

## ***Haemoproteus***

(protist: apicomplexan)

### **Overview**

Protists are single-celled organisms with membrane-bound nuclei (eukaryotes). One protistan supergroup known as SAR comprises the Stramenopiles (with heterokont flagella), Alveolata (with cortical alveoli) and Rhizaria (with fine pseudopodia). Three major alveolate groups are recognized: ciliates, apicomplexans and dinoflagellates. Apicomplexan cells possess a distinctive apical complex of organelles, comprising a conoid, polar ring, rhoptries, micronemes and subpellicular microtubules, which facilitate entry into host cells as they are obligate intracellular parasites for most of their life-cycles. There are three main apicomplexan groups: gregarines, coccidia and haematozoa. Haematozoa are small blood-borne parasites which undergo merogony (= schizogony) and gamogony (gamete formation) in vertebrates and sporogony (sporozoite formation) in blood-sucking invertebrate vectors. Two main groups are recognised in terrestrial vertebrates: haemosporidia with insect vectors; and piroplasms with arachnid vectors. Haemosporidian parasites multiply in the tissues of vertebrates before forming gamonts in blood cells. Most species produce haemozoin pigment granules as a byproduct of haemoglobin metabolism. Gametes ingested by insect vectors undergo fertilization in the gut forming motile zygotes (ookinetes) which form oocysts and then thousands of sporozoites which invade the salivary glands. Haemoproteid infections are transmitted by biting midges, hippoboscids and tabanid flies and are frequently detected in birds and some reptiles. Most apparently causing no harm.

### **Classification:**

Domain: Eukaryota (membrane-bound nucleus)  
Supergroup: SAR (Stramenopiles + Alveolata + Rhizaria)  
Group: Alveolata (with cortical alveoli)  
Phylum: Apicomplexa (with apical complex, all parasitic, sexual development (gamogony))  
Class: Aconoidasida (asexual stages without conoid)  
Order: Haemosporida (pleomorphic stages in blood of vertebrates, insect vectors. motile zygote (ookinete))  
Family: Haemoproteidae (schizogony in tissues, gamonts in blood cells, haemozoin pigment)  
Genus: *Haemoproteus* (parasitic in endothelia/erythrocytes of birds/lizards/turtles)  
Species: various species cause infections mainly in birds

**Parasite biodiversity and host range:** Protists are unicellular eukaryotes that move using undulipodia (flagella or cilia), pseudopodia (false-feet) or a unique gliding motion. Cells with different modes of locomotion do not form separate monophyletic assemblages as previously thought, but rather are distributed across several disparate supergroups (as evidenced by recent molecular phylogenetic analyses). One protistan supergroup known as SAR comprises the Stramenopiles (with heterokont flagella), Alveolata (with cortical alveoli) and Rhizaria (with fine pseudopodia). Three diverse alveolate groups are recognized: Ciliophora (with cilia), Dinoflagellata (with flagella) and Apicomplexa (with gliding motion, some also with flagellated microgametes). Over 4,000 species of Apicomplexa have been described as obligate parasites from vertebrate and invertebrate hosts. At some stage in their development, these possess unique cytoskeletal and membrane-bound organelles (conoid, rhoptries, micronemes, subpellicular microtubules) forming an apical complex that facilitates host cell invasion. Apicomplexans undergo cyclic development involving up to three different divisional processes: asexual merogony (schizogony) either by fission (splitting of maternal cell) or endogony (internal formation of daughter cells); gamogony involving formation of gametes (macrogametes = female, microgametes = male) which undergo fertilization to recombine by fusion (syngamy) with or without paired alignment (syzygy); and sporogony (formation of infective sporozoites).

Three main apicomplexan groups are recognized: haematozoa, gregarines, and coccidia. Haematozoa are small blood-borne parasites in vertebrates which complete their development in blood-sucking invertebrate vectors; with pleomorphic haemosporidia being transmitted by insects and pear-shaped piroplasms being transmitted by ticks. Gregarines are lumen-dwelling parasites that form large extracellular (sometimes septate) gamonts with an anterior holdfast organelle (mucron or epimerite) used to attach to the gut or body cavity of invertebrates. Coccidia are tissue-invading parasites that form small intracellular gamonts (lacking a mucron or epimerite) and most species undergo sexual reproduction by anisogamous fusion without syzygy forming non-motile resistant spores (oocysts) containing infective sporozoites usually confined within secondary spores (sporocysts). Three groups of coccidia are recognized: coelotrophiid coccidia in marine annelids; adeleid coccidia in marine and terrestrial animals (including blood parasites paradoxically known as 'haemogregarines' in reptiles and amphibians with leech or arthropod vectors); and eimeriid coccidia in vertebrates. Many eimeriid coccidia are monoxenous gut parasites undergoing faecal-oral transmission, but some are heteroxenous alternating between enteric stages in predators and encysted stages in prey (there are also a few enigmatic 'haemococcidia' in the blood of reptiles and birds).

Higher taxonomy	Family	Genera	Hosts	Site	Transmission*	
Class: Aconoidasida (asexual stages without conoid)						
Subclass: Haematozoa (clade of vector-borne spore-forming haemo-protozoa)						
Order: Haemosporida (pleomorphic blood stages, insect vectors, motile ookinete)	Plasmodiidae (schizogony in tissues then blood cells, haemozoin pigment)	<i>Plasmodium</i>	mammals, birds, reptiles	liver, erythrocytes	indirect (v-b)	
	Haemoproteidae (schizogony in tissues, haemozoin pigment)	<i>Haemoproteus</i>	birds	endothelia, erythrocytes	indirect (v-b)	
	Leucocytozoidae (schizogony in tissues, no haemozoin pigment)	<i>Leucocytozoon (Akiba)</i>	birds	tissues, leucocytes	indirect (v-b)	
Order: Piroplasmida (pear-shaped blood stages, tick vectors)	Babesiidae (merogony in erythrocytes, trans-stadial + trans-ovarian transmission)	<i>Babesia</i>	mammals	erythrocytes	indirect (v-b)	
	Theileriidae (merogony in leucocytes, trans-stadial transmission in ticks)	<i>Theileria</i>	ruminants	leucocytes, erythrocytes	indirect (v-b)	
Class: Coccidiomorpha [Conoidasida] (with conoid)						
Subclass: Coccidia [Coccidiasina] (small intracellular gamonts)						
Order: Eucoccidiorida (cyclic merogony (schizogony), gamogony, sporogony)						
Suborder: Adeleina (syzygy, 1-4 microgametes)	Haemogregarinidae (ookinete, gamonts in blood cells, invertebrate vectors)	<i>Haemogregarina</i>	reptiles, amphibia, fish	tissues, blood	indirect (v-b)	
		<i>Hepatozoon</i>	mammals, reptiles	tissues, blood	indirect (v-b)	
	Klossiellidae (sporocysts)	<i>Klossiella</i>	mammals	kidney	direct (f-o)	
Suborder: Eimeriorina (no syzygy, >4 microgametes)	Eimeriidae (monoxenous, endogenous merogony and gamogony, exogenous sporogony)	<i>Caryospora</i>	birds, reptiles	gut	direct (f-o)	
		<i>Cyclospora</i>	mammals, reptiles	gut	direct (f-o)	
		<i>Isospora</i>	birds, reptiles	gut	direct (f-o)	
		<i>Eimeria</i>	vertebrates	gut, tissues	direct (f-o)	
		<i>Epieimeria</i>	fish	gut	direct (f-o)	
		<i>Goussia</i>	fish	gut	direct (f-o)	
	Sarcocystidae (heteroxenous, 1:2:4 oocyst:sporocyst:sporozoite configuration)					
	subfamily Cystoisosporinae (monozoic cysts)	<i>Cystoisospora</i> (no Stieda bodies)	carnivores, omnivores	gut, tissues	direct (f-o), indirect (p-p)	
	subfamily: Sarcocystinae (thick-walls, metrocytes)	<i>Sarcocystis (Frenkelia)</i>	mammals, birds, reptiles	gut, muscles	indirect (p-p)	
	subfamily: Toxoplasmatinae (thin-walled cysts without metrocytes)	<i>Besnoita</i>	mammals, reptiles	gut, tissues	indirect (p-p)	
<i>Hammondia</i>		mammals	gut, tissues	indirect (p-p)		
<i>Neospora</i>		herbivores, dogs	gut, tissues	indirect (p-p)		
	<i>Toxoplasma</i>	vertebrates, cats	gut, tissues	indirect (p-p)		
Class: Gregarinomorpha (gregarines, trophonts with specialized attachment epimerite or mucron, syzygy)						
Subclass: Cryptogregarina (epicellular parasites of vertebrates with feeder organelle but lacking apicoplast)						
	Cryptosporidiidae (naked sporozoites)	<i>Cryptosporidium</i>	vertebrates	gut, lungs	direct (f-o)	

\* f-o = faecal-oral transmission; p-p = predator-prey transmission; v-b = vector-borne transmission.

Haemosporida are spore-forming apicomplexan parasites with heteroxenous life-cycles, with merogony in cells of fixed tissues and in the blood of vertebrate (intermediate) hosts and sporogony in haematophagous invertebrate vectors (definitive hosts). In vertebrate blood cells, haemosporidia develop intracellularly forming sexually dimorphic gametocytes: macrogametocytes (female) with compact nuclei and dark-stained cytoplasm (plentiful ribosomes for protein synthesis), and microgametocytes (male) with larger diffuse nuclei (ready for microgamete production) and pale-staining cytoplasm [a simple mnemonic often used is “blue for girls, pink for boys”]. Gametocytes develop independently (without syzygy) and each microgamont produces about eight flagellated microgametes. Haemozoin granules (residual pigment formed due to incomplete haemoglobin digestion) may or may not be produced in infected erythrocytes. In the vector, the zygote is motile (ookinete) and ultimately forms numerous naked sporozoites (without sporocysts). Around 590 species belonging to some 19 haemosporidian genera have been described from a wide range of mammalian, avian and reptilian hosts around the world.

Four haemosporidian families are recognized mainly on the basis of their developmental cycles and whether haemozoin pigment is produced: namely, Plasmodiidae (merogony in tissues then cyclic in erythrocytes, pigment present); Haemoproteidae (merogony in tissues only, pigment present); Leucocytozoidae (merogony in tissues, pigment absent) and Garniidae (merogony in leucocytes, pigment absent). Vertebrates act as intermediate hosts in which the parasites undergo asexual multiplication within tissues and/or blood cells. Even though parasites begin gamete formation in vertebrates, sexual multiplication is not completed until after they are transmitted to their haematophagous invertebrate vectors, which therefore act as definitive hosts. Three genera are recognized in the family Haemoproteidae on the basis of multiple biological characters (including morphology, development, host specificity and range): *Haemoproteus* (syn. *Halteridium*) in birds; and *Johnspretia* and *Sprattiella* in bats. Two subgenera are recognized in the genus *Haemoproteus*: *H. (Haemoproteus)* in columbiform birds with hippoboscids (louse fly) vectors; and *H. (Parahaemoproteus)* in non-columbiform birds with ceratopogonid (biting midge) vectors. Species in another genus *Simondia* (in tortoises) and all reptilian *Haemoproteus* species have recently been transferred to the plasmodiid genus *Haemocystidium* on the basis of contemporary morphological, biological and molecular studies.

Haemosporidian genera	No. spp.	Site* of development in vertebrate		Vertebrate hosts	Invertebrate vector
		meronts	gamonts		
Family: Plasmodiidae (merogony in tissues and erythrocytes, haemozoin pigment present)					
<i>Plasmodium</i>	225	liver, rbc	rbc	mammals, birds, reptiles	diptera
<i>Hepatocystis</i>	25	liver	rbc	primates/bats	midges
<i>Polychromophilus</i>	5	viscera	rbc	bats	nycterids
<i>Nycteria</i>	7	liver	rbc	bats	
<i>Biguetiella</i>	1	liver	rbc	bats	
<i>Bioccala</i>	2	RE cells	rbc	bats	
<i>Dionisia</i>	1	liver	rbc	bats	
<i>Rayella</i>	3	liver	rbc	flying squirrels	
<i>Billbraya</i>	1	rbc	rbc	lizards	
<i>Mesniliium</i>	1	RE cells, rbc	rbc	fish	leeches/insects
<i>Haemocystidium (Simondia)</i>	33	RE cells	rbc	lizards/tortoises	arthropods
Family: Haemoproteidae (merogony in tissues (not in blood cells), haemozoin pigment present in gametocytes)					
<i>Haemoproteus (Halteridium)</i>	6	RE cells	rbc	birds	louse flies
<i>Haemoproteus (Parahaemoproteus)</i>	150	RE cells	rbc	birds	midges
<i>Johnspretia</i>	1	RE cells	rbc	flying foxes	
<i>Sprattiella</i>	1	RE cells	rbc	bats	
Family: Leucocytozoidae (merogony in tissues (not in blood cells), haemozoin pigment absent)					
<i>Leucocytozoon (Akiba)</i>	100	RE cells	blood cells	birds	black flies
<i>Sauocytozoon</i>	3	viscera	leucocytes	lizards	mosquitoes
Family: Garniidae (merogony in leucocytes, haemozoin pigment absent)					
<i>Fallisia</i>	12	leucocytes	leucocytes	lizards	arthropods
<i>Garnia</i>	10	leucocytes	leucocytes	lizards	arthropods
<i>Progarnia</i>	1	leucocytes	blood cells	crocodiles	

\*rbc = red blood cells (erythrocytes); RE = reticuloendothelial cells

Many molecular phylogenetic studies using nuclear, mitochondrial and apicoplast gene sequences have demonstrated a clear relationship between haemosporidian genera not only with their vertebrate hosts but also their invertebrate vectors. There were clear groupings of *Leucocytozoon* from birds, *Haemoproteus (Haemoproteus)* from birds, *Haemoproteus (Parahaemoproteus)* from birds, *Plasmodium* from birds and reptiles, *Plasmodium* from rodents and primates, and *Hepatocystis* from bats. These groups were clearly associated with different vectors; namely, simuliids (black-flies), hippoboscids (louse-flies), ceratopogonids (midges), culicine mosquitoes, anopheline mosquitoes, and midges, respectively. There appears to have been a transition from haemosporidia which do not form haemozoin pigment (*Leucocytozoon* in white blood cells) to genera that do form pigment indicating haemoglobin digestion by parasites in red blood cells (*Haemoproteus*, *Plasmodium* and *Hepatocystis*). This was followed by a transition from haemosporidia which undergo schizogony exclusively in host tissues (*Leucocytozoon* and *Haemoproteus*) to those that undergo schizogony in blood cells (*Plasmodium*). While there appears to be a general shift in haemosporidian genera from birds and reptiles to mammals (from nucleated to non-nucleated blood cells), each genus is associated with a particular vector group: black-flies transmitting *Leucocytozoon* to birds; louse-flies transmitting *Haemoproteus (Haemoproteus)* to birds; midges transmitting *Haemoproteus (Parahaemoproteus)* to birds; culicine mosquitoes transmitting *Plasmodium* to birds and lizards; and anopheline mosquitoes transmitting *Plasmodium* to mammals. The exception to this general trend was *Hepatocystis* which does not undergo blood schizogony and is transmitted to bats by midges.

Haemoproteids are malaria-like parasites found mainly in birds, but a few species in bats. They are characterized by exoerythrocytic schizogony occurring in fixed tissues followed by intraerythrocytic gametogony (no erythrocytic merogony). Most species form haemozoin pigment and they are transmitted by insect vectors other than mosquitoes, including biting midges, hippoboscids and tabanid flies. Six species assigned to the subgenus *Haemoproteus* (*Haemoproteus*) occur mainly in columbiform birds and have hippoboscids as vectors, while over 180 species placed in the subgenus *Haemoproteus* (*Parahaemoproteus*) occur in many non-columbiform bird families and have ceratopogonid vectors. Haemoproteids have a widespread distribution, species richness (biodiversity) being richest in Holarctic, Ethiopian and Oriental regions, and poorest in Neotropical and Australasian regions, with infections recorded in 18 bird orders, particularly Passeriformes, Coraciiformes, Galliformes, Piciformes, Falconiformes and Columbiformes. The zoogeographic boundaries of individual species are unclear as most studies have consisted of patchy surveys and the life-cycles and vectors for most species are unknown. Nevertheless, observations suggest that the dispersal of several species has been assisted by anthropogenic activities (aviary trade) and annual bird migrations (where overwintering sites appear to be more important for transmission than breeding sites).

<i>Haemoproteus</i> species*	Intermediate hosts [pathology]	Gamont shape	Definitive hosts (vectors)	Geographic distribution
<b>Subgenus: <i>Haemoproteus</i></b> (definitive hosts: hippoboscids; intermediate hosts: columbiform birds)				
<i>H. (H.) columbae</i> (syn. <i>maccallumi</i> , <i>melopeliae</i> ) [type species]	Columbiformes: columbid (pigeons, doves), Cuculiformes: cuculid (coucals, cuckoos), Passeriformes: emberizid (buntings), estrildid (mannikins), fringillid (finches), laniid (shrikes), nectariniid (sunbirds), passerid (sparrows), ploceid (bishops, weavers); Strigiformes: strigid (pygmy owls, wood owls); Accipitriformes: accipitrid (goshawks) [megalomeront lesions in tissues]	halteridial	Diptera: hippoboscid ( <i>Microlynchia pusilla</i> , <i>Pseudolynchia brunnea</i> , <i>canariensis</i> (= <i>Lynchia</i> <i>capensis</i> , <i>lividicolor</i> , <i>maura</i> ))	cosmopolitan (except Antarctica)
<i>H. (H.) krylovi</i>	Columbiformes: pteroclid (sandgrouse)	halteridial		Palaearctic
<i>H. (H.) palumbis</i>	Columbiformes: columbid (wood-pigeons)	halteridial	Diptera: hippoboscid ( <i>Ornithomyia avicularia</i> , <i>Pseudolynchia</i> <i>canariensis</i> )	Palaearctic
<i>H. (H.) pteroclis</i>	Columbiformes: pteroclid (sandgrouse)	halteridial		Palaearctic
<i>H. (H.) sacharovi</i>	Columbiformes: columbid (pigeons, doves)	pleomorphic	Diptera: hippoboscid ( <i>Ornithomyia avicularia</i> , <i>Pseudolynchia canariensis</i> (= <i>maura</i> ), <i>brunnea</i> , <i>capensis</i> , <i>Microlynchia</i> <i>pusilla</i> )	Holarctic, Neotropical, Ethiopian, Oriental
<i>H. (H.) turtur</i>	Columbiformes: columbid (pigeons, doves)	halteridial	Diptera: hippoboscid ( <i>Pseudolynchia</i> <i>canariensis</i> )	Palaearctic
<b>Subgenus: <i>Parahaemoproteus</i></b> (definitive hosts: biting midges; intermediate hosts: non-columbiform birds)				
<i>H. (P.) abdusalomovi</i>	Charadriiformes: glareolid (pratincoles)	halteridial		Palaearctic
<i>H. (P.) aegithinae</i>	Passeriformes: aegithinid (ioras), chloropseid (leafbirds)	halteridial		Oriental
<i>H. (P.) aegyptius</i>	Strigiformes: strigid (eagle- owls)			Palaearctic
<i>H. (P.) africanus</i>	Passeriformes: fringillid (finches), ploceid (weavers)	halteridial		Ethiopian
<i>H. (P.) alaudae</i>	Passeriformes: alaudid (larks)	halteridial- circum-nuclear		Holarctic, Ethiopian, Oriental

<i>H. aluci nomen dubium</i>	Strigiformes: strigid (barn owls, eagle-owls, marsh owls, wood owls)			Holarctic, African, Oriental
<i>H. americanae nomen nudum</i>	Coraciiformes: coraciid (Indian rollers)			Oriental
<i>H. (P.) ammoperdix</i>	Galliformes: phasianid (partridges)	halteridial		Palaearctic
<i>H. (P.) anthi</i>	Passeriformes: motacillid (pipits, wagtails)	halteridial		Oriental, Ethiopian, Palaearctic
<i>H. (P.) antigonis</i>	Gruiformes: gruid (cranes); Otidiformes: otidid (bustards)	halteridial		Oriental, Ethiopian, Holarctic
<i>H. (P.) apodus</i>	Apodiformes: apodid (swifts)	micro-halteridial		Neotropical
<i>H. (P.) archilochus</i>	Apodiformes: trochilid (hummingbirds)	circum-nuclear		Nearctic, Neotropical
<i>H. (P.) asturisdussumieri (incertae sedis)</i>	Accipitriformes: accipitrid (goshawks)			Oriental, African
<i>H. (P.) attenuatus</i>	Passeriformes: muscicapid (robins)	halteridial		Palaearctic
<i>H. (P.) balearicae</i>	Gruiformes: gruid (cranes)	micro-halteridial		Holarctic, Ethiopian
<i>H. balfouri nomen nudum</i>	Galliformes: numidid (helmeted guineafowl)			African
<i>H. (P.) balmorali</i>	Passeriformes: muscicapid (flycatchers), turdid (thrushes)	halteridial	Diptera: ceratopogonid ( <i>Culicoides impunctatus</i> )	Palaearctic, Ethiopian, Oriental
<i>H. (P.) bambusicolae</i>	Galliformes: phasianid (bamboo partridge)			Oriental
<i>H. (P.) beckeri</i>	Passeriformes: mimid (thrashers, catbirds, mockingbirds)	halteridial		Nearctic
<i>H. (P.) belopolskyi (syn. sylvae)</i>	Passeriformes: sylviid (warblers)	halteridial-circum-nuclear	Diptera: ceratopogonid ( <i>Culicoides impunctatus</i> )	Oriental, Ethiopian, Palaearctic
<i>H. (P.) bennetti</i>	Piciformes: picid (yellownapes)	rhabdosomal		Oriental
<i>H. (P.) bilobata</i>	Piciformes: capitonid (barbets)	micro-halteridial		Oriental
<i>H. (P.) borgesii</i>	Piciformes: picid (woodpeckers, wrynecks)	halteridial		Oriental, Ethiopian, Neotropical
<i>H. (P.) brachiatus</i>	Falconiformes: falconid (kestrels)	halteridial-circum-nuclear		Holarctic
<i>H. (P.) bramae (species inquirenda)</i>	Strigiformes: strigid (little owl)			Palaearctic
<i>H. (P.) bubalornis</i>	Passeriformes: ploceid (weavers)	halteridial		Ethiopian
<i>H. bubonis nomen dubium</i>	Strigiformes: strigid (barn owl, short-eared owl)			Holarctic, Oriental African
<i>H. (P.) bucconis</i>	Piciformes: bucconid (puffbirds)	rhabdosomal		Neotropical
<i>H. (P.) bucerotis</i>	Bucerotiformes: bucerotid (hornbills)	halteridial		Ethiopian
<i>H. (P.) burhini</i>	Charadriiformes: scolopacid (curlews)	halteridial		Ethiopian
<i>H. (P.) buteonis</i>	Falconiformes: falconid (buzzards, hawks, harriers)	halteridial		Holarctic
<i>H. (P.) calandrellae</i>	Passeriformes: alaudid (larks)	halteridial		Palaearctic
<i>H. (P.) caprimulgi</i>	Caprimulgiformes: caprimulgid (nightjars,	halteridial-circum-nuclear		Holarctic, Oriental

	nighthawks)			
<i>H. (P.) cellii</i> (syn. <i>noctuae</i> var. <i>cellii</i> )	Strigiformes: strigid (bay owls, boobooks, eagle-owl, owlets, pygmy owls, scops owls, screech owls, wood owls)			cosmopolitan
<i>H. (P.) centropi</i> (syn. <i>froilanoi</i> )	Cuculiformes: cuculid (cuckoos, anis)	halteridial		Oriental
<i>H. (P.) cerchneisi</i> ( <i>species inquirenda</i> )	Falconiformes: falconid (Eurasian kestrel)			Palaearctic
<i>H. (P.) chapini</i> ( <i>species inquirenda</i> )	Galliformes: phasianid (Congolese peafowl)			African
<i>H. (P.) chelidonis</i> ( <i>incertae sedis</i> )	Passeriformes: hirundinid (martins, swallows)			Holarctic, Oriental
<i>H. (P.) circumnuclearis</i>	Passeriformes: muscipid (flycatchers)	circum-nuclear		Neotropical
<i>H. (P.) circus</i> ( <i>incertae sedis</i> )	Accipitriformes: accipitrid (harriers)			Palaearctic
<i>H. (P.) clamatoris</i>	Cuculiformes: cuculid (pied cuckoo)	halteridial		African
<i>H. (P.) clelandi</i>	Passeriformes: meliphagid (honeyeater)			Australasian
<i>H. (P.) coatneyi</i> (syn. <i>coereba</i> , <i>paruli</i> , <i>thraupi</i> )	Passeriformes: emberizid (buntings), fringillid (finches), passerid (sparrows), sylviid (warblers), thraupid (tanagers)	halteridial	Diptera: culicid ( <i>Anopheles balabacensis</i> )	Holarctic, Neotropical
<i>H. (P.) contortus</i>	Charadriiformes: glareolid (waders), scolopacid (whimbrels)	circum-nuclear		Oriental (Philippines)
<i>H. (P.) coraciae</i> (syn. <i>coraciae</i> var. <i>benghalensis</i> , <i>cruzferreirae</i> , <i>fontesi</i> , <i>fontessi</i> var. <i>cyanogaster</i> , <i>velascoi</i> )	Coraciiformes: coraciid (rollers)	halteridial-circum-nuclear		Oriental, Ethiopian
<i>H. (P.) cornuata</i>	Piciformes: capitonid (barbets)	halteridial		Oriental, Ethiopian
<i>H. corvi</i> <i>nomen dubium</i>	Passeriformes: corvid (corvids)			Europe
<i>H. (P.) cracidarum</i>	Galliformes: cracid (chachalacas, guans)	halteridial		Neotropical
<i>H. (P.) crumenium</i> (syn. <i>brodkorbi</i> )	Ciconiiformes: ciconiid (storks)	halteridial		Ethiopian, Nearctic
<i>H. (P.) cublae</i>	Passeriformes: laniid (shrikes), malaconotid (boubous)	micro-halteridial		Ethiopian
<i>H. (P.) cuculis</i>	Cuculiformes: cuculid (Asian koel)	halteridial		Australasian
<i>H. (P.) danilewskii</i> [type species]	Passeriformes: corvid (crows, jays, nutcrackers)	circum-nuclear-halteridial	Diptera: ceratopogonid ( <i>Culicoides arboricola</i> , <i>crepuscularis</i> , <i>downesi</i> , <i>edeni</i> , <i>sphagnumensis</i> , <i>stilobezzioides</i> )	Nearctic (North America)
<i>H. (P.) dicaeus</i>	Passeriformes: dicaeid (flowerpeckers)	halteridial		Oriental
<i>H. (P.) dicruri</i>	Passeriformes: dicrurid (drongos)	halteridial		Oriental, Ethiopian
<i>H. (P.) dolniki</i>	Passeriformes: fringillid (finches)	halteridial	Diptera: ceratopogonid ( <i>Culicoides impunctatus</i> )	Palaearctic
<i>H. (P.) elani</i>	Falconiformes: falconid (kites, hawks, vultures, eagles)	halteridial		Oriental, Ethiopian, Holarctic
<i>H. (P.) enucleator</i>	Coraciiformes: alcedinid (kingfisher)	rhabdosomal		Ethiopian

<i>H. (P.) eurylaimus</i>	Passeriformes: eurylaimid (broadbills)	halteridial		Oriental
<i>H. (P.) eurystomae</i>	Coraciiformes: coraciid (rollers)	halteridial		Ethiopian, Oriental
<i>H. (P.) fallisi</i> (syn. <i>hipiduris</i> )	Passeriformes: muscicapid (forktails, nightingales, redstarts, robins, robinchats), passerid (sparrows), parulid (warblers), ploceid (weavers), timaliid (babblers), turdid (chats, thrushes)	micro-halteridial		Holarctic, Neotropical, Ethiopian, Oriental
<i>H. (P.) figueiredoi</i>	Accipitriformes: accipitrid (eagles, sparrowhawks)			Eurasia, Nearctic
<i>H. (P.) formicarius</i>	Passeriformes: thamnophiliid (antbirds)	halteridial		Neotropical
<i>H. (P.) forresteri</i>	Coraciiformes: brachypteraciid (ground rollers)	halteridial-circum-nuclear		African
<i>H. (P.) fringillae</i> (syn. <i>chloriis</i> )	Passeriformes: corvid (jays), emberizid (buntings), estrildid (pytilias), fringillid (canaries, crossbills, finches, grosbeaks, redpolls), laniid (shrikes), muscicapid (robins, shamas), parid (tits), parulid (warblers), passerid (sparrows), prunellid (accentors), ploceid (weavers), sittid (nuthatches), sturnid (starlings), thraupid (bananaquits, grassquits, orangequits, tanagers), turdid (thrushes)	halteridial	Diptera: ceratopogonid ( <i>Culicoides crepuscularis</i> , <i>impunctatus</i> , <i>sphagnumensis</i> , <i>stilobezzioides</i> )	cosmopolitan (except Australia, Antarctic)
<i>H. (P.) furnarius</i>	Passeriformes: parulid (ovenbirds)	halteridial		Neotropical
<i>H. (P.) fusca</i>	Coraciiformes: alcedinid (kingfishers)	circum-nuclear		Oriental, Ethiopian, Palearctic
<i>H. (P.) gallinulae</i>	Gruiformes: rallid (crakes, rails, coots, waterhens)	halteridial		Oriental, Ethiopian, Holarctic
<i>H. (P.) gavrilo</i>	Coraciiformes: meropid (bee-eaters)	rhabdosomal		Palearctic
<i>H. (P.) geocichlae</i> ( <i>species inquirenda</i> )	Passeriformes: turdid (ground-thrush)			Palearctic
<i>H. glaucidii</i> <i>nomen dubium</i>	Strigiformes: strigid (owlets)			Oriental, Neotropical
<i>H. (P.) glaucidiumi</i> ( <i>species inquirenda</i> )	Strigiformes: strigid (pygmy owls)			Neotropical
<i>H. (P.) globulosus</i> ( <i>species inquirenda</i> )	Passeriformes: fringillid (finches)	circum-nuclear		Palearctic (Spain)
<i>H. (P.) goodmani</i>	Coraciiformes: brachypteraciid (ground rollers)	halteridial		African
<i>H. (P.) greineri</i>	Anseriformes: anatid (ducks, geese, swans)	circum-nuclear		Holarctic
<i>H. (P.) halcyonis</i>	Coraciiformes: alcedinid (kingfishers)	halteridial		Oriental, Ethiopian, Palearctic
<i>H. (P.) handai</i> (syn. <i>desseri</i> )	Psittaciformes: cacatuid (cockatoos), psittaculid (parakeets, budgerigars, lorikeets, parrots) [megalomeront lesions in tissues]	circum-nuclear	Diptera: ceratopogonid ( <i>Culicoides nubeculosus</i> )	Australasian, Oriental, Ethiopian, Neotropical
<i>H. (P.) hartmanni</i>	Pelecaniformes: ardeid (night			Holarctic

( <i>species inquirenda</i> )	herons)			
<i>H. (P.) hedymelis</i>	Passeriformes: fringillid (grosbeaks, rosefinches)			Holarctic
<i>H. (P.) herodiadis (incertae sedis)</i>	Pelecaniformes: ardeid (herons, bitteren)	halteridial		Oriental, Holarctic
<i>H. (P.) hirundinis</i>	Passeriformes: hirudinid (swallows, martins)	halteridial		Holarctic, Ethiopian, Oriental
<i>H. (P.) indicator</i>	Piciformes: indicatorid (honeyguides)	halteridial		Ethiopian
<i>H. (P.) iwa</i>	Suliformes: fregatid (frigatebirds)	halteridial		Hawaii
<i>H. (P.) janovyi</i>	Falconiformes: falconid (hawks), cathartid (vultures)	circum-nuclear		Ethiopian
<i>H. (P.) kairullaevi</i>	Passeriformes: sturnid (starlings)	micro-halteridial		Palaearctic
<i>H. (P.) khani</i>	Passeriformes: dicurid (drongos)	circum-nuclear		African
<i>H. (P.) killangoi</i>	Passeriformes: zosteropid (white-eyes)	halteridial		Oriental, Ethiopian
<i>H. (P.) lairdi</i>	Coraciiformes: meropid (bee-eaters)	rhabdosomal		Ethiopian
<i>H. (P.) lanii</i>	Passeriformes: laniid (shrikes)	halteridial-circum-nuclear	Diptera: ceratopogonid ( <i>Culicoides impunctatus</i> )	Oriental, Ethiopian, Palaearctic
<i>H. (P.) larae (syn. lari)</i>	Charadriiformes: larid (gulls, terns)	circum-nuclear		Palaearctic, Ethiopian
<i>H. (P.) lophortyx</i>	Galliformes: phasianid (quail)	circum-nuclear	disputed (initially proposed to be hippoboscids <i>Stilbometopa impressa</i> , <i>Lynchia (Icosta) hirsuta</i> )	Holarctic, Ethiopian
<i>H. (P.) macropigmentatus</i>	Passeriformes: fringillid (finches, canaries)	halteridial		Holarctic, Ethiopian
<i>H. (P.) madagascariensis</i>	Passeriformes: vangid (vangas)	halteridial		African
<i>H. (P.) magnus</i>	Passeriformes: fringillid (finches)	halteridial-circum-nuclear		Palaearctic
<i>H. (P.) majoris (syn. machlolophi)</i>	Passeriformes: parid (tits), parulid (warblers)	halteridial		Holarctic, Ethiopian, Oriental
<i>H. (P.) mansonii (syn. canachites, meleagridis)</i>	Galliformes: phasianid (grouse, partridges, turkeys, pheasant) [megalomeront lesions in tissues, acute disease in turkeys]	halteridial-circum-nuclear	Diptera: ceratopogonid ( <i>Culicoides arboricola</i> , <i>edeni</i> , <i>haematopotus</i> , <i>hinmani</i> , <i>knowltoni</i> , <i>sphagnumemsis</i> )	Holarctic
<i>H. (P.) manwelli</i>	Coraciiformes: meropid (bee-eaters)	halteridial		Oriental
<i>H. (P.) mathislegeri (syn. herodiadis var. mathislegeri)</i>	Pelecaniformes: ardeid (little bitterns)	micro-halteridial		African, Palaearctic
<i>H. (P.) mazzai</i>	Passeriformes: fringillid (golden grosbeaks)	halteridial		Neotropical
<i>H. (P.) megapodius</i>	Galliformes: megapodid (scrubfowl)	micro-halteridial		Oriental
<i>H. (P.) meliornis (species inquirenda)</i>	Passeriformes: meliphagid (honey-eater)			Australasian
<i>H. (P.) meropis</i>	Coraciiformes: meropid (bee-eaters)	halteridial		Oriental, Ethiopian, Palaearctic
<i>H. (P.) minutus</i>	Passeriformes: turdid (blackbirds)	micro-halteridial		Palaearctic

<i>H. (P.) monarchus</i>	Passeriformes: monarchid (monarchs)	halteridial		Oriental, Ethiopian
<i>H. (P.) montezi</i>	Musophagiformes: musophagid (turacos)	halteridial		Ethiopian
<i>H. (P.) morneti</i>	Passeriformes: sturnid (glossy starlings, wattled starlings)			African
<i>H. moruony nomen dubium</i>	Passeriformes: muscicapid (shamas)			African, Oriental
<i>H. (P.) motacillae</i>	Passeriformes: motacillid (wagtails, pipits)	halteridial		Ethiopian, Oriental, Palearctic
<i>H. (P.) multiparasitans (species inquirenda)</i>	Strigiformes: strigid (little owls)			Palearctic
<i>H. (P.) nascimentoi (incertae sedis)</i>	Charadriiformes: charadriid (lapwings)	micro-halteridial		African
<i>H. (P.) nebraskensis (syn. noctuae var. nebraskensis)</i>	Strigiformes: strigid (horned owl)			Nearctic
<i>H. (P.) neseri</i>	Passeriformes: turdid (robin-chats)	halteridial		Ethiopian
<i>H. (P.) nettionis (syn. anatis, anseris, eulabeiae, gabaldoni, hermani)</i>	Anseriformes: anatid (ducks) [anaemia with heavy parasitaemia]	halteridial	Diptera: ceratopogonid ( <i>Culicoides downesi</i> )	cosmopolitan (except Antarctica)
<i>H. (P.) nipponensis</i>	Passeriformes: tyrannid (flycatchers)	halteridial-circum-nuclear		Oriental, Ethiopian
<i>H. (P.) nisi</i>	Falconiformes: falconid (hawks, eagles, buzzards, harriers, kites)	halteridial-circum-nuclear		Holarctic, Ethiopian, Oriental
<i>H. (P.) noctuae (syn. tytoni)</i>	Strigiformes: strigid (boobooks, eared owls, horned owls, little owls, owlets, pygmy owls, scops owls, true owls, wood owls), tytonid (barn owls): Falconiformes: falconid (falcons)	circum-nuclear		cosmopolitan (except Antarctica)
<i>H. (P.) nucleophilus</i>	Passeriformes: dicaeid (flowerpeckers), melanocharitid (berrypeckers)	micro-halteridial		Australasian
<i>H. (P.) orioli (syn. pintoii)</i>	Passeriformes: oriolid (orioles)	halteridial		Oriental, Ethiopian, Palearctic
<i>H. (P.) orizivorae (syn. paddae)</i>	Passeriformes: estrildid (seedcrackers, bluebills, waxbills), fringillid (finches)	halteridial		Oriental, Ethiopian, southern Palearctic
<i>H. (P.) ortalidum (syn. rotundus ortalidium)</i>	Galliformes: cracid (chachalacas, guans)	discosomal		Neotropical
<i>H. (P.) otocompsae</i>	Passeriformes: pycnonotid (bulbuls)	halteridial		Oriental, Ethiopian, South Palearctic
<i>H. (P.) pachycephalus</i>	Passeriformes: pachycephalid (whistlers)	micro-halteridial		Australasian, Oriental
<i>H. (P.) pallidus</i>	Passeriformes: tyrannid (flycatchers)	halteridial-circum-nuclear		Palearctic, Ethiopian
<i>H. (P.) parus</i>	Passeriformes: parid (tits)	discosomal		Nearctic
<i>H. (P.) passeris (syn. danilewskii var. urbanensis, garnhami, granulosum, gymnorhidis, wenyoni, zasukhini)</i>	Passeriformes: alaudid (crested larks, skylarks), cisticolid (tailorbirds), parulid (warblers), passerid (petronias, sparrows), ploceid (weavers) [megalomeront lesions in	halteridial		cosmopolitan (except Antarctica)

	tissues]			
<i>H. (P.) pastoris</i>	Passeriformes: sturnid (starlings, mynas)	halteridial		Oriental, Ethiopian, Palearctic
<i>H. (P.) payevskyi</i>	Passeriformes: parulid (warblers)	micro- halteridial		Palearctic, Ethiopian
<i>H. (P.) peircei</i>	Ciconiiformes: ciconiid (saddle-billed stork, yellow- billed stork)	circum-nuclear		African, Oriental
<i>H. (P.) pelouroi</i>	Ciconiiformes: threskiornithid (ibis)	micro- halteridial		Ethiopian
<i>H. (P.) philemon</i> ( <i>species inquirenda</i> )	Passeriformes: meliphagid (honey-sucker)			Australasian
<i>H. (P.) philippinensis</i>	Passeriformes: pycnonotid (bulbuls)	micro- halteridial		Oriental, Ethiopian, South Palearctic
<i>H. (P.) picae</i>	Passeriformes: corvid (magpies, crows, jays)	halteridial		Holarctic
<i>H. piresi</i> <i>nomen dubium</i>	Columbiformes: columbid (pigeons)			Holarctic
<i>H. (P.) pittae</i>	Passeriformes: pittid (pittas)	halteridial- circum-nuclear		Oriental
<i>H. (P.) platalea</i> (syn. <i>galathea</i> )	Ciconiiformes: ciconiid (storks), threskiornithid (spoonbills, ibis)	halteridial- circum-nuclear		cosmopolitan (except Antarctica)
<i>H. (P.) porzanae</i>	Gruiformes: rallid (crakes, rails, marsh hens)	micro- halteridial		Palearctic, New Guinea
<i>H. (P.) pratasi</i>	Galliformes: numidid (guineafowl)	halteridial		Ethiopian
<i>H. (P.) prognei</i>	Passeriformes: hirudinid (martins, swallows)	halteridial		Holarctic, Neotropical
<i>H. (P.) psittaci</i>	Psittaciformes: psittaculid (parrots)	micro- halteridial		Ethiopian
<i>H. (P.) ptilotis</i> ( <i>species inquirenda</i> )	Passeriformes: meliphagid (honeyeaters, friarbirds)	halteridial- circum-nuclear		Australasian
<i>H. (P.) quelea</i> ( <i>species inquirenda</i> )	Passeriformes: fringillid (finches), ploceid (weavers)	halteridial		Ethiopian, Oriental
<i>H. (P.) quiscalus</i>	Passeriformes: icterid (grackles, cowbirds), turdid (blackbirds)	halteridial		Nearctic, Neotropical
<i>H. raymundi</i> <i>nomen dubium</i>	Passeriformes: nectariniid (sunbirds)			Oriental
<i>H. (P.) rileyi</i> ( <i>species inquirenda</i> )	Galliformes: phasianid (peafowl, pheasant, partridges, quail, junglefowl)	halteridial		Oriental, Ethiopian, South Palearctic
<i>H. (P.) rotator</i>	Charadriiformes: glareolid (waders)	halteridial- circum-nuclear		Oriental (Philippines)
<i>H. rotundus</i> <i>nomen nudum</i>	Galliformes: phasianid (chachalacas, grouse): Charadriiformes: scolopacid (woodcock)			Palearctic, Neotropical
<i>H. (P.) sanguinis</i>	Passeriformes: pycnonotid (bulbuls)	micro- halteridial		Oriental, Ethiopian
<i>H. (P.) santosdiasi</i> ( <i>species inquirenda</i> )	Galliformes: phasianid (chickens, partridges)			Oriental
<i>H. (P.) savianae</i> ( <i>incertae sedis</i> )	Accipitriformes: accipitrid (lizard hawks, bald eagle)			African, Nearctic
<i>H. (P.) scolopaci</i>	Charadriiformes: glareolid (waders), scolopacid (woodcocks, phalaropes, sandpipers)	halteridial- circum-nuclear		Palearctic, Oriental
<i>H. (P.) sequeirae</i>	Passeriformes: nectariniid	halteridial		Oriental,

	(sunbirds)			Ethiopian
<i>H. (P.) serini</i> ( <i>species inquirenda</i> )	Passeriformes: fringillid (canary)			Nearctic
<i>H. (P.) silvai</i> ( <i>species inquirenda</i> )	Galliformes: numidid (guineafowl)			Oriental
<i>H. (P.) sitta</i>	Passeriformes: sittid (nuthatches)	halteridial		Oriental, Holarctic
<i>H. (P.) souzalopesi</i>	Passeriformes: muscicapid (flycatchers)	discosomal		Neotropical
<i>H. (P.) stableri</i>	Galliformes: phasianid (grouse)	circum-nuclear		Nearctic
<i>H. (P.) stellaris</i>	Passeriformes: hirudinid (swallows)	halteridial		Ethiopian
<i>H. (P.) sturni</i>	Passeriformes: sturnid (mynas, starlings)			cosmopolitan
<i>H. (P.) syrni</i> (syn. <i>phodili</i> )	Strigiformes: strigid (owls)	halteridial		Holarctic, Neotropical, Ethiopian, Oriental
<i>H. (P.) tartakovskyi</i>	Passeriformes: fringillid (crossbills, grosbeaks, siskins)	rhabdosomal	Diptera: ceratopogonid ( <i>Culicoides impunctatus</i> )	Palaearctic
<i>H. (P.) telfordi</i>	Otidiformes: otidid (bustards)	circum-nuclear		Ethiopian
<i>H. (P.) tendeiroi</i>	Otidiformes: otidid (bustards)	halteridial		African
<i>H. (P.) tephrodornis</i> ( <i>species inquirenda</i> )	Passeriformes: campephagid (cuckoo-shrikes)	halteridial		African, Oriental
<i>H. (P.) thereicerycis</i>	Piciformes: capitonid (barbets)	halteridial		Oriental, Ethiopian
<i>H. (P.) timalus</i>	Passeriformes: leiotherichid (sibas), timaliid (babblers), turdid (thrushes)	halteridial		Oriental, Ethiopian
<i>H. (P.) tinnunculi</i>	Falconiformes: falconid (falcons, kestrel); Accipitriformes: accipitrid (buzzards, eagles, harriers, kites, sparrowhawks)	halteridial- circum-nuclear		Holarctic, Ethiopian, Oriental
<i>H. (P.) trochili</i>	Apodiformes: apodid(hummingbirds)	halteridial		Neotropical
<i>H. (P.) trogonis</i>	Trogoniformes: trogonid (trogons)	halteridial		Oriental, Neotropical
<i>H. (P.) tyranni</i>	Passeriformes: tyrannid (flycatchers)	halteridial		Neotropical, Nearctic
<i>H. (P.) undulatus</i>	Coliiformes: coliid (mousebirds)	halteridial to circum-nuclear		Ethiopian
<i>H. (P.) upupae</i>	Bucerotiformes: upupid (hoopoes)	halteridial		Oriental, South Palaearctic
<i>H. (P.) uraeginthus</i>	Passeriformes: estrildid (cordonbleus)	rhabdosomal		Oriental
<i>H. (P.) vangii</i>	Passeriformes: vangid (vangas)	halteridial		African
<i>H. (P.) velans</i>	Piciformes: picid (woodpeckers, wrynecks)	circum-nuclear	Diptera: ceratopogonid ( <i>Culicoides</i> <i>sphagnumensis</i> , <i>stilobezzioides</i> )	Nearctic, Oriental
<i>H. vilhenai</i> <i>nomen dubium</i>	Anseriformes: anatid (spur- winged goose)			African
<i>H. (P.) vireonis</i>	Passeriformes: vireonid (vireos)	halteridial		Neotropical, Nearctic
<i>H. (P.) witti</i>	Apodiformes: apodid (hummingbirds)	halteridial		Neotropical (Jamaica)
<i>H. (P.) xantholaemae</i>	Piciformes: capitonid (barbets)	halteridial		Oriental, Ethiopian
<i>H. (P.) zosteropis</i> (syn. <i>johnstoni</i> )	Passeriformes: parulid (warblers), rhipidurid	halteridial		Oriental, Ethiopian,

	(fantails), zosteropid (white-eyes)			Australasian, Palearctic
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\**incertae sedis* (uncertain placement), *species inquirenda* (doubtful identity requiring further investigation), *nomen dubium* (doubtful name), *nomen nudum* (name unavailable due to lack of description, reference or indication)

**Parasite morphology:** *Haemoproteus* spp. form 6 different types of developmental stages: meronts and gametocytes in avian hosts; and gametes, ookinetes, oocysts and sporozoites in insect vectors. In birds, there are at least 2 generations of exo-erythrocytic merogony in host tissues before the appearance of gametocytes in blood cells (there is no erythrocytic merogony). Invading sporozoites form primary (first-generation) meronts which appear as basophilic bodies (10-100  $\mu\text{m}$ ) which become multinucleated as they divide internally to form numerous elongate merozoites (5-6  $\mu\text{m}$ ). Most meronts are rounded, but some may be elongate, vermiform, branched or even split into separate parts (cytomeres) containing several nuclei. Secondary meronts are similar in appearance and location, and further generations may persist contributing to relapses and chronic infections. Some parasite species also produce large ellipsoidal megalomeronts (200-500  $\mu\text{m}$ ) surrounded by thick hyaline walls and producing hundreds of small rounded merozoites (~1  $\mu\text{m}$ ). Merozoites from second and subsequent meront generations invade erythrocytes and transform directly into gametocytes (10-24 x 2-4  $\mu\text{m}$ ) which are often crescentic and curved around the host cell nucleus, although 5 morphogroups have been recognized: halteridial, microhalteridial (bilobulated), circum-nuclear, rhabdosomal (elongate) and discosomal (discoidal). Gametocytes are uninucleated and contain granular cytoplasm with brown-black pigment granules (haemozoin) as well as some violet volutin granules. They exhibit sexual dimorphism: with female macrogametocytes having more intensive cytoplasmic staining (due to abundant ribosomes), a compact nucleus with a nucleolus, and numerous scattered pigment granules; and male microgametocytes having a paler cytoplasm, a diffuse nucleus without a nucleolus, and pigment granules usually gather at either end. In insect vectors, microgametocytes produce and release 5-20 slender (10-18  $\mu\text{m}$ ) microgametes (process known as exflagellation) while macrogametocytes mature to form single robust (6-7  $\mu\text{m}$ ) macrogametes. Fertilization produces a motile zygote (ookinete) and becomes elongated (8-18  $\mu\text{m}$ ), develops a distal residual body containing most of the pigment granules, and those of some species may form short blunt or long digitiform outgrowths of the wall to aid attachment. The ookinete transforms into a rounded oocyst which undergoes sporogony to produce numerous sporozoites from germinative centres. In midge vectors, *Haemoproteus (Parahaemoproteus)* spp. form smaller oocysts (< 20  $\mu\text{m}$ ) that have one germinative centre producing < 100 long (> 10  $\mu\text{m}$ ) sporozoites. In hippoboscid vectors, *Haemoproteus (Haemoproteus)* spp. form larger oocysts (> 20  $\mu\text{m}$ ) with multiple germinative centres producing > 100 shorter (< 10  $\mu\text{m}$ ) sporozoites.

**Site of infection:** In birds, the parasites undergo several cycles of exoerythrocytic merogony in vascular endothelial cells and then fixed macrophages in various organs (mainly the lungs, liver and spleen, sometimes the kidneys, heart, skeletal muscles and skin). Some species also form large megalomeronts, usually within capillary endothelial cells and myofibroblasts in striated musculature (skeletal and cardiac muscles). Merozoites released into the circulation invade erythrocytes and develop into gametocytes. Around 180 haemoproteid species have been found in birds belonging to 90 families in 23 orders: including 6 *Haemoproteus (Haemoproteus)* spp. described in birds belonging to 12 families in 5 orders (mainly Columbiformes); and 170 *Haemoproteus (Parahaemoproteus)* spp. in birds belonging to 82 families in 22 orders (mainly Passeriformes (45 families)). It has been estimated from discordant data-base records that haemoproteid infections have so far been found in around 2,200 bird species (around 20% of the global avifauna). The host specificities of the different parasite species remain to be established. Epidemiological observations and some experimental transmission studies suggest specificity may operate at level of bird family (or even order), but there are numerous contradictory findings suggesting it may wider than expected. In dipteran vectors, gametes and fertilization occur in the gut while the motile ookinete penetrates the peritrophic membrane and develops into an oocyst under the basal lamina, ultimately producing sporozoites and releasing them into the haemocoel where they invade the salivary glands. Little is known about the extent of vector specificity for most parasite species, but it is an important distinguishing character for differentiating subgenera, with *Haemoproteus (Haemoproteus)* spp. utilizing hippoboscid louse flies, and *Haemoproteus (Parahaemoproteus)* spp. using ceratopogonid biting midges, sometimes culicid mosquitoes, as vectors.

**Pathogenesis:** Birds are hosts for both tissue and blood stages of haemoproteid parasites. The proliferative tissue stages (meronts) ultimately result in host cell lysis to liberate parasite progeny, but infections by most species are benign because few meronts are involved and they are small fast transient stages causing little inflammation. The exceptions are those species that form numerous meronts or large megalomeronts which can damage tissue integrity resulting in structural and functional abnormalities. Heavy infections in pigeons have been associated with capillary blockages leading to airsac congestion, pneumonia-like symptoms, hepatosplenomegaly with pigment deposits, anaemia, anorexia, restlessness and occasional deaths, particularly in young squabs. Megalomeronts in ducklings and chickens have caused cardiomyopathies, and infections in turkeys and currawongs have caused seasonal lethal myopathies in several countries. Megalomeronts in other birds, especially parrots, have caused intense inflammation in various tissues and their rupture has been associated with the formation of necrotic nidi, calcificates and myopathies. In contrast, the blood stages (gametocytes) do not proliferate in host cells but reside as persistent transmissive stages. Parasitaemias are usually low (< 0.1%) although higher parasitaemias (up to 30%) may occasionally be found in individual birds but apparently with little effect on host. In some instances, mild anaemia may develop in the course of infection, due not to overt haemolysis but to erythrophagocytosis when infected cells are removed from the circulation by reticuloendothelial cells of the spleen, liver, bone marrow and some other organs. Hepatosplenomegaly may result due to hyperplasia of lymphoid-macrophage cells, and organ rupture may occasionally occur due to accumulations of insoluble pigments. Infections in birds often become chronic, with

parasitaemia maintained for weeks-months by successive cycles of merogony. Relapses of infection have also been recorded, often coincident with the onset of bird reproduction. There is also growing evidence suggesting that subclinical but persistent haemoproteid infections may reduce host fitness by decreasing growth rates (especially around peak parasitaemias), change food acquisition behaviours (birds become more sedentary), altering fright behaviours (hide rather than flight), and affecting migration success (poorer accumulation of migratory fat reserves).

**Developmental cycle and mode of transmission:** *Haemoproteus* spp. have obligative heteroxenous (2-host) life-cycles involving asexual proliferation in birds (acting as intermediate hosts) and sexual development in dipteran vectors (acting as definitive hosts). Vector-borne transmission occurs when haematophagous dipteran insects feed on bird blood. Sporozoites injected into birds invade endothelial cells in various tissues and undergo asexual multiplication (merogony) by internal division (endogeny) producing numerous merozoites usually within 5 days. The merozoites invade new host cells (often fixed macrophages) and undergo another round of merogony, although some species may also form large megalomeronts in host muscles producing hundreds of merozoites over several weeks. Further merogonous generations may occur in host tissues which facilitates relapses and chronic infections. After at least 2 merogonous cycles, merozoites may then invade host erythrocytes where they do not divide further but transform over 2-6 days into gametocytes (male and female). The prepatent period (time from infection to first appearance of gametocytes) ranges from 11-21 days. The longevity of gametocytes in host erythrocytes is not known, but parasitaemias may persist for long periods (being replenished by merozoites from tissue meronts). Dipteran vectors become infected when they ingest erythrocytes containing gametocytes with their bloodmeals. Although the life-cycles for many parasite species have yet to be determined, studies have implicated different vectors for members of each subgenus. Infections by species in the subgenus *Haemoproteus* are transmitted by hippoboscids, while those in the subgenus *Parahaemoproteus* are transmitted by ceratopogonid biting midges (one species, *H. (P.) coatneyi*, has also been reported to develop in culicid mosquitoes). Within the vectors, the ingested gametocytes complete gamete development within the gut, with male microgametocytes exflagellating to produce microgametes which fertilize female macrogametes. The resultant zygote (ookinete) is motile and invades the gut wall to form an oocyst under the basal lamina in the external wall. The oocysts undergo asexual division from germinative centres to produce numerous sporozoites which are released into the haemocoel and invade the salivary glands. In hippoboscid vectors, oocysts are larger and take more than 10 days to produce hundreds of small sporozoites. In midge vectors, oocysts are smaller and take less than 10 days to produce less than 100 long sporozoites (the quicker development and release of sporozoites accommodates the shorter gonadotrophic cycles of these vectors allowing parasites to be ready for transmission the next time the vector feeds). Birds become infected when vectors feed on their blood injecting saliva containing sporozoites into feeding sites (inoculative transmission). Birds vary enormously in their susceptibility/resistance to infection, with younger birds being more susceptible and infections accumulating in birds with higher exposure to vectors. The abundance, distribution and activity of vectors is often a function of climate, with summer rises in populations recorded in warmer regions. In birds that migrate long distances in order to feed and/or breed, studies have shown infections to be more prevalent in feeding sites where birds overwinter rather than breeding sites. Risk factors for infections include bird species that have open nests or ground nests, produce offspring that stay longer in nests, and those that congregate together in large colonies.

**Differential diagnosis:** Infections may be diagnosed by the direct microscopic detection of intra-erythrocytic gametocytes in fixed thin blood smears stained with Giemsa or Leishman's stains. Multiple serial samples may need to be examined as parasitaemias may be low or intermittent. Merogonous stages may be detected in tissues by the microscopic examination of impression smears or histological sections of tissues/organs collected at autopsy. Several experimental studies have reported some success in maintaining blood samples *in vitro* in moist chambers to induce gametocyte exflagellation, fertilization and ookinete development. Infections may be detected in insect vectors by dissection and examining squash preparations or salivary gland extracts. More recently, great success has been achieved using molecular biological techniques to detect and characterize parasites in birds and vectors following the polymerase chain reaction (PCR) amplification of nuclear (small subunit (18S) ribosomal DNA) and mitochondrial (cytochrome b, cytochrome c oxidase subunits 1 and 3) gene sequences.

**Treatment and control:** Because most infections in birds are asymptomatic, treatment is usually not required. When clinical disease is apparent, parasites are often present as proliferative meronts within host tissues. Treatment with conventional antimalarial drugs may not be effective as many are not active against exo-erythrocytic tissue stages. However, good success has been reported treating infections in poultry, pigeons and raptors using quinacrine, chloroquine and bupavaquone, and moderate success using atebriane and plasmochine (despite some toxicity issues). Preventive control measures applicable to farmed and aviary birds basically involve screening new stock for infections and isolating birds from vectors by protecting holding facilities using screen barriers, insect traps, topical or environmental insecticides, and eliminating potential breeding sites (clearing moist organic wastes and vegetation).

# Haemoproteus

2 subgenera:

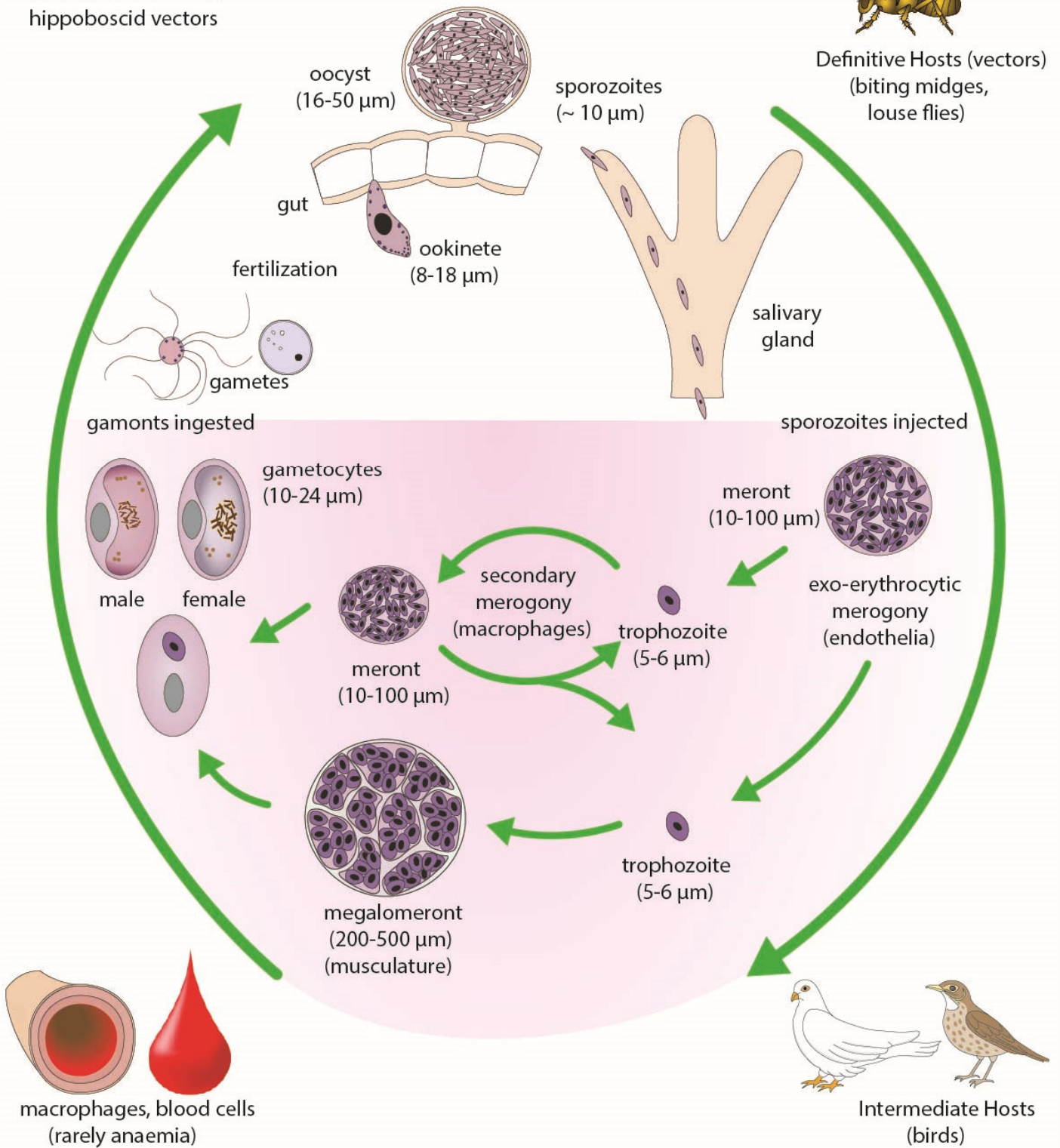
*H. (Parahaemoproteus)*  
mainly in passeriform birds  
with ceratopogonid vectors

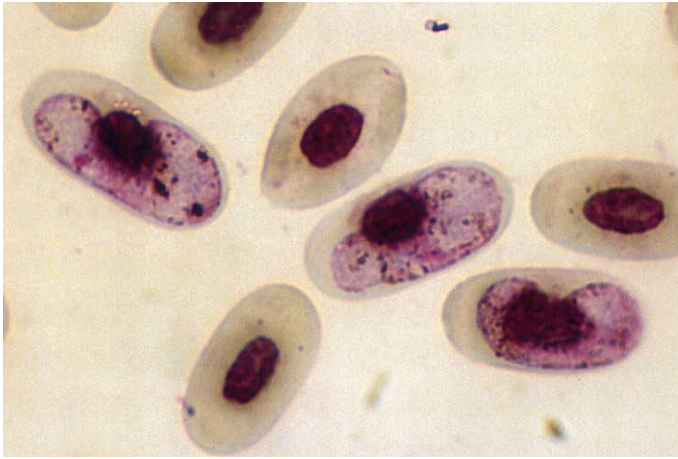
*H. (Haemoproteus)* in  
columbiform birds with  
hippoboscid vectors

heteroxenous (2-host) cycle  
vector-borne transmission  
(sexual development in invertebrate host)  
(asexual development in vertebrate host)

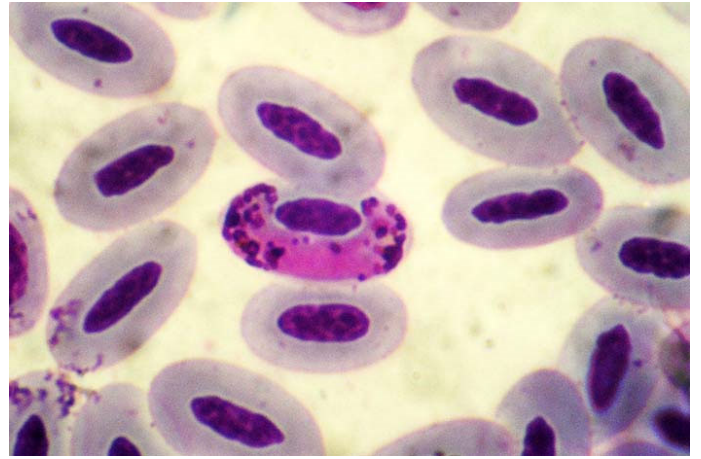


Definitive Hosts (vectors)  
(biting midges,  
louse flies)

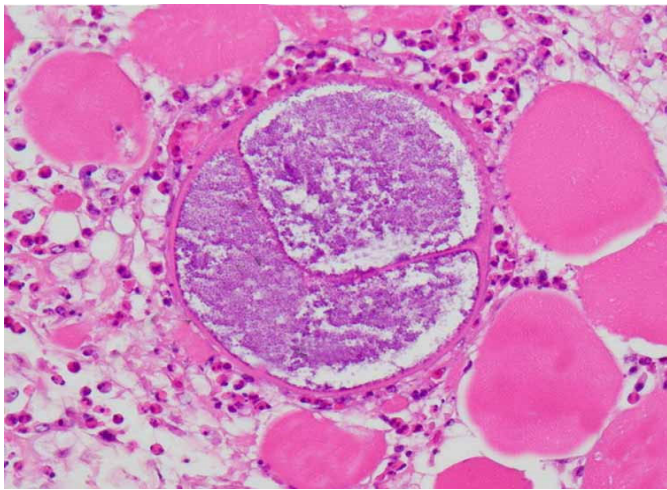




*Haemoproteus* gametocytes in bird blood



*Haemoproteus* gametocyte in bird blood



*Haemoproteus* megalomeront in bird muscle