**Rickettsia rickettsii** (Rocky Mountain Spotted Fever and the Rocky Mountain Fever Group)

**Tick Vectors:** Primarily *Dermacentor variabilis* (the American dog tick) and *D. andersoni* (the Rocky mountain wood tick) are the primary tick vectors. However, both *Rhipicephalus sanguineus* (the brown dog tick) and *Amblyoma americanum* (the Lone Star tick) have also been reported to occasionally transmit the organism.

**Distribution:** *Dermacentor variabilis* (the American dog tick) is widely distributed in the United States from a line drawn from Montana to South Texas extending eastward to the Atlantic coast. It has also been reported in western California and southwestern Oregon. *D. andersoni* (the Rocky mountain wood tick) inhabits a large region in the northwestern United States extending from the Cascade Mountains to the Rocky Mountains. See proceedings on Ehrlichia for distribution of the lone star tick.

**Illness and clinical signs associated with Rickettsia rickettsii pathogens in dogs:**

1) *Rickettsia rickettsii* is the causative agent of Rocky Mountain spotted fever (RMSF).

   - **Clinical signs:** Both clinical and subclinical infections can occur in dogs. Fever is the first and most consistent clinical finding. Other clinical findings primarily occur because of the widespread vasculitis that results from the organism invading and replicating in endothelial cells of small veins and arteries. Purebred dogs, particularly German shepherds may be more prone to developing clinical disease. Vasculitis in affected tissues and organs can cause various clinical signs depending on the areas affected. Some common clinical findings seen early in the course of the disease include hyperemia of ears, lips, extremities, penile sheath and scrotum. Edema may also occur in some of these same areas. Petechial and ecchymotic hemorrhages are frequently noted on surfaces of mucous membranes such as the oral cavity and genitilia. Ocular hemorrhage may also be seen and some animals develop epistaxis or melena. Altered gate and neurological signs may occur as a result of arthritis, myositis, meningitis or cerebral or spinal edema. Mortality can occur in untreated cases.

   - **Onset:** For reasons still unknown, ticks do not appear to transmit infection until they have been attached to a host for a minimum of 5 to 20 hours. Fever can occur as early as 2 to 3 days after tick attachment, but may not develop until up to 14 days after attachment.

   - **Clinical pathology:** As with many vector-borne diseases, the most consistent laboratory finding is thrombocytopenia. Other laboratory findings with include an initial neutropenia followed by a moderate neutrophilia. There may also be a mild left-shift, and toxic changes are often seen in neutrophils. Hyperchlosterolemia and hypoalbuminemia are among the more consistent biochemical abnormalities found in infected dogs.

**Diagnostic Tests**

**Serology:** Serology is the primary method for the diagnosis of RMSF. Because of cross-reactivity of antibodies to nonpathogenic organisms in the spotted fever group and the possibility of subclinical infections in dogs, caution should be used in interpreting positive antibody titers.
The assay most commonly used by most commercial labs is an Immunofluorescent antibody (IFA) test. Active infection in clinically ill dogs can be serologically confirmed by a fourfold increase in titer when evaluating acute and convalescent IgG titers taken 2 to 3 weeks apart. Normal dogs usually have reciprocal titers of less than 64. Acutely affected animals may not have increased levels of IgG at the time of initial presentation, so a reciprocal titer of <64 does not necessarily rule out infection. Conversely, a single reciprocal IgG titer of 1,024 would indicate active infection. Alternatively, a single, increased IgM titer would also indicate active infection.

PCR: PCR analysis is species specific and can distinguish infection with *R. rickettsii* from other rickettsial agents in the spotted fever group. However, due to the low number of circulating organisms, conventional PCR analysis has resulted in a significant number of false negative results. A nested PCR is a more sensitive method of genetic analysis and can be performed using whole blood or biopsies taken from affected tissues.

**Treatment**

Tetracyclines (tetracycline, oxytetracycline or doxycycline) are the drugs of choice for Rocky Mountain Spotted fever. Therapy must be continued for a minimum for 7 days. Choramphenical or enrofloxacin have also been used in cases where tetracyclines are not an option.

**Other Rickettsia spp. in the Spotted Fever Group**

There is evidence that other *Rickettsia* spp., such as *R. amblyommii*, *R. montanensis*, and *R. parkeri*, can infect and may cause clinical illness in people and dogs. *Rickettsia amblyommii* is a bacterium in the spotted fever group of organisms associated with the lone star tick (LST), *Amblyomma americanum*. The LST is most commonly reported tick to parasitize humans in the southeastern US. Within this geographic region, there have been suspected cases of Rocky Mountain Spotted Fever (RMSF) where the causative agent, *R. rickettsii*, was not identified in the tick population. In these same areas, patients with clinical signs of RMSF had low levels or no detectable antibodies to *R. rickettsii*, resulting in an inability to confirm a diagnosis. There has been speculation that infection with *R. amblyommii* may be responsible for these findings.

In a study we conducted in dogs from North Central Florida, samples from canines with clinical findings presentation consistent with RMSF and end-point reciprocal antibody titer to *R. rickettsia* of 32 or greater at the time of presentation were analyzed by IFA using the culture isolate of *R. amblyommii* generated in both AAE-2 and ISE-6 cells. Of the 15 dog serum samples tested, 13 (86.7%) had antibody titers of greater than 1:64 with the antigen of *R. amblyommii*. Of these, 13 samples, 12 had a higher endpoint reciprocal titer to *R. amblyommii*, than to *R. rickettsia*; overall 12 of 15 (80%) canine samples had greater end-point titers to *R. amblyommii* than to *R. rickettsia*
**Babesia canis**

**Etiology and Epidemiology**
Babesia species are intracellular protozoan parasites of RBCs that cause increased RBC destruction and anemia. Babesiosis occurs in dogs in many countries, including the United States. Babesia canis is a large (4-7 μm in length) pear-shaped parasite. Strains present in the U.S. generally cause mild or unapparent disease in adults (unless immunosuppressed), but severe disease in pups. South African strains can cause severe disease and death in adult dogs.

**Transmission**
B. canis is transmitted primarily by bites from infected ticks. Tick vectors in the US include the brown dog tick (*R. sanguineus*) and *Dermacentor* spp. Inoculation with contaminated blood may also result in transmission of the disease.

**Clinical Findings**
The severity of the disease varies with age of the animal and strain of Babesia involved. The course of disease may be acute and fulminating, subclinical or chronic. Clinical signs that may occur in dogs include lethargy, anorexia, pale mucous membranes, fever, emesis, amber to brown urine, splenomegaly, icterus, weight loss, rapid respiration and rapid heart rate. Animals with Babesiosis are usually anemic. The anemia results primarily from intravascular hemolysis although extravascular destruction of erythrocytes also occurs. A regenerative response (reticulocytosis) is present in most cases. Mild to severe thrombocytopenia is often present, but hemorrhage is seldom apparent. Clinical chemistry profiles may demonstrate bilirubinemia and abnormalities related to anemic hypoxia, but profiles can be normal. Bilirubinuria is common, but prominent hemoglobinuria is rarely recognized in dogs in the U.S.

**Diagnosis**
A definitive diagnosis of B. canis infection is made by identification of the organisms in stained-blood films. Serological diagnosis can be made using Indirect fluorescent antibody (IFA) tests, but some cross-reactivity occurs between babesial species. High titers suggest current infection, but IFA tests may be negative in acutely infected animals, especially pups. If parasites are not recognized in the blood, it is difficult to differentiate babesiosis from autoimmune hemolytic anemia, because both disorders may be Coombs' test positive.

**Treatment and Prognosis**
Adult dogs with mild anemia and clinical signs do not require therapy, but can be reservoirs of infection for other animals. Imidocarb dipropionate (Imizol) (6.6 mg/kg SQ or IM, single injection, repeat dose in two weeks) along with supportive care (transfusions or IF fluid therapy) may be efficacious in treating this disease. Antibabesial drugs are potentially dangerous, and can cause neuromuscular signs and liver or kidney injury. Relapse following therapy can occur, but is more likely in dogs with B. gibsoni infections. Treated and untreated dogs often remain carriers of disease.
**Babesia gibsoni**

**Etiology and Epidemiology**
*Babesia gibsoni* is considered to be a small *Babesia*, similar to *B. microti*, the etiological agent of human and rodent babesiosis. The organism is endemic in Africa, the Middle East and Asia. The first report in the US was in 1968, however, the infected Bull Terrier likely contracted the agent while in Malaysia. In 1979 the organism was isolated from a dog that lived in Connecticut and never traveled outside the US. Since that time, infected dogs have been identified in California, the Midwest (Oklahoma) and Southeastern US. Since 1998 there has been a rapid increase in the number of cases reported, predominantly in Pit Bull Terriers and American Staffordshire Terriers.

**Transmission and Pathogenesis**
Known vectors of *B. gibsoni* infections outside the US include the ixodid ticks, *Haemophysalis bispinosa* and *H. longicornis*. The brown dog tick *Rhipicephalus sanguineus* is the suspected vector in the US, but definitive transmission studies have not been done. However, considering the prevalence of this organism in the pit bull and associated breeds, it appears likely that transplacental transmission and inadvertent inoculation with contaminated blood is plays a major role in maintaining this organism in those breeds. Procedures practiced on premises such as during tail docking, ear cropping, vaccinations between animals with single needles, and bite wounds also contribute to the persistent problem in these animals. The vast majority of the reported cases in the US have either been in bull terriers or in animals that were attacked and bitten by bull terriers. Transplacental transmission has been documented. Organisms have been detected in a dam and in 3 of her offspring at 3 days of age. Clinical infections have been seen in animals with a history of attack by Pit Bull Terriers. American Pit Bull Terriers and American Staffordshire Terriers can be subclinically infected carriers (55% PCR positive) MacIntire et al., JAVMA, 220:325-329, 2002. The incubation period for the development of clinical disease is 7 to 21 days. Dogs that survive the acute phase of the disease become chronic carriers and a reservoir for infection.

**Clinical Findings**
Commonly reported clinical abnormalities in dogs include fever, lethargy, pale mucus membranes, lymphadenopathy, splenomegaly, regenerative anemia with intravascular hemolysis, hemoglobinuria, transient but profound neutropenia and thrombocytopenia with increased mean platelet volume. The thrombocytopenia can be severe (<50,000 cells / μl) and may develop before and last longer than the anemia or detectable parasitemia. In addition, persistent thrombocytopenia and anemia without a detectable parasitemia may result in a misdiagnosis of immune-mediated disease or ehrlichiosis. Mild anemia and thrombocytopenia with increased mean platelet volume may be seen in subclinically infected Pit Bull Terriers and Staffordshire Terriers. These findings in terriers living in endemic areas should alert the clinician to potential subclinical infection and prompt further testing.

**Diagnosis**
The clinical diagnosis is often made by microscopic examination of a peripheral blood film. The small (1 -2.5 μm) round to oval piroplasms are usually identifiable in erythrocytes of clinically
infected animals. The organisms are detectable as early as 1 week post-infection and peak parasitemias are seen by 3 to 4 weeks. Peak parasitemias in most dogs range from 2% to 6% of erythrocytes infected, however, parasite numbers may in some cases be much higher. Many infected animals will be Coombs’ test positive. Therefore, the diagnosis must be distinguished from IMHA. Specific species identification is accomplished by PCR analysis of infected, whole blood. PCR analysis is currently available through the North Carolina State University Tick-Borne Disease Testing Laboratory, or through the Department of Pathobiology at Auburn University. The parasitemia in subclinical carriers is too low to be detected microscopically and PCR analysis must be done to confirm a carrier state. Serology using the IFA test demonstrates the presence of antibodies in serum directed against these organisms, but some cross-reactivity occurs between babesial species. Titers > 1:80 are considered significant, but most infected animals have > 1:320. Both false negatives and false positives can occur using the IFA test. Species identification can only be done using PCR analysis.

**Treatment and Prognosis**

The small Babesia, such as *B. gibsoni*, sometimes do not respond well to the typical anti-babesial drugs such as Imidocarb dipropionate. The current recommended treatment is azithromycin 10mg/kg once a day for 10 days, and atovaquone 13.5 mg/kg TID for 10 days, given with a fatty meal. Using this treatment, approximately 80% of the infected animals will be PCR negative in 6 weeks. In addition, some animals may require supportive care with blood replacement products and/or fluid therapy. Imidocarb may be used if azithromycin and atovaquone are not an option. Clinical remission may occur in some cases, but the organism will not be cleared using this drug. Again, there is some question as to whether or not to treat with corticosteroids, although they may be used in cases where the anemia does not respond to anti-microbial therapy alone and eventually required corticosteroids to give clinical improvement.