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ANAPLASMA INFECTIONS IN WILD AND DOMESTIC RUMINANTS: A REVIEW

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ABSTRACT: *Anaplasma marginale* can be transmitted, will grow and can survive in a large number of domestic and wild animals. It is pathogenic in cattle, and usually produces nonapparent or mild infections in other species. *Anaplasma marginale* has been recovered from cattle, sheep, goats, water buffalo (*Bubalus bubalis*), white-tailed deer (*Odocoileus virginianus*), mule deer (*Odocoileus hemionus hemionus*), black-tailed deer (*Odocoileus hemionus columbianus*), pronghorn (*Antilocapra americana americana*), Rocky Mountain elk (*Cervus elaphus nelsoni*), bighorn sheep (*Ovis canadensis canadensis*), black wildebeest (*Connochaetes gnu*), blesbuck (*Damaliscus albifrons*), and duiker (*Sylvicapra grimmii grimmii*). Unidentified anaplasms have been seen in, and in some instances isolated from, Cape buffalo (*Syncerus caffer*), giraffe (*Giraffa camelopardalis*), wildebeest (*Connochaetes taurinus*), Cokes hartebeest (*Alcelaphus buselaphus cokii*), Thompson's gazelle (*Gazella thompsonii*), waterbuck (*Kobus ellipsiprymnus*), and sable antelope (*Hippotragus niger*), with serological evidence of *Anaplasma* infection in an even wider range of wild ruminant species. *Anaplasma ovis*, *A. centrale*, or other as yet unidentified anaplasms may well occur in other ruminants. With the exception of black-tailed deer, the epidemiologic significance of anaplasmosis in wildlife has yet to be determined. The only wild animal in which *Anaplasma* is reported to produce serious clinical disease is the giraffe.

Anaplasmosis is a disease of cattle caused by the intraerythrocytic rickettsial agent *Anaplasma marginale*. While it is true that *A. marginale* is principally pathogenic in cattle, it is not confined to cattle, nor is *A. marginale* the only pathogenic species in this genus.

ANAPLASMA IN DOMESTIC ANIMALS (Table 1)

Soon after Theiler's description of *A. marginale* (Theiler, 1910), he identified a second species of *Anaplasma*, *A. centrale*, which produced a relatively mild pathogenic response in cattle (Theiler, 1911). Its close antigenic similarity to *A. marginale* led to its widespread use as a premunizing vaccine to prevent clinical anaplasmosis (Theiler, 1911). Donatien and Lestoquard (1930) recognized *A. ovis* in sheep. These authors also noted that *A. marginale* could be recovered from sheep that had been previously exposed to *A. marginale*, even

though the animals showed no signs of active infection. *Anaplasma ovis* could not, however, be recovered from calves previously exposed to *A. ovis*. Splitter (1956) described *A. ovis* in the U.S. as an organism causing a mild infection in sheep which was serologically closely related to *A. marginale* but not immunologically identical. Calves were apparently refractory to infection with the *A. ovis* strain identified by Splitter (1956). Kuttler (1981a) was unable to recover *A. ovis* from a splenectomized calf 17 days after inoculation with *A. ovis*, but did recover *A. ovis* 177 and 262 days after exposure. Calves inoculated with *A. ovis* failed to develop a demonstrable parasitemia or any signs of infection except for a delayed low-level, sporadic serologic response to *A. marginale* antigens. Two calves, from which *A. ovis* was recovered, were fully susceptible when challenged with virulent *A. marginale*. Splenectomized sheep inoculated with *A. marginale* showed a low-level parasitemia and a moderate reduc-

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TABLE 1. *Anaplasma* in domestic animals.

| Animal species | Misc. or unknown <i>Anaplasma</i> | <i>A.</i> <i>marginale</i> | <i>A.</i> <i>ovis</i> | <i>A.</i> <i>centrale</i> |
|---|---|-------------------------------|--------------------------|------------------------------|
| Cattle (Theiler, 1910, 1911) | | +++* | ± ^d | ++ |
| Sheep (Donatien and Lestoquard, 1930; Splitter et al., 1956; Gautam et al., 1970; Uilenberg et al., 1979; Magonigle et al., 1981) | + | + ^e | ++ ^f | |
| Goats (Mallick et al., 1979; Maas and Buening, 1981b) | | + | ++ | |
| Horses (Brion, 1943) | ++ ^h | | | |
| Water buffalo (<i>Bubalus bubalis</i>) (Carpano, 1934; Gautam et al., 1970; Singh and Gill, 1977) | + ^e | + | | |

* Uilenberg proposed the name *Anaplasma mesaeterum* for a sheep *Anaplasma* distinct from *A. ovis*.

^b Brion proposed the name *Anaplasma equi*.

^c Carpano proposed the name *Anaplasma buffeli*.

^d ±: *Anaplasma* survives or serologic evidence only.

^e +: Subclinical infection—low parasitemia.

^f ++: Mild clinical response to infection.

^h +++: Severe clinical response to infection.

tion in PCV, as well as a positive serologic response to antigens of *A. marginale* (Kuttler, 1981a). These sheep, when challenged with *A. ovis*, were fully susceptible, confirming the absence of immunologic similarities sufficient to prevent infection. Sera from sheep infected with *A. ovis* react with *A. marginale* antigen, and sera from calves infected with *A. marginale* fix complement in the presence of *A. ovis* antigen.

In addition to these three well-recognized anaplasms, Carpano (1934) identified *Anaplasma buffeli* in water buffalo (*Bubalus bubalis*) in Egypt; and Uilenberg et al. (1979), *Anaplasma mesaeterum* in sheep. This latter organism, which was not infective for cattle, was unique in that fewer than 30% of the inclusion bodies were situated marginally. Infection with *A. mesaeterum* induces incomplete cross immunity to *A. ovis*, a situation somewhat reminiscent of the relationship between *A. centrale* and *A. marginale*.

There is often a common weakness in reports of *Anaplasma* in wildlife and species other than sheep and cattle. Numbers are usually small, and diagnosis is frequently made on the basis of Giemsa-

stained blood smears in the absence of serologic confirmation. For this reason, an anaplasma situated marginally in the erythrocyte is frequently designated as *A. marginale*. While identification of *Anaplasma* species is rather difficult by means of the routinely used serologic tests, there is an indication that cross reactivity of titrated serum samples with the homologous and heterologous antigens may provide a basis for species differentiation (Kuttler, 1967). The presence of *Anaplasma* bodies in erythrocytes of ruminant species other than cattle and sheep poses two possibilities: The organism seen may be antigenically distinct and specific for the species in which it is seen, or it may be one of the recognized anaplasms in a nonbovine or nonovine host.

ANAPLASMA IN NORTH AMERICAN WILDLIFE (Table 2)

There is little or no evidence that American bison (*Bison bison*) are susceptible to *Anaplasma* infections. Peterson and Roby (1975) failed to detect evidence of anaplasmosis in bison using serology and by the inoculation of splenectomized calves, even though the bison were locat-

TABLE 2. *Anaplasma* in North American wildlife.

| Animal species | Misc. or unknown <i>Anaplasma</i> | <i>A.</i> <i>marginale</i> | <i>A.</i> <i>ovis</i> | <i>A.</i> <i>centrale</i> |
|--|---|-------------------------------|--------------------------|------------------------------|
| Bison (<i>Bison bison</i>) (Peterson and Roby, 1975) | — ^a | — | | |
| White-tailed deer (<i>Odocoileus virginianus</i>) (Kreier and Ristic, 1963; Roberts and Lancaster, 1963; Kuttler et al., 1967; Lancaster et al., 1968; Kuttler, 1981a; Maas and Buening, 1981a; Smith et al., 1982) | | + ^b | + | |
| Mule deer (<i>Odocoileus hemionus hemionus</i>) (Howe et al., 1964; Howe and Hepworth, 1965; Renshaw et al., 1977) | | + | | |
| Black-tailed deer (<i>Odocoileus hemionus columbianus</i>) (Boynton and Woods, 1933, 1940; Christensen et al., 1958; Osebold et al., 1959; Howarth et al., 1969) | | + + ^c | | |
| Pronghorn (<i>Antilocapra americana</i>) (Howe et al., 1964; Howe and Hepworth, 1965; Jacobson et al., 1977) | | + | | |
| Rocky Mountain elk (<i>Cervus elaphus nelsoni</i>) (Post and Thomas, 1961; Howe et al., 1964; Magonigle and Eckblad, 1979) | | + | + | |
| Bighorn sheep (<i>Ovis canadensis canadensis</i>) (Howe et al., 1964) | | + | | |

^a —: No reported infection.^b +: Subclinical infection—low parasitemia.^c + +: Mild clinical response to infection.

ed in an anaplasmosis-endemic area of eastern Oregon. I have found no reports in the literature of attempts to infect bison by the inoculation of infected blood.

Anaplasma infections in white-tailed deer (WTD) (*Odocoileus virginianus*) have been studied extensively by numerous workers (Kreier and Ristic, 1963; Lancaster et al., 1968; Kuttler, 1981b). These deer are readily infected with both *A. marginale* and *A. ovis* (Kreier and Ristic, 1963). Even though clinical signs of infection are minimal, WTD may retain a carrier infection for extended periods of time (Kuttler et al., 1967). Efforts by Bedell and Miller (1966) to isolate *Anaplasma* from 270 WTD in the southeastern U.S., an anaplasmosis-endemic zone, were uniformly negative. These results, together with other similar observations, support the view that WTD do not represent a major reservoir of infection for *A. marginale* (Robinson et al., 1968).

A Texas isolate of virulent *A. marginale* (TAM), when inoculated into a splenectomized deer and then passaged in a second deer, produced only mild signs of infection, with parasitemias not exceeding 2% with a 10% and 24% reduction in PCV (Kuttler, unpubl. data). The second passage was made about 30 days after exposure during the parasitemic phase. *Anaplasma marginale* was recovered from the second deer 20 mo later by the inoculation of deer blood into four splenectomized calves. The response of these calves to *A. marginale* (DEAM) of deer origin was unusually mild, in comparison to reactions in splenectomized calves infected with the original TAM maintained in frozen stabilate and an isolate obtained in southern Texas (UAM) (Table 3). It would appear that the TAM, a fully virulent *Anaplasma*, lost most of its virulence for cattle during its 21 mo in WTD.

Mule deer (MD) (*Odocoileus hemionus*

TABLE 3. Response of splenectomized calves to *A. marginale* exposure of different origins.

| | No. of splenectomized calves | Prepatent period (days) | Avg. low PCV % | Avg. % PCV reduction | Avg. high CF titer | Avg. high parasitemia % | Deaths |
|-------------------|------------------------------|-------------------------|-----------------|----------------------|--------------------|-------------------------|--------|
| Inoculum | | | | | | | |
| TAM ^b | 5 | 22 ± 3 ^f | 8 ± 1.8 | 73 ± 6 | 1:80 | 58 ± 31 | 5/5 |
| DEAM ^c | 4 | 28 ± 14 | 21 ± 3.0 | 34.5 ± 6 | 1:95 | 5 ± 2 | 0/4 |
| UAM ^d | 5 | 28 ± 2 | 9 ± 1.8 | 71 ± 4 | 1:80 | 32 ± 15 | 5/5 |
| Significance | | NS | <i>P</i> < 0.01 | <i>P</i> < 0.01 | NS ^e | <i>P</i> < 0.01 | |
| DRS ^e | | | 5.0 | 9.0 | | 37.0 | |

^a NS: Not significant (ANOVA test; Kuttler, unpubl. data).

^b TAM: A Texas *A. marginale* field isolate (stabilate).

^c DEAM: The TAM organism recovered from deer 21 mo later (stabilate and fresh blood).

^d UAM: A Texas *A. marginale* isolate from southern Texas (stabilate).

^e DRS: Difference required for significance.

^f ±: Standard deviation.

hemionus) have been studied less extensively than WTD, but isolations of *Anaplasma* have been made from MD in the anaplasmosis-endemic areas of Wyoming and Idaho (Howe and Hepworth, 1965; Renshaw et al., 1977). Similar efforts in Oregon were unsuccessful (Peterson et al., 1973). *Anaplasma* infection has been induced in MD with carrier infections persisting at least 66 days (Howe et al., 1964). A serologic survey of 87 MD in Idaho, using the serum rapid card agglutination test, revealed that 15% of these animals were positive reactors (Renshaw et al., 1977). Serologic tests on serum from wild animals are often misleading, so should be considered cautiously (Howe and Hepworth, 1965; Howarth et al., 1976). It is unlikely that the presence of *A. marginale* in MD represents a disease threat to this species but infection in MD may provide a nonbovine reservoir of infection with possible epidemiologic significance.

Black-tailed deer (BTD) (*Odocoileus hemionus columbianus*) have been shown to be reservoirs of *A. marginale* infection for cattle (Boynton and Woods, 1933, 1940; Christensen et al., 1958; Christensen and McNeal, 1967). Transmission of *A. marginale* has been demonstrated with adult ticks (*Dermacentor occidentalis*)

collected from BTD (Osebold et al., 1962). Since adults of this species of tick normally feed on both deer and cattle, it is probable that deer-to-deer, deer-to-cattle, and cattle-to-deer transmission occurs. This wildlife reservoir of infection (Osebold et al., 1959) has significant implications in California, where it effectively negates control of anaplasmosis by the conventional methods (test, segregation, and treatment) that are effective elsewhere. Of the three species of deer in the U.S., the black-tailed deer appears to be the most susceptible to *A. marginale* (Kuttler, 1981b).

Pronghorn (*Antilocapra americana americana*), Rocky Mountain elk (*Cervus elaphus nelsoni*) and bighorn sheep (*Ovis canadensis canadensis*) have been infected experimentally with *A. marginale*, which in turn was recovered in cattle (Howe et al., 1964). These animals represent potential reservoirs of infection, but most efforts to recover *Anaplasma* from the wild population have been unsuccessful, suggesting that even though these species are susceptible, they are probably not responsible for maintaining infections or acting as a source of infection for cattle (Post and Thomas, 1961; Howe and Hepworth, 1965; Vaughn et al., 1976; Jacob-

son et al., 1977). In no instance were serious clinical infections in these nonbovine hosts noted following exposure. There is some presumptive evidence that elk may harbor *A. ovis* or a closely related anaplasma (Post and Thomas, 1961). Sheep inoculated with elk blood became positive to the CF test but developed no detectable parasitemia. Challenge of these sheep with *A. ovis* failed to produce an apparent parasitemia, suggesting that an *A. ovis* infection had occurred in sheep after the elk blood inoculation.

The CF test was not reliable when used on pronghorn, bighorn sheep, and elk in that many false positives occurred, and many of the pronghorn sera were anti-complementary (Howe et al., 1964). The rapid card agglutination test, on the other hand, appears satisfactory for use on elk serum (Renshaw et al., 1979) and shows advantages for use on serum from BTB (Howarth et al., 1976) and MD (Renshaw et al., 1977). Even though the CF test is highly sensitive in recognizing induced *Anaplasma* infections in WTD, a capillary tube agglutination test shows advantages in that fewer suspect and false positive reactions occur (Kuttler et al., 1968).

ANAPLASMA IN AFRICAN AND ASIAN WILDLIFE (Table 4)

Serologic evidence of anaplasmosis in Cape buffalo (*Syncerus caffer*) has been observed (Kuttler, 1965). On one occasion *Anaplasma* bodies similar to *A. centrale* were observed in Cape buffalo erythrocytes, but on subinoculation no detectable infection occurred in splenectomized calves (Brocklesby and Vidler, 1966). A mild *A. marginale* isolate has been recovered from Cape buffalo by inoculation of bovines (Potgieter, 1979). It is probable that Cape buffalo would sustain *A. marginale* if splenectomized buffalo calves were inoculated, but evidence confirming this is needed.

There are two reports of acute *Anaplasma* infections in giraffe (*Giraffa ca-*

melopardalis) in which severe clinical signs were seen (Lohr and Meyer, 1973; Agustyn and Bigalke, 1974). In both instances, death occurred in association with the *Anaplasma* parasitemias and severe anemia. The organism was similar to *A. marginale*, but there has been little work done serologically or by animal inoculation to establish conclusively its identity.

There have been a number of reports incriminating species of wildebeest as being infected with *Anaplasma* (Neitz, 1935; Kuttler, 1965; Brocklesby and Vidler, 1966; Lohr and Meyer, 1973; Lohr et al., 1974; Burrridge, 1975). *Anaplasma* has been isolated from the East African blue wildebeest (*Connochaetes taurinus*) (Lohr and Meyer, 1973; Burrridge, 1975), and *A. marginale* infections have been induced in the black wildebeest (*Connochaetes gnu*) under controlled conditions (Neitz, 1935). However, bovine calves that recovered from the *Anaplasma* infection induced by blood inoculation from the East African blue wildebeests were susceptible to *A. marginale* challenge, suggesting antigenic differences (Lohr and Meyer, 1973). The anaplasmas isolated in calves inoculated with blood from Cokes hartebeest (*Alcelaphus buselaphus cokii*), and Thompson's gazelle (*Gazella thompsonii*) resembled *A. marginale*; however, these calves were also susceptible to bovine origin *A. marginale* challenge (Lohr and Meyer, 1973).

Anaplasma marginale, *A. centrale*, and *A. ovis* were recovered from blesbuck (*Damaliscus albifrons*) following experimental exposure to these organisms (Neitz and DuToit, 1932; Neitz, 1939). Efforts to isolate an anaplasma from wild impala (*Aepyceros melampus*) and Grant's gazelle (*Gazella grantii*) have been unsuccessful (Lohr and Meyer, 1973); however, positive serological responses to *Anaplasma* antigens have been observed in impala, waterbuck (*Kobus ellipsiprymnus*), Grant's gazelle, and eland (*Taurotragus oryx*) (Lohr et al., 1974). The significance

TABLE 4. *Anaplasma* in African and Asian wildlife.

| Animal species | Misc. or unknown <i>Anaplasma</i> | <i>A.</i> <i>marginale</i> | <i>A.</i> <i>ovis</i> | <i>A.</i> <i>centrale</i> |
|--|---|-------------------------------|--------------------------|------------------------------|
| Cape buffalo (<i>Syncerus caffer</i>) (Brocklesby and Vidler, 1966; Potgieter, 1979) | + | +(?) | | + |
| Giraffe (<i>Giraffa camelopardalis</i>) (Brocklesby and Vidler, 1966; Lohr and Meyer, 1973; Agustyn and Bigalke, 1974; Lohr et al., 1974) | +++* | | | |
| Wildebeest (<i>Connochaetes taurinus</i>) (Kuttler, 1965; Lohr and Meyer, 1973; Burridge, 1975) | + | + | | |
| Black wildebeest (<i>Connochaetes gnu</i>) (Neitz, 1935) | | + | | |
| Cokes hartebeest (<i>Alcelaphus buselaphus cokii</i>) (Lohr and Meyer, 1973) | + | +(?) | | |
| Thompson's gazelle (<i>Gazella thompsonii</i>) (Lohr and Meyer, 1973) | + | +(?) | | |
| Blesbuck (<i>Damaliscus albifrons</i>) (Neitz and DuToit, 1932; Neitz, 1939) | | + | + | + |
| Impala (<i>Aepyceros melampus</i>) (Kuttler, 1965; Lohr et al., 1974) | ± ^b | — ^a | | |
| Sable antelope (<i>Hippotragus niger</i>) (Thomas et al., 1982) | ++ ^d | | +(?) | |
| Grant gazelle (<i>Gazella grantii</i>) (Lohr et al., 1974) | + | — | | |
| Duiker (<i>Sylvicapra grimmii grimmii</i>) (Neitz and DuToit, 1932) | | + | | |
| Waterbuck (<i>Kobus ellipsiprymnus</i>) (Kuttler, 1965; Lohr et al., 1974) | ± | — | | |
| Siberian ibex (<i>Capra aegagrus</i>) (Matthews, 1978) | +++ | | | |
| Eland (<i>Taurotragus oryx</i>) (Lohr et al., 1974) | ± | — | | |
| Elk (<i>Alces alces</i>) (Grobov, 1961) | | + | | |

^a —: No reported infection.

^b ±: Serological evidence only.

^c +: Subclinical infection—low parasitemia.

^d ++: Mild clinical response.

* + + +: Severe clinical infection.

of these findings is not known in view of serological cross reactions characteristic of the known *Anaplasma* species. A duiker (*Sylvicapra grimmii grimmii*) under natural conditions was not found to harbor hemoparasites transmissible to cattle, but was successfully infected with *A. marginale*. *Anaplasma marginale* was recovered from the exposed duiker, which harbored a nonapparent infection (Neitz and DuToit, 1932).

Blood smears from 124 sable antelope (*Hippotragus niger*) showed only one to be positive for *Anaplasma*. However, splenectomy of a sable calf resulted in a relapsing infection of *Anaplasma* characterized by a serologically positive reaction to antigen of *A. marginale*, and a 12% parasitemia; the agent was susceptible to oxytetracycline therapy. Subinoculation of this organism into a splenectomized sheep and a splenectomized calf resulted in a

low-level parasitemia and serological response in the sheep only. The calf appeared refractory to infection with this anaplasma (Thomas et al., 1982).

The report of *Anaplasma* in an ill Siberian ibex (*Capra aegagrus*) was based entirely on the observation in blood smears of *Anaplasma*-like bodies which were suspected of causing the illness. However, neither serology nor subinoculation of blood into cattle, sheep, or goats was performed to confirm the identity of the organism (Matthews, 1978). Grobov (1961) confirmed the susceptibility of elk (*Alces alces*) in Russia to anaplasmosis. A low but detectable parasitemia accompanied by a modest drop in red cell counts was seen following the inoculation of known *A. marginale* infected bovine blood. The anaplasma was later recovered from the elk by inoculating its blood into a susceptible bovine.

DISCUSSION

In view of the false serologic responses observed in deer, pronghorn, and elk, it is interesting to speculate that if these species were infected with *A. ovis* or a closely related anaplasma, a positive CF response would be expected using *A. marginale* antigen, but recovery of *Anaplasma* from the blood of these wild ruminants in a splenectomized calf would be highly unlikely in view of the extended incubation times required for growth and detection of *A. ovis* in calves, under even optimum conditions. Also, an *A. marginale* challenge of an *A. ovis*-infected calf would result in acute *A. marginale* infection leading to the conclusion that no *Anaplasma* infection existed. Along this same line, there is some evidence from African studies that there may be anaplasmas that are species specific, which may or may not infect cattle.

The apparent reduction in the pathogenicity of *A. marginale* for calves, when maintained in deer for 21 mo, offers a possible explanation for why some of the

organisms isolated from wild ruminants produce only mild infections in calves. If the organism isolated from wild ruminants had its origin with cattle infected with *A. marginale*, then these calves should be reasonably immune to challenge with the bovine *A. marginale*. By contrast, if the organism isolated from wild ruminants is specific for these species or is more closely related to *A. ovis*, then a response similar to that seen when *A. ovis* was inoculated into calves might be expected. In these cases, infections were nonapparent, and the calves were fully susceptible to *A. marginale* challenge.

Although serological cross reactions among anaplasmas cause complications in distinguishing species and strains of *Anaplasma*, the development of new serologic tests and monoclonal antibody techniques offer promise for serologically identifying *Anaplasma* isolates from diverse sources. The study of *Anaplasma* in both wild and domestic ruminants should contribute to a better understanding of this unique microorganism, and possibly lead to the development of safer and more effective live vaccines.

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