A review of the causes of abortion in farm animals with special reference to lesser known bacterial species.

Thesis

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A review of the causes of abortion in farm animals with special reference to lesser known bacterial species

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ABSTRACT

A comprehensive review of abortion in farm animals is presented. Initially it includes a study of the most important non-infectious causes other than bacteria. This is followed by more detailed discussion of the common bacterial agents Brucella and Salmonella. In addition the role of other less well recognised causes of abortion Campylobacter, Leptospira species as well as others the more sporadically reported species of Corynebacteria, Haemophilus, Nocardia, Pasteurella, Neisseria, Mycobacteria, Bacillus and Streptococci is discussed in terms of occurrence, clinical symptoms, pathogenicity and pathology.

Subsequently other contributory factors such as the immune status following production of antibodies in adult and foetus is discussed. The possibility that mixed infections can contribute to abortion mechanisms is examined. The value of recent diagnostic tools in determining the causative agents of abortion is considered and their significance in controlling abortion in farm animals analysed. Future areas of research including diagnostic investigation is briefly discussed.

An extensive Bibliography of references to farm animal abortion is included.
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CHAPTER 1
INTRODUCTION

The cause of abortion in farm animals is still unknown in many cases, despite the intensive research and diagnostic work of veterinarians and animal scientists. For instance Dennis (1969a) in a survey of cattle abortion was unable to find a cause in some 70% of the 200 cases examined and in a recent survey of 2,500 cattle abortions Kirkbride (1979) reported that in over 50% of cases there was no known cause. Even more recently Moojen et al. (1983) reported similar findings.

Abortion is defined as the expulsion of a dead foetus from the uterus at least two weeks prior to parturition (Dennis, 1969a). Arthur (1975) in a review of the causes of abortion in animal species cited infectious agents as a major cause. In Human abortion Gamsu (1977) found that the incidence of bacteria cited as a cause, varied from one country to another, often being dependent upon the socio-economic conditions, local diagnostic procedures and medical practices adopted. This could be equally true for farm animals where worldwide there is a very wide divergence in farming practices and veterinary care. Abortion can have very serious economic consequences for the farmer for it reduces the amount of protein for human consumption available from farm animals. The extent of the financial loss to the farming industry has not been estimated on an international basis but in a conservative study at Reading University Ellis and Jones (1977) reported that the cost of a 2% abortion rate due to Brucellosis in the United Kingdom was some £8 million per annum at 1977 prices.

As well as the loss of the foetus, abortion resulting from infection can lead to slaughter of the infected dam to prevent cross infection in the herd. This additional loss can also adversely affect a planned breeding programme within the herd.

During the past 50 years most abortions in farm animals in the United Kingdom have been attributed to common infectious diseases such
as brucellosis, salmonellosis and trichomoniasis. Also during this period, control and local eradication of these diseases has been maintained by such practices as (a) good management including improvements in housing, hygiene and the rapid removal of infected animals (b) the use of vaccines against Brucella and Salmonella (c) improved veterinary practice involving accurate diagnosis of the causative agent and better treatment of the affected animals.

1.1 NON-INFECTIOUS CAUSES

In a survey of cattle abortion Rowe and Smithies (1978) found 36% were due to infectious causes. They could not establish precisely the percentage that could be attributed to non-infectious mechanisms, as many of the undiagnosed cases could have been due to unidentified infectious agents. The non-infectious mechanisms associated with abortion include:

**Physical**

1. In cattle and horses foetal death caused by torsion of the uterus or twisting of the umbilical cord with subsequent abortion has been reported by Zuk (1975). Induced abortion in cattle caused by veterinary workers accidentally rupturing the amnion during routine manual examination of the rectum has also been reported (Parmigian et al., 1978).

**Genetic**

2. Genetic causes of abortion are mainly a result of inbreeding in pedigree animals. This can increase embryonic deaths by concentrating lethal genes in the zygote, and has led to a significant increase in abortion rate in cattle and pigs (Woodward and Clark, 1959) an observation confirmed by McFeeley (1968) and discussed by Miller (1982).

**Nutritional deficiencies**

3. Reid (1966) found that in a prolonged period of malnutrition the oestrous cycle can be interrupted and if the animal is pregnant an abortion may occur. Vitamin A, Iodine and Selenium deficiency have also been reported as causes of abortion in cattle and sheep (Roberts, 1971;
Taylor et al., 1979) and grass deficient in copper has led to stillbirths and abortion in sheep (Watson, 1962).

Drugs, toxins and miscellaneous chemicals

4 Waterlogged grass with high nitrate levels has been reported as causing abortion in cattle pastured on it (Simon et al., 1958, 1959), and this has been confirmed by Gaytan et al. (1982) and Stuart and Oehme (1982). The latter workers also reported porcine abortion associated with high nitrate consumption. Jones and Jones (1977) observed that a herd of pregnant cattle fed on grass treated with silage, which contains high levels of nitrates, suffered a 20% abortion rate. Experimental induction of abortion in cows by dosing with either nitrates or nitrites alone has been cited by Zermeno and Barra (1978). However, in contrast, nitrate toxicity alone was not sufficient to cause abortion in healthy ruminant animals on a balanced diet (Roberts, 1971).

Consumption of plants such as Sorghum contaminated with Ergot has been reported as causing abortion in cattle and horses. When these contaminated plants are consumed together with grass containing high nitrate levels, higher numbers of abortions have been reported (Romone et al., 1966; Van Kempen, 1970). Boelter and Serodio (1973) reported cattle abortion in Brazil associated with eating aqueous extracts from leaves and stem of the tree Guarea trichilloides.

Van Kempen (1970) observed that Phenothiazine and Thiabenzole used for controlling parasites caused abortion in cattle. In swine, drugs or plants have seldom been associated with abortion although Dunne (1968) cited the drug Dicautoral which is used as a herbicide to be a causative abortive agent.

The use of the lead based paints has been a hazard to farm animals and may lead to encephalitis and breeding problems. Sporadic abortion in cattle associated with ingestion of lead by constant licking of painted surfaces has been reported (Sharma and Buck, 1976; Stuart and Oehme, 1982). Stillbirths in cattle caused by iron deficiency were reported by Moore et al. (1965).
Hormones

5 Oestrogenic compounds including glucocortisone and hydrocortisone if given in excess doses, can induce abortion in cattle (Roberts, 1971). Van Rensberg (1965) (1967) reviewed the close relationship between the activity of the adrenal cortex and the maintenance of pregnancy in farm animals. He found that heifers (pregnant for 193 - 222 days) dosed with cortisones for four to eight days aborted between the fourth and thirteenth day after dosing. Similar finds have been reported (Douglas et al., 1974; Oliva et al., 1976; Brand and Bois, 1976; Jackson and Cooper, 1977; Day, 1977; Copeland et al., 1978; Coulson, 1979; Barth et al., 1981).

Other causes

6 Arthur (1964), Osborne (1966) and Platt (1973) reported a 15-29% incidence of abortion in mares due to twinning. The latter worker suggested that the total foetal loss may be higher since twin abortions are not often submitted for pathological examination. Other infrequent causes of abortion in farm animals include anaphylactic reactions to drugs, antibiotics, poor insanitary housing and poor husbandry (Roberts, 1971).

1.2 INFECTIOUS CAUSES

A wide range of infectious diseases have been associated with abortion in farm animals. Epidemiologically the following types of infections have been recognised.

1 Epizootic, a recurring infection as found in brucellosis and leptospirosis outbreaks.

2 Sporadic with a high infection level of up to 50% in a herd. This type of infection usually found with outbreaks of listeriosis and salmonellosis.

3 Sporadic with a low infection level affecting less than 5% in a herd. Usually found in infections caused by Campylobacter, Corynebacteria, Streptococci and fungal species.

Thus a wide range of micro-organisms have been involved in reports associated with abortion in farm animals and because of their frequency certain species (Table 1) are suggested by Deas (1981) to be "common" agents.
TABLE 1 - Summary of important bacterial genera associated with abortion in farm animals.

<table>
<thead>
<tr>
<th>GENUS</th>
<th>ANIMAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cattle</td>
</tr>
<tr>
<td>Brucella</td>
<td>✓</td>
</tr>
<tr>
<td>Salmonella</td>
<td>✓</td>
</tr>
<tr>
<td>Leptospira</td>
<td>✓</td>
</tr>
<tr>
<td>Listeria</td>
<td></td>
</tr>
<tr>
<td>Campylobacter</td>
<td>✓</td>
</tr>
<tr>
<td>Corynebacteria</td>
<td>✓</td>
</tr>
<tr>
<td>Streptococci</td>
<td></td>
</tr>
</tbody>
</table>

The mechanisms by which these infectious agents may cause abortion is as follows: Organisms invade the reproductive tract following sexual transmission or from infected urine. This causes inflammation and subsequent placentitis with uterine and foetal infection. Alternatively, large numbers of organisms may be ingested in foodstuffs or grass contaminated with infected urine. They become invasive and are then transmitted via the haematogenous route across the placenta leading to uterine and foetal infection.

The infectious agents causing animal abortion can be grouped as follows:

1.2a **NON-BACTERIAL SPECIES**

1 **CHLAMYDIA**

These obligate intracellular organisms occur as small spherical
or rod shaped forms but during their maturation process can be much larger. Except for the small dense forms they can only survive briefly outside animal cells. The spherical forms range from 0.2 to 0.7\(\mu m\) in diameter while the rod forms are in the range of 0.3 to 2.0\(\mu m\). Two species of Chlamydia are now recognised \textit{C. trachomatis} causing disease in humans and \textit{C. psittaci} causing disease in both animals and humans (Carter 1979).

Reports of epizootic abortion in cattle due to the latter species in Germany, France, Italy and Yugoslavia was recorded by Foggie (1959, 1977) and later in Russia (Kurbanov, 1978; Abilgasanov; 1982; Kurbanov et al. 1983) and in the United Kingdom by Robinson and Anderson (1979). This organism has also been cited as the causal agent of enzootic abortion (EAE) in ewes (Shubin and Andryishin, 1977; Blewett et al., 1982, Greig et al., 1982; Sanchis, 1982), a disease first described in Scotland by Stamp et al. (1950). The incidence of abortion in a flock can be as high as 50\% when sheep are first infected but subsequently the disease becomes enzootic with 1 to 5\% of the ewes in the flock aborting each year. In both epizootic abortion in cattle and enzootic abortion in ewes, infection and abortion occur during the last trimester of pregnancy. Control of both diseases is mainly by the use of vaccines (Foggie, 1959, 1977; Durand et al., 1980; Polydorov, 1981; Lohrbach and Frost, 1983), or antibiotics (Rodolakis et al., 1980). Occasional incidences of abortions due to Chlamydia species in horses (Blanco-Loselier et al., 1976) and pigs (Yatsyhin and Bortnichuk, 1976; Plagemann, 1981), have been reported.

2 PROTOZOA

Two of the most important pathogens are the genus \textit{Trichomonas} which mainly effects cattle and the genus \textit{Toxoplasma} which usually causes disease in sheep. Among the \textit{Trichomonas} species, \textit{Trichomonas foetus} has been reported by Laing (1970), Kirkbride (1975) and Kendrick (1975) as a major abortive agent in cattle. Trichomoniasis is worldwide in its distribution and the organism is transmitted by an
infected bull during intercourse (Parsonon et al., 1974). The most effective control procedure is to use semen from non-infected bulls (Clark et al., 1974a). Where this is not possible the preputial mucosa of the bull may be treated locally with acriflavine or dimetridazole may be given orally (McLoughlin, 1970).

Toxoplasmosis caused by Toxoplasma gondii is known to cause abortion in sheep and pigs (Eckerling, 1968; Frei, 1975; Akkermanns, 1977; Waldeland, 1977; Kraft and Stoll, 1978; Nicolas et al., 1978; Quinlivan and Jopp, 1982), and cattle (Miller, 1975; Kolev 1977; Miller et al., 1982). It also causes human abortion and transmission from animals to humans has been documented (Roberts, 1971). However, an infection prior to pregnancy will generally result in maternal immunity and thus no damage to the foetus. This phenomenon has been used to control the disease in sheep by infecting ewes prior to pregnancy (Sim et al., 1963).

3 FUNGAL INFECTIONS

The incidence of abortions in farm animals reported to be due to fungal infections is approximately 1% (Sheridan, 1980) to 20% (Hubbert et al., 1973). The genera most frequently cited in cattle abortion are Apergillus and Mucor (Hill et al., 1971; Matsui et al., 1977; Venec, 1978; Savova and Burdarova, 1978; Stuker et al., 1979; Guarda, 1979, 1980; Higgins et al., 1981). Sporadic abortions occur mainly during the winter period and these may be caused by the consumption of mouldy winter feeds (Hugh-Jones and Austwick, 1967; Blevins et al., 1969; Berthelon, 1975; Matsui et al., 1977). In a flock of pregnant sheep fed with hay infected with Aspergillus fumigatus abortions occurred in 25% (Corbel et al., 1980). Mostaghini (1980) in a survey of infected aborted sheep found Aspergillus spp. in over 50% of foetuses but suggested post-mortem contamination may be a possible source of the fungus. Corbel et al. (1980) suggested that the mycotoxins produced by the fungi following infection once released in the blood stream contributed to the abortions.
Viruses are a unique class of infectious agents in that they multiply only in particular host cells. They can infect species of bacteria (Bacteriophages) or plants or animals.

The most important syndrome caused by an animal virus affecting pregnancy in cattle is Infectious Bovine Rhinotracheitis (IBR). It produces a wide range of clinical symptoms including encephalitis, pneumonitis and septicaemia as well as abortion in cattle. (Wohlegemuth et al., 1972; Durham, 1974; Rowe and Smithies, 1978; Magnani et al., 1978; Reed et al., 1979; Nettleton et al., 1981; Stubbings and Cameron, 1981; Evermann, 1982) and in pigs (Derbyshire and Caplan, 1976). Another widespread viral disease of cattle is Bovine Virus Diarrhoea/Mucosal disease (BVD/MD); caused by organisms of the Togavirus group. In the United Kingdom some 60% of the cattle population have various levels of serum neutralising antibodies to this virus indicating a current or past infection (Phillip, 1973). Similar figures have been reported for the USA and Europe (Roberts, 1971). Viraemia is a feature of the disease and in pregnant animals the virus localises in the alimentary mucosa causing inflammation, subsequently there is a placentitis followed by death of the foetus and abortion (Rowe and Smithies, 1978; Reed et al., 1979; Evermann and Paris, 1981). Recovery of the animal from the disease leads to long lasting immunity but prevention has also been achieved using vaccines (Roberts, 1971).

A viral disease of sheep known as Border disease also belongs to the Togavirus group and was first described in England and Wales by Hughes et al. (1959). Subsequently, it was reported in Australia, New Zealand, USA and Eire (Patterson, 1975). Foetal deaths with or without abortion are now accepted as an important aspect of this disease (Winkler, 1975).

Abortion in mares due to organisms of the Herpesvirus group have been reported (Powell, 1975; Dahle, 1977; Draayer and
Kirkbride, 1977), and isolation of the virus from the foetus has been achieved (Rossdale and Wreford, 1974; Ellis et al., 1976a). Control measures in horses include the removal of infected animals, improved sanitation and vaccination (Eaglesome et al., 1979).

A widespread disease known as Aujeszky's disease occurring primarily in pigs (but also infecting cattle and rodents) is caused by a Herpesvirus and can cause 100% mortality in pigs (Baskerville et al., 1973; Tung et al., 1980). When the pregnant animal becomes infected, the virus spreads via the haemotogenous route and following transplacental passage, foetal infection and abortion occur (Tung et al., 1980). A natural infection prior to pregnancy can lead to the transfer of specific antibodies to the young in colostrum (McFerran and Dow, 1973; Butyanov and Maksimovich, 1979). Vaccines prepared from specific isolates of this virus are available but they lack general effect on the wide range of strains causing the disease. A further drawback is that some animals can become infected by imperfectly prepared vaccines.

Other viruses which can also attack the foetus causing abortion include the Bluetongue virus, a Reovirus which attacks sheep (Young and Cody, 1964) and cattle (Luedke et al., 1977); Parainfluenza type 3 and other enteroviruses which affect cattle and pigs (Dunne et al., 1973; Dilovski and Ognyanov, 1975; Rao et al., 1976); and Adenovirus (Ignatov and Pavlov, 1976), Coronavirus (Eugster et al., 1979) and Parvovirus (Sasaki, 1978; Vannier and Tillon, 1980) all of which cause abortion in pigs.

Finally, equine abortion has been reported to be caused by Equine Rhinopneumonitis Virus (ERV) (Buczek et al., 1976; Benton and Petzold, 1977). Using the electron microscope Dahle (1977) demonstrated the presence of a Herpesvirus from a Rhinopneumonitis abortion case in a mare and Ellis et al. (1976a) reported an abortion association of a mixed Leptospira/Equine Herpesvirus infection.
5 MYCOPLASMA

The mycoplasmas are the smallest of the free living organisms. Unlike bacteria they have no cell wall but are bounded by a membrane. They show pleomorphism and in stained smears are seen as "Ring forms", globules, small coccobacilli or filaments. On agar they produce a typical "fried egg" colony but when first isolated many do not show this colonial morphology. Other species grow as tiny colonies ('T' mycoplasmas or Ureaplasmas).

The first report of the isolation of mycoplasma from an aborted bovine foetus is attributed to O'Berry et al. (1966). Since then M. bovingenitalium, M. bovirhinis, M. bovis, M. arginini, Acholesplasma laidlawii and Ureaplasma spp. have also been isolated from other abortion cases (Volintir et al., 1971a, b; Langford, 1974a; Ball et al., 1978). Recently Rosenfeld and Hill (1980) reported the isolation of M. alkalescens from an aborted bovine foetus. This species has been associated with respiratory tract infections in cattle (Hudson and Etheridge, 1963) and mastitis in cows (Brookbanks et al., 1969). Another species, M. canadense, isolated from a bovine foetus (Boughton et al., 1983) has also been isolated from both male and female bovine genitalia (Ruhrke and Onoviran, 1975; Jasper, 1977; Rae, 1982). M. bovirhinis, M. bovis, and A. laidlawii have been cultured from preputial secretions and semen of bulls (Langford, 1974b).

In cases of abortion caused by Mycoplasma spp. usually there are not any premonitory clinical signs in the dam but the organisms may be isolated from foetal stomach contents, liver, lungs and sometimes placenta. There are also histological changes consistent with intrauterine infection (Rosenfeld and Hill, 1980; Boughton et al., 1983). The placental cotyledons may be soft brown with a wet leathery appearance and the outer skin of the foetus may be oedematous with maceration. The foetal liver may be pale in colour and the lungs may contain neutrophils in the alveoli as well as an increased number of alveolar macrophages.
There have been several reports of the isolation of mycoplasmas from aborted equine foetuses. Kirchhoff et al. (1973) found Acholeplasma spp. and Mycoplasma spp. in aborted foetal lung and liver. Particular species isolated in equine abortion cases include M. bovigenitalium (Langford, 1974a) and Acholeplasma oculi (Moorthy et al., 1977).

In a survey of 845 aborted equine foetuses Heitmann et al. (1979) isolated Acholeplasma spp. from 29 and Mycoplasma spp. from 3 foetuses.

1.2b BACTERIAL SPECIES

1 BRUCELLA

Brucella species are generally accepted throughout the world as a major cause of reproductive failure in farm animals. Most species of Brucella tend to be host specific. Brucella abortus affects cattle (Carter, 1979); whilst Brucella melitensis and Brucella ovis are important agents of abortion of sheep, pigs and goats (Lawrence, 1961; Berthelon, 1975; Fernandez Diez et al., 1978; Nicolette et al., 1979; Kadar and Banfalvi, 1979; Fielden, 1980). Brucellosis is endemic throughout the world except in areas such as N. Ireland and Denmark where it has almost been eliminated following an intensive eradication programme (Joint FAO/WHO expert committee on brucellosis, 1971). Currently, eradication schemes are also in progress in England, France, W. Germany and USA (WHO health report 1979). For example, Kampelmacher (1977) found an incidence of 5% abortion in a 5 year survey (1969-74) of 18,000 cattle abortions in Germany but more recently in a similar survey (1975-79) Kampelmacher et al. (1980) have reported only 0.14% abortions.

Brucellosis in cattle is characterised by abortion after the fifth month of pregnancy followed by a period of infertility. Retained placenta and metritis are frequently noted. The placenta is oedematous with inflammation and necrotic lesions and the dead foetus is usually retained in the uterus for one to three days. Autolysis of the foetal tissue is common. There are no specific lesions of the foetus but suppurative bronchopneumonia often occurs (Kirkbride, 1975; Dennis, 1980; Miller, 1980a).
Abortion in sheep due to Brucella meletensis and Brucella ovis occurs in late pregnancy and the essential lesion is a placentitis. There is oedema and yellow-brown necrosis of the cotyledons and adjacent areas haemorrhagic. The foetus shows the usual autolytic signs of intrauterine death (Manktelow, 1973; Jensen, 1974; Arthur 1975; Fielden, 1980).

The diagnosis of brucellosis is based on the recovery of the organisms from aborted foetuses, milk or other tissue (Dennis, 1969a, b; Kirkbride, 1975; Dennis, 1980; Miller, 1980a; Fielden, 1980). Infection can also be demonstrated by the detection of antibodies to Brucella in the serum of aborted animals and in foetal fluids (Hinton et al., 1977).

2 SALMONELLA

Salmonellosis may be caused by any member of the genus Salmonella in which there are over 1,000 species. The disease may present itself in an acute or chronic form or the animals may be symptomless carriers. In the acute form septicaemia occurs in cattle, sheep, pigs and sometimes horses. Transplacental infection can occur leading to intrauterine infection with foetal death. There are however relatively few species which are important causes of abortion. These include S. dublin in cattle (Hinton, 1977) S. abortus ovis in sheep (Mostaghini, 1980; Favre, 1980; Balbo et al., 1981), S. abortus equi in sheep and horses (Kirkbride, 1975), S. typhimurium in cattle, sheep, pigs and horses (Hunter et al., 1976; Deas, 1981), and S. cholerae-suis in pigs. (Carter, 1979).

Of the 1,618 incidents of salmonellosis reported in cattle in United Kingdom in 1981, 877 were caused by S. typhimurium and 556 were caused by S. dublin (Zoonoses Order (1975); Salmonellosis Report 1982). This finding differs from reports in the previous 10 years (1968 - 1978) when S. dublin was regarded as the most important species (Hinton 1977). In contrast Kampelmacher (1977) in a 5 year survey (1969-74) of 18,000 cattle abortions in Germany found only 113(0.6%) were due to this organism.
In recent years there has been an increasing number of abortions in sheep involving \textit{S. montevideo} (Zoonoses Order (1975), Salmonellosis Report 1982; Linklater, 1983).

There do not appear to be any specific pathological changes associated with Salmonella abortion. The abortion is usually secondary to a severe gastroenteritis and the infected placenta is commonly autolytic, reddish in appearance with marked cotyledonary and intercotyledonary necrosis. The subcutaneous tissue of the foetus is usually oedematous and the stomach contents are blood stained (Dennis, 1969b; Fielden, 1980; Dennis, 1980). The abomasal contents and the intestines are hyperaemic or blood tinged (Hinton, 1971).

Diagnosis is normally based on the isolation of the organisms from either the foetus or placenta (Van Ulsen, 1960; Frik, 1969; Hinton, 1974; Dennis, 1980; Deas, 1981). However serology is a useful adjunct to diagnosis especially if paired sera are examined (Le Guilloux, 1968; Hinton, 1971; Carter, 1979; Fielden, 1980) and the use of a fluorescent antibody technique (FAT) has been suggested by Dennis (1980).

An important feature of salmonellosis is that the affected animals may become convalescent carriers and if exposed to stress reactivation of the disease can occur (Hunter \textit{et al.}, 1976). However, Deas (1981) suggested that after abortion there may be faecal excretion in most cases but this rarely persists for more than three weeks.

Prevention and control methods include good hygiene, quarantine of imported animals until control checks are carried out and the use of commercially prepared vaccines.

3 \textbf{OTHER BACTERIA}

Veterinarians and research workers have included in their reports on animal infections indications of many bacterial species which may be implicated as possible causes of abortion. However, some bacteria because of their frequency of isolation and identification from abortion cases
have become well known and recognised as abortive agents. Brucella and some Salmonella species would be included in this category. However in the past based on evidence emerging from routine serological testing of animals with a history of abortion, other bacterial species such as Leptospira Campylobacter and Listeria were well known as agents possibly associated with abortion. However due to their fastidious growth requirements, these bacteria were isolated and identified less frequently from the aborted foetus. Because of this lack of confirmatory evidence, veterinarians and research workers therefore did not consider these particular species to be equally well recognised as Brucella and Salmonella species were as abortive agents. Equally, other lesser known species which in the past have only rarely been reported as associated with abortion have in recent years been more frequently isolated from aborted foetuses. These include Corynebacteria spp (Guilloux, 1979) Nocardia spp (Kikopa and Bergmann, 1975; Watson and Beverely, 1977; Dohnal et al., 1978), Haemophilus spp (Waldham et al., 1974; Chladek, 1975; Miller, 1980a), Pasteurella spp (Messier et al., 1981; Webb et al., 1980) Mycobacteria spp (Ellesworth et al., 1979), Neisseria spp (Claxton et al., 1974; Neill et al., 1978b) Bacillus spp (Waldeland, 1976) and Mimae/Yersinia spp (Gelev, 1978).

In the past extensive literature has been assembled which shows that Brucella and Salmonella are bacterial abortive agents. However there is much less information available on the lesser recognised and lesser known species referred to above. In chapters 2 and 3 information on each of these lesser known and recognised species will be collated so that in Chapter 4 a comparison of common and contrasting features of and between these species and the traditional species Brucella and Salmonella can be carried out. Finally in Chapter 5 the major areas of diagnosis which require more research i.e. those involving bacterial species which are now more recognised as associated with animal abortion will be discussed.
Fig 1: Aborted bovine fetus infected with *Aspergillus fumigatus*. Note typical encrusted skin lesions.

Fig 2: *Brucella abortus* organisms (coccoid apple green structures) in a section of intercotyledon tissue from an aborted cow. Stained by the FA technique X500.
CHAPTER 2

LESSER RECOGNISED BACTERIAL SPECIES ASSOCIATED WITH ANIMAL ABORTION:

CAMPYLOBACTER, LEPTOSPIRA and LISTERIA.

2.1 CAMPYLOBACTER

Vibriosis in animals is caused by Vibrio fetus a member of the bacterial family Spirillaceae. The organism was first named and its morphological, serological and biochemical characters defined by Smith and Taylor (1919). It was subsequently renamed and reclassified within a new genus Campylobacter as Campylobacter fetus in 1973 by Veron and Chatelain. Two subspecies venerealis and intestinalis were subsequently designated and more recently the latter species was renamed C. fetus subspecies fetus (Skerman et al., 1980).

The disease produced in farm animals by each of the subspecies is quite distinct (Brynner, 1976). C. fetus subspecies venerealis is responsible for genital infections whereas C. fetus subspecies fetus produces a septicaemic condition.

Vibrionic abortion was first reported in sheep (McFadyean and Stockman, 1913) and later in the same year these workers also found Vibrio associated with a case of cattle abortion. Since this date there have been numerous reports of abortion due to Campylobacter species in cattle (Table II) and sheep (Table III) and occasionally in pigs (Higgins and Degre, 1979).

In cattle C. fetus subspecies venerealis is responsible for bovine genital vibriosis, a sexually transmitted disease (Brynner, 1976). The organisms are obligate parasites of the genital mucosa. In the bull the organism primarily infects the penis and fornix of the prepuce causing a mild inflammation (Philpott, 1966; Boyd, 1972). It is transmitted to the cow by coitus (Lawson and McKinnon, 1953; Agumbah and Ogaa, 1979; MacLaren et al., 1980), or by artificial insemination especially when antibiotics are not included in the
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<th>UNITED KINGDOM</th>
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<th>USA/ CANADA</th>
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<tbody>
<tr>
<td>McEwen, 1940</td>
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<td>Barger, 1928</td>
<td>Hindmarsh, 1942</td>
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<td>Lofthouse, 1951</td>
<td>Barner and Oberst, 1950</td>
<td>Plastridge et al., 1947</td>
<td>Leaver and Hart, 1960</td>
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<td>Ellis et al., 1977, 1978a</td>
<td>Fontanelli, 1951</td>
<td>Rhoades and Hardenbrook, 1947</td>
<td>Clark et al., 1969</td>
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<td>Flatla et al., 1952</td>
<td>Bell, 1950</td>
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<td>Trilenko, 1953</td>
<td>Blobel et al., 1957</td>
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<td>Gauthier and Cheve, 1955</td>
<td>Dennis, 1969a, b</td>
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<td>Mundt, 1955</td>
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<td>Shatalov, 1971</td>
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<td>Sesevickova et al., 1976</td>
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| Nishimura, 1936 | |
| Kawashima, 1954 | |
| Kawashima et al., 1955 | |
| Mariyama and Kume, 1975 | |

S. AFRICA

<p>| Snyman, 1931 | |
| Canham, 1948 | |
| Van Rensberg, 1954 | |</p>
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<th>UNITED KINGDOM</th>
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<td>Dikmen and Varder, 1956&lt;br&gt;Ivanov, 1956&lt;br&gt;Al-Khatib and&lt;br&gt;Al-Bassam, 1975&lt;br&gt;Kholeaf et al., 1979</td>
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semen extender (Morgan et al., 1958; Adler, 1966; Clark et al., 1974b, 1975; Clark and Dufty, 1978). An infection in the cow may survive in the cervix through a full gestation period and may possibly infect a different bull at a subsequent breeding (Te Punga and Boyes, 1958; Brynner, 1976). It appears that sexual transmission of the organisms between bull and cows in a herd can be almost 100% successful but there is little or no cross infection occurring between individual cows (Te Punga and Boyes, 1958).

In the cow the vagina, cervix, uterus and oviducts become infected with the organism (Brynner, 1976; Ellis et al., 1978a). Cattle herds infected with C. fetus subspecies venerealis have a characteristically low fertility (Lambelin and Ectors, 1960; Savov, 1968; Ellis et al., 1977). The infected cows do not however remain permanently sterile and fertility usually returns four to eight months after initial infection. If the Campylobacter infection has continued in the herd for several years, older cows will have developed immunity and infertility is likely to be found only in the younger animals (Brynner, 1976).

Abortions due to C. fetus subspecies venerealis usually occur in late pregnancy and in herds with a history of infertility. In an infected herd the incidence of abortion is usually below 10%, but an incidence as high as 50% has been reported (Ellis et al., 1977). With abortion caused by C. fetus subspecies venerealis, the female genital organs become infected and acute endometritis, placentitis with subsequent infection, death and expulsion of the foetus follow (Brynner, 1976; Ellis et al., 1978a). The placentitis is a constant, though not pathognomonic, lesion. The areas between the cotyledons are usually oedematous, hyperaemic and may be leathery in appearance. The cotyledons themselves may be necrotic, haemorrhagic, yellow, and soft. The foetal lesions are specific with little or no autolysis and the
lungs are often only partially expanded. Slight dehydration of the foetal carcase with fibrinous pericarditis, pleuritis or peritonitis may occur. Intra-abdominal or abdominal haemorrhage from a ruptured liver may be evident (Dennis, 1969b, Brynner, 1976; Ellis et al., 1978a).

*C. fetus subspecies fetus* is a ubiquitous bacterium widely distributed in nature. In contrast to *C. fetus subspecies venerealis* it may affect the intestine and liver but also following ingestion of the organism it may cause sporadic abortion in cattle (Hoppe, 1968; Brynner, 1976; Agumbah and Ogaa, 1979; Fossum and Aanestad, 1979). During pregnancy a bacteraemia may originate from the infection of the intestine or liver, subsequently affecting the uterus. The organism localises in the placentomes causing placentitis and abortion often during the last trimester of pregnancy (Brynner 1976; Fossum and Aanestad 1979). The lesions in the placenta or foetus are similar to those produced by *C. fetus subspecies venerealis* (Dennis, 1969b, Brynner, 1976).

There appears to be a distinct difference between the vibrionic disease in cattle and that in sheep especially with respect to the route of infection and its subsequent course in a flock. In cattle, transmission is mainly by coitus whereas in sheep the ram is not the source. Instead the possibility of ewes becoming carriers following infection to other ewes in the flock is more likely (Buxton, 1930; Firehammer et al., 1956; Gorrie, 1962; Dennis 1975). The main organism involved in sheep is *C. fetus subspecies fetus* and abortion of a sporadic nature usually appears in late pregnancy. The incidence of abortion among pregnant ewes in a flock is usually less than 10% (Gorrie, 1962) although in the USA Biswal et al. (1953) reported an incidence of 28%.

Clinical signs suggestive of an impending abortion such as
depression or a rise in temperature in the pregnant ewe have only rarely been reported (Redman et al., 1963). More common is the sudden expulsion of the foetus with no premonitory signs. However, in several cases the ewes may show malaise, depression and lethargy for several days after abortion and during this period there is usually a pronounced dark uterine discharge (Fielden, 1980).

Placental changes vary from a generalised hyperaemia to focal or diffuse placentitis. Affected cotyledons are usually enlarged yellow to pink in colour, soft and necrotic with enlarged margins. The intercotyledon areas are oedematous, thickened and have a "wet leathery" appearance with a reddish brown exudate (Jensen et al., 1961; Gorrie, 1962; Dennis, 1975; Fielden, 1980).

At autopsy, the aborted foetus usually shows subcutaneous oedema in the foetal organs and the abdominal and thoracic cavities contain blood stained fluid (Gardiner, 1961; Redman et al., 1963; Dennis, 1975; Fielden, 1980). Necrotic foci are found on the surface of the liver and are "rosette like" raised, and pale orange to yellow with a depressed reddish brown centre (Fielden, 1980).

In pigs abortions associated with C. fetus subspecies fetus have been reported in the United Kingdom by Ellis et al., (1977), Higgins and Degre (1979) and in Europe by Shatalov (1971), Djakov and Pejeev (1973), Rezashka and Pejeev (1973), Ganchev et al. (1974).

Pathological changes were described in one case by Djakov and Pejeev (1973). Although the aborted pig foetus showed no gross external changes, histological examination showed hyperaemia and oedema of the foetal organs with diffuse leucocyte infiltration. Degenerative changes in the blood vessels were also evident.

**DIAGNOSIS**

Diagnosis of abortion in farm animals caused by either of the Campylobacter subspecies is by use of the following criteria:-

1. Isolation of the organism from placental and foetal tissues or foetal fluids (Kuzdas and Morse, 1956; Hubrig and Rohr, 1956;
Smibert, 1964; Kozhukharova, 1969; Ellis et al., 1977; Clark and Dufty, 1978; George et al., 1978; Neill et al., 1980; Tilse and McAlister, 1981), and identification using routine bacteriological techniques (Bryner, 1976; Neill et al., 1978a, 1979). Colonies of both subspecies grow on blood agar after two to five days incubation in atmosphere containing 10% CO₂.

2 Dark field or phase contrast microscopy of foetal fluids to demonstrate the presence of organisms with the characteristic and morphological features of Campylobacter (Bryner, 1976; Ellis et al., 1977; Fossum and Aanestad, 1979; Higgins and Degre, 1979; Fielden, 1980).

3 Demonstration of the organisms in placental or foetal tissues or fluids using fluorescent antibody and immunofluorescence techniques (Belden and Robertstaad, 1965; Kita et al., 1966; Philpott, 1968; Bingol and Blobel, 1970; Ardrey et al., 1972; Ellis et al., 1977).

4 Determination of agglutinating antibodies in the sera of aborting animals within one month following abortion (Levi, 1950; Pestano de Castro et al., 1967; Kostakev, 1969; Ganchev et al., 1970; Bingol and Blobel, 1970; Corbeil et al., 1974).

CONTROL

The use of vaccination to control vibriosis is mainly confined to countries where cattle are kept under free range conditions. This is because other methods such as artificial insemination using non-infected semen, or the segregation of infected from non-infected animals in the herd are not practical (Beckenhauer, 1967; Clark et al., 1968; Horlein and Carroll, 1970; Clark et al., 1970; Allen and Hutch, 1971; Boyd, 1972; Clark and Fitzpatrick, 1972; Bouters et al., 1973, Clark et al., 1974a, 1976, 1977; Leite et al., 1980). In the United Kingdom vaccination has only been used on a limited scale (Lincoln and Trout, 1967; Boyd, 1972). Philpott (1969) suggested that infection
with *Campylobacter* species in the United Kingdom was no longer a problem because of the increased efficiency of diagnosis and the widespread use of artificial insemination with antibiotic-treated semen. Reports by Adler, (1966) and Bouters et al. (1973) confirm this viewpoint. But more recently Ellis et al. (1978a) and MacLaren et al. (1980) have reported further outbreaks in Northern Ireland and SW Scotland. These infections may have been due to the development of antibiotic-resistant strains of *Campylobacter*.

In sheep, both in United Kingdom and in other countries, vaccination is the main method of control (Storz et al., 1966; Meinershagen et al., 1971; Gilmour and Thompson, 1972; Gilmour et al., 1975).

### 2.2 LEPTOSPIRA

Leptospirosis is the term used to cover a disease syndrome in man and animals caused by a slender spiral-shaped bacteria of the genus *Leptospira*. This genus is currently considered to include the *L. biflexa* complex which includes those species pathogenic to man and animals. A summary of the serogroups and species within the *L. interrogans* complex of approximately 150 species which are particularly associated with abortion in farm animals is given in Table IV. (Page 24).

In cattle the two main species associated with abortion are *L. pomona* and *L. hardjo*. In the USA, Reinhard (1953) and Bridges (1958) in Australia and New Zealand showed that *L. pomona* was the most prevalent species leading to abortion. Bryans (1954) found evidence of serological titres indicating *L. pomona* infection in 20% of breeding cows tested in USA. However, Hanson et al. (1965) and Stoenner (1964) found the level of infection in cattle had decreased from 20% in 1955 to 5.5% in 1964. This was due to the successful use of vaccines in controlling the disease. Other workers also cited this decline in *L. pomona* infection but also reported an increasing incidence of
L. hardjo infection (Hanson and Brodie, 1967; Andress, 1976; Nervig and Ellingausen, 1977). Sullivan (1974) suggested that the serological evidence reported in Australia and the USA would indicate that L. hardjo had replaced L. pomona as the most important leptospiral species causing cattle abortion in these countries.

TABLE IV - Leptospira species associated with abortion in farm animals

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Species</th>
<th>Animal</th>
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<tbody>
<tr>
<td>Icterohaemorrhagiae</td>
<td>icterohaemorrhagiae, copenhagenii</td>
<td>Cattle, pigs, horses</td>
</tr>
<tr>
<td>Pomona</td>
<td>pomona</td>
<td>Cattle, pigs, horses</td>
</tr>
<tr>
<td>Hebdomadis</td>
<td>hardjo, sejroe</td>
<td>Cattle, sheep, horses</td>
</tr>
<tr>
<td>Australis</td>
<td>bratislava, muenchen, lora</td>
<td>Sheep, pigs, horses</td>
</tr>
<tr>
<td>Canicola</td>
<td>canicola</td>
<td>Cattle, pigs</td>
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<tr>
<td>Tarassovi</td>
<td>mitis</td>
<td>Pigs</td>
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<tr>
<td>Grippotyphosa</td>
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<td>Cattle</td>
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<tr>
<td>Ballum</td>
<td>ballum, mus</td>
<td>Horse</td>
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In the United Kingdom and Europe abortion resulting from infection by L. hardjo or L. sejroe (both members of the Hebdomadis group of Leptospira) appears to have been recognised a few years later than in USA and Canada. This may have been due to the importation of the infectious agent, or to the development of techniques to diagnose this more fastidious species. Increasing serological evidence of antibodies
to the Hebdomadis group in aborted cows has been reported (Reis et al., 1973; Zamora and Reidemann, 1978; Little et al., 1980; Witt et al., 1981). In healthy breeding cattle Michna (1967) and Coghlan and Norval (1967) found antibodies to *L. sejroe* in 14% to 20% of cattle with a history of undiagnosed abortion. However almost ten years later Ellis and Michna (1976) found 41.4% to 46.8% of similar cattle had *L. sejroe* antibodies. The first isolation in United Kingdom of *L. sejroe* was from the kidney of a cow which had aborted in Scotland (Michna and Campbell, 1969).

However in the last decade the species *L. hardjo* and not *L. sejroe* has become recognised throughout the world as a common Leptospiral pathogen of cattle. It causes serious outbreaks of Agalactia "Mastitis" (Sulzer et al., 1964; Robertson et al., 1964; Ellis et al., 1976b; Higgins et al., 1980; Pearson et al., 1980) and abortions (Hanson et al., 1965; Martin et al., 1967; Hoare and Claxton, 1972; Ellis et al., 1976c; Little et al., 1980; Ellis et al., 1982a). Ellis et al. (1982b) reported 60.3% of sera from aborted cows on problem farms had antibodies to *L. hardjo* at a titre of 1:10 or over. Turner (1968) pointed out that serological evidence may indicate infection, but only isolation and characterisation of the organism could confirm the abortive agent. In the past, isolation of *Leptospira* spp. from aborted material had only been accomplished on rare occasions (Podgwaite et al., 1955; Dacres and Kiesel, 1958). In the last ten years however, *L. hardjo* has been isolated more frequently from dam and foetal tissues (Ellis et al., 1976b, c, 1981; Orr and Little, 1979). In 1968 Stoenner reported that cattle which had recently aborted as a result of leptospiral infection had a high serum titre (1:10,000 or over) and this may have led Kirkbride et al. (1973) to use a titre of 1:1000 or more as diagnostic of leptospiral abortion. However, Ellis et al. (1982b) suggested that where the predominant
infecting leptospires was *L. hardjo* these criteria were of limited value. This apparent discrepancy between the views of these workers could be due to differences in the species studied. Stoenner's work was mainly with cases of *L. pomona* infection where high antibody titres after abortion were usual. In dealing with cases of *L. hardjo* abortion however, Hoare and Claxton (1972) and Ellis and Michna (1977) observed that titres had fallen to 1:100 by the time of abortion. Ellis *et al.* (1982b) noted that no detectable antibodies were present in 22.8% of 149 cows aborting with *L. hardjo* as the causative agent.

In pigs the main Leptospiral species associated with abortion is *L. pomona*. This has been found in the USA (Bohl *et al.*, 1954); Hungary (Kemenes *et al.*, 1962); S. Africa (Anon, 1966) and Australia (Sullivan, 1974; Edwards and Daines, 1979); although the importance of *L. tarassovi* as an abortive agent in Europe has been suggested by Baryshev and Drozhzhin (1963), Akkermanns *et al.*, (1964) and in Australia by Sullivan (1974). *L. canicola* a pathogen primarily of dogs has also been reported as causing abortion in pigs, in Ireland (McErlean, 1964), in the United Kingdom (Michna, 1965; Lawson and Michna, 1966), in Russia (Lubazenko and Malachow, 1963) and in S. Africa (Renzberg, 1973). The results of serological tests against *L. pomona* in the USA, Europe, S. America and Australia indicate that abortion in swine due to this species can be as high as 20% in a herd but there is no serological evidence to suggest that *L. tarassovi* or *L. canicola* can cause similar abortion levels.

Recently the Australis serogroup of *Leptospira* has been associated with abortion in pigs. Hathaway and Little (1981) in a survey of pigs in the United Kingdom between 1978 and 1980 reported titres to this serogroup of 1:100 or higher in over 20% of blood samples from pigs. This significant finding has also been observed in W. Europe by Farina
et al. (1977) and Weber and Fenske (1978). Isolation from pigs of species in the Australis serogroup including: - L. lora (Hartmann et al., 1975); L. muenchen (Hathaway et al., 1982a); L. muenchen and L. bratislava (Ellis et al., 1985) may account for the increase in titres reported. Hathaway and Little (1981) suggested that the possible source of these Leptospiral species was wildlife as the sows were not housed and had extensive contact with free living animals. Identification of Leptospires of the Australis serogroup in several species of wildlife has been reported (Hathaway et al., 1983).

In horses the major disease symptom caused by Leptospira spp. is periodic opthalmia and uveitis, both infections of the eye (Alston, 1972). However, several cases of equine abortion caused by L. pomona have been reported in the world literature: - in Russia (Sova, 1963), Poland (Zweirz et al., 1965a, b); Australia (Baird et al., 1972, Sullivan, 1974). Giorgi et al. (1981) in Brazil reported an abortion due to L. icterohaemorrhagiae. This was also observed in the United Kingdom by Ellis et al. (1976a) who isolated L. icterohaemorrhagiae from an equine foetus. Subsequently, Ellis et al. (1983b) isolated L. hardjo, L. pomona, L. bratislava and L. icterohaemorrhagiae from aborted equine foetuses.

Sullivan (1974) suggested that sheep are relatively resistant to infection with Leptospira and this accounted for the sporadic reports of abortion in this animal (Beamer et al., 1953; Cacchione et al., 1964). However during the last ten years an increased significance of L. hardjo as an abortive agent in sheep has been suggested in Italy by Andreani et al. (1974) and in USA by Glosser and Diesch (1979) and Schmitz et al. (1978) and in Ireland by Ellis et al. (1983a). These latter workers also reported isolations of L. pomona, L. bratislava as well as L. hardjo from aborted ovine material.
PATHOLOGY OF LEPTOSPIRAL ABORTION

In cattle many abortions occur in the winter feeding period during the last trimester of pregnancy (Mitchell, 1960; Robertson et al., 1964; Stoenner, 1967; Dennis, 1969a, b; Ellis and Michna, 1977; Deas, 1981). In the majority of cases the disease is asymptomatic and cannot easily be recognised by farm staff (Deas, 1981). In pregnant cows the onset of disease is marked by fever, depression and a reluctance to move (Sullivan, 1974). Ellis and Michna (1977) have shown that the pyrexia can be as high as 106 to 107°F. During this bacteraemic phase of infection a sharp reduction in milk yield is found and "mastitis" is often present (Hoare and Claxton, 1972; Pearson et al., 1980; Little and Hathaway, 1983). The milk of infected animals is blood tinged, thickened and colostrum-like and leptospires have been isolated from it (Ellis et al. 1976b, c). The dam may suffer from general jaundice, fever and haemoglobinuraemia and post-mortem will reveal a yellow jaundiced liver and necrotic foci in the kidney. Reddish vulvae and blood tinged urines are also common (Fennestad and Borg Petersen, 1958; Kirkbride, 1975; Deas, 1981). In cows upon recovery, and up to six weeks after infection abortion can occur with the death of the foetus. The foetus has no specific external lesions but subcutaneous oedema and haemorrhagic fluid is common (Dennis, 1969a, b; Kirkbride, 1975; Deas, 1981). The intercotyledon areas of the placenta are covered with brown gelatinous fluid between the amnion and allantois and the cotyledons themselves are usually light tan to yellow in colour, atonic, avascular and uniformly affected (Te Punga and Bishop, 1953; Dennis, 1969a, b; Ezhkova, 1976). No microscopic lesions occur consistently in the foetal tissues (Kirkbride, 1975) but leptospires have often been demonstrated in the tissues and foetal fluids (Ellis et al., 1982a).

Abortion in pigs can occur at any period of gestation and the sow
usually has an enlarged jaundiced liver with numerous haemorrhagic and necrotic foci in the kidney (McErlean, 1964; Akkermanns, 1966; Lawson and Michna, 1966; Sullivan, 1974; Little and Hathaway, 1983). Post-mortem examination of the foetus often reveals characteristic focal areas with necrosis of the liver and thickened necrotic oedematous foetal membranes. Leptospires can often be demonstrated by microscopic examination of the peritoneal fluid (Sullivan, 1974).

**DIAGNOSIS**

A rising serological titre to leptospires in serum samples taken at the time of abortion and 14 days later has been used in the past to implicate them as an abortive agent. However, sometimes an animal will not develop a demonstrable titre (Robertson et al., 1964). Kirkbride (1975) suggests that such a failure to produce antibodies does not rule out Leptospira as the causative agent. Hoare and Claxton (1972) and Ellis and Michna (1977) have indicated that serological titres can be falling at the time of abortion and Ellis et al. (1982b) have reported that 22.8% of 149 cows with aborted infected foetuses had no detectable antibodies.

Demonstration of leptospires in the placenta and foetal tissues by histological staining methods has also been used (Gochenour, 1953; Bryans et al., 1953; Ryley and Simmons, 1954; Dennis, 1969a,b; Roberts, 1975; Kirkbride, 1975; Hodges et al., 1979) but isolation of the organism is the major definitive criterion. However isolation can be difficult because of the sophisticated culture techniques and specialised media that are necessary (Ellis and Michna, 1976). It is now generally accepted (Ellis, 1980) that diagnosis of leptospira abortion should be based on a combination of the following criteria:-

1. The isolation of leptospires from maternal blood, urine or foetal tissues and fluids using a selective medium (Johnston and Harris, 1967). However, Ellis (1984) has suggested that isolation of leptospires from the urine of recently aborted animals may be of little value as it may only indicate the animal as a renal carrier.
Demonstration of leptospira in sections of foetal liver, kidneys, lung, brain or cotyledon by silver impregnation staining technique (Ellis and Michna, 1977) or by immunofluorescence (Ellis et al., 1982a).

Demonstration of leptospiral antibodies in the aborted animal and in foetal serum and thoracic fluids (Stoenner, 1968; Ellis, 1980, 1983b).

TRANSMISSION OF INFECTION

The transmission of the disease in cattle is usually by genital or oral contact between animals congregating during periods of heavy rainfall or when they are housed indoors during the winter (Hanson et al., 1965; Hoare and Claxton, 1972; Ellis and Michna, 1977; Nervig et al., 1977). The drinking of contaminated urine has also been reported as a means of transmitting the disease (Ellis et al., 1976b). Leptospires of the Hebdomadis serogroup have been isolated from badgers, field mice and voles and it has been suggested that these and other animals may act as a reservoir (Brown and Coghlan, 1958; Michna and Campbell, 1969, Salt and Little, 1977). However, Ellis et al. (1981) in a survey of field mice and badgers and Hathaway et al. (1982b) studying mice, failed to demonstrate the Leptospira organism in these animals. Ellis et al. (1981) suggested that the only way to resolve this difference would be by definitive typing of a number of strains isolated from wildlife species and bovine abortion cases by cross-agglutination studies and/or factor analysis (Dikken and Kmet, 1978).

Mice and hedgehogs have been reported by Sova (1963) as the main reservoir of leptospires transmitting infection to horses.

Similar to cattle, transmission in pigs can also be due to urine ingestion (Mitchell et al., 1966; Perianu et al., 1974), but venereal transmission has also been suggested by Van der Hoeden (1958), Sleight et al. (1964), Turner (1967), and Ellis et al. (1985). Transmission of Leptospirosis to pigs from contaminated water, soil or grass has been reported by Hathaway and Little (1981).
PREVENTION AND CONTROL

The control of Leptospirosis has been mainly by the use of vaccines to *L. pomona* for cattle and pigs and to *L. hardjo* for cattle. These have had some success in reducing abortion losses in these animals (Cook, 1964; Killinger *et al.*, 1971; Negi *et al.*, 1971; Crawford, 1972; Hanson, 1972; Huhn *et al.*, 1975; Holyroyd and Smith, 1976; Nervig *et al.*, 1977; Holyroyd, 1980; Allen *et al.*, 1982; Mackintosh *et al.*, 1980). Where it has been possible to recognise the disease in its early stages, preventative treatment with dihydrostreptomycin, auranomycin and oxtetracycline has proved fairly successful (Ferguson and Powers, 1956; McErlean, 1964; Michna, 1965). Ellis (1984) has suggested that a combination of vaccine with dihydrostreptomycin can be administered and in young calves and piglets that feeding with colostrum rich in maternal antibodies can give them passive protection (Kemenes *et al.*, 1962; Baglioni *et al.*, 1966; Perianu *et al.*, 1974). Finally, Hathaway (1981) has emphasised that *L. hardjo* vaccination programmes must be completed as any interruption or wrongly applied vaccine may result in a severe outbreak of clinical disease.

2.3 LISTERIA

This organism is a small gram positive bacillus which was first isolated by Murray *et al.* (1926) from rabbits having a disease characterised chiefly by a mononuclear leucocytosis. It was originally named *Bacterium monocytogenes* but since 1953 is more generally called *Listeria monocytogenes* (Mollello and Rue Jensen, 1964).

It was first isolated from sheep by Gill (1933) in New Zealand. Subsequently infections with *Listeria monocytogenes* have also been reported in cattle, pigs and horses (Jones and Woodbine, 1961), in birds (Killinger and Scubert, 1966), and in humans (Gray, 1964; Gray and Killinger, 1966).
Listeria monocytogenes has been suggested as a cause of abortion in animals and also in humans. Graham et al. (1939) first reported Listeria associated bovine abortion and Patterson (1940) cited this organism as a possible cause of abortion in sheep in England. Subsequently abortions associated with cattle and sheep have been reported worldwide: United Kingdom (Gitter, 1966; McCleod et al., 1974; Clegg, 1975; Woodbine, 1975; Vet. Invest. Ser. Rep., 1979); USA (Ferguson et al., 1951; Olson et al., 1953; Osebold et al., 1960; Njoku et al., 1972; Smith, 1975a); Europe (Van Ulsen, 1960; Donker Voet, 1963; Weis, 1974; Ivanov, 1975; Chwalibog, 1975; Guilloux, 1979; Kampelmacher and Jansen 1979; Korukov, 1981), Australia and New Zealand (Gill, 1963; Dennis, 1975; Hughes, 1975; Broadbent, 1972). From Germany there have been single reports of Listeric abortion in horses (Mayer et al., 1975) and in pigs (Weber and Schleisser, 1972). Despite these widespread incidences, the abortion caused by this organism in cattle, sheep and other animals has not received similar attention to the more traditionally recognised bacterial abortive agents. It was suggested by Clegg (1975) that this may be due to Listeria producing a low grade non-fatal inapparent infection in pregnant animals which at farm level may go undetected. Also contributing, was the failure to recognise the causative organism in aborted foetal materials. However in some incidences of abortion in cattle and sheep there is some evidence of rising serological titres to Listeria in successive adult blood samples and foetal blood titres are also seen to be relatively high.

In surveys of cattle in the USA Listeria has been reported to cause up to 50% abortions in one herd (Osebold et al., 1960; Clegg, 1975), and up to 20% of abortions in sheep flocks (Clegg, 1975). Gorrie (1962) found that abortion due to Listeria did not recur in sheep with a previous history of Listeric abortion. However, reports by Osebold et al. (1960) and Korukov (1981) conflict with this view as they cited cases of listeric abortion recurring seasonally in the same animals. Clegg (1975)
in a review of abortion in cattle and sheep, found higher incidence in cattle than sheep. A possible reason for this is that cattle are of a higher economic value and therefore the cause of abortion in them is investigated more thoroughly. As early as 1966 Gitter suggested that the incidence of Listeric abortion in sheep was under-reported.

**PATHOLOGY OF LISTERIC ABORTION**

The epidemiology of listeriosis in its encephalitic form has been understood for some time (Broadbent, 1975) although the epidemiology of abortion caused by the organism remains obscure. The clinical symptoms in cattle are pyrexia, depression, retained placenta and purulent genital exudate (Osebold et al., 1960; Dennis, 1969a, b; Smith, 1975a).

In both cattle and sheep abortion is usually caused by an ascending infection of the genital tract. The organism attacks the placenta and then the foetus which then dies and is aborted (Njoku and Dennis, 1973). The dead foetus is usually retained for between three to five days and once expelled examination can generally show necrotic yellow foci in the liver, spleen and lungs (Dennis, 1969b; Fielden, 1980). Autolysis of the placenta may occur with marked necrosis and haemorrhage between the cotyledons. The cotyledons themselves become thickened and oedematous and the placenta is often covered with a reddish brown yellow exudate (Mollello and Rue Jensen, 1964; Dennis, 1969a, b; Njoku et al., 1972). Similar clinical symptoms and placentitis have been recorded in cases of listeric ovine abortion (Fielden, 1980).

**DIAGNOSIS**

On histological examination of the liver, placentomes and cotyledons of the aborted foetus, necrotic foci can be detected and gram stained sections of these organs will often reveal small bacilli morphologically identical to *L. monocytogenes* (Dennis, 1969a, b; Kirkbride, 1975; Fielden, 1980). The identity of the organism can be
confirmed in these sections using a fluorescent antibody technique (Baublis and Eveland, 1966; Kral et al., 1977) and using specific immunofluorescent conjugate, L. monocytogenes serotypes 1 and 4b have been found in cattle (Osebold et al., 1960; Seeliger, 1961; Gray and Killinger, 1966; Bellhouse et al., 1975; Kummeneje, 1975), and serotype V in sheep (McCleod et al., 1974; Ivanov, 1975; Srivasta and Kitera, 1980). After treating bovine serum samples with mercaptoethanol to eliminate cross reactions, Srivasta and Kitera (1980) also found three additional serotypes and they suggested further studies to classify these. The organism can be cultured from foetal blood, lung, liver, kidney, brain and placental tissues as well as from stomach, pleural, and peritoneal fluids. Tryptose agar or blood agar base with 5% defribinated ovine or bovine blood is used and the plates are incubated either aerobically or microaerophilically (Gray, 1957; Larsen, 1966; Kirkbride, 1975; Fielden, 1980).

TRANSMISSION OF INFECTION

The connection between silage and the transmission of listeric infection leading to abortion has been emphasised in several reports (Killinger and Hatch, 1966; Dijkstra, 1966; Welshimer and Donker Voet, 1971; Gronstol, 1979). Blenden et al. (1966) and Kampelmacher and Jansen (1979) found that abortion was significantly reduced if silage contaminated with Listeria was removed from the diet. However this cannot be the only method of transmission as silage is not part of normal farm animal diet in Australia yet abortions due to Listeria have occurred (Broadbent, 1975).

PREVENTION AND CONTROL

Broadbent (1975) has shown that antibiotics are effective in the treatment of encephalitis but were less so against genital infections and abortion. Vaccines have been used with limited success in attempts to control abortions in cattle (Gray et al., 1956; Osebold et al., 1959;
Gray, 1963a; Smith, 1975a), and in sheep (Osebold and Inouye, 1954; Molello and Rue Jensen, 1964; Njoku et al., 1972; Njoku and Dennis, 1973).

During the last decade improved methods of diagnosis, isolation, and identification of these organisms (Broadbent, 1975; Fielden, 1980) has indicated that listeric abortion in cattle and sheep is a more widespread and possibly important cause of perinatal loss in farm animals than had been previously realised.
Fig 3: Salmonella dublin in kidney tissue from an aborted bovine fetus. Stained by the FA technique X500.

Fig 4: Mycobacterium bovis in lung tissue. Modified Zeihl Neilsen stain X1000.
INTRODUCTION

The genera discussed in this chapter are less frequently associated with abortion than those described in chapter 2. They include the genera Corynebacteria, Haemophilus, Pasteurella, Neisseria, Mycobacterium, Bacillus and Streptococcus.

3.1 CORYNEBACTERIUM PYOGENES

Corynebacterium pyogenes is a small pleomorphic gram positive rod shaped bacterium generally accepted to be one of the most frequently isolated organisms from pyogenic conditions in farm animals (Bruner and Gillespie, 1973). It is also commonly associated with sporadic infection of the reproductive system which may lead to abortion (Smith et al., 1971; Hinton, 1972). A general review of C. pyogenes was published by Purdom et al. (1958) and Lovell (1959) described the clinical aspects of Corynebacterial diseases.

C. pyogenes has been recorded as a sporadic cause of abortion in sheep by Sorum (1953), Beverley and Watson (1962), Hughes (1964), Dennis and Bamford (1966), Rosca (1971), Smith et al. (1971) and Deas (1981). Abortion occurred during the last trimester of pregnancy and Smith et al. (1971) and Addo and Dennis (1979) noted that prior to abortion there was no systemic illness and the most common lesion was a placentitis. On gross examination the placentas were found to be brown to reddish brown in colour. They were also oedematous and had enlarged cotyledons with varying degrees of autolysis. Foetal changes were primarily autolytic except for small necrotic foci in the liver and small areas of gliosis in the brain. C. pyogenes could be isolated from foetal fluids, tissues and maternal caruncle of the aborting ewes. In pigs C. pyogenes has been associated with genital infections and infertility (Vet. Invest. Ser. Reps. 1959, 1960) although only a single case of abortion has been recorded (Kirkbride and McAdaragh, 1978). In horses an abortion due to C. pyogenes has been reported in India by Krishnappa et al., (1979).
Surveys of abortion caused by *C. pyogenes* in cattle have been carried out by Traum (1923); Gilman (1939) and Lawson (1963). More recently Hinton (1972) estimated the prevalence of abortion in cattle herds attributable to this organism to be between 0.3 and 19.6% with a mean of 5.3%. Smith (1975b) suggested that abortion in breeding cattle was generally sporadic in nature and minor outbreaks in single animals have also been reported (Scheiferi et al., 1974; Deas, 1981). Scheiferi et al. (1974) reported an apparent increase in *C. pyogenes* bovine abortions in Canada but suggested that this could be explained on improved diagnostic methods. In Eastern Europe the sporadic nature was noted by Kolar (1963) when he reported that during a seven year period in 131 (64%) of 204 cattle herds with *C. pyogenes* abortion problems only one animal in each herd was involved. However in one herd he also recorded seven abortions in a period of 14 months, whilst in another only nine cases were recorded in five years. Again in Eastern Europe Kozlowski and Kozlowska (1969) and in 14 out of 18 bovine herds examined, only a single animal aborted and in two of the herds only two animals aborted due to *C. pyogenes* infection.

Smith (1975b) reported that most cattle abortions occurred during the last trimester of pregnancy and Kolar (1963) found that in most cases clinical symptoms were absent prior to abortion, except in a few cases where it was preceded by a systemic illness. Maxwell (1943), Smith (1970) and Deas (1981) suggested that abortion may follow mastitis or a generalised infection caused by *C. pyogenes* and Kolar (1963), Smith (1975b) and Deas (1981) noted that retention of the placenta, sometimes with a purulent metritis frequently occurred. Varying degrees of autolytic changes were often evident in the foetus and placenta.

The mode of infection is not fully understood as the organism is ubiquitous in cattle (Deas, 1981); however, the ascending and haematogenous routes of uterine infection seem to be the most likely (Hinton, 1972). Subsequent septicaemic infection of the foetus is
probably due to aspiration of contaminated amniotic fluid following transplacental passage (Smith, 1975b). Smith et al. (1971) found corynebacterium-like organisms on histopathological examination of foetal lungs but failed to isolate and confirm as *C. pyogenes*. In further investigations Scheiferi et al. (1974) noted that these corynebacterium-like organisms were mainly confined to the bronchioles of the lung, often with little or no inflammatory change. Kolar (1963) had earlier reported that foetal infection was not always reported in abortion cases. In contrast, Hinton (1972) has reported isolations from foetal lung. However, because *C. pyogenes* is a vaginal commensal Kirkbride (1975) and Deas (1981) have suggested that the significance of its presence in foetal lung tissue needs further investigation.

Despite this reservation current diagnosis of abortion is based on the isolation of *C. pyogenes* from the foetal tissue, placenta or vaginal mucus immediately following abortion. However, as *C. pyogenes* may also cause a secondary uterine infection (Hinton, 1972) the longer the time that elapses between the abortion and the collection of samples, the greater the likelihood that the organism is a secondary invader.

*C. pyogenes* grows as small haemolytic colonies on tryptose agar or blood agar base with 5% defribinated bovine or ovine blood when incubated in an atmosphere containing 10% CO₂.

The control of infection by *C. pyogenes* has proved difficult as the organism can be isolated from apparently normal animals and also it can infect all farm animals causing mastitis and skin abscesses. Cross infection between cattle and sheep has also been reported (Roberts, 1971). The organism seems to pose little threat to normal healthy animals but when under stress the pregnant animal during the last trimester seems especially vulnerable to infection. Control of the disease depends upon good sanitation, good management and sound nutrition (Deas, 1981). Rosca (1971) suggested that in sheep the
isolation of infected animals, attention to hygiene and treatment of affected ewes with penicillin, streptomycin or chlortetracycline was of value. On the other hand Kolar (1963) found that in cattle there was no correlation between the abortion rate and herd management as in one outbreak involving seven cases the herd management was excellent.

In conclusion _C. pyogenes_ can be regarded as a primary cause of abortion in cattle and sheep, although care is needed in interpreting the statistics as many of the isolations may represent secondary infection.

3.2 **HAEMOPHILUS**

_Haemophilus_ species have been recovered from most farm animals, cattle, swine and poultry are subject to clinical disease (Biberstein 1981) and in horses a purulent contagious metritis occurs (Brewer, 1983).

Swine are subject to infection with _H. suis_, _H. parasuis_ and _H. pleuropneumonia_ (previously known as _H. parahaemolyticus_). In the past _H. suis_ and _H. parasuis_ have generally been associated with an influenza-like disease (Shope, 1931) but _H. parasuis_ has also been found to be associated with Glassers disease, a systemic infection producing fibrinous inflammation of membranes lining body cavities, joints and meninges. (Hjarre Wramby, 1942; Neilsen, 1981).

_H. pleuropneumonia_ primarily produces an infection of the respiratory tract (Shope, 1964) but also a contagious, often fatal, septicemia (Neilsen, 1973). It has also been reported to cause abortion in sows (Wilson and Kierstead, 1976). Prior to abortion the sows exhibited signs of swollen red vulvae for seven days and when expelled all the foetuses had gross inflammatory lesions. These included swollen and haemorrhagic kidneys, enlarged and congested livers and spleens which were bright red in colour. Microscopically all tissues were heavily congested and the organism could be isolated from placenta, pericardial fluid, lungs, liver and stomach contents.

_Haemophilus_ infections of cattle have been recognised to be of major importance and were first described by Griner et al. (1956) and
experimentally produced in calves by Kennedy et al. (1960) who suggested the name *Haemophilus somnus* for the causative organism. The further involvement of the organism in cattle disease has been demonstrated in the USA, Canada and Europe (McDonald et al., 1973; Van Dreumel et al., 1970; Crandell et al., 1977; Saunders and Janzen, 1980). A wide range of conditions associated with septicaemia occur during infection with *H. somnus*, including thromboembolic meningoencephalitis (Esteme), pneumonia, arthritis (Van Dreumel and Kierstead, 1975; Biberstein, 1981; Stephens et al., 1981).

Following genital infections of cattle with this organism birth of underweight calves (Waldham et al., 1974) and several cases of abortion have been reported (Chladek, 1975; Van Dreumel and Kierstead, 1975). *Haemophilus somnus* has been identified as causing a common infection of the prepuce of bulls (Humphrey et al., 1982), and Corboz and Nicolet (1975) showed that the organism could be transmitted by the infected bull semen and that the bull may thus be a reservoir of infection. In recent studies Van Dreumel and Kierstead (1975) and Miller et al. (1983b) speculated that the possible route of foetal infection was direct cervical invasion, as they had isolated *H. somnus* from the vagina of breeding cows. Although the organism has been isolated from aborted foetuses and placentas (Chadlek, 1975; Van Dreumel and Kierstead, 1975) and experimentally several strains of *H. somnus* have caused abortion following intra-amniotic inoculation (Miller et al., 1983a), the route of infection has not yet been determined without doubt. Miller et al. (1983a) suggested a sexual transmission of the disease whereas a haemotogenous spread of infection leading to transplacental passage and death of the foetus has also been suggested by Smith and Biberstein (1977).

Abortions usually occur between seven and a half and nine months of gestation and are of fairly low incidence with 2 to 3% of cattle within the herds being affected. Van Dreumel and Kierstead (1975) reported that cows
aborting due to *H. somnus* infection had no previous history of illness.

In all cases of abortion the placenta is retained and exhibits inflammatory lesions. Some necrosis of the stromal arteries is evident and the cotyledons are oedematous. Lesions in the foetus are characterised by vascular necrosis, thrombosis and infiltration of leucocytes into brain, lung, myocardi and kidney. In addition, interstitial pneumonia and myocarditis are prominent. Small gram negative *Haemophilus*-like bacilli may be observed in the necrotic tissues of the placenta and foetus and *H. somnus* can often be isolated from placenta, lung and stomach contents (Biberstein, 1981). Although most of the reports of abortion in cattle have been identified as being due to *H. somnus*, an earlier report by Firehammer (1959) of a case with similar clinical symptoms suggested that the causative organism isolated from vagina and foetus was *H. citreus*. However as the classification was based on a limited range of tests it is possible that, if additional modern techniques had been included, this isolate may have been classified as *H. somnus*.

Diagnosis as a causative agent of abortion depends upon the successful isolation of the *H. somnus* from foetal tissues and fluids. For this high oxygen tension and an unidentified growth factor found in the blood agar is required (Kennedy et al., 1960; Garcia Delgado et al., 1977; Foster and Scheer, 1980; Stephens et al., 1981), in addition to the requirements for x and v factors (Zinnemann, 1967; Zinnemann and Biberstein 1974). Biochemically *H. somnus* is oxidase positive and catalase negative and its indole and nitrate reactions are variable (Biberstein, 1981). A more positive identification can be obtained by agglutination with antisera (Shigidi and Horlein, 1970; Dierks et al., 1973), and can be compared using gel diffusion, immunoelectrophoresis, and complement fixation techniques (Garcia Delgado et al., 1977).

No work has been published on the prevention and control of abortion by *Haemophilus* species other than the work of Van Dreumel and
Vaccination against abortion has not been attempted but Brown et al. (1970) and Williams et al. (1978) have successfully used vaccines to control the Esteme disease and further work is required to see if a similar vaccine prepared from other isolates would be effective in controlling abortion. Husbandry appears to be unimportant as a control measure as Van Dreumel and Kierstead (1975) indicated that abortions still occurred when good management practices had been maintained. This finding also requires further confirmation.

3.3 OTHER LESSER KNOWN BACTERIA

A number of other bacteria have been found occasionally in the genital tract following abortion. However, their importance as abortive agents has not yet been established.

(a) Nocardia. The genus Nocardia are acid fast, gram positive, branching filamentous bacteria which may break up into coccoid and bacillar forms and contained within are many saprophytic and several pathogenic species although only Nocardia asteriodes is regarded as an important cause of disease in farm animals. In cattle the organism produces acute and chronic mastitis as well as abortion (Austwick and Venn, 1961; Zanella, 1961; Kikopa and Bergmann, 1975; Dohnal et al., 1978; Monge et al., 1978; Mugarula and McHomba, 1980) and abortion in sheep has been reported (Watson and Beverley, 1977). The first recorded porcine abortion caused by N. asteriodes was described by Cole and Holzinger (1972) and further cases have been reported (Kirkbride and McAdaragh, 1978; Mason et al., 1981; Koehne and Giles, 1981). In a recent survey of 850 cases of cattle abortion, 0.1% were reported as being due to this species (Kirkbride, 1979).

Following abortion the organism can be demonstrated histopathologically in affected adult and foetal tissues and it may be isolated from the foetal lung and stomach contents. In the lung there is usually a generalised pneumonia with numerous
leucocytes and branching nocardial filaments in the alveoli
(Cole and Holzinger, 1972; Mason et al., 1981). These branched
nocardial filaments have also been found in necrotic lesions of
the placenta. *N. asteriodes* will grow on blood agar or
Sabouraud dextrose agar, although plates need to be incubated at
37°C for approximately one week (Carter, 1979). No work has been
found on the control of *N. asteriodes* infection in farm animals.

(b) *Pasteurella*. Members of this genus are small non-motile gram
negative rods or coccobacilli and *P. multocida* and *P. haemolytica*
are the main species causing disease in farm animals. Both species
occur in the upper respiratory and digestive tracts of a wide range
of birds and mammals (Carter, 1979; Gibbs et al., 1983) and are
often secondary invaders in a number of pathological conditions
such as bronchopneumonia (Carter, 1979).

They can produce a septicaemia in farm animals with subsequent
intrauterine infection and abortion. Sporadic abortions in cattle
have been reported to be caused by *P. multocida* (Roberts, 1971;
Zaki et al., 1974) and by *P. haemolytica* (Messier et al., 1981) in
horses (Webb et al., 1980). Two other species *Francisella
tularensis* (formerly known as *P. tularensis*) and *Yersinia
pseudotuberculosis* (formerly known as *P. pseudotuberculosis*) have
been reported as causes of abortion in sheep. (Jellison et al.,
1964).

At post-mortem the foetus may not show any specific lesions
but *Pasteurella* spp. have been isolated from lungs, stomach
contents and abdominal fluids (Webb et al., 1980; Messier et al.,
1981). Examination of the placenta may reveal a purulent
placentitis with numerous necrotic foci. *Pasteurella* spp. can
be recovered on blood agar incubated at 37°C and selective media
for the growth of *P. multocida* and *P. haemolytica* are
available (Morris, 1958; Carter, 1979).
(c) *Neisseria/Branhamella.* Species of the genus *Neisseria* and *Branhamella* are microaerophilic gram negative diplococci which can occasionally occur in farm animals as commensals on mucous membranes including those of the genital tract. However, *Branhamella catarrhalis* (formerly known as *Neisseria catarrhalis*) and *Neisseria ovis* are the two species associated with abortion in cattle.

*B. catarrhalis* is frequently isolated from the nasopharynx of man and animals and also has been associated with pneumonia in calves (Hunter and Harbourne, 1964; Carter, 1979). It was isolated from the stomach contents of an aborted foetus of cow at five and a half months gestation (Claxton et al., 1974). The foetus lacked external lesions but autopsy revealed oedema and yellow fluid in the body cavities. The stomach wall was oedematous with thickened folds and covered with grey yellow mucosa. The lungs were mildly oedematous and the alveoli were filled with an inflammatory exudate containing many gram negative diplococci subsequently identified as *B. catarrhalis*.

*Neisseria ovis* has been isolated from both cattle and sheep suffering from keratoconjunctivitis (Lindquist, 1960; Fairlie, 1966) and has also been reported as the cause of a bovine abortion (Neill et al., 1978b). The foetus showed no obvious gross lesions and histopathological examination revealed slight bronchial hyperplasia in the lung. However, the organism was cultured from the lung, liver, stomach contents, thoracic fluid of the foetus and vaginal mucus and placental tissue of the dam.

(d) *Mycobacteria.* The genus includes many saprophytic species as well as *M. bovis, M. avium* and *M. tuberculosis* known pathogens causing disease in farm animals (Davis et al., 1973; Carter, 1979). Infections of the genital tract and abortions in cattle due to *M. bovis* and *M. tuberculosis* have been reported (Williams, 1943; Blood and Henderson, 1963; Merkal et al., 1982). *M. avium* commonly causes
tuberculous lymphadenitis among swine in the USA (Ellesworth et al., 1979) but for pigs reports of abortion have come mainly from Europe (McErlane, 1959; Ratz and Molnar, 1972; Billie and Larsen, 1973) with one report from the USA (Ellesworth et al., 1979).

The features of abortions in farm animals caused by these three pathogenic species include slight autolysis of the foetus and at autopsy, numerous small white foci in the liver.

Saprophytic mycobacteria are widespread in soil, plants and fresh and salt water (Lennette et al., 1974) but can also cause pulmonary disease in man and animals (Fogan, 1970; Aaneland and Roland, 1972; Edwards et al., 1978). A case of equine abortion due to one of these saprophytic species Mycobacterium terrae has been reported (Tasler and Hartley, 1981). The organism was isolated from an eight and a half month old foetus. The placenta was not available for examination and the foetus showed no autolysis or gross lesions. Histological examination of the lung revealed moderately severe bronchopneumonia with microscopic lesions and many mononuclear cells. Histologically no organisms were demonstrated in the other foetal tissues.

(e) Bacillus. As Bacillus species can be commonly found in the environment, they are usually considered to be contaminants when recovered from clinical specimens. However, although it is generally saprophytic, Bacillus cereus can occasionally infect the bovine udder causing an acute, and often fatal, mastitis (Carter, 1979). Additionally B. cereus has been incriminated in cases of bovine abortion (Hartley and Boyes, 1955; Hartley and Kater, 1964; Wohlegemuth et al., 1972). Other abortions associated with Bacillus species include a single report of an equine abortion caused by B. cereus (Ranganatha et al., 1981) and a report of
abortion in cattle and sheep caused by unidentified Bacillus spp. (Mason and Munday, 1968).

In the few cases where histopathological examination was performed following abortion a necrotising placentitis with no visible abnormalities was evident. On examination however, B. cereus was isolated from blood and stomach contents of the foetus and in one case also from the cervical mucus of a mare (Ranaganatha et al., 1981).

(f) Streptococci. Streptococcal species can be grouped serologically by the method of Lancefield (1933). There are currently 21 recognised groups of which B. C, D, E, G and L (Jones, 1976; Riising, 1976; Carter, 1979) are significant causes of disease in farm animals. Streptococcus zooepidemicus (Group C) a betahaemolytic Streptococcus is the most common species and causes abortion in mares. Abortion can occur at any stage of gestation (Roberts, 1971) and tends to be found on poorly managed farms where proper washing of the external genitalia of the mare and stallion before and after intercourse are not carried out (Berthelon and Rampin, 1970). The abortions are usually sporadic in nature and the organism can usually be recovered from the foetus and the mares genital discharges. Control of the disease is achieved by local antibiotic therapy of the genital tract or artificial insemination using antibiotic treated semen. Douching of the uterus within 12 to 24 hours after intercourse has also been suggested (Roberts, 1971).

Streptococci belonging to groups C and L have also been involved as agents of abortion in sows (Saunders, 1958; USDA Symposium, 1969; Swann and Kjar, 1980). Streptococci belonging to these groups are the most common isolates obtained from vagina and uterus of sows and the prepuce of boars (Olsen, 1964). In cases of abortion the organisms were isolated from vagina, placenta and foetuses (Swann and Kjar, 1980). There were inflammatory areas on the foetal skin and in the thoracic and abdominal cavities of the foetus.
Fig 5: *Campylobacter fetus* sub *sp fetus* isolated from foetal stomach contents. Stained with Methylene blue X750.

Fig 6: *Neisseria ovis* organisms isolated from aborted bovine foetus. Stained by Indirect FA technique X1000.
CHAPTER 4

COMPARISON OF THE INCIDENCE AND OCCURRENCE OF
THE BACTERIAL SPECIES REVIEWED

In previous chapters both the traditional and less common
bacterial agents associated with abortion have been described. In this
chapter the infectious mechanisms and the pathology of these organisms
will be compared under the following headings (1) Occurrence
(2) Clinical Symptoms (3) Pathogenicity (4) Pathology.

4.1 OCCURRENCE

There have been many surveys carried out which have considered the
frequency of abortion due to infectious agents (Bolton et al., 1969;
Rowe and Smithies, 1978; Fernandez-Diez et al., 1978; Kholeaf et al.,
1979; Kirkbride, 1979; Guarda, 1979; Guarda et al., 1979; Balbo
et al., 1981; Mostaghini, 1980; Higgins et al., 1981; Moojen et al.,
1983). Most of these surveys were limited in both the number of animals
investigated and the geographical areas covered. Their relative importance
has been assessed mainly on the incidence of the abortive agent rather
than economic loss considerations. Generally it is difficult to make
comparisons between these surveys, as many tend to be biased towards a
particular organism, possibly because of the laboratory specialisation in
that particular area. Other factors included size of area, time of year
and number of animals involved as well as laboratory techniques as pointed
out by Hubbert et al. (1973).

However, the surveys carried out on Brucella and Salmonella tend to
be more meaningful as internationally agreed methods have been used to
identify these pathogens from affected animals. Tests from suspect herds
include the regular examination of blood, milk and vaginal mucus and the
routine screening of blood and milk from all herds for antibodies to
Brucella or Salmonella. Surveys have shown that the incidence of abortion
in cattle caused by Brucella spp. has decreased in United Kingdom from
13% in 1959 (Holt, 1952) to 1.6% in 1980 (Gordon, 1981) and in the USA
from 11.5% in 1935 (Manthei, 1968) to less than 1% in 1973 (Kirkbride
et al., 1973). It has been suggested by Deas (1981) that this was due to the eradication programmes for Brucellosis in cattle and the subsequent increase in Brucella free herds. However, in some countries because of the lack of suitable eradication programmes, Brucella spp. can still cause major outbreaks of abortion for example in France (Sanchis, 1982); Switzerland (Nicolette et al., 1979), Italy (Guarda et al., 1979; Balbo et al., 1981) Spain (Fernandez-Diez et al., 1978), Egypt (Kholeaf et al., 1979; El-Nagger et al., 1980). Brucella abortus has been associated with abortion in all farm animals with up to 80% of unvaccinated animals becoming infected in an outbreak. A carrier state can be established in animals after acute infection which can persist for the life of the animal in some cases. Following genital infection a carrier state may also exist in bulls and Bartlett (1968) has reported a case of semen infected with Brucella abortus that caused abortion after artificial insemination. However, despite this isolated case Manthei (1968) and Roberts (1971) suggest there is no evidence that the bull acts as a reservoir for Brucella abortus as it may do, for example, in the case of Campylobacter fetus subspecies venerealis (Boyd, 1972).

Salmonellosis is also a worldwide disease; although in the more developed countries it has been largely controlled by vaccination programmes (Hinton, 1974; Hunter et al., 1976). However, outbreaks of abortion caused by Salmonella spp. are still being reported especially among sheep where vaccination programmes are more difficult to administer because of the nomadic nature of these animals (Dennis and Armstrong, 1965; Vujic et al., 1965; Hunter et al., 1976; Quai and Turdean, 1976; Fernandez-Diez et al., 1978; Oof and El Ghani, 1979).

Infection of the foetus by Salmonella spp. usually follows a gastroenteritis in the adult animal caused by ingestion of faecally contaminated materials. As with Brucella spp. a passive carrier state may often be established although its epidemiological significance in the occurrence of abortion is still unresolved (Hinton, 1971).
As *Brucella* and *Salmonella* have been recognised as major causes of abortion, it could be expected that their eradication or control in the United Kingdom and USA would reduce the total numbers of abortions due to infectious causes. However, despite their decline Kiupel *et al.* (1979) reported that the total number of abortions had increased and Miller (1977) stated that the proportion of infectious abortions diagnosed was on the increase as more bacterial species were being demonstrated in the foetus. As farmers usually only report the occurrence when several animals have aborted, the percentage that are due to infectious agents is likely to be higher than the figure of about 25% usually recorded (Mitchell, 1960; Bolton *et al.*, 1969; Moojen *et al.*, 1983). On the other hand, the percentage will be lower if incorrect tissues or tissues and fluids in poor condition are examined or inappropriate diagnostic criteria applied. Also however, some of the abortions may not be due to infectious agents.

*Campylobacter fetus* subsp *venerealis* can be found throughout the world causing an abortion rate in cattle herds of usually less than 10%. It is a sexually transmitted disease and as with *Brucella* and *Salmonella* infections, a carrier state can be established in the female animal, with the organism surviving in the cervix for up to one year. These organisms may then cause abortion in subsequent pregnancies. The role of the bull as a reservoir of infection and the cow as a passive carrier has been more clearly established in relation to abortion with *C. fetus* subsp *venerealis* than with *Brucella* spp. and *Salmonella* spp. This is because more extensive experimental investigations on transmission of the *Campylobacter* spp. between bull and cow have been carried out (Adler, 1966; Florent *et al.*, 1966; Clark *et al.*, 1975; Clark and Dufty, 1978).

*Campylobacter fetus* subsp *fetus* is also widely distributed and tends to cause sporadic abortions in farm animals. It is similar to *Salmonella* spp. in that the foetus becomes infected following a primary intestinal infection of the pregnant female (Miller, 1977). After the acute infection the organisms may survive in the female intestine for
several months but their epidemiological role as passive carriers in the cause of abortion has not been extensively investigated.

Leptospiral abortion has been reported to occur in most areas of the world with animals acting as reservoirs of infection for example Rat (Rattus norvegicus), Hedgehog (Erinaceus europaeus), Badger (Meles meles), Fox (Vulpes vulpes). The frequency of abortion among cattle herds varies between 5% and 40% (Hubbert et al., 1973; Deas, 1981; Ellis et al., 1982a). As with Brucella spp. infection occurs both through mucous membranes and abraded skin. The organism can localise in a number of organs particularly the kidney and female genital tract (Thièrmann, 1982; Ellis, 1983a).

Localisation in the kidney leads to urinary excretion particularly of L. hardjo. This is an important element in the transmission of the disease. Localisation of Leptospiral spp. in the male genital tract of farm animals has not been widely established but some evidence of leptospiral antibodies in the semen of bulls may indicate a local genital tract infection (Vaz and Oliveira, 1978). Whether or not this is sexually transmissible in a way similar to Campylobacter fetus subsp. venerealis has not been fully investigated.

Listeria monocytogenes has also been reported to occur widely and the incidence of abortion can either be of a sporadic nature as with Campylobacter fetus subsp. fetus or multiple as with Salmonella spp. In the same way as Leptospiral spp., Listeria spp. can be found in a wide range of wild life such as Deer (Cervus elaphus), Fox (Vulpes vulpes), Badger (Meles meles), Pine martin (Martes martes), Hare (Lepus caponsis) and may be associated with its transmission to farm animals (Weis, 1974). Unlike the other bacteria discussed Listeria monocytogenes is unique in its ability to resist adverse conditions including the high pH found in silage, and dessication in faeces for up to two years (Miller, 1980a). Consumption by farm animals of the contaminated silage can lead to infection. As with Salmonella spp. the organism can survive in the intestine or like Brucella spp. and Leptospiral spp. be shed in the milk.
of infected animals.

*Corynebacterium pyogenes* is a fairly frequent commensal in the mucous membranes of farm animals (Deas, 1981). An increasing number of sporadic abortions due to this species have been reported in cattle herds with abortion levels of between 3 and 5% and also multiple abortions in up to 64% of the animals (Miller, 1977). Unlike the other species discussed *Corynebacterium pyogenes* is regarded as an opportunist pathogen which takes advantage of stress conditions during pregnancy.

*Haemophilus somnus* has been reported as a cause of infertility and abortion in cattle (Miller, 1982). With the limited numbers of abortions reported as being due to *Haemophilus spp.* the mechanism of transmission to the foetus is still obscure. However, the organism has been found in the bovine vagina (Miller, 1980a,b) and ascending invasion of the foetus by the organism following cervical infection has been suggested by Van Dreumel and Kierstead (1975). *H. somnus* has also been found in the genitalia of the bull (Humphrey et al., 1982). Its role in natural and experimentally-induced genital tract infections has been recently reviewed by Stephens et al. (1981) and Miller et al. (1983a) who suggest a sexual transmission similar to *Campylobacter fetus subsp. venerealis*. However this hypothesis requires further investigation.

### 4.2 CLINICAL SYMPTOMS

In order to make a more accurate diagnosis of abortion in farm animals Dennis (1980) suggested that more detailed clinical histories of abortions were required. These should include (a) The stage of gestation at which the abortion occurred and the number of animals involved (b) Any signs of illness such as coughing or other respiratory symptoms, nasal discharges and diarrhoea (c) Premonitory signs such as pyrexia or signs of depression such as listlessness or loss of appetite. Further useful diagnostic information would be (d) whether or not the placenta had been retained (e) if metritis had occurred or (f) mastitis accompanied by a milk drop syndrome was present. Unfortunately in many
cases of farm animal abortion not all the above information has been reported. However, based on available data some comparison of these clinical features can be made.

(a) **Stage of gestation.** With *Brucella spp.*, *Leptospiral spp.*, *Campylobacter fetus subsp. venerealis* and *Listeria monocytogenes*, abortion tends to occur in late pregnancy. Exceptions to this are *Salmonella abortus ovis* in sheep (Fielden, 1980) and *Campylobacter fetus subsp. fetus* in cattle (Dennis, 1969a,b) where abortion can occur in mid-pregnancy. With *Corynebacterium pyogenes* abortion can occur at any stage (Kirkbride, 1979).

(b) **Signs of illness** have not been generally reported in farm animal abortions but with *Salmonella spp.* (Dennis, 1969a,b), *Campylobacter fetus subsp. fetus* (Kirkbride, 1979) and *Listeria monocytogenes* (Dennis, 1969a,b) severe diarrhoea has been noted in cattle and sheep.

(c) **Premonitory signs** such as high fever and pyrexia have been reported with *Brucella spp.* (Dennis, 1980; Fielden, 1980), *Salmonella spp.* (Hinton, 1971; Fielden, 1980), *Leptospiral spp.* (Kirkbride, 1979) *Listeria spp.* (Dennis, 1969a,b; Smith, 1975a) and *Corynebacterium pyogenes* (Kolar, 1963; Hinton, 1972). In Listeric abortion cases a severe depression has been noted (Smith, 1975a).

(d) **Retention of placenta** is observed more frequently in dairy cattle than other farm animals. However, as cattle generally receive more frequent attention, its incidence relative to that occurring in other farm animals is likely to be overstated. However, it should be noted that placental retention can occur not only in cases of infectious abortion but also following more general disease such as metabolic disorders or nutritional deficiency. This is substantiated by the 7% incidence of retained placenta found in Brucella-free areas with apparently normal pregnancies. In contrast in herds with abortions due to *Brucella spp.*, *Campylobacter subsp. venerealis* and *Listeria monocytogenes* the abortion level can be greater than 50%. With
Corynebacterium pyogenes (Kolar, 1963) and Haemophilus somnus abortions (Miller et al., 1983b) retention of the placenta has also been reported.

(e) Metritis In most abortions involving bacteria, inflammation of the genital tract has been reported (Dennis, 1980). Its possible role as a host factor in the mechanism of abortion will be discussed in the concluding chapter.

(f) Mastitis accompanied by a milk drop syndrome has been a clinical feature reported especially in cases of cattle abortion due to Brucella spp. (Dennis, 1980), Leptospira spp. (Pearson et al., 1980), Corynebacterium pyogenes (Hinton, 1972), Nocardia asteriodes (Mugarula and McHomba, 1980) and Bacillus spp. (Carter, 1979).

Although not included in the list of major clinical symptoms lameness associated with joint swellings has been reported as a feature in sheep abortion due to Brucella spp. (Fielden, 1980). Also symptoms related to malfunctioning of the central nervous system (CNS), such as blindness and staggering have been reported in animal abortions caused by Brucella spp. and Listeria spp. (Broadbent, 1975; Fielden, 1980). It is likely that with the continuing improvements in the diagnosis of abortion, CNS symptoms may also be reported for other bacterial species.

4.3 PATHOGENICITY

The mechanism by which the infectious agents can gain entry to the uterus and interrupt the pregnancy is not fully understood. For the bacterial species under study the initiation of spread and route of infection may be different.

With Brucella spp. an inflammatory infection of the mucous membranes of farm animals may lead to an invasion of the alimentary canal and subsequent infection of the lymph nodes, udder and uterus. Leptospira spp. may gain entrance via the abraded skin and mucous membranes and localise in the kidney especially in cattle. As with Brucella spp. the udder and uterus can become infected. Abortion with both species can be the result of a primary infection which can occur up to six months prior
to the abortion in the case of *Brucella* spp. and up to six weeks with *Leptospira* spp. The organisms which are known to invade the genital tract and uterus such as *Campylobacter fetus subsp. venerealis*, *Haemophilus somnus* and *Corynebacterium pyogenes* usually do so by sexual transmission. A pregnant animal with a *Campylobacter* spp. infection may not abort for at least eight months whereas, with a *Corynebacterium pyogenes* infection abortion may occur in less than one month (King et al. 1981). The time between infection and abortion has not been established for *Haemophilus* spp. but recent experimental evidence in cattle suggests that a period of five days is usual (Miller et al., 1983a). *Salmonella* spp., *Listeria monocytogenes* and *Campylobacter fetus subsp. fetus* usually cause severe intestinal infection with spread of infection to the liver and other organs including the uterus. Occasionally *Salmonella* spp. have been reported as following the genital route of infection (Hinton, 1971).

**4.4 PATHOLOGY**

As most foetal pathogens act primarily by causing a placentitis, careful examination of the placenta is particularly important pathologically (Dennis, 1980; Miller, 1982). It should be examined for shape, colour, consistency, signs of discolouration, necrosis and autolysis. A comparison of the important diagnostic placental lesions due to some of the bacterial species under review is presented in Table V.

The survival of the organism in the placenta may be influenced by low oxygen tension (Kirschbaum and De Haven, 1968; Miller, 1982) and nutrients found in high concentrations such as erythritol, which encourages the growth of *Brucella* (Pearce et al., 1962). The growth of *Salmonella* spp. is found to be stimulated by other non-specific extracts from the placenta (Wray and Corbel, 1980).

The nature of survival and multiplication of other bacterial species on the placenta is in general not understood. Therefore more investigations into the mechanism of placentitis caused by the more
recently recognised and lesser known fastidious species discussed in
this review would be helpful in diagnosis.

Depending upon its virulence when the infectious agent reaches the
placenta, placentitis may be severe or mild and the foetus may or may
not become infected. In severe infections the placenta is usually
retained although death of the foetus and abortion can occur (Miller,
1982).

An important pathological manifestation correlated with bacterial
infection is mummification and maceration of the foetus. The mechanism
of mummification is not yet understood but Roberts (1971) has suggested
without evidence that it may be associated with infection and genetic
factors. More investigative work on this aspect of abortion is needed.
When the foetus dies it continues to autolyse in-utero with maceration
being brought about by proteolytic breakdown promoted by the invading
organism (Miller, 1982). It is quite common in cases of Salmonella
abortion to find that severely autolysed foetuses are expelled during
the latter part of gestation.
TABLE V - Placental lesions following infection by bacteria Ref (1) - (6)

<table>
<thead>
<tr>
<th></th>
<th>Brucella (1) (2) (5)</th>
<th>Salmonella (3)</th>
<th>Campylobacter (1) (2) (5)</th>
<th>Leptospira (1) (2) (5)</th>
<th>Listeria (1) (2) (5)</th>
<th>Corynebacteria pyogenes (4)</th>
<th>Haemophilus somnus (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLACENTITIS</strong></td>
<td>Acute or chronic</td>
<td>With uniform reddish appearance</td>
<td>Similar to Brucella but less severe</td>
<td>Diffuse appearance can be confused with virus infection</td>
<td>No specific lesions</td>
<td>Diffuse reddish brown appearance</td>
<td>Diffuse inflammatory appearance</td>
</tr>
<tr>
<td><strong>COTYLEDON FEATURES</strong></td>
<td>Vary from normal to necrotic red to brownish yellow</td>
<td>Marked necrosis</td>
<td>Haemorrhagic necrotic yellow</td>
<td>Lighten to yellow, atonic, avascular, uniformly affected</td>
<td>Necrotic foci</td>
<td>Oedematous varying degrees of autolysis</td>
<td>Necrotic foci oedematous</td>
</tr>
<tr>
<td><strong>INTER-COTYLEDON FEATURES</strong></td>
<td>Area thick opaque and with wet leathery appearance</td>
<td>Marked necrosis</td>
<td>Area oedematous hyperaemic and possibly leathery</td>
<td>Area diffusely oedematous yellow to brown gelatinous fluid</td>
<td>Necrotic area which tend to be thickened and opaque</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

References:-  
(1) Dennis (1969b)  
(2) Hinton (1971)  
(3) Kirkbride (1979)  
(4) Dennis (1980)  
(5) Hinton (1972)  
(6) Miller (1982)
In other bacterial infections, eg Brucella, Listeria or Leptospira, the foetus can in some cases continue to the last trimester of pregnancy before expulsion with little or no autolysis.

However, in the expelled foetuses following bacterial infection a variety of other pathological lesions occur. These include gross external lesions, necrotic foci on internal organs, with vascular necrosis, bronchopneumonitis or peritonitis. The severity of the pathological findings in foetal organs depends upon the age of foetus and the nature and virulence of the pathogen (Osburn, 1973; Schultz, 1973). Generally the umbilicus, eye, liver and lung are infected (Miller and Quinn, 1975). Infection of the eye and kidney are features of Leptosporial abortion (Ellis et al., 1981), whilst liver lesions and suppurative hepatitis are often found following infections caused by Listeria monocytogenes or Campylobacter fetus subsp. fetus. The foetal lungs may also be affected and interstitial pneumonia is a feature of many abortion cases due to Brucella spp. (Kirkbride, 1979; Dennis, 1980), Corynebacterium pyogenes (Hinton, 1972), Haemophilus somnus (Miller, 1982) and Nocardia asteriodes (Mason et al., 1981).

For some of the bacterial species under study typical pathological lesions of the foetus following abortion are summarised in Table VI.
TABLE VI - Foetal lesions following bacterial infection. Ref (1) - (6)

<table>
<thead>
<tr>
<th>Brucella (1) (2)</th>
<th>Salmonella (3)</th>
<th>Campylobacter (1) (2) (5)</th>
<th>Leptospira (1) (2) (5)</th>
<th>Listeria (1) (2) (5)</th>
<th>Corynebacteria pyogenes (4)</th>
<th>Haemophilus somnus (6)</th>
</tr>
</thead>
</table>

In the previous chapter much of the information on abortion in farm animals has been reviewed under four main headings: OCCURRENCE, CLINICAL SYMPTOMS, PATHOGENICITY and PATHOLOGY. However other topics are important, such as (1) Antibody production in the foetus (2) The role of mixed infections (3) Developments leading to improved diagnosis (4) Future control.

5.1 ANTIBODY PRODUCTION

There are two sources of antibody production; those derived maternally and transferred by passive transplacental passage to the foetus and those that are stimulated by the active response of the foetus. In humans there is evidence of the passive transfer of maternal antibodies to the foetus (Hobart and McConnell, 1975); however, no such transfer is believed to occur in farm animals (Brambell, 1970). Instead following most foetal infections, detectable levels of immunoglobulins can be found in the foetal serum (Silverstein et al., 1963a,b). In most farm animals the foetus produces its own immunoglobulins usually by mid pregnancy. Ellis et al. (1978b,c) and Logan et al. (1981) reported a much higher incidence of immunoglobulins in sera from aborted foetuses (81.5%) than from normal foetuses (32.8%). Also the Ig levels in serum were approximately four times higher in aborted foetuses (140 ± 29 mg/100ml) than in those which did not abort (37 ± 14mg/100ml). Similar findings have been reported by Kirkbride et al. (1977) and Miller and Quinn (1975). However, the specificity of these increased levels of immunoglobulins in the foetus were not always related to a particular abortive agent. For example, with Bovine Viral Diarrohea (BVD) virus increased levels of foetal immunoglobulins were recorded but the minor pathological lesions caused by the virus did not produce abortion (Kendrick, 1971; Braun et al., 1973a,b). Bergeland et al. (1974) noted in a similar situation
that the subsequent abortion was due to a non-infectious agent. The demonstration of antibodies to the virus was simply co-incidental. Similar phenomena could occur with other organisms such as Campylobacter spp., Corynebacteria spp. or Streptococcus spp. In these cases the significance of the immunoglobulin levels to the variety of organisms which can be involved requires more specific investigation. If this is tested a quantitative evaluation of the immunoglobulin classes IgG and IgM could be of diagnostic value (Sawyer et al., 1973; Trainin and Meirom, 1973; Ellis et al., 1978b; Ohmann, 1981).

The low recovery rate of infectious agents from abortion cases may be due to an inhibitory effect on the organisms by the immunoglobulins present (Ellis et al., 1978b). These immunological defence mechanisms could also enable farm animals to eliminate and resist further uterine infections and further study of this possibility has been suggested by Mather and Melancon (1981). Some work which throws light on the possible mechanism of the immune response in farm animals has been demonstrated with bovine venereal vibriosis a disease caused by Campylobacter fetus subsp. venerealis (Winter, 1973; Corbeil, 1980). Following vaginal and uterine infection with this organism the first immunoglobulin classes produced are IgM followed by IgA and finally IgG. The IgM antibodies disappear within a few days and the IgG shortly after the infection ceases. However, the IgA antibodies can be detected for several months. In the vaginal mucus antibodies are primarily of the IgA class and being non-opsonic only immobilise the infectious organism. This could explain the persistence of a vaginal carrier state with Campylobacter spp. In contrast, in the uterus the IgG antibodies can immobilise and opsonise the organisms prior to destruction by neutrophils and macrophages.

A common feature of infected and aborting animals is inflammation
of the genital tract. Most evidence about metritis comes from histopathological demonstration of the disorder in the female which incriminates many bacterial species, including *Brucella abortus*, *Campylobacter fetus subsp. venerealis*, *Corynebacterium pyogenes*, *Haemophilus somnus* and other miscellaneous organisms such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus* spp. and *Streptococcus* spp. (Zemjanis, 1981). The mechanism by which metritis caused by these organisms may lead to abortion is still obscure and simply to report bacterial metritis as a clinical feature is insufficient to implicate the bacterial species involved as the abortive agent. A more reliable approach may be to investigate antibody production by specific organisms at various affected sites in the genital tract. Consideration must also be given to the production of toxins by these organisms and their effect on the foetus. It has also been suggested that metritis can increase oestrogen and prostaglandin levels (Fitzpatrick, 1975). These hormones normally control uterine muscle and a sudden increase could lead to an early expulsion of the foetus.

5.1 ROLE OF MIXED INFECTIONS

This review has concentrated on the role of bacteria acting as single agents. However, more than one infectious agent may be involved and there are many reports of mixtures of aerobic bacteria occurring. There are however fewer reports on organisms which are more difficult to demonstrate such as anaerobic and microaerophilic bacteria and the viruses. This may reflect the ability of present technology to demonstrate some of these organisms.

Amongst the aerobic species the difficulty of ascribing a role to secondary invaders such as saprophytic *Bacillus* spp. is exemplified by the finding of these organisms in the foetus only after death and expulsion (Miller and Quinn, 1975). However, although many species of
the genus are commensals, *Bacillus cereus* can cause mastitis and abortion. Thus if *Bacillus* spp. are found in the foetal tissues they should be specifically identified rather than dismissed as commensals. Similarly other groups of organisms considered to be saprophytic such as *Micrococcus* spp. may act alone or in combination with other organisms to produce abortion. However, Austwick and Venn (1957) found many bacterial species in the stomach contents of foetuses as well as *Aspergillus fumigatus* which they considered to be the abortive agent. The number of these bacteria increased proportionately with the length of time the tissue specimens were delayed in transport to laboratory. Thus some reported isolations may represent only the easily demonstrated secondary invaders and post-mortem contaminants whilst the more obscure pathogen remained undetected.

5.3 IMPROVEMENTS IN DIAGNOSIS

Despite the intensive programmes for the eradication of brucellosis and vaccination programmes for the control of salmonellosis, abortion caused by these and other infections still presents a continuing and serious problem for the farmer. The increased number of reports of infectious abortion has been partly due to the improvements in diagnosis of organisms such as *Leptospira*. Also recently there has been a report indicating a possible resurgence of abortions in cattle due to *Salmonella dublin* (Bulgin, 1983) and *Salmonella montevideo* in sheep (Linklater, 1983). There is also an increasing awareness and knowledge of the many bacterial species involved in abortion. However, a serious drawback in the diagnosis of abortion is the lack of information at farm level. Too often there is a lack of co-ordination between the farmer, veterinary practitioner and the laboratory specialist. A single abortion is often ignored as the farmer and veterinary practitioner do not consider it serious enough to merit a more thorough examination of other animals. However,
at this stage by providing the laboratory specialist with a clinical history, blood samples, foetus and placenta from the animal, some indication of the cause may be provided. In this way diagnosis of the cause of a single abortion could lead to measures which may prevent an outbreak.

In the more developed countries such as United Kingdom and USA most animal abortions tend to be sporadic in nature with a frequency of between 3 to 5% in pregnant animals (Kradel, 1978). Particular care should be taken if the number of abortions rises above this level. In these cases it is even more important to send to the laboratory the specimens previously described. A more accurate history including the age variability of animals, the stage of gestation, management practices and breeding records is essential, because this history would alert the laboratory to carry out more detailed, precise and sophisticated examinations, e.g. histological and fluorescent antibody examination. The quality of specimens is also important. They should be speedily transported in aseptic conditions to the laboratory.

5.4 FUTURE CONTROL

In order to control abortion in farm animals the information obtained from improved diagnostic methods must be applied at farm level. Present methods of control can be grouped as follows:-

(a) Preventive measures. This would include improvements in management such as better hygiene of premises and segregation of infected from non-infected animals to reduce the transmission of the bacterial agent; allowing young and recently purchased non-pregnant animals to be exposed to a natural challenge from carrier animals and encourage the development of natural immunity. However, many carrier animals only excrete the organisms erratically or during certain seasons of the year.

(b) Control measures carried out by or on advice from veterinary practitioner. These include the use of antibiotics, vaccination, or selective culling of infected animals. Antibiotics have been
used in the control of most farm diseases including abortion. However, although the use of antibiotics may reduce infection when it has occurred, they do not protect animals against re-infection, nor can they be used prophylactically in susceptible animals. Another difficulty is in the choice of antibiotic as their continued use has led to development of resistant bacterial strains, e.g. chloramphenicol-resistant strains of *Salmonella dublin* (Hinton, 1977).

Vaccination also has drawbacks as a control measure, especially if live attenuated vaccines are used. Some of the organisms may persist in the animal tissues or alternatively the vaccine may revert to a virulent state and result in infection. Also although vaccination may provide protection against clinical forms of the disease, live organisms can still be excreted with the possibility of being transmitted to other animals. Morgan and MacKinnon (1979) have suggested however the following important criteria that should be applied to assessing the suitability of live vaccines:–

(1) They must be stable and not revert to a virulent state even after repeated animal passages.

(2) No local or general reactions should occur in the injected animal.

(3) The vaccine should survive in animal tissues only long enough to produce the required protective immune response.

(4) The vaccine should not produce a carrier state in animals and should not be transmitted by excreta to other animals.

Another major difficulty resulting from vaccination is its affect on the interpretation of diagnostic serological tests as antibody production stimulated by infection is indistinguishable from that produced as a result of vaccination. A safer alternative is to use inactivated vaccines. However these are less effective and require to be regularly administered (Kahrs 1976). However despite the drawbacks
of inactivated vaccines the future control of abortion seems likely to be by a greater use of commercially prepared inactivated vaccines. Their commercial development is likely to be slow as increased use will only take place following appropriate lengthy trials.

Some experimental work using live and inactivated vaccines has already been carried out with *Listeria* spp (Njoku and Dennis, 1973), *Campylobacter* spp. (Gilmour et al., 1975) and *Leptospira* spp. (Holyroyd, 1980). However, it is also likely that the farmer will be advised to use a combination of control methods which include vaccination. But on economic grounds the farmer may still be prepared to accept sporadic losses caused by abortion, in the hope that other less susceptible animals may gain immunity by cross infection.

### 5.5 CONCLUSION

During the past ten years investigation of the bacteria associated with abortion in farm animals has shifted away from the traditional species *Brucella* and *Salmonella* to others. Leitch (1983) has suggested that since the virtual eradication of *Brucella abortus* the most important bacterial species now implicated as a cause of cattle abortion is *Leptospira hardjo*. Also, Miller (1982) has indicated the increasing importance of *Haemophilus somnus* in cattle.

Although this study has concentrated on evaluating bacterial species associated with abortion reference was made in Chapter 1 to the viruses known to infect the foetus. Consequently it is valuable to note that the IBR/Herpesviruses have also wide disease spectrum and should not be ignored as possible pathogens associated with abortion. Following IBR virus, BVD virus is regarded as a common agent associated with reproductive problems in farm animals.

For a better understanding of the nature of infectious abortion in farm animal species it is most important that future diagnostic investigations and research concentrate on the single or combined role
in the genital tract of such bacterial species as Leptospira, Campylobacter, Haemophilus but not neglecting the viral agents referred to above.

This review has studied different areas of diagnosis and investigation. It would be short-sighted not to suggest that abortion in farm animals could be better controlled if this more detailed biological information emerging from research laboratories was combined with an increase in field investigations and the applied usage of the results obtained at farm level.
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