumonia. The prevalence and significance of this condition in calves is not established, however in a study of infants conducted by Vidyasagar et al. it was found that in spite of oxygen, antibiotics and other supportive therapy many infants with meconium aspiration die. Observations in cattle would suggest that meconium staining of amniotic fluid during live delivery or violent kicking of the legs, would be a bad sign and indication for rapid removal of the fetus with minimal stress. Meconium staining is commonly observed in sheep and pigs following partitution and appears to be of less pathological significance.

Following the development of placentitis the organism may penetrate to the fetus through the amniotic fluid and/or through the circulation. If penetration occurs through the chorion, mesenchyme, allantois and amnion to the amniotic fluid, the fetus is then found to be bathing in an environment contaminated with the organism. In mycotic infections this commonly results in a dermatitis. Approximately one third of bovine fetuses will have gross skin lesions following infection of the placenta with *Aspergillus fumigatus* (Hillman). A much higher proportion of fetuses will have evidence of infection on microscopic examination of eyelid sections (Miller and Quinn).

As the fetus is swallowing amniotic fluid from a very early stage of pregnancy, any organism that is in this fluid will pass into the alimentary tract (Abramovich). In a study conducted by Miller and Quinn of 50 aborted bovine fetuses it was found that 16 of these had lesions in the intestine. These were associated with a variety of agents including viruses, bacteria, fungi and protozoa. The significance of *in utero* infection in the development of neonatal diarrhea in calves has not been established but should not be overlooked as a possible source. In addition to enteritis, a suppurative bronchopneumonia may develop as a consequence of bacteria growing from the pharynx down into the lung following the swallowing of contaminated amniotic fluid.

When the organism travels to the fetus through the circulation the umbilicus and then the liver will be the first organs encountered. Umbilical infection introduced *in utero* is rarely encountered but liver lesions are frequently observed. IBR virus causes coagulation necrosis in the liver (Kennedy and Richards) and a suppurative hepatitis is frequently observed following bacterial placentitis, as in Listeria or Campylobacter fetus infection. Once the organism is in the fetal circulation an interstitial pneumonia may develop. Interstitial pneumonia are commonly seen in tissue sections of bovine fetal lung, however the association with a specific agent is often difficult to determine. Experimentally, PI-3 virus produces as interstitial pneumonia in the fetus (Swift).

Tissues vary in their susceptibility to injury in association with abortion. In a survey of 50 fetuses (Miller and Quinn) where a wide variety of tissues were examined microscopically most tissues examined has some lesions, but it was found that lung, eyelid, liver and placenta were the most frequently affected sites. Placenta was only submitted 16 times, however lesions were observed in 14 of these, and in nine of these 14 a diagnosis was reached, thereby pointing out the importance of submitting placenta with the fetus. Various factors are important in determining the sites of the injury and occurrence of anomalies in the developing fetus. The state of embryogenesis at the time of exposure to the infectious agent or toxic compound may be very important in the development of teratogenic effects. Heart, eye and limbs develop very early in gestation whereas the brain and genitalia may continue development late into gestation and after. Another important factor in determining injury is the development of immunologic competence to various antigens. This varies greatly with the different agents and immunocompetence to the viruses of infectious bovine rhinotracheitis, Bovine virus diarrhea, Parainfluenza-3 and Enteroviruses develop at around the 100 day period. A similar time frame applies with *Brucella abortus,* Anaplasma and Leptospira species (Schultz). Capability to develop antibodies to *Coxiella burnetti, E. coli* and Parvovirus however, develop much later in gestation, usually after 250 days (Schultz). The interaction between the stage of development of the fetus and the state of immune competence is well illustrated by *in utero* infections with Bovine virus diarrhea virus. If the fetus is infected within the first three months of gestation, death and abortion, necrosis of bronchiolar epithelium and necrosis in basal epithelial skin are common findings. If infection occurs between 100 and 150 days; fetal mummification, non-suppurative meningitis, destruction of external granular cell layer, cerebellar hypoplasia and ocular lesions including the development of cataracts and retinal degeneration are common manifestations. After 168 days of infection it is common to find fetal antibody production and only moderate, if any, lesions (Casaro et al.; Scott et al.).

Some of the clinical manifestations commonly observed with *in utero* infections are as follows. During the first trimester, mummification, maceration or abortion may be observed. The mechanism of mummification is not well established but is associated with genetic factors and infection with BVDV (Roberts). Maceration is associated with bacterial infections in the developing fetus. During the last half of gestation it is not uncommon to have severely autolysed fetuses aborted and during the last trimester, particularly towards the end, the emphysematous fetus is commonly encountered with dystocia. Emphysema may develop in the fetus when the cervix is dilated and the fetus fails to be discharged immediately and becomes infected with bacteria from the environment and in the vagina. With the autolysed fetus, the fetus dies, fails to be discharged immediately, and continues to autolyse *in utero.* Eventually the fetus is usually expelled. The mechanism which stimulates the abortion is not clearly understood but probably involves

the production of prostaglandin, lysis of the corpus luteum and subsequent uterine contractions resulting in expulsion of the fetus.

Part II: Diagnosis of the Causes of Bovine Abortion

Using conventional methods the diagnostic rate in bovine abortion is usually between 25 and 40 percent (Hubbert et al.). Why is the diagnosis of the cause of abortion such a difficult problem? First, the lack of knowledge of the daily fetal experience. The clinician or livestock producer does not know how the fetus is feeling today except as it is reflected in the maternal compartment. The fetus may be feverish, hypoxic, fighting a viral or bacterial infection and no signs of this state are reflected in the health of the dam until after the fetus has perished. Another reason for the low diagnostic rate is that three compartments are involved: maternal, placental and fetal. The diagnostician rarely adequately examines the maternal compartment. Samples other than serum samples are seldom taken, swabs and caruncles are not collected and even the temperature is frequently not taken. The portion of the placenta which is submitted is commonly that portion which is hanging out of the vulvar lips and this is frequently amnion, is severely contaminated by fecal material and the surrounding environment, straw, shavings, etc. Amnion is usually the least preferred segment of placenta for examination. The fetus itself is often severely autolysed or partially missing having been eviscerated by dogs or other animals, pigs and cats in the environment. Another major problem is that dedication from the beginning of the discovery of the abortus until the completion of the diagnosis is required by all parties involved. First the owner must have complete records of the breeding history, exposure to diseases, travel and other stresses to which the dam may have been exposed. Also records of feeds, treatments and the general health of the animal are desirable. The clinician should take adequate samples and examine the animal carefully to discover other reasons besides the fetal-placental unit that may have been associated with the abortion. The pathologist also must take adequate samples at the time of necropsy so that later on when the disease is not the one that was suspected, another approach may be utilized and the diagnosis reached. Last but not least our knowledge of the clues related to the causes of abortion is limited. The pathologist's knowledge of the causes of abortion related to specific lesions is woefully inadequate. In the survey conducted by Miller and Quinn, generally as many tissues were examined with lesions where the cause of the abortion was not diagnosed as where it was. For example in the eyelid, lesions were observed in 20 cases of the 50 however only ten of these were diagnosed. The same applies in the lung where lesions were observed in 32 animals but only 16 were diagnosed. Lesions associated with IBRV, *Listeria monocytogenes* and *Aspergillus fumigatus* are widely recognized, however other equally common infections in the environment such as BVDV, Leptospirosis, Coronavirus, Sarcocystitis and Ureaplasma may produce lesions in the fetal-placental unit which would not be recognized.

The management of a single abortion or outbreak may be conducted in the following manner. First the laboratory preference has to be considered. Some laboratories, especially in the early spring of the year, may be so inundated with fetuses that they do not wish to conduct necropsy examinations on single fetuses but would prefer only to have second and third abortions submitted. The preference of the laboratory may vary during the year in regard to this. An ideal individual and herd history is outlined in Table I. Examinations to be conducted on the cow and possibly on other cows in the herd is illustrated in Table II.

Table I
Ideal Individual History

General
- Age
- Breed
- Lactation status
- Illness during pregnancy
- Previous illness
  - Types
  - Dates
- Health during and after abortion
- Purchased: Yes_____No_____
  - Before breeding
  - After breeding
- Transport
  - Date
  - Distance
  - Condition

Reproductive
- Age
- Breeding: Artificial_____Natural _____
  Other_____
  - Dates _____ _____ _____
- Parturitions
  - Number_____
  - Date of Last_____
- Abortion
- Infertility
- Retained Placenta
- Dystocia
- Biopsy
- Other

Treatments
- Previous to abortion
- After abortion

Prophylaxis
- Previous exposure
- Vaccination

Table I (cont'd)
Ideal Herd History

Nutritional
- Water
- Vitamin
- Mineral
- Protein
- Carbohydrate
- Fat
- Other substances

Number of breeding females
Category of herd
- Beef
- Dairy

Calving interval

Signs of disease in herd - during abortions
- prior to abortions

Other abortions - this season
- last season

Additions
- during gestation
- prevous to breeding

Other animals on premise in association with cows
- other age groups
- other species

Examination of the fetal membranes should include a description of their condition, whether fresh, decomposed or retained. The placenta should also be weighed and normal weight may range from nine to 18 pounds in the cow (Wright). An excessively light placenta may be more important than a very heavy one and reflect placental insufficiency. This may be associated with recurring abortion in the same animal. Increased weight of the placenta may be induced by edema fluid as well as inflammatory exudates. The cause of edema usually goes unrecognized and may be observed with a viable as well as a non-viable birth. The number of cotyledons may be important and normally ranges from 75 to 120 (Roberts). The presence of adventitial placentation may indicate a need for more placental area. This may be associated with placental insufficiency, hypoxia in the uterine circulation, decreased numbers of cotyledons, uterine fibrosis, or twin births. Cows with excessive adventitial placentation should be examined carefully as this may reflect inadequate caruncular reserve. Sometimes the size of the cotyledons may be increased excessively and this may also be a reflection of placental insufficiency. Roberts states that placentome diameters exceeding 15 cm. should be considered abnormal. Retention of the placenta may result from inadequate preparation for parturition or be due to inflammation in the maternal septa. In studying maturation of maternal septa, Grunert found that cows at seven months gestation have approximately 53 cells surrounding fetal villi in the caruncle. These decreased at eight months to approximately 25, by 272 days were down to as few as nine, and by 276 days as low as two cells. The type of placenta is therefore changing with maturation in the cow, from an epitheliochorial to a syndesmochorial placentation in the last months of gestation. Grunert also observed that with normal parturition retention of the placenta would occur usually when the number of cells on the uterine epithelium surrounding the fetal villus exceeded 30. In an induced parturition, retention occurred when the number of cells was greater than or equal to 25 and no

Table II

Examination of Cow

- Temperature, Pulse, Respiration
- Condition
- Respiratory System
- Ocular
- Digestive System
- Genito-urinary System
  - Urine
  - Mammary
  - Vulva
    - inflamation
    - discharge
  - Vaginal
    - scope
      - inflammation in vagina or cervix
      - condition of vagina and cervix
        - tears
        - prolapse of cervical rings
      - retention of fetal membranes
  - Examination per rectum
    - cervix
    - uterus
    - ovaries

Examination of Herd
- Condition
- General
- Ocular
- Mammary
- Lactation
- Vulvar discharges
- Examinations per rectum
  - pregnancy
  - mummified fetus
  -pyometra

retention occurred when the number of cells was greater than or equal to 25 and no retention occurred when the number was as low as 14. So again, retention of fetal membranes frequently is the result of inadequate preparation for parturition. The placenta should also be examined for uniformity of cotyledonary size. The largest cotyledons are usually just inside the pregnant horn and correspond to the site of umbilical vessel attachment. Uniformity in size and state of the cotyledons may be a clue to whether they are diseased or not. Fresh and relatively healthy cotyledons may be very dark red or hemorrhagic as associated with separation. Other cotyledons seriously affected may retain portions of carunclar material as is commonly observed in mycotic abortions. It is important to examine the clarity and texture of the intercotyledonary placenta as well. Frequently a rather minor lesion may be observed in the immediate pericotyledonary region and may be detected because of slight thickening, change in colour, or unevenness. So-called "cupping" is frequently observed in the cotyledon and is a reflection of infiltration of inflammatory cells or exudates into the cotyledon causing it to retain the same conformation as when it is attached to the caruncle. Commonly, changes in the placenta following parturition are the results of autolysis. In autolysis the intercotyledonary zone loses its normal translucency and becomes an opaque uniform dark red or grey due to the breakdown of red blood cells and imbibition. So-called amniotic plaques are present on the inner surface of the amnion and are most conspicuous in the region of the umbilicus. These are multifocal to coalescent, raised, firm, white regions which on microscopic examination consist of heaped up mounds of epithelial cells. They are normal structures usually being most conspicuous from three to seven months gestation. The extremities of the chorioallantoic placenta in the tips of each of the uterine horns in cattle normally have a region of necrosis and this is not associated with any recognized disease process but is normal and due to failure of vascularization. Mineralization of the placenta may occur normally in the first few months of gestation and should not be considered pathological during that period. Towards the end of gestation however, mineralization may reflect previous placental injury as associated with bacterial, mycotic or viral infection.

Examination of the fetus should include measurements of the crown-rump length, hair pattern and color, all of which may be used to estimate the age of the fetus. The condition of the fetus, whether fresh, decomposed or mummified should be recorded. Examination of the teeth may reveal pitting as a result of *in utero* viral infection such as with BVD virus. Edema around the jaw and face, conjunctival hemorrhage and swelling of the tongue may reflect dystocia. One of the causes of dystocia may be illness in the calf. Careful examination of the newly haired regions over the eyelid, ears, withers or tail head may reveal slightly raised white crusts typical of mycotic dermatitis. Fetuses aborted as a result of mycotic placentitis may be meconium stained and frequently are fresh as the slowly developing lesion stimulates premature delivery. The color of the conjunctiva should be observed and if white may reflect excessive bleeding as associated with umbilical vessels broken off too long. In pigs excessive bleeding has been associated with ascorbic acid deficiency (Sandholm et al.). This has not been described in cattle and was not expected in pigs since primates and guinea pigs are the only mammalian species known to require exogenous ascorbic acid (chatterjee et al.). Other causes such as a decrease in vitamin K-dependent coagulation factors however should be considered as in association with moldy sweet clover poisoning (Fraser & Nelson). White putty-like precipitates are frequently observed on the hair of aborted fetuses and newborn calves. These are of unknown significance and have not been associated with any specific disease. The container that an animal is shipped in may be very important. Fertilizer bags containing small amounts of fertilizer produce gross lesions on the skin of fetuses and may be confusing to the pathologist. Mineralization occasionally occurs in the epidermis and may be associated with an old mycotic infection or other unrecognized causes of dermatitis. The skin and oral cavities should always be examined for the presence of meconium staining as evidence of *in utero* fetal distress. An estimate of the chronicity of fetal distress may be made based on the intensity and the degree of penetration of meconium into the fetal hair. This should not be mistaken for the normal progression of staining which occurs in the fetal eponychium of the developing fetal hoof. At three months gestation the eponychium is becoming stained yellow, this increases in intensity to five months when it becomes quite a brillant gold. By seven months the intensity is again decreased and by term only a small tip of yellow staining remains. This correlates with the changes observed in the aminiotic fluid and in the stomach contents however the latter clear more rapidly than the eponychium. Failure to lose this staining may indicate *in utero* distress. The eponychium is shed immediately as the calf starts to walk and may be eaten by birds in stillborn calves.

Internal findings of subcutaneous thoracic and abdominal serosanguinous fluid is consistent with autolysis and not a lesion associated with any specific disease. It is due to prolonged retention *in utero* following death (Dillman and Dennis). Fetal kidney is one of the first organs to show marked autolysis and may be surrounded by blood-stained fluid. Hemorrhage around the umbilical vessels indicates that the animal was alive shortly before or during parturition (McFarlane). Inflation of the lungs generally indicates that the animal has breathed, however vigorous resuscitation such as mouth to nose breathing has been shown to partially inflate the lungs in an already dead fetus. Stomach contents should always be examined and may reflect *in utero* fetal distress if they contain meconium swallowed when the fetus was alive or may contain white clotted material indicating that the animal has been given colostrum. Mucus present in the abomasum may be difficult to distinguish grossly from

milk in some circumstances. Trauma *in utero* with severe injury to the fetus can occur as the fetus is being discharged, especially in a fetus less than five months old, and would not be the cause of the abortion. Ruptured liver and inflated lungs in newborn calves are frequently observed and are thought to be associated with trauma following birth. Healed rib fractures have been observed in aborted fetuses verifying severe trauma *in utero*. Whether this was the cause of the subsequent abortion however was not determined.

Criteria used for the diagnosis of fetal abortion include the history, isolated agents, lesions and the development of fetal anitbody. Samples which may be collected from the cow are listed in Table III and from the herd in Table IV. With regard to the samples of placenta, a specimen should always be obtained even if the placenta is retained *in utero*. A portion of cotyledon and caruncle obtained from deep within the uterus is generally cleaner and more representative of the

Table III
Samples To Be Collected From The Cow

Clotted blood samples with another in two to three weeks	
Urine sample	- culture
	- cytology
Vagina	- cervical swab
Placenta	- even if retained remove a portion for culture
	- histological examination
Caruncle	

disease than the portion hanging from the vulva. The importance of the placenta (cotyledon and caruncle) cannot be over-emphasized and a clear relationship between the diagnosis of mycotic abortion and placental submission has been shown (McEntee). Where placenta was submitted mycotic abortions constituted 20 percent of the total diagnoses, however when the placenta was not submitted mycotic agents contributed only four percent. Samples, ideal and essential, to be obtained from the fetus are shown in Table V.

As the fetus is immunologically competent at a relatively early age and as chronic *in utero* infections result in antibody production it was originally thought that these antibodies could be used as a specific indicator of *in utero* infection. The relationship of the stage of illness to the presence of virus in test material and to the appearance of antibody has been indicated by Swift in his experiments with PI-3. Virus was recovered in fetuses from six to 20 days following inoculation but not after 35 to 56 days. On the other hand fetal antibodies were not demonstrated from six to 10 days after inoculation but were present between 20 to 56 days. Miller and Quinn found that two and one-half times as many aborted fetuses as non-aborted fetuses have substantial quantities of immunoglobulins in their fetal fluids. Dunne et al., and Miller and Wilkie showed however that antibodies to many agents may be present in the aborted fetus. The presence of antibodies to several agents makes their useage in diagnosis difficult. The passage of immunoglobulins from the cow to the fetus following placental injury has been suggested by different authors (Brown et al., Dunne et al., Miller and Wilke). Experiments to determine whether this occurs or not are being conducted and until this problem is clarified, antibodies in fetal fluids, unless titers are very high, are of doubtful use in diagnosis in abortion.

Table IV
Samples To Be Collected From The Herd

Blood samples
Vaginal Swabs
Urine samples
Milk?

Part III: Diagnostic Criteria For a Few of the Causes of Abortion and Samples Desired

Tables illustrating the common causes of abortion, prevalence, source of agent, incubation to abortion, probable pathogenesis, usual history, abortion rate, stages of gestation in which abortion occurs, diagnostic method preferred, duration of carrier state, recurrence of abortion, prevention and control and samples to be submitted have been published previously (Miller, 1980). A summary of some of this information follows.

In abortion associated with infection by IBR virus the agent is usually transmitted directly from an infected cow and any animal with a positive titer may be carrying the virus (Davies and Duncan). The agent is widespread throughout the world and following contact, abortion may occur any time from two weeks to four months after. The virus is carried in the blood leukocytes and localized in the placental vessels (Dellers) and on entering the fetus kills the fetus usually within 24 hours (Kendrick and Straub). Frequently there will have been some previous respiratory or conjunctival form of the disease, however there may be no

Table V
Samples from the Fetus

Ideal		
	Entire placenta	
	Placental fluids	
	Entire fetus	
Essential		
Fixed	(Liver	
	(Adrenal)	
	(Kidney)	
	(Lung)	Fresh
	(Placenta)	
	Stomach content)	

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signs in the cow nor evidence of introduction of infected animals. The abortion rate may range from five to 60 percent, may occur at any time in gestation but has a predilection for the last trimester (Kennedy and Richards). Lesions observed in the fetus may or may not be diagnostic however the demonstration of the antigen in frozen tissue sections of kidney by the fluorescent antibody technique is a reliable test (Reed et al). A four-fold rise in titer from abortion to two weeks may occur in the dam, however frequently animals will have an elevated titer before abortion and this finding makes it an unreliable indicator of the cause of abortion. Animals, once infected, probably carry the virus for life, however recurrence of abortion is generally considered to be unlikely (Davies and Carmichael). Vaccination of heifers at six months of age is considered protective (Kahrs). The vaccination of animals during preganancy with virulent virus is discouraged, however temperature sensitive and certain other strains of virus administered intranasally give protection and can be administered during pregnancy (Kucera et al., Smith et al.). Both temperature-sensitive and other strains however remain latent (Postoret et al.). Vaccination confirms humoral immunity for several years but as cell mediated immunity may be more important in controlling IBR viral infections, annual vaccinations may be indicated (Rosner, Kahrs).

Infections with BVD virus are widespread throughout the world and infected cattle housed or pastured together will spread the disease possibly by nasal passages. The virus is also excreted in the urine (Mills et al.). Some evidence of spread by fomites should be considered. Results of a study by Archbald et al. indicate that BVD virus in uterine horns may interfere with normal development of pre-implantation embryos. The virus has been isolated from semen (McClurkin et al.). Persistently infected but seronegative cattle occur and cows so infected may give birth to sick calves or abort (McClurkin et al.). Outbreaks of abortion may follow an epizootic of bovine viral diarrhea-mucosal disease in the herd (Kahrs et al.). A wide variety of manifestations can occur in the fetus and are related to the time in gestation that the virus reaches the fetus. Important aspects are the stage of embryogenesis and development of the immune response. Abortion with abnormalities in the skin, lung and bones occur in the first trimester or early second trimester. Infection in mid-gestation may not produce abortion but calves born frequently have lesions in eye and brain. Specific antibody may be present in pre-colostral calf sera as immune responsiveness to BVD virus develops between 90-100 days (Shultz). After 168 days no lesions may be observed and antibody is produced. The abortion rate is generally low even when the rate of infection is high. Abortion usually occurs early but may be up to four months of gestation. In an experiment conducted by Done et al 15 heifers were inoculated at gestation day 100 with Pestivirus bovis (BVD). Six fetuses died *in utero* and ten calves were born alive (there was one set of twins). Of the 16 offspring, 15 had intrauterine growth retardation and ten of these had central nervous system defects, seven of which were not visible clinically. Analysis of fetal organ weights showed that there was marked decrease in the weights of the thymus, gastrocnemius, lung, body weight, tibia and cerebellum. Growth arrest lines were present on the longitudinal section of the bones. Of the six fetuses that died in utero, five were aborted and one was mummified. On culture, all of these were negative for virus. Uterine cultures were not reported. Of the ten calves born alive, three were clinically abnormal and seven were normal. Of the clinically abnormal calves the signs were generally related to the nervous system. Of the ten calves born alive, eight were positive for virus isolation but negative for serum neutralizing antibody. Two were negative for virus isolation but were positive for serum neutralizing antibody. The importance of these findings is, of the six dead *in utero,* the usual procedure would be to culture for virus however they were all negative, therefore the difficulty of diagnosing this condition in fetuses which die *in utero* is great. Perhaps uterine cultures will be found to be more profitable. Previously the usual practice has been to use serum neutralizing antibody to diagnose BVD viral infections in calves that are born alive however in this experiment of the ten calves born alive only two were positive for serum neutralizing antibody whereas eight were positive for virus. In the diagnosis of *in utero* infections with BVD virus, it is therefore recommended that both serum neutralizing antibody tests and virus isolation be conducted on aborted fetuses and calves born alive. It also appears advisable to culture caruncle from cows having aborted or mummified fetuses associated with BVD virus (Miller, unpublished data).

In herd health programs, serum from blood samples drawn from the dam at the time of pregnancy diagnosis may be saved and in the event of abortion, titers compared with another sample. This would increase the diagnostic value of the second sample and aid in the diagnosis of BVD virus infections and other causes of abortion, eg Leptospira. Vaccination is reported as being effective however untoward effects do occur (Lambert) and effectiveness may be questioned in some circumstances. Steck et al. studying immune responsiveness in cattle fatally affected by bovine virus diarrheal-mucosal disease found that some animals developed good antibody titers to one strain of BVD virus but remain sensitive to other antigenic strains. They concluded that a broad spectrum of antigen variants is needed in BVD (mucosal disease) vaccines. Similar times and precautions for vaccination to those for IBR virus are generally recommended.

Parainfluenza-3 virus infection is widespread but it is probably not a common cause of abortion (Swift and Trueblood). The transmission is probably by respiratory tract and the incubation period following experimental *in utero* inoculation required 45 to 56 days. Viremia in the dam with establishment of infection in the fetus is suggested as the

pathogenesis. The ideal diagnostic method would be isolation of virus from the fetus however this is unusual and the demonstration of the specific antibody to PI-3 virus in the serum of aborted fetuses is so common as to make the results questionable (Dunne et al; Miller and Wilkie). Lesions in the fetus typically include an interstitial pneumonia but as this lesion is not specific, other methods of diagnosis are required. Recurrence of abortion is unlikely as a low titre prevents infection (Swift and Trueblood). Vaccination would therefore appear to be effective in prevention.

Ureaplasma is a group of organism which are becoming more frequently isolated from aborted bovine fetuses (Langford) and appear to be commonly associated with infertility (Doig et al.). The organism is widespread and is commonly found in the vulvar region of the cow and genital tracts of bulls (Onoviran et al.). In an experiment conducted by Miller et al., ureaplasma was inoculated into the amniotic cavity of four pregnant cows varying from four to eight months gestation. Of these four, two aborted premature dead feti, one was born alive and died shortly after and one was born alive and appeared as though it would have lived. All four cows retained their placenta and ureaplasma was recovered from four placentas and three feti. The organism was recovered for up to 97 days from vulvar discharges and urine. Lesions in the placenta consisted of a mononuclear cell infiltrate with some foci of mineralization in amnion. Major changes in the lung of the fetus consisted of peribronchiolar cuffing and a severe diffuse alveolitis. The specimens to submit for diagnosis of abortion caused by ureaplasma are lung, placenta and caruncle. If swabs are used "Culturette"[1] samples with transport media are preferred. Samples should be delivered to the laboratory preferably immediately, or at least in less than 24 hours, or frozen at -70°C if early delivery is impossible. Freezing at -20°C appears to damage the organism (Ruhnke). Preventive measures have not been developed.

Haemophilus somnus has been incriminated as a cause of infertility and abortion and is frequently found in the bovine vagina (Miller, 1980a) and even more often in the prepuce of the bull (Humphrey et al., 1982). In experiments conducted by Miller (1980a), 31 cows were inoculated with *H. somnus* by various routes. Of these 31, 18 became infected for more than a week. Seventeen of the 18 either failed to conceive, recycled, developed a placentitis, aborted or developed an endometritis from which at least one animal died. The organism is widespread in Canada and United States (Stephens et al.) and has been isolated in association with reproductive problems in many other countries of the world (Miller, 1980a). Lesions associated with abortion include a severe placental vasculitis (Van Dreumel and Kierstead). In experimental infections organisms were more frequently recovered from placenta and uterine swabs than stomach and intestinal contents. Most satisfactory results were obtained by culturing vulvar discharges accompanying or just previous to abortion (Miller, 1980a). The organism is carried for prolonged periods in the vagina of infected cows and is commonly resident in the major vestibular gland normally producing little or no lesions in this site. It is frequently shed in the urine (Humphrey et al., Miller, 1980a). The effectiveness of vaccination procedures in preventing *H. somnus* infections of the reproductive tract have not been thoroughly investigated.

Abortions in cattle associated with Leptospira infections are usually diagnosed by demonstrating a high titer in the dam. Recent work in Ireland indicates that some leptospira can be readily demonstrated in fetal tissues using the fluorescent antibody technique and also contrary to previous results, by culture. Antibodies to leptospira may also be present in fetal fluid. As lesions diagnostic of leptospirosis are only occasionally present, adoption of these techniques on this continent should facilitate diagnosis of this disease (Ellis et al., 1976, 1978; Ellis and Michna). Vaccines are available which effectively prevent Leptospiral infections

[1]*Culturette, Marion Scientific Corporation, Kansas City, Missouri, U.S.A. 32720*

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