Neosporosis in cattle

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Abstract

During the past decade, Neospora caninum infection has emerged as an important reproductive disease in cattle throughout the world. Abortion, occurring during the middle of gestation, is the primary clinical sign of the infection in cattle. Surveys in several countries from three continents have identified N. caninum infection as the major diagnosed cause of bovine abortion. Both endemic and epidemic patterns of abortion may occur in herds. An important feature of this disease is that the protozoan parasite is maintained in cattle as a chronic infection which can be passed on to the fetus during pregnancy. Two methods for the transmission of the infection in cattle have been proposed and are the subject of current investigations. Horizontal transmission utilizes a two-host life cycle whereby the cow is infected from ingestion of coccidial oocyst stages shed by the definitive host. Experimental infections have confirmed that the dog is a definitive host for the parasite. There is epidemiological evidence that the dog has a role in the prevalence of the infection but, as yet, no confirmation that the dog is the source for natural infections in cattle. Vertical transplacental transmission of the infection is an important route of infection in many herds. Vertical transmission occurs because fetal infection frequently does not result in abortion but rather the fetus survives to be a persistently infected animal. A heifer calf that is born congenitally infected is capable of transmitting the infection to the next generation when she becomes pregnant, thus maintaining the infection in the herd. The clinical outcome of transplacental fetal infection with N. caninum is likely determined by maternal and fetal immune responses which involve humoral, and most importantly, cell-mediated immune factors. The diagnosis of the infection is assisted through histopathology and immunohistochemical examination of aborted fetuses and serologic testing of cattle for evidence of infection. Several types of serologic tests, based on the use of culture-derived organisms or recombinant N. caninum antigens are available. There are no proven control methods for the prevention or treatment of neosporosis. Suggested control measures focus on programs to reduce the number of congenitally infected animals.
1. Introduction

In the past decade, neosporosis has emerged as a major cause of abortion in cattle throughout the world (Anderson et al., 1991; Barr et al., 1991a; Thornton et al., 1991; Nietfeld et al., 1992; Mainar-Jaime et al., 1999; Wouda et al., 1999a). *Neospora caninum* was first identified in dogs with encephalomyelitis and myositis (Bjerkas et al., 1984; Dubey et al., 1988a,b; Bjerkas and Dubey, 1991). In addition to cattle, the protozoan has been associated with sporadic disease in other livestock species including sheep (Dubey et al., 1990), goats (Barr et al., 1992) and horses (Marsh et al., 1996; Hamir et al., 1998). In cattle, the parasite was first isolated from aborted fetuses (Conrad et al., 1993a). The pathogenic potential of this isolate has been confirmed by experimental infection of pregnant cattle resulting in fetal death and/or congenitally infected calves (Barr et al., 1994). This paper is intended to provide current information about neosporosis in cattle. Several review papers are available for additional information (Anderson et al., 1994; Dubey and Lindsay, 1996a; Abbitt, 1997; Dubey, 1999; Thurmond and Hietala, 1999a).

Bovine neosporosis was first associated with an abortion storm in 1987 on a dairy in New Mexico and numerous reports of *Neospora* abortion have confirmed this infection as a significant cause of abortion, particularly among dairy cattle (Thilsted and Dubey, 1989; Anderson et al., 1991; Thornton et al., 1991; Barr et al., 1992; Nietfeld et al., 1992; Thornton et al., 1994; Dubey and Lindsay, 1996a; Campero et al., 1998; Fondevila et al., 1998; Gottstein et al., 1998; Schares et al., 1998; Thurmond and Hietala, 1999a). Neosporosis has a worldwide distribution, having been diagnosed in many countries from six continents, and is prevalent throughout North America. Bovine neosporosis is probably not a new disease, but rather a newly recognized one. Retrospective studies in California have confirmed that the parasite has been endemic since 1984, and a decade earlier, the infection was identified retrospectively in a stillborn calf in Australia (Dubey and Lindsay, 1996a). Surveys in California (Anderson et al., 1991; Barr et al., 1991a), the Netherlands (Wouda et al., 1998b) and New Zealand (Thornton et al., 1991) indicate that approximately 20% of all aborted bovine fetuses submitted to diagnostic laboratories are diagnosed with this infection. In abortion submissions from dairy herds with a history of *Neospora* endemic abortion, the proportion of *Neospora* infection in aborted fetuses is as high as 44% (Anderson et al., 1995). In 50 Dutch dairy herds experiencing epidemic abortions, the proportion of confirmed *N. caninum*-infected fetuses was 77% of 226 fetuses submitted for diagnosis (Wouda et al., 1999a).

1.1. Clinical presentation

There are no signs of clinical illness in cows that abort due to *Neospora* infection. The aborted fetuses are usually autolyzed with no gross lesions and placentas are not
retained. Abortions may occur throughout the year in both heifers and cows. The majority of *Neospora* abortions occur during the fourth to sixth month of gestation. This pattern of mid-gestation abortion can be useful to initially assess whether *Neospora* infection is a probable cause in an abortion outbreak. It has not been established whether *Neospora* infection can cause reproductive problems in the earliest stages of pregnancy, but death and mummification of fetuses approximately 3 months in gestational age has been associated with *Neospora* outbreaks. *Neospora* infections associated with abortion and congenital infections have been reported in both dairy and beef cattle, but there are more reports attributing significant numbers of abortions in dairy cattle, particularly those in drylot dairies. A sampling bias in favor of the diagnosis of abortion in dairies might be involved since it is likely that the mid-gestation fetuses, typical of *Neospora* abortion, would be more easily found and submitted in a dairy environment. However, it also may be that the environment of the drylot dairy is conducive to the transmission and clinical expression of this disease. Comparison of the seroprevalence among dairy and beef cattle in Spain found a significantly greater (35.9%) seroprevalence in dairy cattle compared to beef cattle (17.9%) (Quintanilla-Gozalo et al., 1999).

The estimated seroprevalence in dairy cattle in England and Wales is 6% (Trees et al., 1998; Davison et al., 1999b) and a similar level of seroprevalence was identified in New Zealand cattle (Reichel, 1998). A survey of beef cattle in Canada found a seroprevalence of 30% (Waldner et al., 1998). In individual herds the seroprevalence can be quite variable, serologic evidence of *N. caninum* infection in dairies in the United States ranges from 2% to 98% (S. Hietala, personal communication, CVDLS data).

Cattle with serologic evidence of infection have an increased risk of abortion (Paré et al., 1997; Thurmond and Hietala, 1997a; Moen et al., 1998; Waldner et al., 1998; Wouda et al., 1998b; Davison et al., 1999b). In a California study, seropositive congenitally infected cows had a 7.4 increased risk of abortion in their first pregnancy. The risk in the second pregnancy was considerably lower, though this may have been influenced to some degree by selective culling of aborting cows from the first pregnancy (Thurmond and Hietala, 1997a). In the Netherlands, a 3-fold increased abortion risk was observed in seropositive cows compared to seronegative herdmates (Wouda et al., 1998b). In England and Wales, a serologic survey identified a 3.5-fold increased risk of abortion in seropositive dairy cattle and it was estimated that 12.5% of abortions in dairy cattle could be attributed to neosporosis (Davison et al., 1999b). In addition to abortion and congenital infection, *Neospora* infection may cause reduced milk production and shortened production life based on a study of seropositive cows which produced less milk and were culled earlier than seronegative herdmates (Thurmond and Hietala, 1996, 1997b). Seropositive beef cattle have an increased risk of abortion and stillbirth, in addition to increased risk of culling for any reason and culling for poor reproductive performance (Waldner et al., 1998).

Two patterns of abortion, endemic and epidemic, have been described in association with neosporosis in herds of cattle (Thurmond and Hietala, 1999a). In the endemic pattern of abortion, the herd experiences an elevated abortion rate of greater than 5% per year which persists for years. In investigations of two California dairies with endemic *Neospora* abortions, the annual abortion rate attributable to neosporosis was estimated to be 10.6% and 17.3% (Thurmond et al., 1997c). The epidemic pattern of abortion is less
common and is characterized by abortions in a high proportion of pregnant cattle over a relatively brief period of time. In some instances, over 30% of pregnant cattle have aborted due to neosporosis within several months (Thilsted and Dubey, 1989). An apparent mixture of these patterns may be observed in some herds that have experienced a prolonged history of sporadic cases of Neospora abortion and occasional outbreaks of abortions attributable to Neospora.

In most instances, cows that abort a Neospora-infected fetus will have either additional abortions (Anderson et al., 1995; Dubey and Lindsay, 1996a) or infected fetuses in subsequent pregnancies (Barr et al., 1993; Dubey and Lindsay, 1996a). The clinical outcome of these subsequent pregnancies is variable, but a seropositive cow that has an abortion may have an up to 5.7 greater risk of abortion in the subsequent pregnancy (Thurm and Hietala, 1997a).

An uncommon manifestation of fetal Neospora infection is the birth of a clinically affected full-term calf which exhibits variable nervous system abnormalities. These neurological signs are manifested as limb dysfunctions, which range from mild proprioceptive defects to complete paralysis. Microscopically there is a multifocal protozoal encephalomyelitis which may be particularly localized in the spinal cord gray matter (Barr et al., 1993; Dubey and Lindsay, 1996a).

The majority of calves that acquire a Neospora infection during gestation are born clinically normal. These calves will have a high precolostral antibody titer to N. caninum which is useful in detecting in utero infection. A high percentage, 80% to over 90%, of calves born to seropositive cows are congenitally infected based on serology (Barr et al., 1993; Paré et al., 1996; Schares et al., 1998; Thurmond and Hietala, 1999a). As will be discussed in the section on transmission, these clinically normal, congenitally infected calves are important in maintaining the infection in the herd.

1.2. Diagnosis

The confirmation of a suspect Neospora infection will require the assistance of a veterinary diagnostic laboratory. The preferred samples in cases of abortion include one or more aborted fetuses submitted with placenta and sera from the dam. The aborted fetus is usually autolyzed with serosanguinous fluid accumulation in body cavities. Rarely, white linear foci may be seen grossly in the muscles. Histologically, widely disseminated changes are present in many organs but the most diagnostically significant lesions are found in the brain and consist of scattered foci of nonsuppurative cellular infiltrates with occasional foci of necrosis. Other histologic lesions that are consistently found include nonsuppurative epicarditis and/or myocarditis, focal nonsuppurative myositis and nonsuppurative portal hepatitis, frequently with focal hepatic necrosis and focal nonsuppurative interstitial pneumonia (Barr et al., 1991a; Anderson et al., 1994).

The presumptive diagnosis of protozoal infection can usually be made on the basis of histologic lesions. Immunohistochemistry using antibodies to Neospora is an effective method to identify the parasites (both tissue cyst and tachyzoite stages) in fetal tissues. Neospora immunohistochemistry is most successful on sections of fetal brain, although the parasites are also frequently present in the lung, kidney and skeletal muscle. Immunohistochemistry has been successfully employed to diagnose Neospora infections.
in mummified fetuses although the autolytic state of these fetuses diminishes the diagnostic accuracy (Anderson et al., 1994).

Since fetal infection can result in either fetal death and abortion or in the birth of a live congenitally infected calf, there are questions about what are the appropriate methods to diagnose Neospora abortion. The use of pathology and immunohistochemistry on aborted fetuses to establish a diagnosis of N. caninum as the cause of an abortion has been questioned (Thurmond et al., 1999b). N. caninum is adapted to cattle and utilizes vertical transmission, in which the birth of a live infected calf helps to maintain the infection in the herd. A fetus that acquires the infection prior to sufficient development of an immune response may become overwhelmed with a disseminated infection leading to death. This may occur through the sixth month of gestation, but later in gestation, the number of N. caninum-induced fetal deaths is greatly reduced (Anderson et al., 1994). In fetal death and abortion due to neosporosis, there are characteristic disseminated inflammatory lesions in the brain, lungs, heart, liver, kidney, muscles, placenta and other organs (Anderson et al., 1994). An accurate diagnosis of Neospora abortion can be achieved if various criteria for the diagnosis are met. These diagnostic criteria include a compatible gestational age, autolyzed postmortem condition of the fetus, the presence of compatible disseminated inflammatory fetal lesions, the presence of detectable parasites with immunohistochemistry in the fetus and/or serologic evidence of infection, and the absence of other abortifacients associated with the abortion. Conversely, a N. caninum-infected fetus that is aborted with mild focal lesions such as focal encephalitis, may have an incidental Neospora infection and other causes for the abortion should be investigated.

Serological diagnosis of N. caninum infection was reviewed recently (Björkman and Uggla, 1999). At present, the two major types of serologic tests most commonly employed for the diagnosis of Neospora infection are the indirect fluorescent antibody test (IFAT) (Conrad et al., 1993b; Dubey et al., 1996b) and the enzyme-linked immunosorbent assay (ELISA) (Paré et al., 1995; Baszler et al., 1996; Dubey et al., 1996b; Lally et al., 1996b; Björkman et al., 1997; Jenkins et al., 1997; Louie et al., 1997; Williams et al., 1997; Björkman and Lunden, 1998; Osawa et al., 1998; Packham et al., 1998; Romand et al., 1998; Wouda et al., 1998a). There are a variety of different procedures for conducting these tests, though most are based on the use of culture-derived tachyzoites of either bovine or canine isolates of N. caninum. Some modifications to improve the specificity of N. caninum ELISA tests include the use of immune stimulating complexes (Björkman and Lunden, 1998), monoclonal antibodies to specific immunoglobulins (Björkman et al., 1997; Williams et al., 1997; Björkman and Lunden, 1998) or tachyzoite surface antigens (Baszler et al., 1996) and molecularly cloned Neospora-specific antigens (Lally et al., 1996b; Jenkins et al., 1997; Louie et al., 1997). Direct agglutination tests (DAT) (Packham et al., 1998; Romand et al., 1998), which do not require species-specific secondary antibodies, will also have practical applications in the diagnosis of bovine neosporosis.

Regardless of the serologic tests employed, laboratories must establish appropriate cut-off titers for each test, using standardized sera. Often reports of test validations are based on comparisons between the titers of aborted and nonaborted cows or on the use of the IFAT as a gold standard. Ideally, comparisons should be made with sera from
cattle whose infections have been confirmed by the identification of parasites in their aborted fetuses or congenitally infected calves. These sera are often difficult to obtain, as are confirmed negative control sera. Therefore, serologic test comparisons should be viewed with some caution.

Careful consideration must always be given to the most appropriate use and interpretation of serologic results, particularly in the diagnosis of abortions. Serodiagnosis is best employed for evaluation of herd exposure and risk of *Neospora* infection rather than as a means of assessing whether an individual cow has aborted due to neosporosis. A single serum sample from an individual cow may not accurately reflect her infection status. Most naturally infected cows are seropositive at the time of abortion (Otter et al., 1997; Paré et al., 1997; Stenlund et al., 1999). In rare instances, however, cows that abort a *Neospora*-infected fetus may not have a significantly elevated titer at the time of abortion (Otter et al., 1997). In one study, a portion of congenitally infected heifers that had a history of positive *Neospora* titers had antibody levels below the cut-off of the IFAT at the time that they gave birth to infected calves (Anderson et al., 1997). Specific antibody titers vary between naturally infected cows and may fluctuate considerably throughout pregnancy (Stenlund et al., 1999), sometimes even dropping below the positive cut-off level with some tests (Conrad et al., 1993b; Paré et al., 1997). Despite reported fluctuations in titers, there is no conclusive evidence to show that serologically positive cows can revert to a consistently seronegative status.

*Neospora* serology can be used in the diagnosis of a herd abortion problem by comparing the serologic titers in groups of aborting and nonaborting cows to determine if a significant association exists between *Neospora* titers and abortion (Thurmond and Hietala, 1999a). Serodiagnosis of *Neospora* infection can be achieved in aborted fetuses with the IFAT, particularly if they are 6 months or more in gestational age (Barr et al., 1995; Otter et al., 1997; Wouda et al., 1997; Slotved et al., 1999). However, negative IFAT results do not always rule-out the possibility of infection, particularly in younger fetuses which may not be immunologically developed and capable of producing detectable levels of antibodies to the parasite. A positive IFAT indicates infection but, by itself, does not confirm that the abortion was caused by the *Neospora* infection. Thus far, immunological tolerance to *Neospora* infection has not been reported. However, in a recent study one of the eight full-term fetuses taken prior to parturition from naturally infected cows had disseminated neosporosis without evidence of an antibody or detectable cellular immune response to *N. caninum* antigen (unpublished data). The IFAT have proven to be superior to the whole parasite or recombinant antigen ELISAs for the detection of fetal antibodies to *Neospora* (Wouda et al., 1997). The DAT also works well for this purpose, unless the fetal sera are hemolyzed (Packham et al., 1998).

Congenital infections can be diagnosed in calves with high titers to *Neospora* which are detectable with either the IFAT, ELISA or DAT (Barr et al., 1991b, 1993; Jenkins et al., 1997; Louie et al., 1997; Packham et al., 1998).

Methods have been developed for the amplification of various nucleotide sequences of *N. caninum* using the polymerase chain reaction (PCR) procedure (Barta and Dubey, 1992; Ho et al., 1996, 1997; Holmdahl and Mattsson, 1996; Kaufmann et al., 1996; Lally et al., 1996a; Müller et al., 1996; Payne and Ellis, 1996; Yamage et al., 1996; Ellis, 1998; Ellis et al., 1999; Gottstein et al., 1998; Liddell et al., 1999). Recent
progress on the development of PCR-based detection methods for Neospora has been rapid (Ellis, 1998) but thus far, only a few of these tests have been evaluated for their applicability for the diagnosis of infections in cattle (Ho et al., 1996, 1997; Gottstein et al., 1998, Ellis et al., 1999). Molecular diagnostic techniques have the advantage of being highly specific and sensitive, as well as being able to amplify small amounts of parasites in a larger quantity of tissue than is generally available for histopathologic examination on a microscope slide. The disadvantages are the costs, time, equipment and expertise required to perform these tests. In our experience, PCR amplification of parasite DNA does not work well when fetuses are autolysed, which is often the case with Neospora abortions. At present, PCR-based detection systems are primarily used as investigative tools in a relatively limited number of diagnostic and research laboratories. However, they may become more applicable as this technology continues to become more widely used and cost-effective in the diagnosis of other diseases of importance in human and veterinary medicine.

1.3. Immune responses to Neospora infection

Studies of the immune responses to N. caninum infection are needed to understand the mechanisms of this disease. Cell-mediated immunity is the major protective immune response against infections caused by intracellular protozoan parasites, including the closely related Toxoplasma gondii (Gazzinelli et al., 1993). Resistance to toxoplasmosis is associated with a T lymphocyte helper type 1 immune response mediated by the cytokines interferon-γ (IFN-γ), interleukin 12 (IL-12) and IL-2 (Sharma et al., 1985; Suzuki et al., 1988; Gazzinelli et al., 1994). There is evidence that cell-mediated immunity is involved in the resistance of inbred A/J mice to Neospora infection and that in vivo neutralization of IFN-γ and IL-12 ablates this immunity (Khan et al., 1997). A more recent paper confirms the critical role of IFN-γ and type 1 immune responses in the control of acute Neospora infection in BALB/c mice (Baszler et al., 1999). The only published data about bovine cellular immune responses to N. caninum infection are from experimentally infected non-pregnant cattle. Following a subcutaneous or a combined intravenous/intramuscular inoculation of N. caninum tachyzoites, non-pregnant cattle mount Neospora-specific cellular immune responses as determined by lymphoproliferative responses and production of IFN-γ (Lunden et al., 1998; Marks et al., 1998; Andrianarivo et al., 1999). Calves orally infected with N. caninum oocysts from dogs also develop Neospora-specific lymphoproliferative responses (De Marez et al., 1999). However, whether similar immune responses are induced in pregnant naturally or experimentally infected cattle and whether they influence the fetal outcome of the infection remain to be investigated.

Earlier studies in our laboratory suggested that the outcome of Neospora infection on the bovine fetus depends on the gestational age of the fetus and its immune competence at the time of maternal infection (Barr et al., 1994). Other reports indicate that some capability to elicit cell-mediated immune responses (CMI) in the bovine fetus may exist by 120–160 days of gestation (Higgins et al., 1983; Hein et al., 1988; Jensen et al., 1988). Therefore, we decided to evaluate immune responses in bovine fetuses from dams experimentally infected with Neospora tachyzoites between 159 and 169 days of
gestation (Andrianarivo et al., manuscript in preparation). Preliminary results showed that all fetuses mounted strong humoral immune responses to *Neospora*, as detected by the IFA test. In contrast, *Neospora*-specific CMI, as determined by lymphoproliferative responses and production of IFN-\(\gamma\), were highly variable among the fetuses. The humoral and CMI responses were not able to prevent infection in any of the fetuses. Moreover, there was no correlation between the fetal CMI responses and the severity of the histopathological lesions. Previous studies indicate that cytokines influence the subclasses of antibody responses. While the type 1 cytokine IFN-\(\gamma\) stimulated the production of IgG2 antibodies (Estes et al., 1994), the type 2 cytokine IL-4 up regulated the production of IgG1 antibodies (Estes et al., 1995) by bovine B cells in vitro. In our study, production of the type 1 cytokine IFN-\(\gamma\) was detected in four of the five fetuses examined. However, a predominant type 2 immune response was also indicated by the production of significantly more *Neospora*-specific IgG1 than IgG2 antibodies in all five infected fetuses. Altogether, these data suggest an imbalance between the production of type 1 and type 2 cytokines, in favor of type 2 cytokines, possibly IL-4, in these fetuses which may have affected their ability to resolve the infection. Alternatively, other factors, including maternal immune responses, may play a role in the prevention of fetal infection.

1.4. Transmission

There are several routes by which cattle may acquire *Neospora* infection, either by horizontal postnatal infection or by vertical transmission of the infection transplacentally during pregnancy. Both routes are the subject of active investigations. The asexual forms of the parasite, tachyzoites and tissue cysts, have been identified in infected fetuses and calves. Tachyzoites can spread through the body and invade the cells of a variety of organs resulting in tissue damage. The persistent tissue cyst stage, containing multiple bradyzoites surrounded by a thick cyst wall, is found in neural tissues and elicits minimal inflammatory reaction. The dog was recently shown to be a definitive host for *N. caninum*. Dogs fed tissues from experimentally infected mice with tissue cyst stages of *N. caninum* shed oocysts in their feces (McAllister et al., 1998; Lindsay et al., 1999). Calves orally infected with oocysts from experimentally infected dogs have serologic and PCR evidence of infection (De Marez et al., 1999). Experimental transplacental transmission of the infection to the fetus with oocysts in pregnant cattle has not yet been reported. Several epidemiological studies found an association between *Neospora* seroprevalence and the presence of dogs in the herds or on the farm, suggesting that dogs may play a role in the transmission of neosporosis (Pare et al., 1998; Bartels et al., 1999; Mainar-Jaime et al., 1999; Wouda et al., 1999b). Bartels et al. (1999) also identified an increased risk of abortion storms due to *Neospora* associated with poultry and moldy feed. In addition to the oocyst stage, there is a potential that postnatal *N. caninum* infection could be acquired from the asexual stages of the parasite based on an experiment in which calves were infected by feeding colostrum inoculated with tachyzoites (Uggla et al., 1998).

Although there are close similarities between *Neospora* and *Toxoplasma* parasites, there are differences between neosporosis in cattle and toxoplasmosis in sheep. When
sheep are infected with *T. gondii* during pregnancy, the ewe seroconverts to the parasite, and fetal infection and/or abortion may occur. In subsequent pregnancies the ewe is resistant to infection (Anderson et al., 1994). Unlike ovine toxoplasmosis, cows that abort a *Neospora*-infected fetus are susceptible to repeat fetal infection in subsequent pregnancies. Moreover, neosporosis in pregnant cattle differs in that the cow does not need to acquire *Neospora* infection or seroconvert during pregnancy for her fetus to become infected.

Vertical transmission of *Neospora* through generations of cattle appears to be the major method by which the infection is maintained in herds (Pare et al., 1994; Björkman et al., 1996; Paré et al., 1996, 1997; Anderson et al., 1997; Thurmond et al., 1997c; Schares et al., 1998; Wouda et al., 1998b; Thurmond and Hietala, 1999a). In a Swedish study, the role of congenital transmission of neosporosis was supported by evidence of the familial distribution of seropositive cattle through successive generations (Björkman et al., 1996). In a German study, 93% of the descendants of seropositive cows were also seropositive, indicating that vertical transmission was the major mode of transmission of infection in the herds examined (Schares et al., 1998). In California dairies, several serologic studies also offer evidence of vertical transmission (Pare et al., 1994; Paré et al., 1996; Thurmond et al., 1997c). In endemic herds, the majority of calves born to seropositive cows have serologic evidence of congenital infection and the rate of seropositivity is similar among the calves and adult cattle in the herd. Three studies have found that the rate of seropositivity in the herd is not associated with the age of the cow, suggesting that the rate of acquired infection after birth is low (Thurmond et al., 1997c; Moen et al., 1998; Bartels et al., 1999; Davison et al., 1999a; Wouda et al., 1999a). There is additional pathologic and serologic evidence which indicates that these congenitally infected calves have a chronic persistent infection which can be passed on transplacentally to their offspring. In a survey in a known *Neospora* dairy herd, heifer calves with serologic evidence of congenital exposure were compared with serologically negative cohorts. The two groups were similar until calving, at which time all the offspring of the seropositive heifers had elevated *Neospora* titers and all seronegative heifers had serologically negative calves (Anderson et al., 1997). A portion of the calves were necropsied, and the calves from seropositive heifers had histologic lesions in the brain and spinal cord consistent with congenital *Neospora* infection and protozoa were identified by immunohistochemistry. A sample of calves from seronegative heifers had no lesions or other findings suggestive of congenital *Neospora* infection.

While vertical transmission appears to be the major way that cattle become infected with *Neospora* in endemic herds, there is serologic evidence that cows that have aborted during an epidemic probably acquired the infection after birth, based on analysis of the seropositivity of dams and daughters (Thurmond et al., 1997c). In addition, the pattern of abortion outbreaks in epidemic neosporosis is suggestive of a point source exposure with acquired infection (Nietfeld et al., 1992; Thornton et al., 1994; Dubey and Lindsay, 1996a; McAllister et al., 1996). At present, there has been no confirmation that the cattle aborting in an epidemic acquired the infection during their pregnancy. In endemically infected herds which have been sampled extensively, there is serologic evidence that a low level of postnatal infection from unknown sources may occur (Schares et al., 1998; Thurmond and Hietala, 1999a).
2. Control and prevention

A major method of Neospora transmission in herds is through the infection of fetuses in cows that are chronically infected. These infected animals can be identified based on their serologic titers or from a history of previous Neospora abortion or congenital infection. With this knowledge, control of the infection could be focused on reducing the numbers of infected cows in the herd and limiting the introduction of infected replacement cattle into the herd. Culling decisions concerning cows that have had a confirmed Neospora abortion can be made with the knowledge that there is a higher risk of repeat abortion in these animals (Moen et al., 1998; Thurmond and Hietala, 1997a). Seropositive cows also have a greater risk of abortion and there is a very high probability of congenital infection in the calves born to these cows (Paré et al., 1997; Thurmond and Hietala, 1997a; Moen et al., 1998; Waldner et al., 1998; Wouda et al., 1998b). In addition, seropositive heifers have been shown to have a reduced milk production (Thurmond and Hietala, 1997b). In both dairy and beef cattle, epidemiological studies have found that seropositive cattle have an increased rate of culling for a variety of reasons (Thurmond and Hietala, 1996; Waldner et al., 1998).

Although various antimicrobial agents have been tested against *N. caninum* in vitro, there is currently no known method whereby an infected cow can be cleared of the infection (Dubey and Lindsay, 1996a).

A provisional killed *N. caninum* vaccine has recently become available but there is no information on its efficacy in regard to reducing fetal infection or abortion in an infected cow or in preventing postnatal infection in a non-infected cow.

There are no proven methods available to prevent postnatal infection. The details of the life cycle are still incomplete. However, based on the experimental evidence that the dog can be a definitive host (McAllister et al., 1998) and the epidemiological association between dogs and seroprevalence in the herd (Pare et al., 1998; Bartels et al., 1999; Mainar-Jaime et al., 1999), it would be prudent to take measures to reduce the potential for this type of transmission. The removal of all potentially infected tissues, such as aborted fetuses and placentas from the environment, that might serve as a source of infection for susceptible hosts would be advisable. In addition, fecal contamination of feed and water sources by potential host animals should be minimized.

References


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