Introduction and Zoonotic Potential of Hemoplasmas

Blood-borne mycoplasmas, known collectively as hemotropic mycoplasmas or hemoplasmas, are small, pleomorphic, epicellular bacteria that adhere to the host’s red blood cells. They cannot be cultured. They can be detected microscopically in blood smears and, more reliably, through use of PCR assays on whole blood. The hemoplasmas vary in severity of disease caused to the host and most infected animals appear healthy. Concurrent infections, stress, and immunosuppression may induce signs of disease that include fever, lethargy, anorexia, and mild to severe anemia. Severe forms of disease are characterized by hemolytic anemia, which can be treated with antibiotics and blood transfusions. Although often effective at eliminating signs of disease, treatment is not likely to completely clear hemoplasmas from the body and the infected animal remains a carrier. Transmission of hemoplasma is by arthropod vectors, blood transfusions, common use needles and surgical instruments, and, possibly, by animals fighting with each other. Vertical transmission from mother to offspring occurs with several of the hemoplasmas. The focus of this presentation will be hemoplasmas of large animals and will include Mycoplasma wenyonii (formerly Eperythrozoon wenyonii) and Mycoplasma hemobos of cattle, Mycoplasma ovis and Mycoplasma hemovis of sheep, and hemoplasmas of horses and deer. Before that discussion begins, it is important to consider the hemoplasmas as potential zoonotic agents. Recent reports listed below are examples of human infection with animal hemoplasmas.

**Hemoplasma Infection in HIV-positive Patient, Brazil.** *Emerging Infectious Diseases*, 14 (12):1922-1924, 2008. Patient with 5 cats at home was diagnosed with disseminated *Bartonella henselae* and was also infected with *Mycoplasma hemofelis*

**Co-infection with Anaplasma platys, Bartonella henselae, and Candidatus Mycoplasma haematoparvum in a veterinarian.** *Parasites & Vectors* 2013, 6:103; [http://www.parasitesandvectors.com/content/6/1/103](http://www.parasitesandvectors.com/content/6/1/103). 27-year-old female veterinarian experienced migraine headaches, seizures, including status epilepticus, and other neurological and neurocognitive abnormalities, she was primarily a dog and cat practitioner that had a history of contact with fleas, ticks, lice, biting flies, mosquitoes, spiders and mites and had also been scratched or bitten by dogs, cats, birds, horses, reptiles, rabbits and rodents.

numbness of the left leg and left hand subsequently developed an acute febrile illness with nausea and malaise. He had a history of frequent bites or scratches from cats, dogs, rodent pocket pets, and an assortment of wild and zoo animals. He had also worked with sheep, goats, llamas, and camels and had frequent contact with deer during his career.

**Prevalence of Mycoplasma suis (Eperythrozoon suis) infection in swine and swine-farm workers in Shanghai, China.** *American Journal of Veterinary Research, 70:*890–894, 2009. The first case of human infection with *M. suis* was reported in 1986. Infected humans can show mild pyrexia, hemolytic anemia, and icterus. Moreover, congenital infection via transplacental transmission has been reported. Blood from 172 swine and blood from 65 workers and veterinarians from 19 commercial swine farms were tested using a PCR assay and 32 (49%) blood samples from humans and 148 (86%) blood samples from swine contained *M. suis* DNA.

**Infection with Hemotropic Mycoplasma Species in Patients with or without Extensive Arthropod or Animal Contact.** *Journal of Clinical Microbiology, 51* (10):3237–3241, 2013. The study groups were people with peripheral or central neurological deficit and/or chronic joint pain or were people with self-reported histories of chronic, poorly defined illnesses. Those found infected with hemoplasmas were predominately veterinarians, veterinary technicians, spouses of veterinary professionals, and others with extensive arthropod exposure and/or frequent animal contact. A *Mycoplasma ovis*-like species was the most prevalent organism detected.

**Hemoplasmas of Cattle**

The hemoplasmas of cattle are thought to induce latent infections that seldom manifest as overt clinical disease. There are two recognized hemoplasmas of cattle, *Mycoplasma wenyonii* and *Mycoplasma hemobos*. The former has been known for decades, has worldwide distribution, and is common; while the latter, *M. hemobos*, is newly recognized and information on its distribution is limited. *M. hemobos* has been locally reported in Asia, Europe, and South America. In areas where both organisms are found, dual infections occur and there is some thought that this may increase the risk for clinical disease developing. When clinical signs associated with hemoplasmas occur in cattle they are often mild and include mild depression, mild anemia, and transient low grade fever. Other clinical signs may include anorexia, lymphadenopathy with enlarged and palpable prefemoral lymph nodes, edematous hind legs, scrotal edema, udder and teat edema, weight loss, drop in milk production, and reproductive inefficiency. Signs of reproductive inefficiency associated the hemoplasmas in cattle are abortion and delayed estrus in cows, and lowered fertility in bulls. Reports indicate that young calves are most susceptible to severe anemia. With the exception of cases of severe disease, most cattle recover without treatment in 7 to 10 days.

Clinical disease caused by the bovine hemoplasmas may be seen in cattle of all ages. However, disease has been reported most often in adult animals. In dairy cattle, disease is often seen in periparturient animals and likely is stress associated. Recent reports suggest transplacental transmission of the bovine hemoplasmas can occur. A small study of pregnant cattle infected with *M. wenyonii* or *M. hemobos* found 10% of calves born to the infected dams were infected
with either \textit{M. wenyonii} or \textit{M. hemobos}. As with other hemoplasmas, biting insects are important in the spread of the bovine hemoplasmas. In one study done on a farm with known presence of \textit{M. wenyonii}, PCR assays were used to detect the hemoplasma in over 50\% of the lice (18 of 26), flies (20 of 30), and mosquitos (21 of 26) that were collected. In the United Kingdom, outbreaks of \textit{M. wenyonii} show a seasonal trend and peak in late summer and early fall, reflecting the seasonal presence of biting insects.

A recent study done in Japan focused on the effects of chronic infection of cattle with hemoplasmas. The stimulus for the study was the known negative effects of chronic hemoplasmosis (\textit{Mycoplasma suis}) on reproduction in swine. Those effects are delayed estrus, early embryonic death, and late term abortions. The Japanese study involved 93 dairy cattle and their 80 live calves (13 stillborn calves were excluded). Testing blood from the cows using PCR assays showed 83 cows were infected, 33 cows had \textit{M. wenyonii}, 18 cows had \textit{M. hemobos}, and 32 cows were infected with both hemoplasmas. Blood was tested from 71 of the calves and only 10 calves were found infected. Of those 10 calves, 5 calves had \textit{M. wenyonii}, 2 calves had \textit{M. hemobos}, and 3 calves had dual infections. None of the infected calves were born to non-infected dams. Milk yield was measured for all cows for the first four months after parturition. For the first month after parturition, all groups (grouped by hemoplasma infection) of infected cows had statistically significant lower milk yield than the non-infected cows. For the second month, the group of cows infected with \textit{M. hemobos} and the group of dually infected cows had statistically significant lower milk yield than non-infected cows. Statistically significant differences in milk yield were not seen in months 3 and 4. The only other significant finding was lower birth weight of calves from infected cows. A long term study of the infected calf was not done.

Hemoplasmas of Sheep

The hemoplasmas of sheep, \textit{Mycoplasma ovis} and \textit{Mycoplasma haemovis}, are still being sorted out, as at this time is not clear if there are multiple hemoplasmas or multiple variants of the known hemoplasmas. \textit{Mycoplasma ovis} (formally \textit{Eperythrozoon ovis}) is widespread and common, while \textit{M. haemovis} is newly described and its distribution is not yet known. \textit{M. ovis} may induce poor weight gain, severe anemia, hypoglycemia, and mortality in infected lambs and infected young adults. The severe signs of disease are most common during an acute infection and often associated with recent stress such as weaning and yarding. Double digit mortality rates have been reported. More frequently, infection of sheep with the hemoplasmas results in subclinical to mild disease that my manifest as mild anemia and marginal hematologic changes associated with red blood cells. As with the hemoplasmas of other species, chronic infection occurs. Indicators of chronic infection include reduced weight gain, ill thrift, and reduced wool production. Seasonality of clinical disease has been noted and, like the hemoplasmas of cattle, there is a correlation with seasonal presence of arthropods in some outbreaks.

Hemoplasmas of Horses

The first report of hemoplasma infection in horses appeared in 1978 and described an outbreak of ‘‘haemobartonellosis’’ in horses in Nigeria. The clinical signs exhibited by the horses included fever, apathy, lymphadenitis, circulatory disorders, and pale mucosa. At that time, the diagnosis was made by detection of the organism in blood smears and a definitive classification
of hemoplasmas was not possible. In 2010, a hemoplasma infection of horses was verified and preliminary characterization of the agent was done using nucleic acid sequencing. The report involved two horses that were presented to a veterinary clinic showing rough hair coat, unthriftiness, loss of weight and condition. Hematologic evaluations showed that both horses had a mild anemia. A hemoplasma was suspected and a PCR assay used to detect hemoplasmas of dogs and cats was used to amplify DNA from the organism. Nucleic acid sequencing of 900 bases or the 16S rDNA gene indicated that the equine hemoplasma was most closely related to *M. hemobos* of cattle. The newly derived nucleic acid sequence was used to design PCR primers specifically targeting the equine hemoplasma and a survey of 117 horses at a single breeding farm was done to estimate the prevalence of the hemoplasma. The hemoplasma was detected in 31 horses and 7 of those horses were reported with poor condition and poor performance. Nine of the 31 horses had anemia (Ht < 0.32), 10 horses had a low level hematocrit (Ht = 0.32–0.34) and 12 horses were non-anemic (Ht > 0.34). Younger horses (< 1yr) were affected more by the infection than older horses.

**Hemoplasmas of deer**

Reports of hemoplasmas in white-tailed deer and reindeer in the U.S., and in other species of deer in Brazil and Japan, indicate there may be multiple hemoplasmas infecting cervids. In addition, prevalence studies involving relatively small numbers of captive and free-living deer suggest that a high percentage of deer may be infected. Anemia has been detected in several reindeer and a white-tailed fawn infected with hemoplasmas. Most of the affected reindeer, and the white-tailed fawn, were infected with hemoplasmas that were closely related to *M. ovis* or *M. wenyonii*, but one reindeer was infected with a hemoplasma that clustered with *M. hemofelis* and *M. hemocanis*. In Brazil, 32 deer representing 3 species were studied and hemoplasmas were found in 27 of the deer. Most of the hemoplasmas were closely related to *M. ovis*, but one hemoplasma was distinctly different. In a recent study that involved 73 deer from a hunting preserve in the U.S., 65 of the deer were infected with hemoplasmas. PCR amplifications of the 16S rDNA gene and the RnaseP gene of hemoplasmas from 12 deer, followed by nucleic acid sequencing of the amplicons, showed that *M. ovis* like hemoplasma was present in some deer. Interestingly, 2 other hemoplasmas were identified that were divergent from *M. ovis* and more similar to hemoplasmas from deer in Brazil.