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INTRODUCTION

Tick-borne pathogens are of tremendous historical importance to both veterinary and human medicine. Recent events emphasize an expanding role for newly discovered, as well as previously recognized tick-transmitted organisms, as a cause of animal and human suffering. One of the most important new developments related to ehrlichiosis is the realization that a given mammalian species can be infected simultaneously or sequentially by several Ehrlichia species. As an example, both dogs and people can be infected with Ehrlichia chaffeensis, Ehrlichia canis, Ehrlichia ewingii, Anaplasma platys and Anaplasma phagocytophilum. During the past decade observations related to ehrlichiosis in animals have contributed substantially to the rapid expansion of new knowledge related to human anaplasmosis and ehrlichiosis. Increasingly, veterinarians in practice are being called upon to provide comparative medical information about ehrlichiosis in animals and to discuss the zoonotic risks that are attributable to members of the genus Ehrlichia. Without question, the increased spectrum of human and companion animal recreational activities continue to bring each of us, as well as our pets, into contact with competent tick vectors. Therefore, so as to decrease disease transmission, drug manufacturers should continue to search for effective acaricides and products with strong repellent characteristics, so as to prevent tick attachment and the need to treat ehrlichiosis in pets.

COMPARATIVE MEDICAL IMPORTANCE OF ANAPLASMA AND EHRLICHIA SPECIES INFECTIONS.

Of comparative medical interest, cats, dogs, humans, as well as other domestic and wild animal species, can all be infected with the same Anaplasma or Ehrlichia sp. For example, E. chaffeensis has been shown to infect dogs, goats, deer, and human beings. Similarly, A. phagocytophilum can induce similar disease manifestations in cats, dogs, horses and human beings and has also be detected in blood samples from a wide range of wild animals. With the recent application of new molecular diagnostic techniques, the study of vector-borne disease problems has been enhanced. This technology continues to result in substantial clarification of the role of established agents in the pathogenesis of previously undocumented disease sequelae. In many respects, the immunopathogenic consequences of tick-borne infections, such as anaplasmosis and ehrlichiosis, are nearly
identical among infected animal species and human patients. Often, the experimental characterization of the immunopathological response of a specific Ehrlichia sp. in animals has provided important insights as to the potential pathogenic consequences induced when the same organism infects human patients. Conversely, observations in human patients have contributed to the recognition of an increased spectrum of disease manifestations in animals, such as acute renal failure or acute respiratory distress syndrome (ARDS) in dogs infected with Ehrlichia sp.

Canine ehrlichiosis is an infectious rickettsial disease of dogs, caused by E. canis, E. chaffeensis, and E. ewingii and potentially E. ruminantium. Although the clinicopathologic course of disease will vary depending upon the infecting Ehrlichia species, illness is typically characterized by an acute reduction in cellular blood elements, most often thrombocytopenia. Canine ehrlichiosis, caused by E. canis, has been reported from tropical and subtropical regions throughout the world. The distribution of E. canis infection is related to the geographic distribution of the vector tick, Rhipicephalus sanguineous, the brown dog tick, which spends all 3 life stages on dogs. Canine ehrlichiosis, caused by E. chaffeensis and E. ewingii, have been diagnosed in the United States and Africa. Amblyomma americanum, the Lone Star tick, is the most important vector for E. chaffeensis and E. ewingii in North America. Co-infection with multiple Ehrlichia species or Ehrlichia and Anaplasma spp. is not uncommon.

Based upon experimental infection studies, canine ehrlichiosis has been divided into 3 phases: an acute, subclinical and chronic disease phase. Although these 3 phases of disease can be utilized to infer some clinical utility, the onset and duration of infection is rarely known in the clinical setting. Clinical signs during the acute phase of disease are highly variable and can include: depression, anorexia, fever, severe loss of stamina, weight loss, ocular and nasal discharges, dyspnea, lymphadenopathy, and edema of the limbs or scrotum. Thrombocytopenia and leukopenia generally occur 10 to 20 days following infection. Despite moderate to severe thrombocytopenia, hemorrhages are rarely observed. A variety of central nervous system signs, including hyperesthesia, muscle twitching, and cranial nerve deficits, may occur due to inflammation and bleeding into the meninges. Clinical findings in the acute phase of ehrlichiosis can be identical to canine Rocky Mountain spotted fever or canine distemper.

Serologic diagnosis utilizing the indirect fluorescent antibody technique (IFA) is currently recommended for confirming a diagnosis of ehrlichiosis. The IFA test for E. canis is sensitive and reasonably specific; however, based upon Western immunoblot (WI) analysis, low IFA titers are not diagnostic and may represent exposure to other infectious organisms. Current modalities that detect E. canis antibodies in serum samples obtained from dogs for diagnostic purposes, such as the microimmunofluorescent assay (IFA), do not facilitate differentiation of the infecting Ehrlichia species. There is substantial serologic cross reactivity between E. canis and E. chaffeensis, whereas E. ewingii infected dogs generally do not recognize E. canis antigens or do so at very low titers. Dogs generally become seronegative within 3 to 9 months after effective treatment, although some dogs maintain persistent and stable titers for years. Polymerase chain reaction (PCR) amplification can facilitate a molecular confirmation of the diagnosis of canine ehrlichiosis, determine of the infecting Ehrlichia species or help to confirm the therapeutic elimination of infection. EDTA blood is required for PCR and should optimally be collected for diagnostic confirmation prior to antibiotics or to confirm therapeutic elimination of infection after cessation of antibiotics.
Tetracycline (22 mg/kg given every 8 hours) or doxycycline (5 mg/kg every 12 hours), administered daily for 4 weeks, represent the treatment of choice for canine and feline anaplasmosis and ehrlichiosis. Clinical improvement may be observed in E. canis infected dogs with penicillin, sulfonamides, enrofloxacin or imidocarb dipropionate but the therapeutic response is incomplete and therefore these antibiotics cannot be recommended. Dramatic clinical improvement generally occurs within 24 to 48 hours after initiation of a tetracycline derivative in dogs with acute phase or mild chronic phase disease. Hemorrhage, immunosuppression and concurrent infections with Babesia or Bartonella species may contribute to the death of chronically affected dogs, despite the initiation of tetracycline therapy. The duration of treatment of chronically affected dogs with severe pancytopenia or aplastic anemia is controversial. Despite clinical improvement and presumable clearance of the infection, bone marrow regeneration may require up to 120 days following treatment. Supportive therapy, including fluids, blood transfusion, vitamins, and anabolic steroids are required in some patients. Long-term tetracycline prophylaxis (6.6 mg/kg once daily), repositol oxytetracycline (200 mg IM twice weekly) or doxycycline have been utilized in military working dogs or dogs maintained in tick infested kennels to prevent ehrlichiosis during deployment to tick endemic regions. Following therapeutic elimination of Ehrlichia spp., dogs do not develop protective immunity and can be re-infected when re-introduced to a vector-competent tick. Experimentally, dogs have been re-infected with E. canis by both homologous and heterologous challenge. Although not well characterized, the long term prognosis following treatment for ehrlichiosis does not appear to be predictable. The reasons for variability in post-treatment outcomes in dogs with ehrlichiosis remains to be established through long term follow-up studies.

Zoonotic Implications of Ehrlichiosis

Based upon isolation from patients, E. canis, E. chaffeensis and E. ewingii can all cause human ehrlichiosis. However, the zoonotic role of dogs as a reservoir for human infection has not been clearly established for any Ehrlichia species. In South America, E. canis causes human monocytic ehrlichiosis and dogs are the probable reservoir host.

References