Bovine Leptospirosis and Infertility

Lyle E. Hanson, *D.V.M.*
College of Veterinary Medicine and
Agricultural Experiment Station
Urbana, Illinois 61801

Bovine leptospirosis was first identified as a disease of cattle in 1935 in Russia (Mikhin and Azhinov, 1935). Although bovine leptospirosis has been in the U.S. for many years, it was primarily associated with the *pomona* serovar (Baker and Little, 1948). At least 6 additional serovars have since been isolated from U.S. cattle and agglutinins for other serovars have been detected in U.S. cattle. Serologic surveys indicate that *hardjo* is the most common serovar in U.S. cattle which are the natural reservoir host. It was first isolated in 1959 in dairy cattle in Louisiana (Roth and Galton, 1960). Other serovars also isolated from U.S. cattle include *canicola* (Turner *et al.,* 1958), *grippotyphosa* (Hanson *et al.*, 1964), *icterohaemorrhagiae* (Schnurrenberger *et al.*, 1970), *szwajizak* (Glosser *et al.*, 1974), *balconica* (White *et al.,* 1982). In addition, urine from Florida cattle with *tarassovi* agglutinins have stimulated agglutinins in inoculated hamsters (White *et al.,* 1982).

Prevalence studies based on serolgic surveys indicate *hardjo* is the most widespread serovar with reactor rates varying from a low of 6% for the midwest to a high of 62% for Florida cattle (Stoenner, 1975; Rubin, 1977). The reactor rates to all serovars ranged from 12.5% for the midwest states to 70% for Florida cattle in the same studies. Isolation studies conducted on kidney tissues randomly collected at Florida slaughter plants resulted in isolation of leptospires from 36% of the tissues (White *et al.,* 1982). Of these isolates, 80% were *hardjo,* 17% were *balconica,* and 3 *pomona.*

Clinical signs of leptospirosis in cattle vary with the serovars involved, the herd susceptibility, and between acute and chronic infections. Considerable variation exists between the serovars of *pomona* and *hardjo*. *Pomona* infections usually are more severe but persist for shorter intervals while *hardjo* infections are less severe but more persistent. However, considerable variation can occur depending on stress and whether the infection is the initial exposure or endemic in the herd. *Pomona* is generally reservoired in the pig while the cow is the natural reservoir of the *hardjo* serovar.

Acute leptospiral infections in the cow usually cause an elevation of body temperature, malaise, and anorexia. However, these signs can go unrecognized, especially if they involve nonlactating cows, calves, or beef cattle. In the dairy cow, mastitis and agalactia are often present even when only mild signs are evident. The reduction in milk production in nursing beef cattle can create a stress in the young calves which in turn can stimulate secondary infections. The kidneys generally are involved with an interstitial nephritis, but when only scattered lesions are present no signs are apparent.

The more severe signs of acute leptospirosis generally are associated with *pomona* and *grippotyphosa* infections. These signs include pyrexia, anorexia, hemaglobinuria, jaundice, anemia, pneumonia, and encephalitis. Orchitis may occur in some bulls (Sleight *et al.,* 1974). Mastitis characterized by yellow-thickened blood tinged milk and followed by a severe agalactia may persist from 1 to 2 weeks. Most cows return to production but some never reach original levels during that year's lactation period.

Leptospiremia occurs during acute leptospirosis and leptospires usually can be isolated for a few days from the blood. A noninflammatory leptospiral mastitis occurs in many acute leptospiral infections due to infections by a variety of serovars. Initially, the milk produced is yellow, thickened, and may contain flecks of blood. Agalactiae, which usually follows the initial infection persists from a few days to 1 to 2 weeks. Leptospires have been isolated from the abnormal milk (Baker and Little), 1948; Mitchell and Boulanger, 1959; Higgins *et al.*, 1980; Thiermann, 1982). The lesions consist primarily of degeneration of the alveolar epithelium with only minor inflammatory infiltration of lymphocytes and plasma cells.

Chronic leptospirosis in cattle is recognized primarily as a reproductive disease causing abortions, stillbirths, early fetal deaths, and weak calves. These signs occur from 10 days to 6 weeks but some researchers have followed the acute leptospiremia in the dam. If the acute signs are very mild, abortion may be the first recognized evidence of the disease.

The initial associations of leptospirosis with abortions in cattle were based upon serologic evidence. Various studies indicate *pomona* (Sipple *et al.*, 1952; Bryan, 1955; Borg-Peterson and Fennestad, 1956; Morse *et al.*, 1955), *hardjo* (Summers *et al.*, 1974; Nervig *et al.*, 1980; and Higgins *et al.*, 1980) and *sejroe* (Michna and Campbell, 1969) were all associated with bovine abortion.

Later this association was strengthened by isolations of leptospires from dams following abortions. Serovars isolated from aborting cows include *sejroe* (Michna and Campbell, 1969), *hardjo* (Sulzer *et al.*, 1964; Robertson *et al.*, 1964; Hoare and Claxton, 1972), *grippotyphosa* (Hanson *et al.*, 1964) and *szwajizak* (Glosser *et al.*, 1974).

Leptospires have also been isolated from weak newborn calves. Turner *et al.* (1958) isolated *canicola,* Giles *et al.* (1983) isolated *hardjo,* and Baxter and Pearson (1956) isolated *icterohemorrhagiae* from calves. A direct association of leptospires with abortions has been demonstrated by the isolation of *pomona* (Podgwaite *et al.*,

1955; Dacres and Kiesel, 1958), and *hardjo* (Hathaway and Ellis, 1983; Ellis *et al.*, 1982) from aborted fetuses. The failure to make isolation from aborted bovine fetuses is generally due to death of leptospires resulting from the tissue autolysis present at time of abortion. However, recently Ellis and coworkers (Ellis *et al.*, 1982) made 56 isolates of *hardjo* from bovine fetuses. Further, in a study of 245 randomly selected aborted bovine fetuses they diagnosed leptospires as the cause of 41.6% by using isolation, immunofluorescent and serologic tests on fetal sera. The authors concluded that the extensive cultural techniques would not lend themselves to routine diagnostic services so techniques should be included in their diagnostic program. Fennestad and Borg-Petersen (1958) had previously demonstrated leptospires in bovine fetuses with silver stains even though they were unable to make isolations from the tissues. They also had previously demonstrated that bovine fetuses were capable of developing leptospiral antibodies and the presence of these antibodies in serum from the fetus or stillborn calf at birth provides a positive diagnosis of a fetal infection (Fennestad and Borg-Peterson, 1957).

Experimental inoculation of pregnant cattle has been conducted by a number of researches. Ferguson *et al.* (1957) inoculated 9 pregnant cows with *pomona* and observed abortions in 3 pregnant cows on days 19, 20 and 47 following exposure but did not make isolations. Murphy and Jensen (1969) inoculated 27 heifers in a study in which cows were in the third trimester, with *pomona.* Leptospires were isolated from 5 viable fetuses, and placentas, but not from the 6 dead fetuses examined. Fennestad, Borg-Peterson (1958) inoculated passively immunized cows intraplacentally with *pomona, sejroe,* and *saxkoebing.* Fetal deaths occurred in all *but* the *saxkoebing* inoculated cows and leptospires were isolated from fetal tissues demonstrated by silver stain in fetal tissues. Thiermann (1982) inoculated 8 pregnant cows, 6 with *hardjo* and 2 with *szwajizak* during the fifth month of pregnancy. All the cows which received *hardjo* cultures developed mild signs, malaise, and pyrexia and 1 aborted a dead calf, 2 delivered premature weak calves, and 2 delivered normal calves. All the cows that lactated, developed mastitis, and isolations of leptospires were made from the milk of 5 cows. Leptospires were observed in the cotyledons from 5 cows and the placenta of 3 cows that were infected with *hardjo.* The 2 cows which received *szwajizak* did not show acute signs and delivered normal calves. However, *szwajizak* organisms were isolated from the kidney of 1 calf.

Ellis and Michna (1977) inoculated 20 pregnant heifers with a *hardjo* culture which has been isolated from a cow 5 weeks after an abortion. One of the inoculated heifers aborted and 2 delivered weak calves. Leptospires were demonstrated in the liver, kidney and lungs of the aborted fetus. Although leptospires were not isolated from the fetus, they were isolated from the placental tissue. Leptospires were demonstrated in the placentae of 5 heifers for 14 to 60 days and for as long as 174 days in the kidneys of the heifers. This study indicated the role of *hardjo* in abortions and the persistence of the organisms in the tissues of the cow following abortions.

Abortions due to leptospiral infections are not unique to cattle as they have been demonstrated in other domestic animals and wildlife. Leptospires have been demonstrated in aborted fetuses in swine (Gochenour *et al.*, 1952; Bryan *et al.*, 1953) sheep (Beamer *et al.*, 1953), horses (Ellis *et al.*, 1976), and man (Coghlan and Bain, 1969). In wildlife leptospires have been isolated from fetuses of rats (*Rattus norveigicus*) by Schnurrenberger *et al* (1970), from deer (*Odocolileus vinginianus*) by McGowan *et al.,* 1963, and from sea lions (*Zalaphus californeamus*) by Smith *et al.* (1974).

Lesions in fetal tissues following abortions and stillbirths include severe edema of the placentas, necrosis of the fetal villa (Murphy and Jensen, 1969), edema and scattered necrotic foci in the kidneys and liver tissues (Murphy and Jensen, 1969; Fennestad and Borg-Petersen, 1958; and Thiermann, 1982), and dark red fluids in both the thoracic and abdominal cavities (Fennestad and Borg-Petersen, 1958; Ellis *et al.*, 1982).

Leptospires have been isolated from weak calves at birth and for as late as 7 weeks of age (Giles *et al.*, 1983). Also isolations of leptospires from the urine of cattle have been made continuously for as long as 454 days after the initial infection with a *hardjo* culture (Thiermann, 1982). The lack of readily recognized acute signs in many *hardjo* infections results in the reporting of no apparent acute clinical illness associated with many of these infections. As the cow is the natural maintenance reservoir host for *hardjo* serovar the host-parasite relationship between the cow and the *hardjo* organisms often results in a mild clinical disease, but a long term carrier associationship (Hathaway *et al.*, 1983). The same long term maintenance host-parasite relationship has been demonstrated in the rat with *icterohemorrhagiae* and the mouse with *ballum* (Hathaway *et al.*, 1983).

The reports on serologic, bacteriologic, and histologic studies indicate leptospiral infections have been associated with early fetal deaths, as well as abortions, stillbirths, and weak calves. Herd disease histories indicate leptospires contribute to early fetal deaths reported as infertility (Bryan, 1955; Hanson and Brodie, 1967; Hanson *et al.*, 1972; Bellani and Ruggeri, 1968). The major problem of obtaining isolates from aborted fetuses appears to be due to the very small numbers of leptospires still viable in the bovine fetus due to autolytic changes in the tissues and lack of a satisfactory laboratory medium for some of the fastidious serovars, such as *hardjo.*

Diagnosis of leptospiral infertility cases in cattle usually requires a combination of clinical history, serologic, microbiologic, and histologic examinations. Serologic testing may be inconclusive as the tests may be positive for a short or long interval which does not coincide with the shedding of leptospires in the urine (Killinger *et al.*, 1970; White *et al.*, 1982). However, demonstration of leptospiral agglutinins in fetal or stillborn calves is a positive indication

of an intrauterine infection (Fennstad and Borg-Peterson, 1958). Although isolation of leptospires from a fetus or a stillborn calf constitutes a positive diagnosis, many attempts have been negative from known infected fetuses (Murphy and Jensen, 1969; Thiermann, 1982). Therefore, the use of several techniques should be utilized.

A combination of antibiotic therapy and vaccination with the homologous leptospiral serovars has been shown to be effective if administered early in an initial outbreak (South and Stoenner, 1974). Endemic infections with *hardjo* have been more difficult to contain. Semiannual vaccination along with treatment of the cows during the dry period with a single treatment with dihydrostreptomycin appears to show promise.

As leptospirosis can be an occupational hazard for the dairy worker, the veterinarian should inform the dairy owner of the public health aspects of the disease whenever an outbreak occurs (White *et. al.*, 1981; Hanson, 1982). The augmentation of control measures with antibiotic therapy and vaccination both decrease the hazard by reducing the shedding of leptospires in the urine (Ryan *et al.*, 1982; MacKintosh *et al.*, 1982).

Summary

Leptospirosis is primarily recognized as a reproductive disease in cattle as the disease is most often associated with mastitis in acute infections and early fetal deaths, abortions, stillbirths, and weak calves in chronic infections. A variety of antigenetically distinct serovars can infect cattle. In the United States, 7 serovars have been isolated from cattle with *hardjo* being the most common. *Hardjo* which generally causes a milder disease than the *pomona* serovar is endemic in cattle, the reservoir host.

Serologic, histologic, and microbiologic techniques along with experimental inoculation studies have established the role of some leptospiral serovars in bovine reproductive problems. These findings have been supported with epidemiological studies.

Diagnosis of leptospirosis as the cause of reproductive problems in a cattle herd generally requires several laboratory techniques as clinical signs and lesions usually alone are not distinct. Serologic tests alone are often inadequate to diagnose leptospirosis due to the persistence of leptospires in chronic infections without stimulation of generalized humoral responses.

Control of bovine leptospirosis can most economically be accomplished by yearly vaccination with bacterins containing the prevalent leptospires. Treatment with antibiotics may be a necessary supplemental procedure when endemic infections are present in large herds.

The dairyman should be informed of the zoonotic aspects of leptospirosis whenever the active disease is present in a dairy herd.

References

1. Baker, J.A. and Little, R.B. 1948. Leptospirosis in cattle. J. Exp. Med. 88:295-307. 2. Baxter, J.T. and Pearson, J.K.L. 1956. *Leptospira icterohaemorrhagiae* infection in calves in Northern Ireland. Vet. Rec. 68:6-8. 3. Beamer, P.D.; Hardenbrook, H., Jr. and Morrill, C.C. 1953. Studies on leptospirosis in domestic animals. I. Leptospirosis in sheep. Vet. Med. 48:365-366. 4. Bellani, L. and Ruggeri, L. 1968. Endemic abortion and infertility among cattle caused by leptospirosis in the Po Valley (Italy). Clinica. Vet. Milano 91:237-243. 5. Borg-Petersen, C. and Fennestad, K.L. 1956. Studies on bovine leptospirosis and abortion. I. Serological examination of aborting and "normal" cattle in Denmark. Nord. Vet. Med. 8:465-480. 6. Bryan, H.S.; Rhoades, H.E. and Willigan, D.A. 1953. Isolation of *Leptospira pomona* from aborted swine fetuses. Vet. Med. 48:438-442. 7. Bryan, H.S. 1955. Some effects of leptospirosis on reproduction in cattle. Proc. J. Am. Vet. Med. Assoc. 92:371-373. 8. Coghlan, J.D. and Bain, A.D. 1969. Leptospirosis in human pregnancy followed by death of the foetus. Brit. Med. J. 1:228-230. 9. Dacres, W.G. and Kiesel, G.K. 1958. Isolation of *Leptospira pomona* from a bovine fetus. JAVMA 132:525-526. 10. Dazas, L. and Sudhir S. 1970. Endometrial changes in nonpregnant ewes infected with *Leptospira pomona.* Cornell Vet. 60:254-264. 11. Ellis, W.A., Bryson, D.G. and McFerran, J.B. 1976. Abortion associated with mixed leptospira/equid herpesvirus 1 infection. Vet. Rec. 98:218-219. 12. Ellis, W.A. and Michin, S.W. 1977. Bovine leptospirosis: Experimental infection of pregnant heifers with a strain belonging to the Hebdomadis serogroup. Res. Vet. Sci. 22:229-236. 13. Ellis, W.A., O'Brien, J.J., Neill, S.D., Hanna, J. and Bryson, D.G. 1977. The isolation of a strain of *Leptospira* serogroup *icterohaemorrhagiae* from an aborted bovine foetus. Brit. Vet. J. 133:108-109. 14. Ellis, W.A., O'Brien, J.J., Neill, S.D., Ferguson, H.W. and Hanna, J. 1982. Bovine leptospirosis. Microbiological and serological findings in aborted fetuses. Vet. Rec. 110:147-150. 15. Fennestad, K. L. and Borg-Petersen, C. 1957. Leptospira antibody production by bovine foetuses. Nature 180:1210-1211. 16. Fennestad, K.L. and Borg-Petersen, C. 1958. Fetal leptospirosis and abortion in cattle. J. Infect. Dis. 102:227-236. 17. Ferguson, L.C.; Ramge, J.C. and Sanger, V.L. 1957. Experimental bovine leptospirosis. Am. J. Vet. Res. 18:43-49. 18. Giles, N., Hathaway, S.C. and Stevens, A.E. 1983. Isolation of *Leptospira interrogans* serovar *hardjo* from a viable premature calf. Vet. Rec. 113:174-176. 19. Gochenour, W.S. Jr., Johnston, R.V., and Yager, R.H., Gochenour, W.S. 1952. Porcine leptospirosis. Am. J. Vet. Res. 13:158-160. 20. Glosser, J.W., Sulzer, C.R. and Whitsett, D. 1974. Serotype *szwajizak* isolated from bovines in Oregon: First time in the US *Proc. US Anim. Hlth. A. 78:119-125. 21. Hanson, L.E., Ellinghausen, H.C. and Marlow, R. 1964. Isolation of Leptospira grippotyphosa* from a cow following an abortion. Proc. Soc. Exp. Biol. Med. 117:495-497. 22. Hanson, L.E., Tripathy, D.N. and Killinger, A.H. 1972. Current status of leptospirosis immunization in swine and cattle. J. Amer. Vet. Med. Ass. 161:1235-1243. 23. Hanson, L.E. and Brodie, B.O. 1967. *Leptospira hardjo* infection in cattle. Proc. US An. Hlth. Assoc. 71:210-215. 24. Hanson, L.E. 1982. Leptospirosis in domestic animals: the public health perspective. J. Am. Vet. Med. Assoc. 181:1505-1509. 25. Hoare, R.J. and Clapton, P.D. 1972. Observations on *Leptospira hardjo* infections in New South Wales. Aust. Vet. J. 48:228-232. 26. Hathaway, S.C. and Little, T.W.A. 1983. Epidemiological study of *Leptospira hardjo* infection in second calf dairy cows. Vet. Rec. 111:215-218. 27. Hathaway, S.C., Blackmore, D.K. and Marshall, R.B. 1983. Leptospirosis and the maintenance host: A laboratory moust model. Res. Vet. Sci. 34:82-89. 28. Higgins, R. J., Harbourne, J.F., Little, T.W.A. and Stevens, A.E. 1980. Mastitis and abortion in dairy cattle associated with leptospira of the serotype *hardjo.* Vet. Rec. 107:307-310. 29. Killinger, A.H., Hanson, L.E., Mansfield, M.E. and Reynolds, H.A. 1970. Vaccination of cattle with leptospiral bacterins. I. Serologic and cultural results of challenge. Proc. US Anim. Hlth. A. 74:165-177. 30. McGowan, J.E., Karstad, L. and Fish, N.A. 1963. Leptospirosis in Ontario cervidae, isolation of *Leptospira pomona* from a deer fetus. Tran. North Am. Wildlife Nat. Res. Conf. 28:199-206. 31. MacKintosh, C.G., Schallum, L.M., Blackmore, D.K., and Marshall, R.B. 1982. Epidemiology of leptospirosis in dairy farm workers in the Manquatu. Part II. A case – control study of high and low risk farms. NZ. Vet. J. 30:73-76. 32. Michna, S.W. and Campbell, R.S.F. 1969. The isolation of *Leptospira sejroe* from the kidneys of aborting cattle. Vet. Rec. 84:83-96. 33. Mikhin, N.A. and Azhinov, S. A. 1935. Spirochaetal jaundice and haemoglobinuria in calves

and adult cattle in North Caucasus. Sovet. Vet. 10:23-27. 34. Michell, D. and Boulanger, P. 1959. Leptospirosis in Canada. IV. An atypical mastitis in cattle due to *Leptospira pomona.* Can. J. Comp. Med. 23:250-255. 35. Morse, E.V., Allen, V., Pope, E.P. and Krohn, A.F. 1955. Leptospirosis in Wisconsin. II. Serological studies. J. Am. Vet. Med. Assoc. 127:422-426. 36. Murphy, J.C. and Jensen, R. 1969. Experimental pathogenesis of leptospiral abortion in cattle. Am. J. Vet. Res. 30:703-713. 37. Nervig, R.M., Beran, C.W. and Hill, H.T. 1980. Bovine leptospirosis in Iowa: A serological survey. Iowa State Vet. 51:62-64. 38. Podgwaite, G.C., Tourtellotte, M.E., Jacobs, R.E., Helmobaldt, C.F., Easterbrooks, H.L., Williams, L.F., Jungherr, E.L. and Plastridge, W.N. 1955. Isolation of *Leptospira pomona* from three aborted bovine fetuses. Vet. Med. 50:164-165. 39. Robertson, A., Boulanger, P. and Mitchell, D. 1964. Isolation and identification of a leptospire of the Hebdomodis serogroup (*L. hardjo*) from cattle in Canada. Can. J. Comp. Med. 28:13-18. 40. Roth, E.E. and Galton, M.M. 1960. Isolation and identification of *Leptospira hardjo* from cattle in Louisiana. Amer. J. Vet. Res. 21:422-426. 41. Rubin, H.L. 1977. Serologic incidence of leptospirosis in Florida cattle. Proc. US An. Hlth. Assoc. 81:197-200. 42. Ryan, T.J., Hellstrom, J.S. and Penniket, J.H. 1982. Leptospirosis in dairy farmers: prevention by vaccination of cattle. NZ. Vet. J. 30:107-108. 43. Schnurrenberger, P.R., Hanson, L.E. and Martin, R.J. 1970. Leptospirosis: Long-term surveillance on an Illinois farm. Am. J. Epid. 92:223-239. 44. Sipple, W.L., Boyer, C.I. and Chambers, E.E. 1952. Bovine leptospirosis in Georgia. J. Am. Vet. Med. Assoc. 120:278-282. 45. Sleight, S.D., Atallah, O.A. and Steinbauer, D.J. 1964. Experimental *Leptospira pomona* infection in bulls. Am. J. Vet. Res. 25:1663-1668. 46. Smith, A.W., Brown, R.J. and DeLong, R. 1974. Leptospira abortion and other possible causes of reproductive failure in wild California sea lions (*Zalaphus californiamus*). J. Am. Med. Assoc. 165:996-998. 47. South, P.J. and Stoenner, H.G. 1974. The control of outbreak of leptospirosis in beef cattle by simultaneous vaccination and treatment with dehydrostreptomycin. Proc. US An. Hlth. Assoc. 78:126-130. 48. Stoenner, H.G. 1975. Summary report on the 1975 survey for leptospirosis in the United States. Proc. US An. Hlth. Assoc. 79:145-149. 49. Sulzer, C.R., Shotts, E.B., Jr., Olsen, C.D., Galton, M.N. and Stewart, M.A. 1964. Leptospirosis due to serotype *hardjo* in cattle. J. Am. Vet. Med. Assoc. 144:888-890. 50. Summers, P.M., Campbell, R.S.F. and Dennett, D.P. Herd Studies on the genital pathology of infertile beef cows. Aust. Vet. J. 50:150-154. 51. Turner, L.W., Roberts, C.S., Wiggins, A.M., Alexander, A.D. and Murphy, L.C. 1958. *Leptospira canicola* infection in a newborn calf. Am. J. Vet. Res. 19:780-784. 52. Thiermann, A.B. 1982. Experimental leptospiral infections in pregnant cattle with organisms of the *hebdomadis* serogroup. Am. J. Vet. Res. 43:780-784. 53. White, F.H., Sutherland, G.E., Raynor, L.E., Cottrell, C.R. and Sulzer, K.R. 1981. *Leptospira interrogans* serovars *hardjo* and *pomona:* causes of infections in dairy cows and humans in Florida. Public Health Reports 96:250-254. 54. White, F.H., Sulzer, K.R. and Engel, B.S. 1982. Isolations of *Leptospira interrogans* serovars *hardjo, balconica* and *pomona* from cattle at slaughter. Am. J. Vet. Res. 43:1172-1173.