

BASICS

DEFINITION

Most avian hemoparasites are protozoal and of little clinical significance, however many types of avian hemoparasites can become pathologic under stressful conditions (e.g., captivity, breeding season, migration), when they infect a host species that is out of its natural ecosystem (e.g., captivity), or when vector species invade new geographic areas (e.g., due to climate change).

PATHOPHYSIOLOGY

- Lifecycle of *Plasmodium*: An infected vector (typically a *Culex* spp. mosquito) bites an uninfected bird: parasite sporozoites are passed into the bird's blood and via the bloodstream reach the liver; in the liver the sporozoites develop into pre-erythrocytic schizonts which then become merozoites; merozoites enter erythrocytes and develop into macrogametocytes (female), microgametocytes (male), or segments (schizonts). Schizonts divide in erythrocytes (intraerythrocytic merogony) indefinitely until the bird dies or the bird's immune system responds, therefore there is potential for persistence of infection with frequent relapses. Second-generation and subsequent generation exoerythrocytic schizonts can be seen in tissues other than the liver. Birds typically undergo an acute phase of infection where parasitemia increases steadily to a peak at 6-12 days after infection, then the host immune system begins to bring the infection under control; chronic infection then persists for the life of the bird, with recurrence of clinical disease possible.
- Lifecycle of *Haemoproteus*: A vector (typically a midge or hippoboscid) ingests gametocytes in RBC's of an infected bird; inside the insect vector the parasites migrate from the insect's GI tract to the bloodstream, then to the salivary glands as sporozoites; sporozoites are injected into the bloodstream of a new bird when the insect feeds; sporozoites migrate from the bird's bloodstream into endothelial cells of various tissues (lung, liver, bone marrow, spleen) where they develop into schizonts; each schizont contains many merozoites that are released into the bloodstream when the endothelial cell dies; merozoites in the bloodstream enter RBC's to become gametocytes. Gametocytes in a bird's RBC's can become infective in as little as 7 days after they enter the bird's RBC's; parasitemia in a host bird peaks at 10-21 days after infection and falls rapidly within 7 days to a low intensity.
- Lifecycle of *Leukocytozoon*: A vector (typically a black fly) ingests gametocyte-containing blood from an infected bird; gametocytes develop into sporozoites inside the fly; the fly injects sporozoites into the bloodstream of a new bird; sporozoites travel from the bloodstream of the new bird to invade endothelial and parenchymal cells of various tissues such as liver, heart and kidney; sporozoites develop into schizonts, which then rupture and release merozoites that infect RBC's and leukocytes. Alternately, released merozoites may be ingested by macrophages to become megaloschizonts in tissues such as the liver, lung and kidney, and from that point the megaloschizonts may release merozoites that develop into gametocytes.
- Possible clinical signs due to direct blood cell effects such as anemia
 - *Plasmodium* spp.

- *Aegyptianella* spp.
- *Leukocytozoon* spp. (not common)
- Possible clinical signs due to multi-organ and muscle tissue destruction as parasites progress through life cycle stages
 - *Plasmodium* spp.
 - *Leukocytozoon* spp.
 - *Atoxoplasma* spp.
 - *Haemoproteus* spp. (unusual)
- Transmitted via mosquitoes (*Culex* spp., *Mansonia crassipes*, *Aedeomyia squamipennis*)
 - *Plasmodium* spp.
 - Some *Trypanosoma* spp.
- Transmitted via hippoboscids flies
 - Some *Haemoproteus* spp.
 - Some *Trypanosoma* spp.
- Transmitted via biting midges (ceratopogonids, *Culicoides* spp.)
 - Most *Haemoproteus* spp.
 - *Leukocytozoon caulleryi*
- Transmitted via black flies (simuliids)
 - Most *Leukocytozoon* spp.
 - Some *Trypanosoma* spp.
- Transmitted via mites, ticks, fleas or other arthropods
 - Some *Trypanosoma* spp.
 - *Hepatozoon* spp.
 - *Babesia* spp.
 - *Aegyptianella* spp.
 - *Borrelia anserina*
- Transmitted via ingestion of sporulated oocysts (feces-contaminated water or food)
 - *Atoxoplasma* spp.

SYSTEMS AFFECTED

- Behavioral – Lethargy and weakness are seen in symptomatic infections of most avian hemoparasites
- Cardiovascular
 - Hemolytic anemia – *Plasmodium* spp., *Aegyptianella* spp., *Haemoproteus* spp. (unusual), *Leukocytozoon* spp. (unusual), *Borrelia anserina*
 - Lymphocytosis, leukocytosis – *Plasmodium* spp., *Leukocytozoon* spp. (unusual)
- Hemic/Lymphatic/Immune
 - Spleen - *Atoxoplasma* spp., *Leukocytozoon* spp.
- Hepatobiliary
 - Liver- *Plasmodium* spp., *Atoxoplasma* spp., *Leukocytozoon* spp.
- Nervous

- Central nervous system signs – *Plasmodium* spp., *Leukocytozoon* spp.
- Neuromuscular
 - Loss of balance, lameness or reluctance to move in galliformes - *Plasmodium* spp.
- Respiratory
 - Lungs - *Atoxoplasma* spp.

GENETICS

N/A

INCIDENCE/PREVALENCE

Prevalence of *Atoxoplasma* spp. can approach 100% in some passerine collections. *Haemoproteus* spp. are the most common blood parasite genus in birds. *Haemoproteus* spp., *Leukocytozoon* spp. and *Plasmodium* spp. are relatively common in wild birds. Seasonality of parasitemia generally coincides with vector prevalence.

GEOGRAPHIC DISTRIBUTION

- *Aegyptianella* spp. usually affects birds of tropical or subtropical climates.
- *Haemoproteus* spp. are distributed worldwide in temperate, tropical and subtropical climates.
- *Plasmodium* spp. and *Leukocytozoon* spp. are found in all zoogeographic regions except Antarctica (due to lack of mosquito vectors).

SIGNALMENT

- Species –
 - *Atoxoplasma* spp. are especially pathogenic in small passerines, especially the families Fringillidae and Sturnidae.
 - *Aegyptianella pullorum* affects galliformes (chickens, turkeys) and anseriformes (ducks, geese).
 - *Trypanosoma* spp. usually affect passerines, galliformes, waterfowl and pigeons.
 - *Borrelia anserina* usually affects galliformes or waterfowl.
 - *Haemoproteus* spp. are found in many species, especially passerines, strigiformes and columbiformes.
 - *Plasmodium* spp. have been found in birds from nearly all avian orders (not yet reported in struthioniformes, colliiformes, or trogoniformes). *Plasmodium relictum* has been found in natural infections of birds of at least 70 avian families. *Plasmodium* spp. appear to be especially pathogenic in penguins, small passerines, galliformes (chickens, turkeys) and anseriformes (ducks, geese).
 - *Leukocytozoon* infections have been most often reported in passerines, galliformes and coraciiformes, but appear most pathogenic in anseriformes (ducks, geese, swans), galliformes (chickens), columbiformes, and less commonly in falconiformes.

Leukocytozoon simondi is especially pathogenic in ducks and geese, and *L. caulleryi* is especially pathogenic in chickens in Asia.

- *Aegyptianella* spp. have been reported in many species including galliformes, pigeons, crows, anseriformes, ratites, falcons, passerines and psittacines. *A. pullorum* is pathogenic in chickens.
- Breed Predilections – N/A
- Mean Age and Range –
 - Atoxoplasmosis is usually a disease of young birds, particularly fledglings, and adults are usually asymptomatic.
- Predominant Sex – N/A

SIGNS

- General Comments - Most avian hemoparasites are of little clinical significance, however many types of avian hemoparasites can become pathologic under stressful conditions (e.g., captivity, breeding season, migration), when they infect a host species that is out of its natural ecosystem (e.g., captivity), or when vector species invade new geographic areas (e.g., due to climate change).
- Historical Findings –
 - Lethargy, listlessness – *Plasmodium* spp., *Leukocytozoon* spp., *Babesia shortti*, *Haemoproteus* spp. (unusual), *Leukocytozoon* spp. (unusual), *Borrelia anserine*
 - Labored breathing – *Leukocytozoon simondi* (unusual)
 - Central nervous system signs (ataxia, convulsions) - *Plasmodium* spp., *Leukocytozoon* spp.
 - Diarrhea - *Leukocytozoon simondi* (unusual), *Aegyptianella pullorum*
 - Erratic flight or other neurologic signs, vomiting – *Leukocytozoon toddi*
 - Loss of balance, lameness or reluctance to move in galliformes – *Plasmodium* spp.
 - Acute death – *Leukocytozoon simondi in juveniles*
- Physical Examination Findings –
 - Weight loss – *Haemoproteus* spp., *Leukocytozoon* spp.
 - Pale mucous membranes – *Plasmodium* spp., *Babesia shortti*, *Haemoproteus* spp. (unusual), *Leukocytozoon* spp. (unusual)
 - Jaundice - *Aegyptianella* spp., *Babesia shortti*
 - Typically asymptomatic – *Trypanosoma* spp., *Hepatozoon* spp., most *Babesia* spp., *Haemoproteus* spp., *Leukocytozoon* spp., *Trypanosoma* spp., microfilaria of filarial nematodes

CAUSES

See pathophysiology section above

RISK FACTORS

- Likelihood of clinical signs due to avian hemoparasites increases with seasonal changes in photoperiod, increased vector prevalence, increased reproductive activity, and exposure to predators. Likelihood of clinical signs is inversely correlated with host immunocompetence.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Most avian hemoparasites are differentiated using their appearance in blood smears. Multiple genera of hemoparasites may be present in the same patient. Numerous other non-parasitic etiologies exist for the nonspecific clinical signs of lethargy and weight loss.

CBC/BIOCHEMISTRY/URINALYSIS

- Parasites inside red blood cells –
 - *Haemoproteus* spp. – elongate pigmented gametocyte, usually alongside or wrapping around rather than deforming the RBC nucleus. The degree of parasitemia can be used as a gauge of general immunocompetence of the host (inverse correlation).
 - *Plasmodium* spp. – usually a round pigmented gametocyte, trophozoite or schizont that may displace the RBC nucleus, but may be elongate and not displace the RBC nucleus. In contrast to *Haemoproteus* spp., *Plasmodium* can show schizogony in RBC's and endothelial cells of various organs, gametocytes can displace the RBC nucleus, and parasite stages can be seen within thrombocytes and leukocytes as well as in RBC's.
 - *Leukocytozoon* spp. - a gametocyte is sometimes round but is typically large, elongate, with wispy ends, and without pigmented granules; may distort the infected host cell so much that the cell's original identification is difficult
 - *Aegyptianella* spp. – tiny nonpigmented vacuole appearance in RBC's.
 - *Babesia* spp. - nonpigmented white vacuole
- Parasites inside white blood cells –
 - *Hepatozoon* spp. – in monocytes or lymphocytes
 - *Atoxoplasma* spp. - a single merozoite or a meront in monocytes or lymphocytes, causing an indentation in the cell's nucleus
 - *Leukocytozoon* spp.
 - *Plasmodium* spp.
- Parasites inside thrombocytes –
 - *Plasmodium* spp.
- Extracellular parasites – *Haemoproteus* spp. (if several hours elapsed between blood collection and smear preparation), *Trypanosoma* spp. (long, flagellated, with an undulating membrane), microfilaria of filarial nematodes, *Borrelia anserina* (spirochete with loose spirals)
- Hemoglobinuria – *Plasmodium* spp.

- Elevation of AST or ALT – *Leukocytozoon* spp. (unusual), *Atoxoplasma* spp., *Haemoproteus* spp., *Plasmodium* spp.
- Hypoalbuminemia – *Plasmodium* spp.
- Hypergammaglobulinemia therefore hyperproteinemia – *Plasmodium* spp.
- Anemia – *Plasmodium* spp., *Aegyptianella* spp., *Haemoproteus* spp. (unusual), *Leukocytozoon* spp. (unusual), *Borrelia anserina*, *Aegyptianella* spp.
- Lymphocytosis, leukocytosis – *Plasmodium* spp., *Leukocytozoon* spp. (unusual), *Haemoproteus* spp.

OTHER LABORATORY TESTS

- Buffy coat smear, looking for parasites amongst white blood cells from a centrifuged hematocrit tube of whole blood – especially used for *Atoxoplasma* spp. and *Trypanosoma* spp.
- PCR of tissues or whole blood
- Fecal direct smear and centrifugation/flotation with Sheather's sugar solution – sometimes used for *Atoxoplasma* spp. The oocysts of organism cannot be differentiated in this manner from typical enteric species of *Isospora* (two sporocysts containing four sporozoites each), however the relative prevalence of *Atoxoplasma* versus enteric *Isospora* in some avian species is so disproportionate that the finding of oocysts in feces is diagnostic for *Atoxoplasma*. However, there is no correlation between presence of *Atoxoplasma* oocysts in feces and the presence of mononuclear merozoites in the same bird at the same time.
- Increased intensity of green color (biliverdin) in feces
- Several serological tests (agar gel precipitation, counter-immunoelectrophoresis, immunofluorescence, enzyme-linked immunosorbent assay, immunoblot analysis, latex agglutination) have been developed for *L. caulleryi*, but not for other *Leukocytozoon* spp.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

See blood analysis recommendations above.

PATHOLOGIC FINDINGS

- Splenomegaly – *Atoxoplasma* spp., *Haemoproteus* spp., *Plasmodium* spp., *Leukocytozoon* spp., *Aegyptianella* spp., *Borrelia anserina*
- Hepatomegaly - *Atoxoplasma* spp., *Haemoproteus* spp., *Plasmodium* spp., *Leukocytozoon* spp., *Aegyptianella* spp., *Borrelia anserina*
- Hepatic necrosis - *Atoxoplasma* spp., *Haemoproteus* spp., *Leukocytozoon* spp., *Aegyptianella* spp.
- Renal necrosis - *Aegyptianella* spp.
- Lung lesions – *Haemoproteus* spp.

- Muscle necrosis (white or hemorrhagic streaks) – *Haemoproteus* spp.
- Atoxoplasmosis – also may see necrotic foci in spleen and/or heart; pancreatic edema and/or hemorrhage; fluid accumulation in intestines; ascites
- Impression smears of spleen, liver or lung can be used to detect *Atoxoplasma* spp. sporozoites.
- *Atoxoplasma* can be confirmed in infected tissues via PCR.

TREATMENT

APPROPRIATE HEALTH CARE

See medications section below.

NURSING CARE

If a patient is symptomatic, general supportive care should be provided (nutrition, hydration, appropriate temperature, calm environment).

ACTIVITY

See “nursing care” section.

DIET

See “nursing care” section.

CLIENT EDUCATION

Chronic infection with some avian hemoparasites (e.g., *Haemoproteus*) may stimulate immunity to reinfection with homologous parasites of the same species, therefore treatment may be elected against in cases of asymptomatic infection. However, immunosuppression due to stress or other factors may cause recrudescence of parasitemia and clinical signs.

SURGICAL CONSIDERATIONS

N/A

MEDICATIONS

DRUG(S) OF CHOICE

- *Atoxoplasma* spp. – reported treatment options include:
 - Sulfachlorpyrazine (ESB3[®]) in drinking water at a dosage of 300 ppm (1 gram of 30% powder added to each 1 liter of drinking water). If sulfachlorpyrazine is used, a vitamin B₆ supplement should be given during the treatment.
 - Sulfachlorpyridazine (Vetisulid[®]) in drinking water at a dosage of 300 ppm. If sulfachlorpyridazine is used, a vitamin B₁₂ supplement should be given during the treatment.

- Toltrazuril 12.5 mg/kg PO SID for 14 days
- Diclazuril
- Ponazuril should show some efficacy, although this remains anecdotal.
- *Haemoproteus* spp. – reported treatment options include atebriane, plasmochin, chloroquine sulfate, quinacrine, primaquine, mefloquine, buparvaquone, pyrimethamine, pyrimethamine-sulfadoxine combinations, and tetracyclines.
- *Plasmodium* spp. – reported treatment options include chloroquine phosphate, primaquine phosphate, pyrimethamine-sulfadoxine combinations, mefloquine, sulfamonomethoxine, sulfachloropyrazine, doxycycline, halofuginone and atovaquone – proguanil combinations (Malarone™).
- *Leukocytozoon* spp. – reported treatment options include pyrimethamine, pyrimethamine-sulfamonomethoxine in combination, clopidol, atebriane, trimethoprim-sulfamethoxazole combination, melarsomine, and primaquine
- *Aegyptianella* spp. – doxycycline
- *Babesia shortti* in falconiformes – imidocarb dipropionate 5-13 mg/kg IM q7days for 2-3 weeks.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

N/A

FOLLOW-UP

PATIENT MONITORING

See blood analysis section above.

PREVENTION/AVOIDANCE

- 2 vaccines were developed for *Plasmodium relictum*; both provided protection for penguins and canaries against natural infection, but immunity was short-lived in canaries and immunity waned to that of unvaccinated control birds when challenged with mosquito vectors a year later.
- 2 vaccines have been developed for protection of chickens against *L. caulleryi*

- Frequent replacement of drinking water, bathing bowls and enclosure substrate to prevent ingestion of sporulated oocysts - *Atoxoplasma* spp.
- Protection from flying insect vectors with screening – *Plasmodium* spp., some *Trypanosoma* spp., *Haemoproteus* spp., *Leukocytozoon* spp.
- Protection from tick vectors with use of acaricides - Some *Trypanosoma* spp., *Hepatozoon* spp., *Babesia* spp., *Aegyptianella* spp.
- Absolute prevention of infection may be counterproductive for protection from some hemoparasite-induced diseases, as birds naïve to infection are much more likely to experience morbidity and mortality if subsequently infected.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Atoxoplasmosis is often a diagnosis made post-mortem. Most other hemoparasites are either asymptomatic, or their numbers are able to be reduced in the host with appropriate medications.

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- The term “malaria” is most accurately associated with *Plasmodium* spp., but some older literature uses the word “malaria” to refer to *Haemoproteus* spp. infections.
- Haemoproteosis, hematozoan disease, haemosporidian disease, blood parasite disease, Bangkok hemorrhagic disease (*L. caulleryi*), “going light” (*Atoxoplasma* spp.) in passerines, “black spot disease” (*Atoxoplasma* spp. – due to liver visible through body wall)
- Note, some older reports of *Lankesterella* infection may have been actually due to *Atoxoplasma* spp.

SEE ALSO

N/A

ABBREVIATIONS

- RBC – red blood cell
- AST – aspartate aminotransferase concentration in serum or plasma
- ALT – alanine aminotransferase concentration in serum or plasma

INTERNET RESOURCES

Norton, Terry M., Ellis Greiner, Kenneth Latimer, and Susan E. Little. 2004. Medical protocols recommended by the U. S. Bali Mynah SSP. Accessed on July 20, 2014. Available at: <http://www.riverbanks.org/subsite/aig/new.htm>

VanWettere, Arnaud J. 2013. Merck Veterinary Manual: Overview of blood borne organisms in poultry. Accessed on May 28, 2014. Available at: http://www.merckmanuals.com/vet/poultry/bloodborne_organisms/overview_of_bloodborne_organisms_in_poultry.html

Suggested Reading

Atkinson, Carter T., Nancy J. Thomas, and D. Bruce Hunter (eds.). 2008 (print) or 2009 (e-book). Parasitic Diseases of Wild Birds. Wiley-Blackwell, Ames, IA and Hoboken, NJ. Relevant chapters include:

Ch. 2: *Haemoproteus*, by Carter T. Atkinson

Ch. 3: Avian Malaria, by Carter T. Atkinson

Ch. 4: Leukocytozoonosis, by Donald J. Forrester and Ellis C. Greiner.

Ch. 5: *Isospora*, *Atoxoplasma* and *Sarcocystis*, by Ellis C. Greiner

Campbell, Terry W. 2012. Chapter 19: Hematology of Birds. In: Veterinary Hematology and Clinical Chemistry, 2nd ed. Thrall, Mary Anna, Weiser, Glade, Allison, Robin, and Terry W. Campbell (eds.). Wiley-Blackwell, Hoboken, NJ. Pp. 262-266.

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