Ehrlichiosis and Anaplasmosis in Mammals

Bovine Anaplasmosis,
Ovine Anaplasmosis
Canine Monocytic Ehrlichiosis,
Canine Hemorrhagic Fever,
Tropical Canine Pancytopenia,
Tracker Dog Disease,
Canine Tick Typhus,
Nairobi Bleeding Disorder,
Canine Granulocytic Ehrlichiosis,
Canine Granulocytic Anaplasmosis,
Equine Granulocytic Ehrlichiosis,
Equine Granulocytic Anaplasmosis,
Tick-borne Fever,
Pasture Fever,
Cyclic Canine Thrombocytopenia,
Human Monocytic Ehrlichiosis,
Human Granulocytic Anaplasmosis,
Human Granulocytic Ehrlichiosis,
Human Ewingii Ehrlichiosis

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Importance

Ehrlichiosis and anaplasmosis are tick-borne diseases caused by obligate intracellular bacteria in the genera *Ehrlichia* and *Anaplasma*. These organisms are widespread in nature, with reservoir hosts that include numerous wildlife as well as some domestic animals. While many infections in pets, livestock and wildlife are subclinical or mild, some organisms can cause more severe illnesses, and certain diseases, such as tick-borne fever of livestock (*Anaplasma phagocytophilum)* or bovine anaplasmosis caused by *Anaplasma marginale*, can be a significant economic burden. Historically, ehrlichiosis and anaplasmosis were seen as strictly animal diseases, but since the 1980s, some organisms have also been recognized to affect people. While human illnesses initially appeared to be rare, increasing numbers of cases have been attributed to these agents since that time, particularly in the U.S. where mandatory reporting has been in place since 2000, and serological studies have uncovered evidence for many subclinical or mild infections.

Etiology

Ehrlichiosis and anaplasmosis are caused by members of the genera *Ehrlichia* and *Anaplasma*, which are pleomorphic, Gram negative, obligate intracellular bacteria in the family Anaplasmataceae, order Rickettsiales. Some species known to affect mammals include *A. phagocytophilum* (tick-borne fever in ruminants; equine, canine and human granulocytic anaplasmosis), *A. marginale* (bovine anaplasmosis), *A. centrale, A. bovis* (bovine ehrlichiosis, bovine anaplasmosis), *A. ovis* (ovine anaplasmosis), *A. capra*, *A. platys* (cyclic canine thrombocytopenia), *A. odocoilei*, *E. canis* (canine monocytic ehrlichiosis), *E. chaffeensis* (human monocytic ehrlichiosis), *E. ewingii* (canine granulocytic ehrlichiosis, human ewingii ehrlichiosis), *E. muris* and its subspecies *E. muris eauclairensis*, *E. ruminantium* (heartwater), *E. minasensis* (previously *E. mineirensis*) and "the Panola Mountain ehrlichia." Additional poorly characterized organisms, which often have descriptors such as "organisms related to *E. canis*," might either be variants of a known species or novel agents. For example, one organism in ruminants originally described as *E. canis*-like became the new species *E. minasensis*, while an *E. muris*-like agent in North America is now *E. muris* subsp. *eauclairensis*. There are also some *Ehrlichia* and *Anaplasma* that have only been reported in ticks, birds or reptiles but might infect mammals.

Each species of *Anaplasma* or *Ehrlichia* tends to infect certain blood cells or cell fragments (platelets), which can help distinguish these organisms in blood smears and is also reflected in the names of some diseases. *E. canis, E. chaffeensis, E. muris* and *A. bovis* are mainly found in monocytes, though they sometimes occur in other leukocytes; *E. ewingii* and *A. phagocytophilum* are primarily detected in granulocytes*;* *A. marginale, A. centrale, A. ovis* and *A. capra* infect red blood cells; and *A. platys* and *A. odocoilei* circulate in platelets.

This factsheet provides an overview of the illnesses caused by most of the organisms in the genera *Anaplasma* and *Ehrlichia* affecting mammals, except *E. ruminantium* (formerly *Cowdria ruminantium*), which causes heartwater in ruminants and is described in a separate factsheet.

Taxonomy note: Major revisions among the Anaplasmataceae in 2001 resulted in a number of name changes. *Ehrlichia bovis* and *E. platys* became *Anaplasma bovis* and *A. platys*, while the former *Ehrlichia risticii*, which causes Potomac horse fever/ equine monocytic ehrlichiosis, and *Ehrlichia sennetsu*, the agent of sennetsu fever in humans, were transferred to the genus *Neorickettsia*, whose members have life cycles involving trematodes rather than ticks. The most controversial change was consolidating three organisms previously considered separate species - *Ehrlichia equi*, the agent of equine granulocytic ehrlichiosis, *Ehrlichia phagocytophila*, responsible for tick-borne fever in ruminants, and "the agent of human granulocytic ehrlichiosis" - into the single species *A. phagocytophilum*. As a result, *A. phagocytophilum* is a particularly heterogeneous organism, with North American variants, for instance, causing illnesses in humans, dogs and horses but not cattle or small ruminants, while all of these hosts are affected by the variants in Europe.

Species Affected

Note: Most infections reported in animals are based on PCR, which sometimes detects related ehrlichia or anaplasma; relatively few hosts have been confirmed by isolation of the organism or experimental inoculation.

Ehrlichia canis, E. minasensis and related organisms

E. canis affects dogs and other canids, which are also the reservoir hosts. Evidence for this or a closely related organism has been reported in cats and other felids, dromedary camels, a goat, a sika deer (*Cervus nippon*), some South American primates (e.g., *Sapajus apella*, *Callithrix* sp.), coatis (*Nasua* spp.), Eurasian otters (*Lutra lutra*) and raccoons (*Procyon lotor*); however, one attempt to inoculate raccoons with *E. canis* was unsuccessful.

E minasensis was originally found in cattle but also seems to infect goats, deer and horses.

Ehrlichia chaffeensis

Clinical signs caused by *E. chaffeensis* have been reported in dogs, captive lemurs and experimentally infected calves, though there are currently no reports of cases in naturally infected cattle. This organism also seems to infect some cervids, cats, various wild canids and felids, black-tailed marmosets (*Mico melanurus*), raccoons, badgers (*Meles meles*), American mink (*Neovison vison*) and some rodents. It has been documented in goats, though they do not seem to be readily infected in the laboratory. There are also reports of *E. chaffeensis* DNA in some birds.

Which species maintain *E. chaffeensis* is not entirely clear, though white-tailed deer (*Odocoileus virginianus*) are thought to be a major reservoir host in North America.

Ehrlichia ewingii

E. ewingii is known to affect dogs and experimentally infected goats. Deer and canids have been proposed as reservoir hosts. This organism has also been detected subclinically in other species, such as cats, captive tigers and a goat, and antibodies were found in coyotes.

Ehrlichia muris and the Panola Mountain *Ehrlichia*

Rodents seem to be the reservoir hosts for *E. muris* subsp. *muris* and *E. muris* subsp. *eauclairensis*. *E. muris* and the Panola Mountain ehrlichia have been found in deer, and goats are susceptible to experimental inoculation with the latter organism. Two dogs that were PCR positive for either *E. muris* or the Panola Mountain ehrlichia had clinical signs consistent with ehrlichiosis, though a causative role for these organisms as canine pathogens remains to be proven.

Anaplasma phagocytophilum

A. phagocytophilum seems to have an exceptionally wide host range that includes dogs, cats, equids, domestic ruminants, camels, South American camelids, reindeer (*Rangifer tarandus*), and many additional species, such as various cervids and other wild ungulates, bears, wild canids and felids, raccoon dogs (*Nyctereutes procyonoides*), pine marten (*Martes martes*), wild boar (*Sus scrofa*), raccoons, opossums, striped skunks (*Mephitis mephitis*), hares (*Lepus* spp.), rodents and nonhuman primates. It has been detected in birds and lizards, though the isolates found in lizards seem to differ significantly from those in mammals. The proposed maintenance hosts are diverse and might vary between regions and *A. phagocytophilum* variants. In North America, they are thought to include rodents and cervids.

Clinical cases have been reported in a number of mammals including domestic ruminants, dogs, wolves (*Canis lupus*), cats, equids, llamas, alpacas and non-human primates. The syndrome known as tick-borne fever mainly affects domestic ruminants, particularly sheep and cattle, but it has also been reported in some cervids. North American variants of *A. phagocytophilum* can affect dogs, cats, horses and llamas, but unlike European variants, they do not seem to cause illness in cattle or small ruminants.

Anaplasma bovis

Cattle and water buffalo are the primary hosts for *A. bovis*, but there are also reports of this organism or a closely related species in other mammals including goats, sheep, horses, various cervids, dogs, cats, wild felids and canids, raccoon dogs, coatis, Mongolian gazelles (*Procapra gutturosa*), giraffes (*Giraffa camelopardalis*), raccoons, wild boars, bears, some rabbits and hares, cynomolgus macaques (*Macaca fascicularis*) and rodents/ small mammals. Clinical cases are usually seen in cattle, but an illness in one horse might have been caused by this organism.

Anaplasma marginale and *A. centrale*

A. marginale infects bovids including cattle, water buffalo, yaks, bison (*Bison* spp.) and African buffalo (*Syncerus caffer*), but it or a closely related organism has also been found in sheep, camels, equids, some cervids, sable antelope (*Hippotragus niger*), and tufted capuchins (*Sapajus apella*). Additional species, such as blesbok (*Damaliscus pygargus phillipsi*), common duiker (*Sylvicapra grimmia*), and black wildebeest (*Connochaetes gnou*) can be infected experimentally. Bovids, particularly cattle, appear to be the reservoir hosts, and illnesses are mainly seen in cattle.

A. centrale has been reported in bovids (cattle, water buffalo, African buffalo) and some other ungulates, such as wildebeest (*Connochaetes* spp.), eland (*Taurotragus oryx*), waterbuck (*Kobus ellipsiprymnus*) and sika deer (*Cervus nippon*). Experimental infections have been established in blesbok, common duiker and black wildebeest.

Anaplasma ovis

A. ovis occurs in sheep, goats, some of their wild relatives (e.g., bighorn sheep, *Ovis canadensis*) and various cervids. Small ruminants and some cervids are thought to be reservoir hosts. This organism also seems to infect cattle and camels occasionally, and it has been reported in sable antelope, red foxes (*Vulpes vulpes*) and donkeys.

Anaplasma capra

A. capra has been detected in sheep, goats, cattle, water buffalo, dogs, wild onagers (*Equus hemionus onager*), Japanese serows (*Capricornis crispus*), takins (*Budorcas taxicolor*) and a number of cervids. At present, it is not known to cause any illness in animals.

Anaplasma platys

A platys affects dogs, but it or a related organism has also been found in red foxes, cats, cattle, water buffalo, small ruminants, Bactrian and dromedary camels, sable antelope and some cervids. At least some of the organisms identified in camels might belong to a proposed new species, Candidatus *A. camelii*.

Anaplasma odocoilei

A. odocoilei has been identified in various cervids, and it or a related organism was found in goats.

Zoonotic potential

Organisms that have been recognized as human pathogens include *E. chaffeensis* (human monocytic ehrlichiosis), *E. ewingii* (human ewingii ehrlichiosis) and *A. phagocytophilum* (human granulocytic anaplasmosis). However, some *A. phagocytophilum* variants might not affect people, or do so only rarely. *E. canis*, *E. muris*, *E. muris eauclairensis, A. capra, A. bovis, A. ovis, A. platys* and the Panola Mountain ehrlichia have been implicated in a few cases, with varying levels of evidence.

Geographic Distribution

E. canis, A. phagocytophilum, A. marginale, A. centrale, *A. ovis*, *A. bovis* and *A. plays* have been found on most or all continents, though their distribution varies with the occurrence and density of their tick vectors. *A. marginale*, *A. centrale* and *A. plays* are particularly common in tropical and subtropical regions, with a more limited presence in temperate climates. Some *A. phagocytophilum* variants seem to occur in limited locations, which influences the hosts affected in an area. *E. chaffeensis* and *E. minasensis*, which were originally detected in only a few areas, now also appear likely to be cosmopolitan.

Other organisms might either be geographically limited or incompletely surveyed. *A capra* was originally identified in China, but it has since been found in a number of other countries in Asia, Europe and North Africa. *E. ewingii* has been documented in parts of North and South America and was also reported from Cameroon, Africa. *E. muris* is known to occur in parts of Eurasia, while *E. muris eauclairensis* was described in North America. *A. odocoilei* has been found in North and South America and the Philippines, and the Panola Mountain ehrlichia has been reported in North America, the Caribbean and Africa.

Transmission

Various hard ticks (family Ixodidae) are the biological vectors for members of the genera *Ehrlichia* and *Anaplasma*. Some organisms seem to be transmitted mainly by a few specific vectors, while others occur in a wide variety of ticks. How long a tick must remain attached to infect an animal is generally not known, but at least 24-48 hours usually seems to be required for *A. phagocytophilum*, with a few mice seroconverting after 12 hours. Some organisms, including *A. marginale* in cattle and *A. ovis* in sheep, establish chronic, low level infections in their hosts. *E. canis* and *E. ewingii* infections can also persist for years in some dogs, while *E. chaffeensis* seems to be eliminated more rapidly, disappearing in a few weeks or months in one study.

Ehrlichia and *Anaplasma* can be acquired occasionally by other routes, especially in procedures that transfer blood. Mechanical transmission on blood-contaminated fomites (e.g., needles, dehorning equipment) or by biting insects seems to be important for some species that infect RBCs, such as *A. marginale*. However, this is not necessarily the case for all species of *Ehrlichia* and *Anaplasma*, and one study found that insects rarely seemed to transmit *A. phagocytophilum* mechanically. A few cases of ehrlichiosis or anaplasmosis in people were apparently acquired in blood transfusions and bone marrow or solid organ transplants. The risk probably depends on the specific organism and blood components, but transfusions of both leukoreduced and non-leukoreduced RBCs have transmitted ehrlichiosis.

Transplacental transmission is also possible, at least for some organisms. *A. marginale* can cross the placenta in cattle, resulting in healthy but persistently infected calves. There is also evidence for *in utero* infections with *A. phagocytophilum* in cattle, sheep, horses and dogs, and perinatal transmission of this organism, either *in utero* or during delivery, was documented in two women. Another study suggested the possibility of transplacental transmission of *A. platys* in dogs. One report found DNA from *A. ovis*, *A. bovis* and *A. phagocytophilum* in the milk of ruminants, though the significance of this finding remains to be determined.

Other routes of transmission are controversial. Direct contact with deer blood might have caused *A. phagocytophilum* infections in three people, but this is still uncertain as other exposures (e.g., tick bites) could not be ruled out. Possible person-to-person transmission of this organism was suggested in a Chinese hospital, after an outbreak in relatives and healthcare workers who had been in close, direct contact with a severely hemorrhaging, intubated patient. However, it now appears possible that another virus might have been responsible for their symptoms.

Disinfection

Disinfection is unimportant for controlling *Ehrlichia* and *Anaplasma*, which are obligate intracellular organisms. Disinfectants employed against other Gram negative bacteria would probably be effective against these agents.

Infections in Animals

Incubation Period

Incubation periods ranging from 7 to 100 days have been reported for bovine anaplasmosis caused by *A. marginale*, with most cases becoming apparent in about 2-5 weeks. *A. phagocytophilum* generally affects ruminants and dogs in appoximately1-2 weeks, and horses in 1-3 weeks. Dogs infected with *E. canis* usually develop the acute form of canine monocytic ehrlichiosis within 2-4 weeks of the tick bite, while the chronic form can occur months or years later.

Clinical Signs

Ehrlichiosis and anaplasmosis generally present as a febrile illness with nonspecific clinical signs, often accompanied by elevated liver enzymes and reductions in leukocyte, RBC and/or platelet numbers. Some agents that infect RBCs also tend to cause overt signs of anemia. Concurrent infections may influence the clinical presentation or increase the severity of the illness.

Organisms that affect white blood cells: E. canis and other species in dogs and cats

E. canis infections in dogs (canine monocytic ehrlichiosis; CME) range from subclinical to severe. Many dogs have no clinical signs when they become infected, but others develop a nonspecific illness with signs such as fever, lethargy, anorexia, lymphadenopathy and splenomegaly, often accompanied by thrombocytopenia and mildly elevated hepatic enzymes. Gastrointestinal signs (e.g., vomiting, diarrhea), edema in the legs or scrotum, respiratory signs (nasal discharge, coughing, dyspnea), and uveitis or other ocular signs may also be seen in some animals. Bleeding disorders (e.g., petechiae, ecchymoses or mild epistaxis) and neurological signs are possible, though less common than in chronic CME. Polyarthropathy with lameness, stiffness or joint swelling has also been described, but some authors suggest this is caused by coinfections and not *E. canis*.

Dogs with acute CME often recover, though severe cases can be fatal. Recovered dogs, as well as those that never developed clinical signs, sometimes remain subclinically infected for months or years. These animals, which may have mild thrombocytopenia, can eventually clear the organism or develop chronic CME. Chronic CME resembles the acute illness, but is more severe, and often includes additional signs such as chronic weight loss and edema, as well as pancytopenia with various combinations of leukopenia, thrombocytopenia and anemia. Some dogs develop bleeding disorders and/or various neurological signs, or other complications such as renal failure, interstitial pneumonia, liver disease, polymyositis or reproductive disorders with prolonged bleeding during estrus, inability to conceive, abortion and/or neonatal death. In addition to being debilitating, chronic CME can eventually be fatal.

Clinical cases caused by *E. ewingii* (canine granulocytic ehrlichiosis), *A. phagocytophilum* (canine granulocytic anaplasmosis) and *E. chaffeensis* can resemble CME; however, dogs infected with *A. phagocytophilum* generally seem to have milder illnesses, with fewer animals developing hemorrhagic or neurological signs and only rare fatalities. Healthy dogs experimentally infected with *E. canis*, *E. chaffeensis* or *A. phagocytophilum* usually remained asymptomatic or had only an intermitent fever, with *A. phagocytophilum* causing the mildest signs in one comparative study.

One clinical case attributed to *E. muris* was characterized by fever, thrombocytopenia, joint stiffness and carpal pain, while a dog infected with the Panola Mountain ehrlichia had hepatomegaly, mild thrombocytopenia and lymphocytosis with atypical lymphocytes. Pre-existing hepatitis could have been responsible for some of the clinical signs in the latter case, though the thrombocytopenia and lymphocytosis resolved with doxycycline.

Ehrlichia and *Anaplasma* have been implicated only rarely in clinical cases in cats. Nonspecific signs of fever, lethargy and inappetence are reported most often, but other clinical signs seen in dogs, including joint pain and rare hemorrhagic or neurological signs, have been documented.

Organisms that affect white blood cells: A. phagocytophilum in equids

Equine granulocytic anaplasmosis, which is caused by *A. phagocytophilum*, is an acute illness that is generally more severe in horses > 3 years old. While signs in animals under a year of age may be limited to fever, older horses are more likely to appear ill, with a decreased appetite, lethargy and icterus, sometimes followed by petechiae, distal limb edema and myalgia, with stiffness of gait, reluctance to move or lameness. A few reports have described animals with apparent neurological signs (e.g., ataxia, reduced alertness), upper respiratory disease with dysphagia due to laryngeal hemiplegia or pharyngeal edema, bicavitary effusion or transient ventricular arrhythmia. Laboratory abnormalities can include thrombocytopenia, anemia and leukopenia. Deaths seem to be very rare.

Organisms that affect white blood cells: A. phagocytophilum in ruminants

Clinical cases caused by *A. phagocytophilum* in sheep (tick-borne fever) mainly occur in young lambs, or in older sheep newly introduced to tick-infested areas. The primary syndrome is a sudden fever that lasts for 4-10 days, which may be accompanied by nonspecific signs of illness, and can be followed by abortions and stillbirths in ewes that become infected during the late stages of gestation. Deaths are uncommon except in some aborting ewes, or in young lambs that develop secondary infections.

In cattle, this disease is most often seen in dairy animals recently turned out to pasture. The clinical signs, which are nonspecific and variable in severity, often include decreased milk production, with some animals also developing respiratory signs and/or edema of the lower limbs. Abortions and stillbirths may be seen in pregnant cows and semen quality is temporarily reduced in bulls.

Organisms that affect white blood cells: A. bovis

A. bovis infections seem to be subclinical in many cattle, but some develop a fever and nonspecific signs of illness, including decreased milk production. Edema, nasal discharge, occasional abortions or rare neurological signs have also been reported. Some infected cattle in Japan had mild to severe anemia, but coinfections with *Anaplasma* and *Theileria* complicate the interpretation of these cases. While deaths are possible, severe cases seem to be uncommon in most regions.

One old horse infected with *A. bovis* had a fever, anorexia, lethargy and severe dehydration.

Organisms that affect white blood cells: Ehrlichia chaffeensis and E. minasensis in ruminants, cervids and other species

Although clinical cases caused by *E. chaffeensis* have not been reported in naturally infected ruminants, experimentally infected dairy calves sometimes developed mild to severe illnesses that ranged from fever alone, accompanied by decreased leukocyte and platelet numbers, to a febrile illness with progressive weakness in the hindlegs, recumbency and death. Most infections in deer seem to be subclinical, but some experimentally infected fawns had a periodic mild fever on days when the organisms were found in the blood. An outbreak in captive ring-tailed lemurs (*Lemur catta*) and red ruffed lemurs (*Varecia variegata rubra*) appeared as a nonspecific febrile illness accompanied by thrombocytopenia and hyperbilirubinemia.

Clinical cases caused by *E. minasensis* in one naturally infected calf and one experimentally infected calf were characterized by fever, lethargy, thrombocytopenia, leukopenia and anemia. Another attempt to inoculate calves with this organism resulted in no clinical signs. The Panola Mountain ehrlichia caused brief or intermittent fevers in two experimentally infected goats, with serous nasal discharge in one animal.

Organisms that affect red blood cells: A. marginale, A. centrale and A. ovis

Clinical anaplasmosis caused by *A. marginale* in cattle is characterized by nonspecific signs of illness and mild to severe anemia, which may result in pale mucous membranes with elevated heart and respiratory rates, and icterus in the later stages. Neurological signs have been reported (probably from oxygen limitation to the CNS), pregnant cows may abort, and bulls may have a transient decrease in fertility. Severely affected animals may die, especially when stressed. Peracute cases, which are uncommon and occur mainly in high- producing dairy cattle, can be fatal within a few hours of the onset of clinical signs. Cases are typically milder in young animals than those first infected as adults, and infections in cattle less than a year of age are usually subclinical. Chronically infected cattle are asymptomatic but may relapse if immunosuppressed.

A. ovis infections in sheep are similar but often milder or subclinical. Overt signs of illness are most common in animals that are stressed or coinfected with other organisms. *A. centrale* infections in cattle also tend to be mild, and this organism is used as a vaccine for *A. marginale*.

Organisms that affect platelets: A. platys and A. odocoilei

Many or most *A. platys* infections in dogs seem to be subclinical, but there are also reports of nonspecific febrile illnesses, accompanied by thrombocytopenia and anemia, with petechiae and other signs of bleeding disorders. Although many cases may be mild, severe hemorrhages and fatalities are possible. Two case reports described sick cats with thrombocytopenia that were infected with *A. platys*, though a causative role in their clinical signs is unclear. One cat had a urinary tract infection that could account for its lethargy and anorexia, while the other had multiple myeloma and several coinfections.

Fawns experimentally infected with *A. odocoilei* sometimes had multiple transient episodes of thrombocytopenia but no overt clinical signs.

Post Mortem Lesions Click to view images

Gross lesions in ehrlichiosis and anaplasmosis are generally nonspecific, and often include enlargement of the spleen. Dogs with canine monocytic ehrlichiosis may also have edema in the legs, ascites, hydropericardium, lymphadenopathy (particularly of the mesenteric nodes) and/or hemorrhagic lesions in various internal organs, subcutaneous tissues and eyes. Hemorrhages are more common and widespread in chronic than acute CME.

Some illnesses, such as bovine anaplasmosis caused by *A. marginale*, also include signs of anemia (e.g., pallor) and icterus. The liver is often enlarged in bovine anaplasmosis, and may be yellowish-orange and mottled; the hepatic and mediastinal lymph nodes may be brown; and petechiae are often found on the serosa of internal organs, especially the heart and pericardium.

The usual lesions in equine granulocytic anaplasmosis are petechiae, ecchymoses and edema in the subcutaneous tissues and fascia, mainly in the legs, though interstitial pneumonitis has been reported in some animals, and other internal organs may have inflammatory lesions and serosal hemorrhages in severe cases.

Diagnostic Tests

Organisms and/or their nucleic acids can sometimes be found in the blood, bone marrow and/or samples from affected sites (e.g., joint fluid) in live animals or in various tissues, such as the spleen, liver, heart, lung, kidney and blood vessels, at necropsy. PCR tests are available for some common species of *Anaplasma* and *Ehrlichia*, and are increasingly employed in diagnosis. They do not always detect very small numbers of organisms, for instance *E. canis* in the peripheral blood of subclinically or chronically infected dogs, or *A. marginale* in chronically infected cattle.

Loop-mediated isothermal amplification (LAMP) assays have also been published for some organisms.

Observing intracytoplasmic inclusions in Wright, Giemsa or Romanowsky (e.g., Diff-Quik™) stained blood, bone marrow or fresh tissue impression smears can help support the diagnosis, though it cannot definitively identify these organisms. Inclusion bodies, which are called morulae in WBCs, are generally stippled blue-gray to dark blue or purple, and are visible at 400x or 1000x magnification. *E. canis*, *E. chaffeensis*, *E. muris* and *A. bovis* inclusion bodies are mainly found in monocytes; *A. phagocytophilum* and *E. ewingii* primarily in neutrophils; *A. marginale, A. centrale, A. ovis* and *A capra* in RBCs; and *A. platys* and *A. odocoilei* in platelets. Organisms found in WBCs have occasionally been detected in leukocytes other than those they usually infect.

Inclusion bodies are most likely to be observed early in the acute illness, and are rarely found in chronically infected animals. They are also more easily detected in some diseases than others. The morulae of *E. canis* and *E. chaffeensis,* for instance, are uncommon in the blood of dogs (though buffy coat may be more successful). The cyclic nature of *A. platys,* as well as the relatively small percentage of platelets with inclusion bodies, can also make this organism difficult to find.

Clinical cases can also be confirmed serologically by seroconversion or a rising antibody titer. Single titers should be interpreted with caution, as antibodies to these organisms are common in healthy animals. Indirect immunofluorescent antibody (IFA) tests and ELISAs, the most commonly used assays, are available for most clinically important organisms. Cross-reactivity can be an issue, but mainly occurs between members of the same genus. It is occasionally exploited to provide evidence of infection with organisms not readily cultivated *in vitro,* such as *E. ewingii.* Immunoblotting (Western blotting), which can distinguish reactivity to different species, is mainly used in research.

Culture is considered impractical for routine diagnosis, as it can take up to 2-6 weeks and requires specialized techniques that are unavailable at most diagnostic laboratories. Most organisms, including some that were previously considered uncultivable (e.g., *E. ewingii, A. ovis*) can be grown *in vitro* for at least a short time.

Treatment

Anaplasmosis and ehrlichiosis are resistant to most antibiotics but can be treated with a few drugs, such as tetracyclines, combined with supportive care as needed. Some organisms may not be cleared completely, though this might depend on the specific antibiotic used and the dose and length of time the animal is treated. Treatment of chronic canine monocytic ehrlichiosis (*E. canis*) may be difficult, though uncomplicated acute cases usually respond promptly.

Control

Disease reporting

Veterinarians who suspect an animal is infected with *Ehrlichia* or *Anaplasma* should follow their national and/or local guidelines for disease reporting. State authorities should be consulted for regulations in the U.S.

Prevention

Limiting tick bites with acaricides, tick repellents and/or environmental modifications that make habitats less attractive to ticks (e.g., brush removal) is expected to reduce the risk of ehrlichiosis and anaplasmosis; however, the widespread nature of some organisms and their tick vectors may make control difficult. Prompt removal of ticks from the animal is also expected to be helpful.

Animal management can reduce disease impacts in livestock, for instance by first introducing animals to infected pastures at an age when they are less likely to develop severe signs. Tetracyclines have sometimes been employed prophylactically in dogs or domestic ruminants. Although vaccines are not available for most organisms, a live vaccine containing *A. centrale* can be used to induce immunity to *A. marginale.*

PCR testing for certain common organisms may be advisable in animals used as blood donors, but might not detect some chronically infected individuals.

Morbidity and Mortality

Asymptomatic infections with some species of *Ehrlichia* and *Anaplasma* seem to be relatively common in mammals, with serological surveillance suggesting that up to 50-60% or more of the animals in some areas have been exposed to these organisms. In one prospective U.S. study, 70-100% of dogs walked in tick habitats without tick control became subclinically infected with *E. ewingii* or *E chaffeensis,* though none of the 10 dogs acquired *E canis.*

Clinical cases are seasonal in temperate regions, usually appearing during or soon after the active tick season. Some diseases, such as tick-borne fever, tend to appear as outbreaks when animals are first exposed to tick habitats (e.g., dairy cattle turned out to pasture after the winter); others can be seen sporadically throughout the season. Clinical cases can also present occasionally outside tick season. Some occur when ticks such as *Rhipicephalus sanguineus*, an important vector for *E. canis,* become established indoors in houses and kennels. Others are caused by illnesses with long or indeterminate incubation periods, such as chronic canine monocytic ehrlichiosis.

Clinical cases vary in severity, depending on the specific organism and host. Bovine anaplasmosis from *A. marginale* can be a serious illness, with reported mortality rates of approximately 30-50% if cattle are first exposed as adults (> 2 years). It is particularly severe in high-producing dairy cows. However, animals raised in some endemic regions are likely to encounter this organism at a younger age, which can reduce its impact. Deaths are uncommon in equine granulocytic anaplasmosis, and tick-borne fever of ruminants is mainly an economic issue, with low mortality but significant decreases in milk production and the potential for reproductive losses. Abortion storms with losses of up to 90% are sometimes seen in previously unexposed pregnant ewes. *A. bovis* infections are also said to be economically important in Africa, though they tend to be mild or subclinical in many other regions. Immunity to some organisms does not seem to be absolute, and may fall quickly if animals are removed from tick-infested areas.

Canine monocytic ehrlichiosis, caused by *E. canis*, is usually the most serious illness in dogs. While asymptomatic infections with this organism are fairly common, and most animals that become acutely ill recover, the disease is potentially severe and chronic cases can be difficult to cure. Infections with *E. chaffeensis* or *A. phagocytophilum* are thought to be overall milder in dogs, though severe illnesses and deaths are possible.

Infections in Humans

Incubation Period

Incubation periods from 5 to 21 days have been reported for human ehrlichiosis and anaplasmosis, with most cases appearing in about 1-2 weeks.

Clinical Signs

As in animals, the consequences of infection with *Ehrlichia* or *Anaplasma* range from asymptomatic infections to a severe, potentially fatal illness. Clinical cases caused by *E. chaffeensis* (human monocytic ehrlichiosis; HME) generally appear as an acute febrile illness with nonspecific signs such as headache, myalgia and arthralgia, often accompanied by thrombocytopenia, mild to moderate leukopenia, elevated levels of liver enzymes, and in some cases anemia. Some patients may also have respiratory or gastrointestinal signs (vomiting, diarrhea, abdominal pain) or a nonpruritic rash that usually spares the palms and soles and may be maculopapular, petechial or characterized by diffuse erythroderma. Gastrointestinal signs and rashes are more common in children than adults.

The reported complications of HME are diverse and include opportunistic infections, meningitis or meningoencephalitis, cardiovascular failure, myocarditis, liver dysfunction, acute renal failure, interstitial pneumonia, respiratory distress syndrome and hemorrhages, as well as a multisystemic disease that resembles toxic shock syndrome or septic shock. Complications, severe cases and deaths are more likely in elderly, very young, or immunocompromised patients, or in those with other concurrent illnesses, but fatal cases have been seen even in previously healthy young patients.

Illnesses caused by *A. phagocytophilum* (human granulocytic anaplasmosis; HGA) and *E. ewingii* (human ewingii ehrlichiosis; HEE) are similar, but tend to be less severe, and leukopenia, thrombocytopenia and abnormal liver function tests are sometimes absent in HEE. Rashes are generally said to be infrequent (< 10%) in both diseases; however, some recent reports found them in up to 15-17% of patients with HGA in the U.S. In European HGA patients, a rash was mostly seen in people coinfected with *Borrelia*. Complications seem to be less frequent in HGA than HME, and have rarely been reported in HEE. CNS involvement is uncommon.

The few clinical cases attributed to *E. canis*, *E. muris*, *E. muris eauclairensis*, *A. ovis*, *A. bovis* or *A. platys* were mostly characterized by similar nonspecific febrile illnesses, though one person PCR positive for *A. platys* had a complicated medical history that included hospitalization for encephalitis of uncertain etiology, with ongoing seizures and migraines after discharge. Because she was not tested for *A. platys* until later, and also had two tickborne coinfections, a role for *A. platys* in her neurological signs is speculative. The Panola Mountain ehrlichia case was also atypical: the main symptom, which resolved promptly with doxycycline, was persistent neck soreness after a tick bite. Some *A. capra* infections and one of the *A. bovis* infections reported from China included one or more eschars, which is not typical of anaplasmosis or ehrlichiosis (but can be caused by some *Rickettsia*), in addition to signs more characteristic of these illnesses. Five of 28 cases attributed to *A. capra* were severe enough to require hospitalization, with one patient developing CNS signs.

Diagnostic Tests

Ehrlichiosis or anaplasmosis in humans is diagnosed similarly to cases in animals. Morulae can be found in the blood or buffy coat of 25-75% of the patients infected with *A. phagocytophilum*, but <10% of those infected with *E. chaffeensis*, and are most likely to be detected during the first week of illness. In rare cases, they may be found in CSF. PCR is more sensitive than microscopic examination for morulae, though it may not detect DNA after the first 2 weeks. Organisms can also be found sometimes in formalin-fixed tissue samples (e.g., bone marrow biopsies; autopsy samples from spleen, lymph node, liver or lung) with immunohistochemistry. Serology, with seroconversion or a fourfold rise in titer, is diagnostic, though single high titers are sometimes employed for a presumptive diagnosis. As in animals, culture is mainly used in research.

Treatment

Ehrlichiosis and anaplasmosis are usually treated with antibiotics, with supportive care as necessary. Uncomplicated early cases usually respond promptly, but prolonged treatment may be necessary for severe illnesses.

Prevention

The risk of ehrlichiosis or anaplasmosis can be reduced by avoidance of tick habitats or by discouraging tick bites with appropriate clothing (e.g., pyrethrin-impregnated garments, long-sleeved shirts and trousers tucked into socks), repellents (e.g., DEET) and insecticides. Any attached ticks should be removed promptly. Treatment of the environment with acaricides and/or modification of tick habitats can also be used to decrease tick populations, but acaricide use may have detrimental effects on non-target species and promotes acaricide resistance.

Morbidity and Mortality

Significant numbers of healthy people, up to 20% or more, have antibodies to *Ehrlichia* or *Anaplasma* in some regions, suggesting that symptomatic infections or mild illnesses might be relatively common. Some prospective studies have also reported subclinical seroconversion in many or most of those who are naturally exposed. Clinical cases tend to be more severe in immunocompromised or elderly patients, very young children, and individuals with other illnesses, though serious illnesses can be seen occasionally in healthy people of all ages. The estimated case fatality rate in the U.S. is approximately 1% for HME, with higher rates of 3-4% in young children less than 5 years of age and adults over 70, and < 1% for HGA. Because many mild cases could be missed, it is possible that these values overestimate the severity of these illnesses.

In the U.S., where mandatory reporting of human ehrlichiosis and anaplasmosis was implemented in 1999, the recorded incidence of HGA rose from 273 cases (1.4 per million persons) in 2000 to approximately 4000 to 5760 cases per year between 2017 and 2019. The incidence of HME likewise increased from 201 cases (< 1 per million persons) to about 1300 to 2100 cases/ year between 2013 and 2019. It should be noted that more than half of these reports describe probable HGA and HME cases, based on a single antibody titer, rather than confirmed cases. The number of clinical cases documented in countries without mandatory reporting is generally much lower, though seroprevalence in some regions is higher than in North America.

Fewer clinical cases have been reported for other organisms, though this might also be influenced by the availability of diagnostic tests. Human ewingii ehrlichiosis (*E. ewingii)* was initially diagnosed in only a few patients, most of whom were immunosuppressed, but an additional 55 cases affecting both healthy and immunocompromised or elderly individuals were reported to U.S. federal authorities between 2008 and 2012. No deaths and few complications have been associated with this organism, as of 2022. Most other species of *Ehrlichia* and *Anaplasma* have been implicated in very few human cases; however, hospital surveillance attributed 28 clinical cases to *A. capra* in China in 2015, and *E. muris* has been implicated in at least 2 PCR-confirmed and 84 serologically diagnosed cases in Russia. Approximately 1% of the residents in Tokyo, Japan had antibodies to the latter organism, though cross-reactions with other organisms could not be ruled out.

Internet Resources

Centers for Disease Control and Prevention (CDC). Anaplasmosis

Centers for Disease Control and Prevention (CDC). Ehrlichiosis

Department of Agriculture, Fisheries and Forestry, Australia. Ehrlichiosis in Dogs

eMedicine.com. Ehrlichiosis

European Advisory Board on Cat Diseases. Guideline for *Anaplasma, Ehrlichia, Rickettsia* infections

International Veterinary Information Service (IVIS)

Medscape. *Anaplasma phagocytophilum*

Sainz et al. Guideline for veterinary practitioners on canine ehrlichiosis and anaplasmosis in Europe

StatPearls. *Anaplasma phagocytophilum*

StatPearls. Ehrlichiosis

The Merck Manual

The Merck Veterinary Manual

World Organization for Animal Health (WOAH). Bovine anaplasmosis

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