

Hepatozoon

(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. Three groups of coccidia are recognized: coelotrophiid coccidia in marine annelids; adeleid coccidia (including the blood parasites paradoxically known as 'haemogregarines') in marine and terrestrial animals; and eimeriid coccidia in vertebrates. Haemogregarines are heteroxenous (2-host) parasites where merogony and gamogony occurs in the vascular system of a vertebrate host while sporogony occurs in a haematophagous invertebrate host (vector). They are common blood parasites in reptiles and some occur in fish, amphibians, birds and mammals. Four main assemblages are recognized: haemogregarinids, karyolysids, hepatozoids and dactylosomatids. Hepatozoids (*Hepatozoon*) produce oocysts containing numerous sporocysts in the gut or haemocoel of various vectors (leeches, insects, acarines). Vertebrates are infected by ingesting vectors, and merogony (= schizogony) occurs in vascular endothelial cells prior to the formation of gamonts in erythrocytes and/or leucocytes. Cystic stages have been associated with tissue lesions and may contribute to persistent infections. Given the paucity of information on the developmental biology of most species, it has been suggested that all members of the genus *Haemogregarina* in snakes, crocodiles, lizards, amphibians, birds and mammals (but not tortoises or fish) be transferred to the genus *Hepatozoon* pending determination of their vectors and developmental cycles.

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: Coccidiorhyncha [Conoidasida] (with conoid)
Subclass: Coccidia [Coccidiasina] (small intracellular gamonts)
Order: Eucoccidiorida (cyclic merogony (schizogony), gamogony, sporogony)
Suborder: Adeleina (syzygy, 1-4 microgametes)
Family: Haemogregarinidae (ookinete, gamonts in blood cells, invertebrate vectors)
Genus: *Hepatozoon* (vector-borne tissue parasites)
Species: various species cause infections in rodents and domestic animals

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 endogeny (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: Gregarinomorpha (gregarines, trophonts with specialized attachment epimerite or mucron, syzygy)					
Subclass: Cryptogregaria (epicellular parasites of vertebrates with feeder organelle but lacking apicoplast)					
	Cryptosporidiidae (naked sporozoites)	<i>Cryptosporidium</i>	vertebrates	gut, lungs	direct (f-o)
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>Isoospora</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</i> (<i>Frenkelia</i>)	mammals, birds, reptiles	gut, muscles	indirect (p-p)	
subfamily: Toxoplasmatinae (thin-walled cysts without metrocytes)	<i>Besnoitia</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: 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</i> (<i>Akiba</i>)	birds	tissues, leucocytes	indirect (v-b)
Order: Piroplasmorida (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)

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

Haemogregarines are heteroxenous (2-host) parasites where merogony (= schizogony) and gamogony occurs in the vascular system of a vertebrate intermediate host while fertilization and sporogony occurs in a haematophagous invertebrate definitive host (vector). They are common blood parasites in reptiles and fish and some occur in amphibians, birds and mammals. Infections are generally considered to be nonpathogenic, even when high parasitaemias are present. Haemogregarines are classified together with other coccidia, specifically with the adeleorine coccidia in marine and terrestrial animals. These parasites undergo sexual reproduction involving the formation of macro- and micro-gametes which associate pairwise in syzygy so comparatively few microgametes are produced (usually 1-4). The resultant zygote forms an oocyst containing infective sporozoites which are

transmitted to vertebrates when infected vectors are eaten (consumptive) or when they feed on vertebrate blood (inoculative). Over 450 haemogregarine species have been described in vertebrate blood, most records being confined to the detection of intra-erythrocytic stages (almost exclusively gamonts) which do not produce haemozoin pigment. Numerous species were described simply on the basis of host occurrence but little is known about their actual host specificity or developmental cycles. Despite early confusion, there has been growing acceptance of the recent classification of haemogregarines into four families: Haemogregarinidae containing the genera *Haemogregarina*, *Cyrlia* and *Desseria*; Hepatozoidae containing the genus *Hepatozoon*; Karyolysidae containing the genera *Karyolysus* and *Hemolivia*; and Dactylosomatidae containing the genera *Dactylosoma* and *Babesiosoma* (in addition to 3 other adeleine families: Adeleidae, Klossiellidae and Legerellidae). It has been suggested that the chelonian (tortoise) haemogregarines be regarded as *Haemogregarina sensu stricto* (*s.s.*, in the strictest sense) whereas fish haemogregarines be classified as *Desseria* or *Cyrlia* or left as *Haemogregarina sensu lato* (*s.l.*, in the broadest sense). It was also suggested that all members of the genus *Haemogregarina* in non-chelonian reptiles (snakes, crocodiles, lizards), amphibians, birds and mammals be transferred to the genus *Hepatozoon* pending determination of their vectors and studies on their developmental cycles. All haemogregarines use vertebrates as intermediate hosts for cyclic merogony (often forming macro- then micro-merozoites) in tissues and gamont development in blood cells (mostly red, sometimes white, blood cells). Gamogony is completed in invertebrate definitive hosts (leeches, acarines or dipterans) followed by fertilization and oocyst formation in the gut or haemocoel. The oocysts undergo sporogony resulting in sporozoites lying directly within oocysts (for Dactylosomatidae), within sporocysts (for Hepatozoidae), within tissues (for Haemogregarinidae) or within eggs (for Karyolysidae). The four families are currently differentiated as follows:

- Haemogregarinids produce oocysts with naked sporozoites in the gut of leech vectors, vertebrates are infected by vector bite, and schizogony occurs in host erythrocytes (although infected cells tend to be sequestered in viscera prior to the development of intraerythrocytic gamonts); genera comprise *Haemogregarina s.s.* in turtles and *Haemogregarina s.l.*, *Desseria* and *Cyrlia* in fish.
- Hepatozoids produce oocysts containing numerous sporocysts in the gut or haemocoel of various vectors (leeches, insects, acarines), vertebrates are infected by ingesting vectors, and schizogony occurs in vascular endothelial cells in host tissues (cystic stages also observed contributing to chronic infections and possible paratenic transport); the genus *Hepatozoon* occurs in mammals, reptiles (crocodiles, snakes, lizards), amphibians and birds.
- Karyolysids produce sporokinetes and motile spores in the gut and ova of mite vectors, vertebrates are infected by ingesting mites, and schizogony occurs in host vascular endothelial cells; genera comprise *Karyolysus* and *Hemolivia* in reptiles and amphibians.
- Dactylosomatids produce oocysts which bud sporozoites directly within epithelial cells in the intestines of leech vectors, vertebrates are infected presumably by vector bite and schizogony occurs in host erythrocytes; genera comprise *Dactylosoma* and *Babesiosoma* in reptiles, amphibians and fish.

Family	Genus	No. species	Site of development in vertebrate		Vertebrate hosts	Invertebrate vector
			meronts	gamonts		
Haemogregarinidae	<i>Haemogregarina</i>	<i>s.s.</i> 38; <i>s.l.</i> 42	erythrocytes	erythrocytes	<i>s.s.</i> in turtles; <i>s.l.</i> in fish	leeches
	<i>Cyrlia</i>	3	erythrocytes	erythrocytes	fish	leeches
	<i>Desseria</i>	35	exo-erythrocytic	erythrocytes	fish	leeches
Hepatozoidae	<i>Hepatozoon</i>	341*	viscera	erythrocytes, leucocytes	mammals, reptiles, birds, frogs, fish	leeches, arthropods
Karyolysidae	<i>Hemolivia</i>	4	RE cells	erythrocytes	lizards, tortoises, toads	ticks
	<i>Karyolysus</i>	11	viscera ± erythrocytes	erythrocytes	lizards, frogs	mites
Dactylosomatidae	<i>Dactylosoma</i>	10	erythrocytes	erythrocytes	reptiles, amphibians, fish	leeches
	<i>Babesiosoma</i>	12	erythrocytes	erythrocytes	fish, amphibians	leeches

*Includes some 200 former *Haemogregarina* spp. from crocodiles, snakes, lizards, amphibians and birds following their mass transfer to the genus *Hepatozoon* pending further characterization

Early phylogenetic studies used cladistics analyses of multiple phenotypic characters (morphology, biology) to reveal several clades apparently associated with different vectors (notably ticks, flies and leeches) rather than particular vertebrate hosts, thus suggesting vector-first evolution. However, such patterns may have arisen due to the environments in which the hosts occurred; e.g. marine hosts with leeches, and terrestrial hosts with ticks or flies. Molecular phylogenetic studies using small subunit (18S) ribosomal RNA sequences revealed any associations between haemogregarines and their vertebrate hosts to be polyphyletic with many mixed clades associated with parasites in snakes, lizards, amphibians and mammals. Detailed analyses revealed five major clades: two *Hepatozoon* clades (clade A associated with carnivores and clade C with reptiles and frogs) separated by an

intermediary *Hemolivia* clade in lizards, and two distant clades, one containing *Haemogregarina* species from tortoises and the other containing *Dactylosoma/Babesiosoma* species from fish and frogs. The five major clades were also well separated with respect to vectors: the former three clades using ticks and flies as vectors and the latter two using leeches. The *Hepatozoon* species in mammals (clade A) were more closely related to *Karyolysus* species from lizards, while the *Hepatozoon* species in frogs and reptiles (clade C) were more closely related to *Hemolivia* species from tortoises and lizards. Several interesting biological associations were evident between polyphyletic clades. *Haemogregarina* s.s. and dactylosome clades use leech vectors without sporocyst formation, and they only formed micro-merozoites in their turtle, frog or fish hosts. In contrast, members of the *Hepatozoon*, *Karyolysus* and *Hemolivia* clades use tick vectors with sporocyst (or sporokinete) formation, and they formed macro-merozoites in their mammal or reptile hosts. Given that *Hepatozoon* did not form a single monophyletic group, it was recently suggested that species from reptiles, amphibians, marsupials, birds and rodents that are transmitted solely by biting insects be transferred to a new genus *Bartazoon*. However, subsequent studies indicated that this genus was not well-supported, so many workers do not recognize *Bartazoon* over *Hepatozoon*.

Infections by *Hepatozoon* spp. have been recorded in tropical and subtropical areas in various vertebrate (reptiles, amphibians, birds, mammals), mostly by the detection of gamonts within erythrocytes and/or leucocytes and the absence of merogonic division in peripheral blood. Instead, merogony occurs with endothelial cells in host tissues, sometimes persisting as cystic forms (monozytic or dizyotic) thus contributing to chronic infections (and potentially paratenic transport). For those few species in which the vectors have been determined, transmission from vertebrate to invertebrate occurs during vector blood-feeding, while transmission from invertebrate to vertebrate occurs by the consumption of infected vectors (and not by inoculation through vector bite). Invertebrate vectors have included acarines (mites, ticks), insects (fleas mosquitoes, bugs) and leeches, in which large multisporecystic oocysts are formed within their internal tissues (whereas *Haemogregarina* spp. have leech vectors in which small asporocystic oocysts are formed). Regrettably, the vectors and sporogonous cycles for many species are not known, so their generic placement is uncertain. Studies conducted on several *Haemogregarina* spp. from snakes, lizards and birds revealed that they had arthropod vectors and formed multisporecystic oocysts, so it was suggested that they be transferred to the genus *Hepatozoon*. It was further suggested that all *Haemogregarina* spp. from non-chelonian reptiles and birds (around 200 species) be similarly transferred to the genus *Hepatozoon* pending identification of their vectors and developmental cycles. This follows the earlier precedents of mass transfers of *Haemogregarina* spp. described from birds and mammals, as well as many non-avian *Leucocytozoon* spp., to the genus *Hepatozoon*. To date, over 340 putative *Hepatozoon* spp. have been described, with 509 spp. in mammals, 139 spp. in snakes, 76 spp. in lizards, 6 spp. in crocodiles, 1 sp. in tortoise, 49 spp. in amphibians and 20 spp. in birds. In the following species lists, synonyms have been provided to provide context to the origins and taxonomic status of the *Hepatozoon* spp.

<i>Hepatozoon</i> species	Gamont dimensions (µm)	Hosts	Location* (disease)	Vectors	Distribution
species in mammals (Mammalia)					
<i>H. acomys</i>		Rodentia: murid (spiny mice)	rbc		Africa, Middle-East
<i>H. akodoni</i> (syn. <i>Haemogregarina</i> , <i>Leucocytozoon</i>)		Rodentia: murid (grass mouse)	wbc		South America
<i>H. alactagae</i> (syn. <i>H. alactaguli</i>)		Rodentia: dipodid (five-toed jerboa, northern three-toed jerboa, thick-tailed three-toed jerboa, dwarf fat-tailed jerboa)	rbc		Asia
<i>H. americanum</i>	8.8 x 3.9	Carnivora: canid (dogs, coyotes, foxes)	wbc	Acari: ixodid (<i>Amblyomma maculatum</i>)	North America, Brazil
<i>H. arvalis</i> (syn. <i>Leucocytozoon</i>)		Rodentia: murid (African grass rat)	wbc		Africa
<i>H. arvicanthis</i> (syn. <i>H. arvicanthis</i>)		Rodentia: murid (African grass rat)	wbc		Africa
<i>H. arvicolae</i> (syn. <i>Karyolysus</i>)		Rodentia: cricetid (water vole)	blood cells		Eurasia
<i>H. balfouri</i> (syn. <i>Haemogregarina</i> , <i>H. jaculi</i>)		Rodentia: dipodid (jerboas)	wbc (pathogenic experimentally)	Acari: laelapid (<i>Haemolelaps aegyptius</i> , <i>longipes</i> , <i>centrocarpus</i>)	North Africa
<i>H. canis</i> (syn. <i>Leucocytozoon</i> , <i>Leucocytozoon</i>)	11 x 4.3	Carnivora: canid (dog, coyote, black-backed jackal, golden jackal,	wbc (fever, anaemia,	Acari: ixodid (<i>Rhipicephalus sanguineus</i> ,	Europe, Middle-East, Far East,

<i>Haemogregarina, H. rotundata, chattoni, pattoni, Microbesnoitia leoni</i>		crab-eating fox, red fox, hoary fox, Pampas fox, spotted hyena); procyonid (coati), viverrid (Asian palm civet), felid (cat, cheetah, lion, leopard); Perissodactyla: tapirid (tapir); Didelphimorphia: didelphid (white-eared opossum)	weight loss, splenomegaly, paralysis?)	<i>decoloratus, microplus, Amblyomma cajennense, maculatum, ovale, sculptum, Haemaphysalis concinna, flava, longicornis, Ixodes ricinus</i>	Africa, Americas
<i>H. citellicolum</i> (syn. <i>Leucocytozoon</i>)		Rodentia: sciurid (ground squirrel)	wbc		North America
<i>H. criceti</i> (syn. <i>Leucocytozoon</i>)		Rodentia: cricetid (European hamster)	wbc	Acari: laelapid (<i>Laelaps echidninus</i>)	Eurasia
<i>H. cricetomysi</i>		Rodentia: nesomyid (Gambian pouched rat)	rbc		Africa
<i>H. cuniculi</i> (syn. <i>Leucocytozoon</i>)		Lagomorpha: leporid (rabbit)	wbc		Europe
<i>H. darjeelingensis</i>		Rodentia: sciurid (flying squirrel)	rbc		Asia
<i>H. dasyuri</i> (syn. <i>Haemogregarina</i>)		Dasyuromorphia: dasyurid (eastern quoll)	rbc		Australia
<i>H. dendromi</i> (syn. <i>H. dendromysi, dendromusi</i>)		Rodentia: nesomyid (African climbing mouse)	rbc		Africa
<i>H. didelphydis</i> (syn. <i>Haemogregarina</i>)		Didelphimorphia: didelphid (American opossum, brown four-eyed opossum, gray four-eyed opossum)	rbc		Americas
<i>H. dolichomorphon</i>		Rodentia: anomalurid (long-eared flying mouse)	wbc		Africa
<i>H. epsteini</i>		Rodentia: murid (brown rat)	wbc		cosmopolitan
<i>H. erhardovae</i>		Rodentia: cricetid (bank vole)	wbc	Siphonaptera: pulicid (<i>Xenopsylla cheopis</i>), hystrihopsyllid (<i>Ctenophthalmus agyrtes, assimilis</i>), ceratophyllid (<i>Nosopsyllus fasciatus</i>)	Eurasia
<i>H. felis</i> (syn. <i>H. felisdomesticae, Haemogregarina felisdomesticae, Leucocytozoon felisdomestici</i>)	10.5 x 4.7	Carnivora: felid (cat, wildcat, serval, leopard cat, iriomote cat, jaguar, lion, tiger, caracal, puma, Eurasian lynx)	wbc	Acari: ixodid (<i>Rhipicephalus sanguineus</i>)	India, Europe, Americas, Africa
<i>H. funambuli</i> (syn. <i>Leucocytozoon</i>)		Rodentia: sciurid (palm squirrel)	wbc		Indo-Asia
<i>H. gaetulum</i> (syn. <i>H. getulum</i>)		Rodentia: sciurid (Barbary ground squirrel)	wbc		North Africa
<i>H. gerbilli</i> (syn. <i>Haemogregarina</i>)		Rodentia: murid (great gerbil, Indian gerbil, Libyan jird)	rbc	Phthiraptera: haematopinid (<i>Haematopinus stephensi</i>)	Asia
<i>H. graomysi</i>		Rodentia: cricetid (gray leaf-eared mouse)	rbc		South America
<i>H. griseisciuri</i>		Rodentia: sciurid	wbc	Acari: laelapid	North

		(eastern grey squirrel)		(<i>Echinolelaps echidninus</i>), haemogamasid (<i>Euhaemogamasus ambulans</i> , <i>Haemogamasus reidi</i>)	America
<i>H. hoogstraali</i>		Afrosoricida: tenrecid (lowland streaked tenrec)	rbc		Madagascar
<i>H. insectivorae</i>		Eulipotyphla: soricid (common shrew, bicoloured shrew)	wbc		Eurasia
<i>H. krampitzi</i> (syn. <i>H. microti p.p.</i>)		Rodentia: cricetid (tundra vole)	wbc		Europe, Asia, North America
<i>H. leporis</i> (syn. <i>Leucocytozoon</i>)		Lagomorpha: leporid (Indian hare)	wbc		Indo-Asia
<i>H. leptosoma</i>		Rodentia: cricetid (deer mouse, brush mouse)	wbc		North America
<i>H. luiperdje</i>		Carnivora: felid (leopard)	wbc		Africa
<i>H. lusitanicum</i>		Rodentia: glirid (garden dormouse)	wbc		Eurasia
<i>H. mereschkowskii</i>		Rodentia: sciurid (speckled ground squirrel, Caucasian ground squirrel)	wbc		Eastern Europe
<i>H. metachiri</i> (syn. <i>Haemogregarina</i>)		Didelphimorphia: didelphid (quica opossum)	rbc		South America
<i>H. microti</i> (syn. <i>H. lavieri</i> , <i>micratai</i> , <i>sylvatici</i> , <i>Haemogregarina</i>)		Rodentia: cricetid (field vole); dipodid (Severtzov's jerboa); murid (wood mouse, yellow-necked mouse, broad-toothed field mouse); plus exptl. infection in cricetid (bank vole)	wbc	Acari: laelapid (<i>Laelaps agilis</i>)	Europe, North Africa
<i>H. muris</i> (syn. <i>H. innoxia</i> , <i>perniciosus</i> , <i>ratti</i> , <i>Haemogregarina</i> , <i>H. ratti</i> , <i>Leucocytozoon</i> , <i>L. ratti</i> , <i>Leucocytozoon</i> <i>innoxia</i>) [type species]		Rodentia: murid (rats, Tullberg's soft-furred mouse)	wbc (pathogenic experimentally)	Acari: laelapid (<i>Laelaps echidninus</i>)	cosmopolita n
<i>H. mustelis</i>	nd	Carnivora: mustelid (Siberian polecat)	macrophages		Eurasia, North America
<i>H. musculi</i> (syn. <i>Leucocytozoon</i> , <i>Leucocytozoon</i> <i>innoxia</i>)		Rodentia: murid (house mouse)	wbc		cosmopolita n
<i>H. normani</i>		Rodentia: anomalurid (long-eared flying mouse)	wbc		Africa
<i>H. peramelis</i> (syn. <i>Haemogregarina</i>)		Peramelemorphia: peramelid (long-nosed bandicoot)	blood plasma		Australia
<i>H. perniciosum</i>		Rodentia: murid (laboratory white rat)	liver, wbc	Acari: laelapid (<i>Echinolaelaps echidninus</i>)	North America
<i>H. peromysci</i>		Rodentia: cricetid (brush	wbc		North

<i>H. bitis</i> (syn. <i>Haemogregarina</i>)		viperid (puff adder)	rbc		Africa
<i>H. boigae</i> (syn. <i>Haemogregarina</i>)		colubrid (green tree snake, brown tree snake)	rbc		Australia
<i>H. boodoni</i> (syn. <i>Haemogregarina</i>)		colubrid (African house snake)	rbc		Africa
<i>H. bornandi</i> (syn. <i>Haemogregarina</i>)		colubrid (grass snake)	rbc		Eurasia
<i>H. bradfordi</i> (syn. <i>Haemogregarina</i>)		colubrid (banded water snake)	rbc		North America
<i>H. brendae</i> (syn. <i>Haemogregarina</i>)		colubrid (short-snouted grass snake)	rbc		Africa, Asia
<i>H. brumpti</i> (syn. <i>Haemogregarina</i>)		colubrid (pine snake)	rbc		North America
<i>H. bungari</i> (syn. <i>Haemogregarina</i> , <i>Laverania</i>)		elapid (banded krait)	rbc		India, Asia
<i>H. calligaster</i> (syn. <i>Haemogregarina</i>)		colubrid (northern tree snake)	rbc		Australia
<i>H. cantliei</i> (syn. <i>Haemogregarina</i>)		boid (sand boa)	rbc		South America
<i>H. capsulata</i> (syn. <i>Haemogregarina</i>)		viperid (tropical rattlesnake)	rbc		South America
<i>H. carinacauda</i>	23-25 x 5-6	colubrid (Wied's keelback)	rbc	Hirudinea: glossiphoniid (<i>Haememteria lutzi</i>)	Brazil
<i>H. cenchridis</i> (syn. <i>Haemogregarina</i>)		boid (rainbow boa)	rbc		South America
<i>H. cevapii</i>	15-20 x 2-4	viperid (neotropical rattle snake)	rbc		South America
<i>H. chartusica</i> (syn. <i>Haemogregarina</i>)		colubrid (spotted desert racer)	rbc		West Asia
<i>H. chironii</i> (syn. <i>Haemogregarina</i>)		colubrid (Boettger's sipo)	rbc		South America
<i>H. colubri</i> (syn. <i>Haemogregarina</i>)		colubrid (false coral, spotted desert racer, Asian racer, Aesculapian snake)	rbc		South America, South Asia
<i>H. confusus</i>	14-17 x 3.5-5	colubrid (eastern racer)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. corallus</i> (syn. <i>Haemogregarina</i>)		boid (Amazon tree boa)	rbc		South America
<i>H. coronellae</i> (syn. <i>Haemogregarina</i>)		colubrid (southern smooth snake)	rbc		Europe
<i>H. crotali</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		viperid (diamondback rattlesnake, tropical rattlesnake)	rbc		North and South America
<i>H. crotaphopeltis</i> (syn. <i>Haemogregarina</i>)		colubrid (herald snake)	rbc		Africa
<i>H. cuestensis</i>	14-19 x 2-5	viperid (neotropical rattle snake)	rbc		South America
<i>H. cyclagrasii</i> (syn. <i>Haemogregarina</i>)		colubrid (false water cobra)	rbc		South America
<i>H. darwiniensis</i> (syn. <i>Haemogregarina</i>)		elapid (king brown snake)	rbc		Australia
<i>H. dendrophidis</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		colubrid (green tree snake)	rbc		Australia
<i>H. denisoniae</i> (syn. <i>Haemogregarina</i>)		elapid (northern small-eyed snake, marsh snake, red-bellied black snake, tiger snake)	rbc		Australia

<i>H. digueti</i> (syn. <i>Haemogregarina</i>)		viperid (massasauga)	rbc		North America
<i>H. dogieli</i> (syn. <i>Haemogregarina</i>)		viperid (Gaboon viper)	rbc		Africa
<i>H. domerguei</i>	14 x 3	lamprophiid (Madagascar night snake); transmissible to lamprophiid (blonde hognose); pythonid (African rock python); Sauria: lacertid (common wall lizard, ruin lizard, viviparous lizard), oplurid (Madagascar swift)	rbc	Diptera: culicid (<i>Culex pipiens</i> , <i>Anopheles stephensi</i>)	Madagascar
<i>H. drymobii</i> (syn. <i>Haemogregarina</i>)		colubrid (Rio tropical racer)	rbc		South America
<i>H. echisi</i> (syn. <i>Haemogregarina</i>)		viperid (saw-scaled viper)	rbc		Indo-Asia
<i>H. eidsvoldensis</i> (syn. <i>Haemogregarina</i>)		elapid (king brown snake)	rbc		Australia
<i>H. enswerae</i> (syn. <i>Haemogregarina</i>)		elapid (forest cobra)	rbc		Africa
<i>H. eristavi</i> (syn. <i>Haemogregarina</i>)		viperid (blunt-nosed viper)	rbc		Middle-East
<i>H. fasciatae</i>	16-18 x 3-5	colubrid (banded water snake, green water snake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. florulentusi</i> (syn. <i>Haemogregarina</i>)		colubrid (flowered racer)	rbc		North Africa
<i>H. franchinii</i> (syn. <i>Haemogregarina</i>)		pythonid (Indian python)	rbc		South Asia
<i>H. fuscus</i> (syn. <i>Haemogregarina</i>)		pythonid (brown water python)	rbc		Australia
<i>H. fusifex</i>	9.2-17.3 x 2.3-8.1	boid (boa constrictor)	rbc	Acari: ixodid (<i>Amblyomma dissimile</i>), exptl. in Diptera: culicid (<i>Culex tarsalis</i> , <i>Aedes togoi</i>)	North America
<i>H. garnhami</i> (syn. <i>Haemogregarina</i>)		psammophiid (Schokari sand racer)	rbc		Egypt
<i>H. ghaffari</i>		viperid (Sahara sand viper)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	Egypt
<i>H. gigas</i> (syn. <i>Haemogregarina</i>)		colubrid (false water cobra)	rbc		South America
<i>H. gightiensis</i> (syn. <i>Haemogregarina</i>)		colubrid (awl-headed snake)	rbc		North Africa, Middle-East
<i>H. guangdongense</i>		colubrid (Chinese ratsnake), exptl. infection in colubrid (Asiatic water snake, radiated ratsnake) homalopsid (Chinese water snake)	rbc		Asia
<i>H. guttata</i>	10-17 x 3.5-6	colubrid (corn snake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. hassleri</i> (syn. <i>Haemogregarina</i>)		colubrid (burrowing snake)	rbc		South America
<i>H. horridus</i>	13-17 x 4-6	viperid (timber rattlesnake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. imperatoris</i> (syn. <i>Haemogregarina</i>)		boid (common boa)	rbc		South America

<i>H. jararacussu</i> (syn. <i>Haemogregarina</i>)		viperid (jararacussu, Neuwied's lancehead)	rbc		South America
<i>H. joannoni</i> (syn. <i>Haemogregarina</i>)		lamprophiid (false smooth snake)	rbc		Mediterranean
<i>H. juxtannuclearis</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		boid (boa constrictor)	rbc		Americas
<i>H. laevicolis</i> (syn. <i>Haemogregarina</i>)		colubrid (sipos)	rbc		South America
<i>H. lahillei</i> (syn. <i>Haemogregarina</i>)		colubrid (grass snake, brown water snake)	rbc		Eurasia, North America
<i>H. lebetina</i> (syn. <i>Haemogregarina</i>)		viperid (blunt-nosed viper)	rbc		Middle-East
<i>H. leimadophis</i> (syn. <i>Haemogregarina</i>)		dipsadid (penarol snake)	rbc		South America
<i>H. lermensis</i> (syn. <i>Haemogregarina</i>)		colubrid (garter snake)	rbc		North America
<i>H. luehi</i> (syn. <i>Haemogregarina</i>)		boid (tree boas)	rbc		South America
<i>H. luisieri</i> (syn. <i>Haemogregarina</i>)		colubrid (horseshoe whipsnake)	rbc		Mediterranean
<i>H. lutzi</i> (syn. <i>Haemogregarina</i>)		boid (green anaconda)	rbc		South America
<i>H. malpoloni</i> (syn. <i>Haemogregarina</i>)		psammophiid (Montpellier snake)	rbc		Mediterranean
<i>H. mancauxi</i> (syn. <i>Haemogregarina</i>)		colubrid (horseshoe whipsnake)	rbc		Mediterranean
<i>H. mansonii</i> (syn. <i>Haemogregarina</i>)	13-16 x 4-6	colubrid (whipsnake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. massardi</i>	15-20 x 2-4	viperid (neotropical rattle snake)	rbc		South America
<i>H. matruhensis</i> (syn. <i>Haemogregarina</i>)		psammophiid (Schokari sand racer)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	Egypt
<i>H. megalocystis</i> (syn. <i>Haemogregarina</i>)		pythonid (carpet python)	rbc		Australasia
<i>H. mehlhorni</i>	17.2 x 5.4	viperid (saw-scaled viper)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	Egypt
<i>H. migonei</i> (syn. <i>Haemogregarina</i>)		colubrid (false water cobra)	rbc		South America
<i>H. miliaris</i> (syn. <i>Haemogregarina</i>)	13-14 x 3-3.5	colubrid (common water snake)	rbc	Hirudinea: glossiphoniid (<i>Haementeria lutzi</i>)	Brazil
<i>H. minchini</i>		colubrid (herald snake)	rbc		Africa
<i>H. mirabilis</i> (syn. <i>Haemogregarina</i>)		colubrid (water snakes, tree snakes)	rbc	Hirudinea: cyclicobdellid (<i>Hirudinaria granulosa</i>)	India
<i>H. mocassini</i> (syn. <i>Haemogregarina</i>)	14-18 x 4-6	viperid (water moccasin)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. modesta</i> (syn. <i>Haemogregarina</i>)		colubrid (modest groundsnake)	rbc		South America
<i>H. moreliae</i> (syn. <i>Haemogregarina</i>)		pythonid (carpet python)	rbc		Australasia
<i>H. mucosus</i>		colubrid (Oriental rat snake)	rbc		Asia
<i>H. musotae</i> (syn. <i>Haemogregarina</i>)		lamprophiid (striped house snake, Seychelles house snake)	rbc		Africa
<i>H. najae</i> (syn. <i>Haemogregarina</i>)	14-18 x 3.5-6	elapid (Indian cobra)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	India
<i>H. pallida</i>		colubrid (Amazon	rbc		South

(syn. <i>Haemogregarina</i>)		coastal house snake)			America
<i>H. pefilievi</i> (syn. <i>Haemogregarina</i>)		viperid (saw-scaled viper)	rbc		Middle-East, Central Asia
<i>H. perrieri</i> (syn. <i>Haemogregarina</i>)		viperid (Neuwied's lancehead)	rbc		South America
<i>H. phisalix</i> (syn. <i>Haemogregarina</i>)		pythonid (black-tailed python)	rbc		Indo-Asia
<i>H. phylodriasi</i> (syn. <i>Haemogregarina</i>)		colubrid (green racers)	rbc		South America
<i>H. pictiventris</i>	11-16 x 4-6	colubrid (banded water snake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. pigmentata</i> (syn. <i>Haemogregarina</i>)		psammophiid (steppe ribbon racer)	rbc		Asia
<i>H. pituophis</i> (syn. <i>Haemogregarina</i>)		colubrid (pine snake, bullsnake)	rbc		North America
<i>H. plimmeri</i> (syn. <i>Haemogregarina</i>)	10-15 x 2.5-4.5	viperid (jararaca, lancehead)	rbc	Diptera: culicid (<i>Culex dolosus</i>)	Brazil
<i>H. pococki</i> (syn. <i>Haemogregarina</i>)		pythonid (black-tailed python, carpet python)	rbc		Australasia
<i>H. poecilogyrus</i> (syn. <i>Haemogregarina</i>)		dipsadid (penarol snake)	rbc		South America
<i>H. polytopis</i>	10-15 x 3-6	colubrid (eastern racers)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. priapus</i>	17-20 x 3.5-6	colubrid (eastern racers)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. prolata</i> (syn. <i>Haemogregarina</i>)		colubrid (spotted whip snake)	rbc		Asia
<i>H. pseudechis</i> (syn. <i>Haemogregarina</i>)		elapid (red-bellied black snake, king brown snake)	rbc		Australia
<i>H. pseudoboa</i> (syn. <i>Haemogregarina</i>)		colubrid (black false boa)	rbc		South America
<i>H. pullatus</i> (syn. <i>Haemogregarina</i>)		colubrid (caninana)	rbc		Mesoamerica
<i>H. punctatus</i>	12-16 x 4-6	colubrid (ringneck snake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. pythonis</i> (syn. <i>Haemogregarina</i> , <i>H. amethystina</i> p.p., <i>colubri</i> p.p., <i>reichenowi</i> , <i>shattocki</i> p.p., <i>Danilewskya</i>)		pythonid (reticulated python, black-tailed python, rock python, carpet python, amethystine python, green tree python)	rbc		Australasia
<i>H. rarefaciens</i> (syn. <i>Haemogregarina</i>)	11-18 x 2.5-9	colubrid (Indigo snake); plus exptl. infections boid (boa constrictor); colubrid (gopher snake)	rbc, wbc	exptl. in Diptera: culicid (<i>Aedes sierrensis</i> , <i>Anopheles albimanus</i> , <i>Culex tarsalis</i>)	North America
<i>H. refringens</i> (syn. <i>Haemogregarina</i>)		lamprophiid (mole snake)	rbc		South Africa
<i>H. robertsonae</i> (syn. <i>Haemogregarina</i>)		pythonid (ball python, rock python)	rbc		Africa
<i>H. rojasi</i> (syn. <i>Haemogregarina</i>)		viperid (crossed pit viper), colubrid (Wagler's snake)	rbc		South America
<i>H. romani</i> (syn. <i>Haemogregarina</i>)		viperid (tropical rattlesnake)	rbc		South America
<i>H. roulei</i> (syn. <i>Haemogregarina</i>)		viperid (crossed pit viper)	rbc		South America
<i>H. samboni</i> (syn. <i>Haemogregarina</i>)		viperid (asp viper, blunt-nosed viper)	rbc		South Europe, North Africa
<i>H. sauritus</i>	13-19 x 2.5-	colubrid (southern	rbc	Diptera: culicid	North

	5.5	ribbon snake, eastern racers, black rat snake, corn snake, garter snake, ringneck snake); viperid (timber rattlesnake)		(<i>Aedes aegypti</i>)	America
<i>H. sebai</i> (syn. <i>Haemogregarina</i>)		pythonid (African rock python)	rbc		Africa
<i>H. seligmanni</i> (syn. <i>Haemogregarina</i>)		viperid (bushmaster)	rbc		South America
<i>H. seminatrici</i>	14-20 x 3-5	colubrid (swamp snake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. serpentium</i> (syn. <i>Haemogregarina</i> , <i>Drepanidium</i> , <i>Karyolysus</i>)		boid (green anaconda, boa constrictor), colubrid (savannah hunter, indigo snake, caninana, false fer-de-lance, green racer, tropical racer), viperid (lancehead, rattlesnakes)	rbc		Americas
<i>H. seurati</i>	12-16 x 3-5	viperid (horned viper)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	North Africa
<i>H. shattocki</i> (syn. <i>Haemogregarina</i>)		pythonid (carpet python, amethystine python), elapid (tiger snake, spotted black snake)	rbc		Australasia
<i>H. sipedon</i>	19 x 3.7	colubrid (northern water snake)	rbc	Diptera: culicid (<i>Culex pipiens</i> , <i>territans</i>), then frogs (Anura: ranid (<i>Rana pipiens</i>))	Canada
<i>H. sirtalis</i>	17-22 x 3-6	colubrid (garter snake, ribbon snake, eastern racers, banded water snake)	rbc	exptl. in Diptera: culicid (<i>Aedes aegypti</i>), then frogs (Anura: ranid (<i>Rana</i>))	North America
<i>H. sistruri</i>	12.6-15.8 x 4.7-6.3	viperid (ground rattlesnake)	rbc	Diptera: culicid (<i>Aedes aegypti</i>)	North America
<i>H. stegonoti</i> (syn. <i>Haemogregarina</i>)		colubrid (slatey-grey snake)	rbc		Australia
<i>H. strigatus</i> (syn. <i>Haemogregarina</i>)	14-18 x 6-8	colubrid (coastal house snake)	rbc	Diptera: culicid (<i>Culex dolosus</i> , <i>fatigans</i>)	Brazil
<i>H. terzii</i> (syn. <i>Haemogregarina</i>)		boid (boa constrictor)	rbc		Americas
<i>H. thamnophis</i> (syn. <i>Haemogregarina</i>)		colubrid (garter snakes)	rbc		North America
<i>H. tigrinae</i> (syn. <i>Haemogregarina</i>)		colubrid (tiger keelback, four-lined ratsnake), viperid (Siberian pit viper)	rbc		Asia
<i>H. trumata</i> (syn. <i>Haemogregarina</i>)		colubrid (Dahl's whip snake)	rbc		Middle-East
<i>H. tucumanensis</i> (syn. <i>Haemogregarina</i>)		viperid (crossed pit viper), colubrid (green racer)	rbc		South America
<i>H. viperini</i> (syn. <i>Karyolysus</i>)		colubrid (viperine snake)	rbc		Mediterranean
<i>H. vubirizi</i> (syn. <i>Haemogregarina</i>)		lamprophiid (Congo file snake)	rbc		Africa
<i>H. wardi</i> (syn. <i>Haemogregarina</i>)		colubrid (chain kingsnake)	rbc		North America
<i>H. weissii</i> (syn. <i>Haemogregarina</i>)		elapid (Egyptian cobra)	rbc		North Africa
<i>H. zambiensis</i>		colubrid (boomslang)	rbc		Africa

(syn. <i>Haemogregarina</i>)					
<i>H. zamenis</i> (syn. <i>Haemogregarina</i>)		colubrid (horseshoe whip snake, oriental ratsnake, golden tree snake)	rbc		Mediterranean, South Asia
<i>H. zumpti</i> (syn. <i>Haemogregarina</i>)		elapid (black mamba)	rbc		Africa
species in lizards (Sauria)					
<i>H. ameivae</i> (syn. <i>Haemogregarina</i>)		teiid (green ameiva)	rbc		South America
<i>H. amphisbaena</i> (syn. <i>Haemogregarina</i>)		amphisbaenid (red worm lizard)	rbc		Eurasia
<i>H. annularis</i> (syn. <i>Haemogregarina</i>)		phyllodactylid (ringed wall gecko)	rbc		Africa
<i>H. argantis</i>		agamid (Mozambique agama), phyllodactylid (wall gecko)	rbc	Acari: argasid (<i>Argas brumpti</i>)	Africa
<i>H. babudierii</i> (syn. <i>Haemogregarina</i>)		lacertid (ruin lizard, wall lizard, European green lizard)	rbc		Europe
<i>H. berestnewi</i> (syn. <i>Karyolysus</i>)		lacertid (European green lizard)	rbc		Europe
<i>H. bicapsulata</i> (syn. <i>Haemogregarina</i>)		lacertid (common wall lizard)	rbc		Europe
<i>H. borreli</i> (syn. <i>Haemogregarina</i>)		varanid (desert monitor)	rbc		Africa, Asia
<i>H. boskiani</i> (syn. <i>Haemogregarina</i>)		lacertid (fringe-toed lizard)	rbc		North Africa, West Asia
<i>H. breinlii</i> (syn. <i>Haemogregarina</i>)	14-16 x 1.5-2.5	varanid (black-headed monitor, lace goanna, sand goanna)	rbc	Diptera: culicid (<i>Culex fatigans</i>)	Australia
<i>H. burneti</i>		phyllodactylid (European common gecko)	rbc		Mediterranean
<i>H. camarai</i> (syn. <i>Haemogregarina</i>)		varanid (rock monitor)	rbc		Africa
<i>H. capsensis</i> (syn. <i>Haemogregarina</i>)		lacertid (fringe-fingered lizards)	rbc		Africa, Eurasia
<i>H. carlosi</i> (syn. <i>Haemogregarina</i> , <i>H. minuta</i> , <i>Schellackia</i>)		lacertid (ocellated lizard)	rbc		Europe
<i>H. chabaudi</i>		chamaeleonid (chameleons)	rbc		Africa, Eurasia
<i>H. chamaeleonis</i> (syn. <i>Haemogregarina</i>)		chamaeleonid (common chameleon, African chameleon)	rbc		Africa
<i>H. cheissini</i> (syn. <i>Haemogregarina</i>)		agamid (Caucasian agama)	rbc		Caucasus
<i>H. cnemidophori</i> (syn. <i>Haemogregarina</i>)		teiid (rainbow whiptail)	rbc		Americas
<i>H. ctenosaurae</i> (syn. <i>Haemogregarina</i>)		iguanid (spinytail iguana)	rbc		Mexico
<i>H. cunninghami</i> (syn. <i>Haemogregarina</i>)		scincid (Cunningham's skink, tree skink)	rbc		Australia
<i>H. curvirostris</i> (syn. <i>Haemogregarina</i>)		lacertid (ocellated lizard)	rbc		Europe
<i>H. dolichopyrena</i> (syn. <i>Haemogregarina</i>)		gekkonid (Caspian thin-toed gecko)	rbc		West Asia
<i>H. egerntiae</i> (syn. <i>Haemogregarina</i>)		scincid (Cunningham's skink, tree skink)	rbc		Australia
<i>H. eremiae</i> (syn. <i>Haemogregarina</i>)		lacertid (racerunners)	rbc		Eurasia
<i>H. eumecei</i>		scincid (Berber skink)	rbc		North

(syn. <i>Haemogregarina</i>)					Africa, West Asia
<i>H. gilruthi</i> (syn. <i>Haemogregarina</i>)		varanid (black-headed monitor)	rbc		Australia
<i>H. gouldii</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		varanid (sand goanna)	rbc		Australia
<i>H. gracilis</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)	18-22.5 x 0.9-1.4	scincid (rainbow skink)	rbc	Diptera: culicid (<i>Culex pipiens</i>)	Sudan
<i>H. hamata</i> (syn. <i>Haemogregarina</i>)		lacertid (Jackson's forest lizard), scincid (speckle-lipped skink)	rbc		Africa
<i>H. heteronotae</i> (syn. <i>Haemogregarina</i>)		gekkonid (Bynoe's gecko)	rbc		Australia
<i>H. hinuliae</i> (syn. <i>Haemogregarina</i>)		scincid (golden water skink)	rbc		Australia
<i>H. iguanae</i> (syn. <i>Haemogregarina</i>)		iguanaid (green iguana, lesser Antillean iguana), teiid (gold tegu)	rbc		Americas, Caribbean
<i>H. jakimovi</i> (syn. <i>Haemogregarina</i>)		agamid (toadhead agamas)	rbc		Eurasia
<i>H. johnstoni</i> (syn. <i>Haemogregarina</i>)		varanid (lace goanna, sand goanna)	rbc		Australia
<i>H. kisrae</i>	12-15 x 2-5.5	agamid (star lizard)	rbc	Acari: ixodid (<i>Hyalomma aegyptium</i>)	Middle-East
<i>H. lygosomarum</i> (syn. <i>Haemogregarina</i>)	13.6-16.8 x 4.2-6.3	scincid (Moko skink)	rbc, liver, spleen	Acari: macronyssid (<i>Ophionyssus scincorum</i>)	New Zealand
<i>H. mabuiae</i> (syn. <i>Haemogregarina</i>)		scincid (bridled skink)	rbc		Middle-East
<i>H. malacitensis</i> (syn. <i>Haemogregarina</i>)		lacertid (wall lizard)	rbc		Mediterranean
<i>H. marceai</i> (syn. <i>Haemogregarina</i>)		lacertid (wall lizard)	rbc		Europe
<i>H. mellisselensis</i> (syn. <i>Haemogregarina</i>)		lacertid (Dalmatian wall lizard)	rbc		Mediterranean
<i>H. mesnili</i>	15-17 x 4-7	gekkonid (dwarf gecko)	rbc	Diptera: culicid (<i>Culex fatigans</i> , <i>Aedes albopictus</i> , <i>Stegomyia albopicta</i>)	Vietnam
<i>H. missoni</i> (syn. <i>Haemogregarina</i>)		teiid (gold tegu)	rbc		South America
<i>H. nana</i> (syn. <i>Haemogregarina</i>)		lacertid (common wall lizard, Italian wall lizard)	rbc		Mediterranean
<i>H. nicollei</i> (syn. <i>Haemogregarina</i>)		lacertid (ocellated lizard)	rbc		North Africa
<i>H. nobrei</i> (syn. <i>Haemogregarina</i>)		lacertid (common wall lizard)	rbc		Mediterranean
<i>H. obscura</i> (syn. <i>Haemogregarina</i>)		scincid (Cunningham's skink)	rbc		Australia
<i>H. octosporei</i>	17.3-19.5 x 3.8-4.9	scincid (keeled Indian mabuya)	rbc	Acari: macronyssid (<i>Ophionyssus</i> sp.)	India
<i>H. ophisauri</i> (syn. <i>Haemogregarina</i>)		anguid (European legless lizard)	rbc		Eurasia
<i>H. palmeri</i> (syn. <i>Haemogregarina</i>)		agamid (Australian water dragon)	rbc		Australia
<i>H. paradoxa</i> (syn. <i>Haemogregarina</i>)		varanid (rock monitor)	rbc		Africa
<i>H. pavlovskiyi</i>		gekkonid (Turkestan)	rbc		West Asia

(syn. <i>Haemogregarina</i>)		thin-toed gecko, Transcaspian bent-toed gecko, wonder gecko)			
<i>H. percomsi</i> (syn. <i>Haemogregarina</i>)		agamid (rock agama)	rbc		Asia
<i>H. petrishchewae</i> (syn. <i>Haemogregarina</i>)		agamid (Lichtenstein's toadhead agama)	rbc		Eurasia
<i>H. phyllodactyli</i> (syn. <i>Haemogregarina</i>)		phyllodactylid (South American leaf-toed gecko)	rbc		South America
<i>H. platydactyli</i> (syn. <i>Haemogregarina</i>)		phyllodactylid (common wall gecko)	rbc		Mediterrane an
<i>H. procteri</i> (syn. <i>Haemogregarina</i>)		phyllodactylid (Elisa's leaf-toed gecko)	rbc		Middle-East
<i>H. prodhoni</i>		oplurid (Madagascar swift)	wbc		Madagascar
<i>H. psammodromi</i> (syn. <i>Haemogregarina</i> , <i>H.</i> <i>lusitanica</i> , <i>pallida</i>)		lacertid (large psammadromus)	rbc, wbc		Mediterrane an
<i>H. ramadani</i> (syn. <i>Haemogregarina</i>)		lacertid (Bosc's fringe- toed lizard)	rbc		Egypt
<i>H. salimbeni</i> (syn. <i>Haemogregarina</i>)		teiid (black tegu)	rbc		South America
<i>H. sauromali</i>	10-21 x 3.3- 7.7	iguanid (chuckwallas)	rbc, wbc	Acari: acarid (<i>Hirstiella</i> sp.)	Mexico
<i>H. schaudinni</i> (syn. <i>Haemogregarina</i>)		lacertid (ocellated lizard)	rbc		North Africa
<i>H. sergentium</i> (syn. <i>Haemogregarina</i>)		scincid (ocellated skink)	rbc		Mediterrane an, India
<i>H. sinimbui</i> (syn. <i>Haemogregarina</i>)		iguanid (green iguana)	rbc		Central and South America
<i>H. taeniolati</i> (syn. <i>Haemogregarina</i>)		scincid (copper-tailed skink)	rbc		Australia
<i>H. thomsoni</i> (syn. <i>Haemogregarina</i>)		agamid (tuberculated agama, steppe agama)	rbc		Indo-China
<i>H. tiliquae</i> (syn. <i>Haemogregarina</i>)		scincid (blue-tongued skink)	rbc		Australia
<i>H. toddi</i> (syn. <i>Haemogregarina</i>)		varanid (Nile monitor)	rbc		Africa
<i>H. triatomae</i> (syn. <i>Haemogregarina</i>)		teiid (tiger lizard); tropicidurid (Amazon lava lizard)	rbc	Hemiptera: reduviid (<i>Triatoma</i> <i>subrovaria</i>)	Central and South America
<i>H. tuatarae</i>	12.5-16.7 x 3.3-4.4	Rhynchocephalia: sphenodontid (tuatara)	rbc		New Zealand
<i>H. tupinambis</i> (syn. <i>Haemogregarina</i> , <i>H.</i> <i>caranii</i>)	14.5-19 x 5-8	teiid (golden tegu)	rbc	Diptera: culicid (<i>Culex fatigans</i>)	Brazil
<i>H. turcomanica</i> (syn. <i>Haemogregarina</i> , <i>H.</i> <i>agamae</i>)		agamid (rock agama, toad-headed agama)	rbc		Central and West Asia
<i>H. varani</i> (syn. <i>Haemogregarina</i>)		varanid (savannah monitor, desert monitor, Nile monitor, Komodo dragon)	rbc		Africa, Indonesia
<i>H. varanicola</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		varanid (lace goanna, black-headed monitor, Gould's goanna, Asian water monitor)	rbc		Australasia
<i>H. veloxi</i> (syn. <i>Haemogregarina</i>)		lacertid (rapid fringe- toed lizard)	rbc		Central Asia
<i>H. waltirensis</i>		agamid (Oriental garden	rbc		India

(syn. <i>Haemogregarina</i>)		lizard)			
species in crocodiles (Crocodylia)					
<i>H. caimani</i> (syn. <i>Haemogregarina</i> , <i>H. brasiliensis</i>)	16.2-25 x 2.5-4	alligatorid (broad-snouted caiman, white caiman)	rbc	Diptera: culicid (<i>Culex dolosus</i> , <i>fatigans</i>)	Brazil
<i>H. crocodilorum</i> (syn. <i>Haemogregarina</i>)	8-11 x 4-6	crocodylid (African dwarf crocodile); alligatorid (American alligator)	rbc	Hirudinea: glossiphoniid (<i>Placobdella multilineata</i>)	North America
<i>H. hankini</i> (syn. <i>Haemogregarina</i>)		gavialid (gharial)	rbc		India
<i>H. pettiti</i> (syn. <i>Haemogregarina</i>)	18-25 x 2.5-5	crocodylid (Nile crocodile)	rbc	Diptera: glossinid (<i>Glossina palpalis</i>)	Senegal
<i>H. serrei</i> (syn. <i>Haemogregarina</i>)		alligatorid (caiman)	rbc		South America
<i>H. sheppardi</i> (syn. <i>Haemogregarina</i>)		crocodylid (Nile crocodile)	rbc		North Africa
species in tortoises (Testudines)					
<i>H. mauritanicum</i> (syn. <i>Haemogregarina</i> , <i>Coelomoplasma hyalomma</i>)		testudinid (Greek tortoise)	rbc	Acari: ixodid (<i>Hyalomma aegyptium</i>)	Europe
species in amphibians (Anura)					
<i>H. aegyptia</i> (syn. <i>Haemogregarina</i>)	12-15 x 6-9	bufonid (African toad)	rbc		Egypt, Sudan
<i>H. aguai</i> (syn. <i>Karyolysus aguai</i> , <i>Haemogregarina</i> , <i>H. minima</i>)		bufonid (cane toad)	rbc		North America
<i>H. andamanensis</i> (syn. <i>Haemogregarina</i>)	14.5 x 3.5	ranid (skipper frog)	rbc		India
<i>H. arabica</i> (syn. <i>Haemogregarina</i>)		bufonid (Dhofar toad)	rbc		Arabia
<i>H. assiuticus</i> (syn. <i>Haemogregarina</i>)	30-38 x 3-5	bufonid (African toad)	rbc		Egypt
<i>H. aurorae</i> (syn. <i>Haemogregarina</i>)		ranid (red-legged frog)	rbc		North America
<i>H. berestneffi</i> (syn. <i>Haemogregarina</i>)	16-28 x 3-6	ranid (grass frog, green pond frog, skipper frog), dicroglossid (Asian bullfrog)	rbc		Sri Lanka, India
<i>H. boueti</i> (syn. <i>Haemogregarina</i> , <i>H. boneti</i>)	16-26 x 3-6	bufonid (African toad, Asian toad)	rbc		Egypt, Guinea-Bissau
<i>H. boyli</i> (syn. <i>Haemogregarina</i>)	8-17 x 4-6	ranid (yellow-legged frog)	rbc		North America
<i>H. bufonis</i> (syn. <i>Haemogregarina</i> , <i>Plasmodium bufonis</i>)		Anura: bufonid (American toad)	rbc		North America
<i>H. catesbiana</i> (syn. <i>Haemogregarina</i>)		ranid (American bullfrog)	rbc	Diptera: culicid (<i>Culex territans</i>)	North America
<i>H. cayennensis</i> (syn. <i>Haemogregarina</i>)		bufonid (cane toad)	rbc		
<i>H. clamata</i> (syn. <i>Haemogregarina</i> , <i>Karyolysus</i>)		ranid (green frog, leopard frog, American bullfrog)	rbc		North America
<i>H. darlingi</i> (syn. <i>Haemogregarina</i>)		bufonid (cane toad)	rbc		
<i>H. epuluensis</i> (syn. <i>Haemogregarina</i>)		ptychadenid (South African sharp-nosed frog)	rbc		Africa
<i>H. faiyumensis</i>	13-17 x 4-5	bufonid (African toad)	rbc		Egypt

(syn. <i>Haemogregarina</i>)					
<i>H. francai</i> (syn. <i>Haemogregarina</i>)	18-20 x 2-3	bufonid (African toad)	rbc		Egypt
<i>H. froilanoi</i> (syn. <i>Haemogregarina</i>)	16-21 x 6-8	bufonid (African toad)	rbc		Angola
<i>H. hijaziensis</i> (syn. <i>Haemogregarina</i>)		bufonid (Arabian toad)	rbc		Arabia
<i>H. hortai</i> (syn. <i>Haemogregarina</i>)		ranid (edible frog)	rbc		Europe
<i>H. hyperoliu</i> (syn. <i>Haemogregarina</i>)		hyperoliid (reed frog)	rbc		Africa
<i>H. involucrum</i>	19-26 x 4-6	hyperoliid (reed frog)	rbc		South Africa
<i>H. ixoxo</i>	12-17 x 6-9	bufonid (Garman's toad, guttural toad, striped toad)	rbc		South Africa
<i>H. kaloulae</i> (syn. <i>Haemogregarina</i>)	16 x 3.6	microhylid (Asian narrowmouth toad)	rbc		India
<i>H. lavieri</i> (syn. <i>Haemogregarina</i>)	20	bufonid (African toad)	rbc		Congo
<i>H. legeri</i> (syn. <i>Haemogregarina</i>)		bufonid (cane toad)	rbc		
<i>H. leptodactyli</i> (syn. <i>Leucocytozoon ranarum</i> , <i>Haemogregarina</i> , <i>H. heteronucleata</i> , <i>ranarum</i>)		leptodactylid (butter frog, smoky jungle frog)	rbc		South America
<i>H. maculatus</i> (syn. <i>Haemogregarina</i>)	16.5 x 3.3	rhacophorid (Indian tree frog)	rbc		India
<i>H. magna</i> (syn. <i>Haemogregarina</i> , <i>H. ranarum p.p.</i> , <i>Drepanidium magnum</i> , <i>krusei</i> , <i>Danilewskyia krusei</i>)	12-18 x 4-6	ranid (green frog, rice field frog, leopard frog, marsh frog), dicroglossid (Asian bullfrog)	rbc		Europe, India
<i>H. magni</i> (syn. <i>Haemogregarina</i>)	21-26 x 5-9	bufonid (African toad)	rbc		Egypt
<i>H. medinensis</i> (syn. <i>Haemogregarina</i>)		ranid (marsh frog)	rbc		Europe
<i>H. moloensis</i> (syn. <i>Haemogregarina</i>)	18 x 8	bufonid (toads)	rbc		Kenya
<i>H. neireti</i> (syn. <i>Haemogregarina</i>)		ptychadenid (grassland frogs)	rbc		Africa
<i>H. nucleobisecans</i> (syn. <i>Haemogregarina</i>)	14.4 x 3	bufonid (Himalaya toad, Asian toad, spotted toad)	rbc		India
<i>H. nutti</i> (syn. <i>Haemogregarina</i> , <i>Pseudohaemogregarina</i>)		pyxicephalid (Nutt's river frog)	rbc		Europe
<i>H. pattoni</i> (syn. <i>Haemogregarina</i>)		dicroglossid (Indian five-fingered frog)	rbc		India
<i>H. perinucleophilum</i> (syn. <i>Haemogregarina</i>)	11.1 x 3.1	dicroglossid (Asian bullfrog)	rbc		India
<i>H. pestanae</i> (syn. <i>Haemogregarina</i> , <i>H. pistanae</i>)	12-17 x 4-5	bufonid (African toad)	rbc		Egypt, Guinea-Bissau
<i>H. pulchra</i> (syn. <i>Haemogregarina</i>)	15.4 x 3	microhylid (chubby frog)	rbc		India
<i>H. scheini</i> (syn. <i>Haemogregarina</i>)		dicroglossid (Asian bullfrog)	rbc		South Asia
<i>H. seychellensis</i>		Gymnophiona: grandisoniid (Stejneger's caecilian)	rbc		Seychelles
<i>H. shirikenimori</i>		Urodela: salamandrid	rbc		Japan

(syn. <i>Haemogregarina</i>)		(sword-tail newt)			
<i>H. systoma</i> (syn. <i>Haemogregarina</i>)	15.3 x 3.9	microhylid (lesser balloon frog)	rbc		India
<i>H. temporariae</i> (syn. <i>Haemogregarina</i> , <i>Nematopsis</i>)		ranid (European grass frog)	rbc		Europe
<i>H. tenuis</i>	11-17 x 4-7	hyperoliid (greater leaf-folding frog, reed frog)	rbc		South Africa
<i>H. theileri</i> (syn. <i>Haemogregarina</i> , <i>Pseudohaemogregarina ranae</i>)		pyxicephalid (Angola river frog, Drakensberg River frog, pixie frog)	rbc		Africa
<i>H. thori</i>	11-17 x 4-7	hyperoliid (marbled reed frog)	rbc		South Africa
<i>H. tonkinensis</i> (syn. <i>Haemogregarina</i>)		bufonid (Asian toad)	rbc		South Asia
<i>H. tunisiensis</i> (syn. <i>Haemogregarina</i>)	12-15 x 8	bufonid (Berber toad)	rbc		Tunisia
species in birds					
<i>H. albatrossi</i>	13 x 6.1	Procellariiformes: diomedeid (albatrosses)	wbc		Southern Ocean
<i>H. aragaoi</i> (syn. <i>Haemogregarina</i>)		Passeriformes: thraupid (yellow-billed cardinal)			South America
<i>H. atticorae</i> (syn. <i>Haemogregarina</i>)	7.9-9.9 x 3.3-3.9	Passeriformes: hirundinid (South African cliff swallow, tawny-headed swallow, blue-and-white swallow, southern rough-winged swallow, western house martin)	wbc	Acari: argasid (<i>Ornithodoros peringueyi</i>); Siphonaptera: pulicid (<i>Xenopsylla trispinis</i>)	South Africa, South America
<i>H. columbae</i> (syn. <i>Haemogregarina</i>)		Columbiformes: columbid (pigeon)	rbc		Eurasia
<i>H. estrildus</i>	8.8 x 3.7	Passeriformes: estrildid (bronze mannikin)	wbc		Zambia
<i>H. kiwii</i>	9.8-13.5 x 6.2-8.3	Apterygiformes: apterygid (kiwi)	wbc		New Zealand
<i>H. lanis</i>	7.8 x 3.6	Passeriformes: laniid (fiscal shrike)	wbc		Africa
<i>H. malacotinus</i>	10.8 x 5.1	Passeriformes: malaconotid (black-backed puffback)	wbc		Africa
<i>H. neophrontis</i> (syn. <i>Leucocytozoon</i> , <i>Toxoplasma</i> , <i>H. adiei</i> , <i>monachus</i>)	9.6 x 4.6	Accipitriformes: accipitrid (hooded vulture, lappet-faced vulture, white-backed vulture, Egyptian vulture, tawny eagle, red-tailed hawk, black kite, osprey)	wbc		Africa
<i>H. numidis</i>	9.5 x 5.3	Galliformes: phasianid (helmeted guineafowl)	wbc		Africa
<i>H. paroariae</i> (syn. <i>Haemogregarina</i> , <i>H. brachyspizae</i>)		Passeriformes: passerellid (Andean sparrow), thraupid (red-cowled cardinal)	wbc		South America
<i>H. parus</i>	9.8-10.6 x 3.6-4.4	Passeriformes: parid (chickadees, titmice)	wbc		North America, Europe
<i>H. passeris</i>	7.9 x 3.9	Passeriformes: ploceid (scaly-feathered weaver)	wbc		Africa
<i>H. pintoii</i>		Accipitriformes:	wbc		Americas

(syn. <i>Haemogregarina</i>)		accipitrid (turkey vulture)			
<i>H. pittae</i>	10.6 x 3.7	Passeriformes: pittid (blue-banded pitta)	wbc		Borneo
<i>H. prionopis</i>	10.6 x 6.1	Passeriformes: vangid (white-crested helmetshrike)	wbc		Africa
<i>H. rhamphocoeli</i> (syn. <i>Haemogregarina</i> , <i>H. tanagrae</i>)		Passeriformes: thraupid (scarlet tanager, palm tanager)	wbc		South America
<i>H. sylvae</i>	9.2 x 3.5	Passeriformes: sylviid (chestnut-vented warbler)	wbc		South Africa
<i>H. travassosi</i> (syn. <i>Haemogregarina</i>)		Passeriformes: thamnophilid (great antshrike)	wbc		Americas
<i>H. zosteropis</i>	8.3 x 3.3	Passeriformes: zosteropid (Orange River white-eye)	wbc		South Africa

*rbc = red blood cells (erythrocytes); wbc = white blood cells (leucocytes)

Parasite morphology: *Hepatozoon* spp. form 4 different types of developmental stages: meronts in the viscera and gamonts in blood cells of vertebrates; and gametes and oocysts in invertebrate vectors. Meronts (often called schizonts) appear as ovoid basophilic stages (around 30 µm in diameter) in vascular endothelial cells in various tissues of vertebrates. The meronts undergo internal (endogenous) division to form merozoites, with 2 patterns of division observed: one type producing 2-4 large robust macro-merozoites; and the other forming over 20 smaller slender micro-merozoites arranged around the periphery (imparting a 'wheelspoke' appearance). Persistent cysts containing 1 or 2 merozoites (sometimes called cystozoites) have also been observed in host organs for several *Hepatozoon* spp. (but are absent in *Haemogregarina* spp.). All species then form elliptical gamonts (9-12 x 4-6 µm) in white blood cells (mainly neutrophils, rarely monocytes) and sometimes in red blood cells. Gamonts are enveloped in a thick membrane and are usually located in the centre of the cell causing lateral displacement of the lobulated host cell nucleus. The gamonts themselves possess a central compact nucleus that stains dark red with Giemsa while the cytoplasm stains blue. Gamonts ingested by vectors form sexually dimorphic gametocytes (8-11 x 3-5 µm) which are associated pairwise (in syzygy), with female macrogametocytes maturing into robust unicellular macrogametes, and male microgametocytes dividing to produce 1-4 slender unflagellated microgametes. Fertilization produces non-motile zygotes that undergo sporogonous development to form large oocysts (200-300 x 150-300 µm) containing numerous (50-70) sporocysts, each of which contains 4-16 or more sporozoites (10-14 x 3-4 µm). Ultrastructural studies have revealed the presence of polar rings, micropores and cristate mitochondria in all stages, anterior conoids in all non-gamete stages, crystalloid bodies in sporozoites, and variable numbers of amylopectin granules (the latter absent in *Haemogregarina* spp.).

Site of infection: In vertebrate hosts, meronts (schizonts) develop in a variety of tissues and organs, including the liver, spleen, kidneys, lymph nodes, bone marrow, heart, lung and muscles. Monozoic or dizoic cysts have also been observed in similar tissues for several parasite species. Gamonts are found in host blood cells, infecting polymorphonuclear leucocytes, and sometimes erythrocytes. Over 340 *Hepatozoon* spp. have been described, which includes some 200 former *Haemogregarina* spp. from non-chelonian reptiles, amphibians and birds. Some 50 parasite species have been reported in 89 mammalian species (belonging to 24 families in 11 orders, mostly carnivores and rodents), almost 140 parasite species in 140 snake species (belonging to 9 families, mostly colubrids), 76 parasite species in 72 lizard species (belonging to 13 families, mainly lacertids), 6 species in 7 crocodile species (belonging to 3 families), one species in a tortoise (testudinid), 49 species in 49 amphibian species (21 species in 12 toad species, 26 species in 31 frog species belonging to 8 families, one species in a salamander and one in a caecilian), and 20 parasite species in 34 bird species (belonging to 18 families in 6 orders, mostly passeriforms and accipitriforms). Of the 340 putative species, the life-cycles have only been determined for some 61 species, all of them utilizing arthropods or leeches as vectors. The parasites completed gametogony in the guts of the vectors, resulting in the formation of polysporocystic oocysts which were found in the haemocoel, Malpighian tubules, stomach, intestines and caeca of the invertebrate hosts. Vectors identified for parasites in mammals included ixodid ticks, laelapid and haemogamasid mites, haematopinid and hoplopleurid lice, and pulicid, hystrichopsyllid and ceratophyllid fleas; those for parasites in snakes included culicid mosquitoes, ixodid ticks, glossiphoniid and cyclobdellid leeches; those for parasites in lizards included culicid mosquitoes, reduviid bugs, acarid and macronyssid mites, argasid and ixodid ticks; those for parasites in crocodiles included glossiphoniid leeches, glossinid tsetse flies and culicid mosquitoes; those for the parasites in tortoises were ixodid ticks; those for parasites in amphibians were culicid mosquitoes; and those for parasites in birds included argasid ticks and pulicid fleas.

Pathogenesis: Most infections in vertebrates are asymptomatic and have not been associated with any clinical disease in wildlife or domesticated animals. Heavy infections by several species, however, may cause disease (hepatozoonosis) when proliferating merogonous (schizogonous) stages damage host tissues, particularly in canids and felids. Developing schizonts may be disseminated throughout many host tissues, including haemolymphatic organs (bone marrow, spleen, lymph nodes) and internal visceral organs (liver, kidney, lungs). Upon maturation, schizonts lyse their host cells thus causing structural deficits, with cumulative losses leading to functional deficits and disease expression. Small lesions may develop in host tissues with necrotic foci and diffuse inflammation contributing to splenomegaly, hepatomegaly, hepatitis with Kupffer cell hyperplasia, pneumonitis, interstitial pneumonia, lymphadenopathy, glomerulonephritis and interstitial nephritis, and blood cell losses leading to progressive non-responsive anaemia (usually normocytic, normochromic, regenerative, sometimes with thrombocytopenia). There may be elevated monocyte counts with increasing numbers of monoblasts detected in peripheral blood (sometimes mistaken for monocytic leukaemia). Clinical signs are generally nonspecific and include fever, diarrhoea, icterus, ulcerative glossitis with hypersalivation, serous nasal-ocular discharge, intermittent anorexia, weight loss, emaciation, and death. Serum chemistry abnormalities include hyperproteinaemia (hyperglobulinaemia but hypoalbuminaemia) with increased creatine kinase (CK) and alkaline phosphatase (ALP) activities. Following schizogony, the parasites form gamonts in blood cells (especially neutrophils) and while many consider these to be latent stages, high parasitaemias (sometimes up to 50-100% of circulating neutrophils) have been associated with severe disease in dogs, characterized by lethargy, fever, severe weight loss and cachexia. Clinical infections are more abundant and severe in young or immuno-compromised animals, as they appear to be more susceptible to new infection or the reactivation of existing infections from persistent cystic stages in tissues. Various immunological studies have suggested that even in the absence of clinical signs, *Hepatozoon* infections of leucocytes may act to compromise and even suppress host immune responses, allowing infections to persist and predisposing animals to secondary infections.

Developmental cycle and mode of transmission: Hepatozoids have obligative heteroxenous (2-host) life cycles involving merogony and gamont formation in vertebrates (intermediate hosts), and gametogony, oocyst formation and sporogony in invertebrate hosts (definitive hosts or vectors). When vertebrates ingest vectors infected with mature oocysts, the oocysts excyst in their intestines releasing the containing infective sporozoites which penetrate the gut wall. The sporozoites invade mononuclear cells and are disseminated haematogenously or via the lymph to various host tissues and organs. They develop into meronts (schizonts) that undergo asexual internal (endogenous) division to form numerous merozoites; either 2-4 macro-merozoites or 20-30 micro-merozoites (depending on the parasite species). When mature, the meronts rupture releasing the merozoites which invade circulating neutrophils (or nucleated erythrocytes in non-mammalian hosts) and develop into gamonts in the peripheral circulation. In some instances, several *Hepatozoon* spp. also form small monozytic or dizoic cysts which persist in host organs resulting in long-term (chronic) infections. It has been suggested that these cystic stages may also facilitate paratenic transport between intermediate hosts by predation within the food chain (i.e. when carnivorous predators eat smaller infected prey). In one exceptional instance, vertical transmission has been reported for one species (*H. canis*) when proliferative stages cross the placenta in pregnant dogs. The life-cycles have been determined for over 60 *Hepatozoon* spp. and they all involve haematophagous invertebrate vectors (including leeches, ticks, mites, lice, fleas, mosquitoes, and tsetse flies). Infections are acquired by the vectors when they feed on vertebrate blood and ingest blood cells containing gamonts. The blood cells are digested in the vector gut releasing the gamonts which initiate extracellular gametogenesis by pairing up and developing into sexually dimorphic gametes. Macrogametocytes (female) form single 'egg-like' macrogametes while microgametocytes (male) form several 'sperm-like' flagellated microgametes. Fertilization occurs producing non-motile zygotes that develop into oocysts which undergo endogenous sporulation to form numerous sporocysts, each containing numerous sporozoites. Mature oocysts occur within various vector tissues, and they tend to accumulate in the haemocoel after moulting. In arthropod vectors, parasites may be transferred trans-stadially from larvae to nymphs to adults, but not trans-ovarially from females to their eggs (as occurs for some piroplasms). Infections are transmitted to vertebrate hosts when infected vectors are eaten and not via vector bite (i.e. transmission is consumptive rather than inoculative). Vectors are often consumed during grooming processes (self or communal grooming) and many vectors move between vertebrate hosts as larvae, nymphs and adults may feed on different individuals. The biogeographic distribution of many parasite species therefore closely follows that of their vectors. Transmission is often greatest during warm-hot seasons when vectors are more active, but infections in vertebrates may still be found throughout the year presumably due to persistent tissue stages replenishing gamont populations, particularly in immunosuppressed hosts.

Differential diagnosis: Infections may be indicated in certain hosts (esp. dogs and cats) by a history of tick infestation with compatible clinical signs, including leucocytosis, non-regenerative anaemia, hypoalbuminaemia and increased serum alkaline phosphatase activity. However, other infectious, immune-mediated or metabolic diseases and several neoplasias may cause similar signs. Infections are conventionally diagnosed by the direct microscopic detection of gamonts in blood smears stained with Giemsa or Wright's stains. Several studies have found the examination of buffy coat smears from centrifuged samples to be more sensitive than examining routine blood smears. Schizonts are usually detected by the histological examination of autopsy (sometimes biopsy) material, and radiological studies have been used to reveal periosteal reactions in the long bones of dogs infected with *H. americanum*. Infections in leech or arthropod vectors may be detected by the microscopy of wet smear/squash preparations of tissues looking for the presence of large polysporocystic oocysts. Several serological tests (fluorescent-antibody tests, enzyme immunoassays) have been developed to detect specific host antibodies against gamont antigens, but little is known about test

sensitivity or specificity, and they have mainly been used for research and several epidemiological studies. More recently, molecular biological techniques have been used to detect and characterize parasites in both vertebrates and vectors following the polymerase chain reaction (PCR) amplification of nuclear gene sequences (predominantly small subunit (18S) ribosomal DNA).

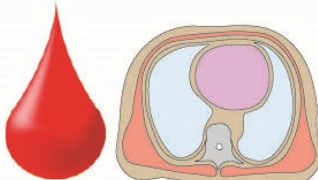
Treatment and control: Asymptomatic or subclinical infections are usually not treated, but those infections producing clinical disease (particularly in dogs and cats) often require chemotherapeutic intervention to prevent their persistence, escalation or potentially fatal outcome. A range of antiprotozoal (antimalarial and coccidiostatic) drugs have been used with variable efficacy to treat animals, including sulphonamides (sulfamethoxazole, sulfadimethoxine, sulfadoxine/pyrimethamine), diaminopyrimidines (trimethoprim), aminoquinolines (primaquine), hydroxyquinolones (decoquinate), diamidines (diminazene aceturate) and imidazolines (imidocarb), with or without antibiotics (oxytetracycline, doxycycline, clindamycin, chloramphenicol). Some treatments produced adverse side-effects in the hosts, including cholinergic conditions requiring atropine. They varied considerably in their efficacy against schizonts and/or gamonts, with none eliminating infections and none effective against persistent cystic stages. Relapses in treated animals were common but could be forestalled by prolonged treatment (sometimes extending to years). Preventive measures are based around vector control to limit transmission to susceptible hosts. Topical or systemic insecticides and acaricides may be used to reduce infestations by ectoparasitic arthropods, together with the regular cleaning and grooming of individual animals to prevent them from ingesting vectors. As some parasite species may also be transmitted horizontally via predation on infected prey or vertically via transplacental transfer, carnivores in endemic areas should be restricted from hunting or consuming raw meat, and infected dams should be treated before mating.

Hepatozoon

(includes all non-chelonian *Haemogregarina* species)



Intermediate Hosts
(mammals, birds, reptiles, amphibians)

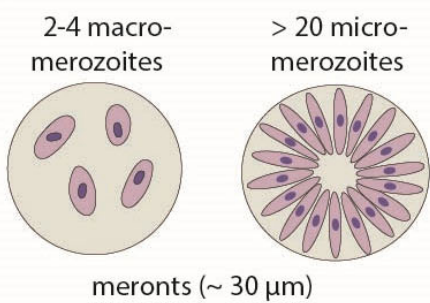


blood, viscera
(occasional
visceral
lesions)

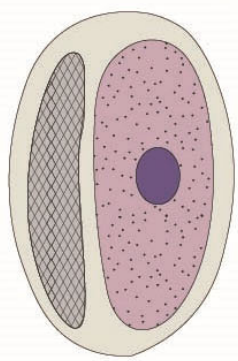
heteroxenous
(2-host)
cycle

asexual merogony
in viscera

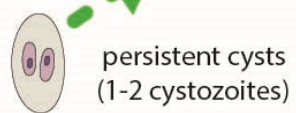
gamont formation
in blood cells



meronts (~ 30 μ m)



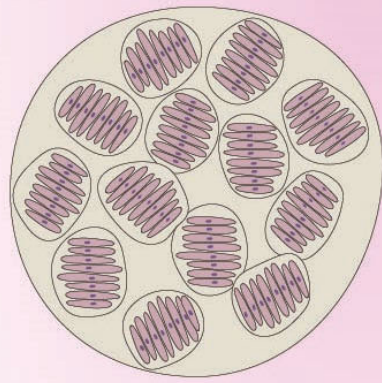
gamonts (9-12 μ m)



persistent cysts
(1-2 cystozoites)

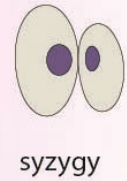
consumptive transmission
(vector ingested)

ingested with
bloodmeal

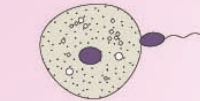


oocyst (200-300 μ m)
(numerous sporocysts)

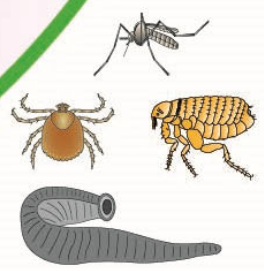
sexual development
completed in vector



syzygy



fertilization

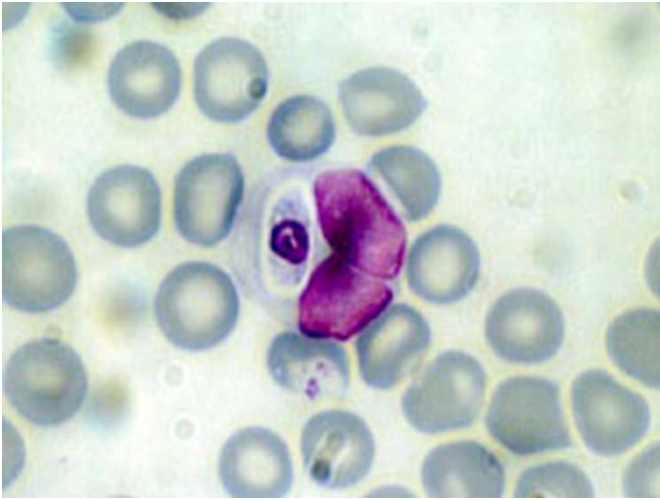


Definitive Hosts
(tick/flea/mosquito/leech vectors)
(tissues, haemocoel)

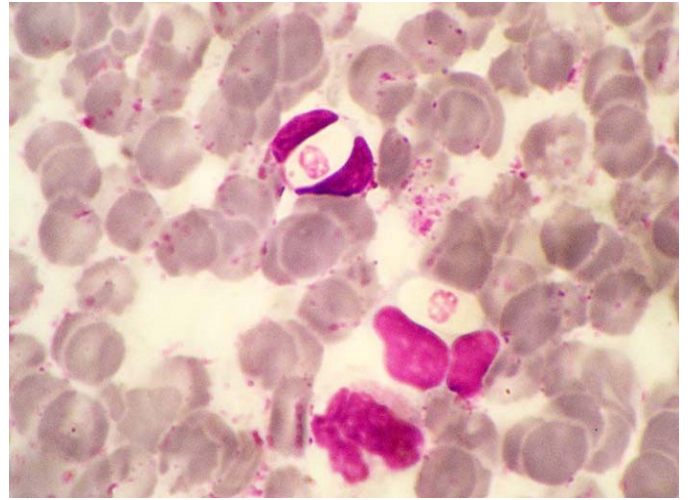


Possible paratenic transport
within foodchain (predators
may become infected when
consuming prey harbouring
persistent tissue stages)

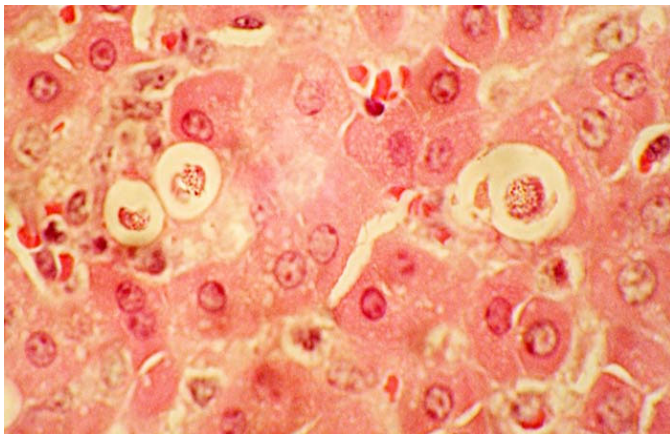
vector-borne transmission



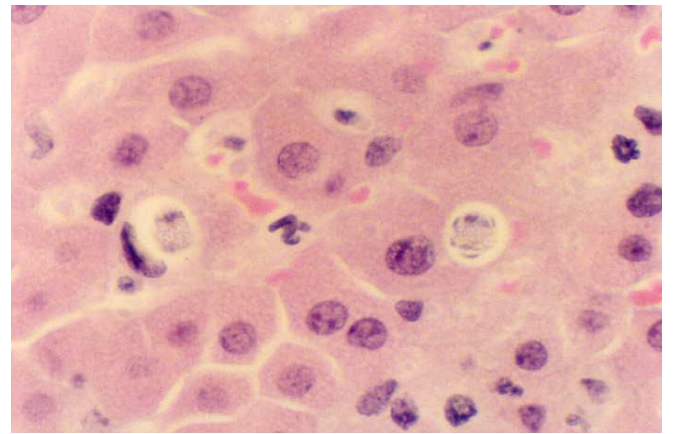
Hepatozoon gamont in dog blood



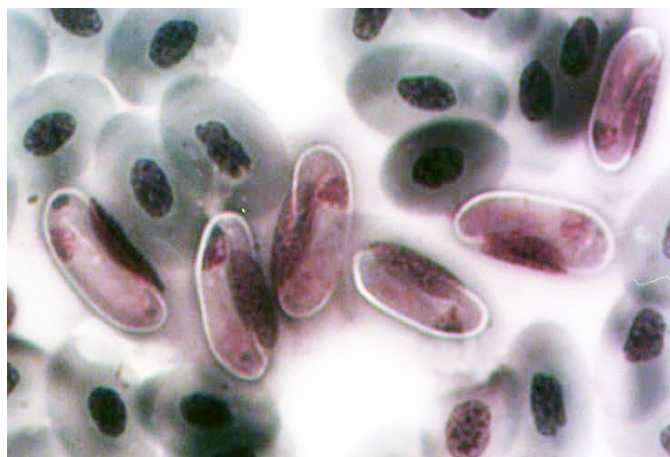
Hepatozoon gamont in dog blood



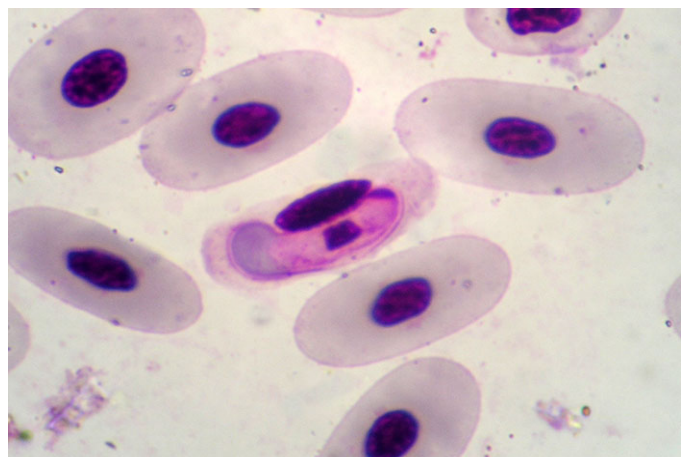
Hepatozoon schizonts in dog liver



Hepatozoon schizonts in dog liver



Hepatozoon (Haemogregarina s.l.) gamonts in snake blood



Hepatozoon (Haemogregarina s.l.) gamont in snake blood