Babesia
(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. In mammals, piroplasm parasites multiply in blood cells by a form of merogony forming small characteristic pear-shaped merozoites. When ingested by ixodid ticks, the parasites form unique paired bodies (strahlenkorper) which give rise to numerous schizonts leading to the production of numerous sporozoites in the salivary glands. Infections persist in ticks during metamorphosis (trans-stadial transmission) and are passed by female ticks to their progeny (trans-ovarian transmission). Many *Babesia* spp. have been detected in mammalian hosts and have been associated with severe disease syndromes (tick fevers).

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: Piroplasmida (pear-shaped stages in blood cells of vertebrates, tick vectors)
Family: Babesiidae (merogony in erythrocytes, trans-stadial + trans-ovarian transmission in ticks)
Genus: *Babesia* (mammals, erythrocytes, indirect (ixodid tick vectors))
Species: various species cause tick fever (babesiosis) in mammals

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	Trans-mission*
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)	*Plasmodium*	mammals, birds, reptiles	liver, erythrocytes	indirect (v-b)
	Haemoproteidae (schizogony in tissues, haemozoin pigment)	*Haemoproteus*	birds	endothelia, erythrocytes	indirect (v-b)
	Leucocytozoidae (schizogony in tissues, no haemozoin pigment)	*Leucocytozoon* (*Akiba*)	birds	tissues, leucocytes	indirect (v-b)
Order: Piroplasmida (pear-shaped blood stages, tick vectors)	Babesiidae (merogony in erythrocytes, trans-stadial + trans-ovarian transmission)	*Babesia*	mammals	erythrocytes	indirect (v-b)
	Theileriidae (merogony in leucocytes, trans-stadial transmission in ticks)	*Theileria*	ruminants	leucocytes, erythrocytes	indirect (v-b)
Class: Coccidiomorphea [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)	*Haemogregarina*	reptiles, amphibia, fish	tissues, blood	indirect (v-b)
		Hepatozoon	mammals, reptiles	tissues, blood	indirect (v-b)
	Klossiellidae (sporocysts)	*Klossiella*	mammals	kidney	direct (f-o)
Suborder: Eimeriorina (no syzygy, >4 microgametes)	Eimeriidae (monoxenous, endogenous merogony and gamogony, exogenous sporogony)	*Caryospora*	birds, reptiles	gut	direct (f-o)
		Cyclospora	mammals, reptiles	gut	direct (f-o)
		Isospora	birds, reptiles	gut	direct (f-o)
		Eimeria	vertebrates	gut, tissues	direct (f-o)
		Epieimeria	fish	gut	direct (f-o)
		Goussia	fish	gut	direct (f-o)
	Sarcocystidae (heteroxenous, 1:2:4 oocyst:sporocyst:sporozoite configuration)				
	subfamily Cystoisosporinae (monozoic cysts)	*Cystoisospora* (no Stieda bodies)	carnivores, omnivores	gut, tissues	direct (f-o), indirect (p-p)
	subfamily: Sarcocystinae (thick-walls, metrocytes)	*Sarcocystis* (*Frenkelia*)	mammals, birds, reptiles	gut, muscles	indirect (p-p)
	subfamily: Toxoplasmatinae (thin-walled cysts without metrocytes)	*Besnoita*	mammals, reptiles	gut, tissues	indirect (p-p)
		Hammondia	mammals	gut, tissues	indirect (p-p)
		Neospora	herbivores, dogs	gut, tissues	indirect (p-p)
		Toxoplasma	vertebrates, cats	gut, tissues	indirect (p-p)
Class: Gregarinomorphea (gregarines, trophonts with specialized attachment epimerite or mucron, syzygy)					
Subclass: Cryptogregaria (epicellular parasites of vertebrates with feeder organelle but lacking apicoplast)					
	Cryptosporidiidae (naked sporozoites)	*Cryptosporidium*	vertebrates	gut, lungs	direct (f-o)

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

Piroplasms undergo unique ‘sexual’ reproduction involving pairing of ray-bodies (Strahlenkorper) in tick ‘vectors’ (making them definitive hosts) and then asexual developmental (merogony) in erythrocytes, and sometimes other circulating and fixed cells, in vertebrates (making them intermediate hosts). They differ from other blood-borne Apicomplexa (haemosporidia and haemococcidia) in that they do not form conoids, oocysts, spores or pseudocysts. Infections by piroplasms have been detected in over 130 species in mammals and in some birds and reptiles. Three families are recognized essentially on the basis of their site of development in their vertebrate hosts: Babesiidae (in erythrocytes of mammals and some birds); Theileridae (in lymphocytes then erythrocytes of mammals); and Haemohormidiidae (in nucleated erythrocytes of reptiles). The parasites undergo trans-stadial transmission in their tick vectors (parasites persist when ticks metamorphose from larvae to nymphs to adults) while some babesiids also undergo trans-ovarian (vertical) transmission (eggs become infected in gravid female ticks).

Piroplasms	No. spp.	Site of development in vertebrates		Vertebrate hosts	Invertebrate vectors
		meronts	'gamonts'		
Family: Babesiidae (erythrocytes of mammals and birds)					
Babesia	100	erythrocytes	erythrocytes	mammals, birds	ticks
Family: Theileridae (lymphocytes then erythrocytes of mammals)					
Theileria	15	lymphocytes	erythrocytes	ruminants	ticks
Cytauxzoon	4	vascular endothelia	erythrocytes	carnivores	ticks
Family: Haemohormidiidae (nucleated erythrocytes of reptiles and fish)					
Sauroplasma (*Serpentoplasma*)	3	erythrocytes	erythrocytes	lizards, snakes	ticks?
Haemohormidium (*Haematractidium*)	12	erythrocytes	erythrocytes	tortoises, frogs, fish	leeches

Two broad *Babesia* spp. morphotypes occur in host erythrocytes; some species forming small (1-2 µm) merozoites shorter than the erythrocyte radius (e.g. *B. bovis, B. divergens, B. gibsoni, B.ovis*); and others forming large (2-5 µm) merozoites longer than the erythrocyte radius (e.g. *B. bigemina, B. canis, B. major, B. motasi*). Molecular biological studies on comparative gene sequences have shown that the Babesiidae may be divided into two major clades: *Babesia s.s.* (*sensu stricto,* in the narrowest sense) comprising those species forming two merozoites in the erythrocytes of carnivores and rodents and undergoing trans-stadial and trans-ovarian transmission in ticks (e.g. *B. bovis, B. canis*); and *Babesia s.l.* (*sensu lato,* in the broadest sense) comprising those species forming four merozoites in the erythrocytes of rodents, carnivores and deer and only undergoing trans-stadial transmission in ticks (e.g. *B. microti, B. conradae*). These clades are apparently split by an intermediary *Theileria/Cytauxzoon* clade comprising species which exhibit pre-erythrocytic schizogony before forming four merozoites in erythrocytes in ungulates and felids and undergoing trans-stadial transmission in ticks (e.g. *T. parva, C. felis*).

Babesia infections have been detected in most domestic animals (cattle, sheep, goats, horses, pigs, dogs, cats) and numerous wild animals (over 70 species) and humans. Five species cause tick fever in cattle: two small piroplasms *B. bovis* (syn. *B. argentina, B. berbera*) and *B. divergens*; and three large piroplasms *B. bigemina, B. major* and *B. ovata.* Two species were originally thought to infect horses, large *B. caballi* and small *B. equi*, but the latter was recently re-classified as *Theileria equi* due to the discovery of exo-erythrocytic (intra-lymphocytic) merogony. A similar discovery resulted in *B. microti* from rodents being re-classified as *Theileria microti* (both re-classifications supported by contemporary molecular biological studies). The host specificities of *Babesia* spp. for both vertebrate and invertebrate hosts is variable, but most are stenoxenous with parasite species only infecting closely-related hosts, although zoonotic infections in humans have been attributed to *B. divergens* and *B. venatorum* from ruminants in Europe and *T. microti* from rodents in North America. All parasite species are limited in their distribution in accordance with that of their tick vectors.

Parasite species	Vertebrate hosts	Merozoite size (µm)	Vectors	Distribution
Species in mammals				
B. alberti	Carnivora: hyaenid (spotted hyena)			Africa
B. avicularis	Rodentia: murid (striped zebra mouse, Abyssinian grass rat)			Africa
B. bandicootia	Rodentia: murid (greater bandicoot rat), plus experimentally murid (brown rats, gerbils), cricetid (hamsters)			Asia
B. beliceri	Artiodactyla: bovid (cattle)			Russia
B. bigemina	Artiodactyla: bovid (cattle, buffalo, zebu, yak, bison, sheep, Soemmerring's gazelle), cervid (brocket deer, white-tailed deer)	large (1.5-5.0)	one-host ticks (*Rhipicephalus annulatus, R. australis, R. decoloratus, R. geigyi, R. microplus*), two-host ticks (*R. evertsi*)	Europe, Africa, Asia, Australia, Americas
B. bovis (syn. *B. argentina, B. berbera*) [type species]	Artiodactyla: bovid (cattle, zebu, buffalo), cervid (red deer?, European roe deer, Panama white-tailed deer?)	small (1.0-2.4)	one-host ticks (*Rhipicephalus annulatus, R. australis, R. calcaratus, R. geigyi, R. microplus*), 2-host ticks (*R. bursa*), 3-host ticks (*Ixodes ricinus, I. persulcatus*)	Europe, Africa, Asia, Australia, South & Central America

B. brachyceri	Artiodactyla: bovid (dwarf buffalo)			Africa
B. brasiliensis	Didelphimorphia: didelphid (four-eyed opossums, white-eared opossum, black-eared opossum)			Central and South America
B. brygooi	Afrosoricida: tenrecid (hedgehog tenrecs)			Madagascar
B. caballi	Perissodactyla: equid (horse, donkey, mule, plains zebra)	large (2.0-5.0)	one-host ticks (*Dermacentor albipictus, D. nitens, Hyalomma scupense*), two-host ticks (*Hy. excavatum, Hy. truncatum, Rhipicephalus bursa, R. evertsi*), three-host ticks (*D. marginatus, D. reticulatus, D. silvarum, D. variabilis, R. sanguineus*)	Europe, Asia, Africa, Americas, Australia
B. campana	Rodentia: murid (field mice)			Africa
B. canis canis	Carnivora: canid (dog, raccoon dog, red fox, coyote), plus molecular detection in felid (cat) [haemolytic disease in dogs)	large (2.0-5.0)	three-host ticks (*Dermacentor marginatus, D. reticulatus, D. variabilis, Rhipicephalus sanguineus*)	Europe, now cosmopolitan
B. canis presentii	Carnivora: felid (cat)	large (2.0-5.0)	?	Israel
B. canis rossi (syn. *B. rossi*)	Carnivora: canid (dog, African wild dog) [haemolytic disease]	large (2.0-5.0)	three-host ticks (*Haemaphysalis elliptica* syn. *leachi*)	Southern Africa
B. canis vogeli (syn. *B. vogeli*)	Carnivora: canid (dog) [mild disease]	large (2.0-5.0)	three-host ticks (*Rhipicephalus sanguineus*)	cosmopolitan
B. capreoli	Artiodactyla: cervid (European roe deer, red deer)			Europe
B. cati	Carnivora: felid (cat)	3.0	unknown	South Africa, India
B. cheirogalei	Primates: cheirogaleid (greater dwarf lemur)			Madagascar
B. citelli	Rodentia: sciurid (leopard ground squirrel)			North America
B. civettae	Carnivora: viverrid (African civet)			Africa
B. colesi	Rodentia: murid (wood mouse)			Europe, Africa
B. conradae	Carnivora: canid (dog)	small (1.0-3.0)	three-host ticks (*Dermacentor variabilis, Rhipicephalus sanguineus*)	North America
B. crassa	Artiodactyla: bovid (sheep, and experimentally goats); Primates: hominid (human)		three-host ticks (*Ixodes persulcatus*, *Haemaphysalis concinna*)	Asia
B. cricetuli	Rodentia: cricetid (Daurian hamster)			Eurasia
B. crocidurae	Eulipotyphla: soricid (bicolored shrew, Eurasian shrew)			Africa, Eurasia
B. cynicti	Carnivora: herpestid (yellow mongoose)			Africa
B. decumani	Rodentia: murid (brown rat, and experimentally house mouse)			Africa, Asia
B. divergens	Artiodactyla: bovid (cattle, mouflon), cervid (fallow deer, red deer, reindeer, European roe deer); and splenectomized Rodentia: murid (gerbil); Primates:	small (1.5-2.0)	three-host ticks (*Dermacentor marginatus, Ixodes ricinus, I. persulcatus*)	Western & Central Europe, North Africa

	cercopithecid (rhesus macaque), hominid (chimpanzee, human)			
B. duncani (WA1)	Primates: hominid (human); Artiodactyla: cervid (mule deer), bovid (bighorn sheep); Perissodactyla: equid (horse); Rodentia: cricetid (hamster)	variable (0.5-4.0)	one-host tick (*Dermacentor albipictus*)	North America
B. eliomysi	Rodentia: glirid (garden dormouse)			Europe
B. epsteini	Rodentia: sciurid (little souslik)			Asia
B. equi [now *Theileria equi*]	Perissodactyla: equid (horse, donkey, mule, zebra)	small (2.0-3.0)	one-host ticks (*Dermacentor albipictus, D. nitens, Hyalomma scupense*), two-host ticks (*Hy. anatolicum, Hy. dromedarii, Hy. marginatum, Rhipicephalus bursa, R. evertsi*), three-host ticks (*D. reticulatus, D. variabilis, R. sanguineus*)	Europe, Africa, Asia, Americas
B. ernestoi	Didelphimorpha: didelphid (black-eared opossum, white-eared opossum)			Central and South America
B. felis (syn. *Babesiella felis, Nuttallia felis, Nicollia felis*)	Carnivora: felid (cat, lion, leopard, Sudanese wild cat, puma, American lynx)	small (1.5-3.0)	three-host ticks (*Haemaphysalis elliptica* syn. *leachi*)	Africa, now cosmopolitan
B. foliata	Artiodactyla: bovid (sheep)			India
B. galagolata	Primates: galagid (brown greater galago), and experimentally Primates: cercopithecid (rhesus monkey), Rodentia: murid (brown rat, house mouse, gerbil), cricetid (golden hamster), caviid (guinea pig)			Africa
B. garnhami	Carnivora: viverrid (common genet, Cape genet)			Africa
B. genettae	Carnivora: viverrid (common genet)			Africa
B. gerbilli	Rodentia: murid (great gerbil)			Asia
B. gibsoni	Carnivora: canid (dog, wolf, jackal, dhole, fennec fox), herpestid (mongoose), mustelid (Burmese ferret-badger)	small (1.0-3.0)	three-host ticks (*Haemaphysalis bispinosa, Ha. longicornis, Rhipicephalus sanguineus*), also transmitted transplacentally and via dog bites	India, Asia, North Africa, North America
B. golundae	Rodentia: murid (striped grass mouse)			Africa
B. graingeri	Rodentia: sciurid (striped ground squirrel)			Africa
B. heischi	Carnivora: herpestid (African dwarf mongoose)			Africa
B. herpailuri	Carnivora: felid (jaguarundi, ocelot, cat)	2.3-3.0		Americas
B. herpestedis	Carnivora: herpestid (Egyptian mongoose)			Africa
B. hoarei	Carnivora: herpestid (dwarf mongoose)			Africa
B. hylomysci	Rodentia: murid (Stella wood mouse), plus experimentally Rodentia: murid (Cairo spiny mouse, European wood mouse, Natal multimammate mouse, Mongolian gerbil, Shaw's jird, house mouse, brown rat), cricetid (bank vole, Syrian hamster, Chinese hamster, steppe			Eurasia, Africa

	lemming, deer mouse, hispid cotton rat), sciurid (chipmunk); Primates: cercopithecid (rhesus macaque)			
B. kolzovi	Rodentia: sciurid (little ground squirrel)			Asia
B. legeri	Carnivora: herpestid (water mongoose)			Africa
B. lemniscomysi	Rodentia: murid (striped grass mouse)			Africa
B. leo	Carnivora: felid (lion)			Africa
B. leporis	Lagomorpha: leporid (hare)			Europe
B. lotori	Carnivora: procyonid (raccoon); Rodentia: cricetid (hamster)	small		North America
B. loxodontis	Proboscidea: elephantid (African bush elephant)			Africa
B. macaci	Primates: cercopithecid (long-tailed macaque, rhesus macaque, vervet monkey)			Asia, Africa
B. macropus	Diprotodontia: macropodid (eastern grey kangaroos, agile wallabies)	1-5		Australia
B. major	Artiodactyla: bovid (cattle)	large (1.8-3.0)	three-host ticks (*Haemaphysalis longicornis, Ha. punctata*)	Europe, North Africa, Asia, Americas
B. meles	Carnivora: mustelid (European badger)			Europe
B. mephitis	Carnivora: mephitid (striped skunk)	large		North America
B. meri	Rodentia: murid (fat sand rat), and experimentally murid (spiny mouse, unstriped grass mouse, multimammate mouse, house mouse, rats, gerbil), cricetid (hamster)			
B. merionis	Rodentia: cricetid (gerbils, jirds)			Eurasia
B. microti [now *Theileria microti*]	Rodentia: murid (mice, field mice, white-footed mice, thicket rats), cricetid (deer mice, pack rats, voles, red-backed voles); sciurid (ground squirrels); Eulipotyphla: soricid (shrews, water shrews); Lagomorpha: leporid (cottontail rabbits), occasionally Primates: hominid (human), plus experimentally Rodentia: murid (gerbils, mice, multimammate mice), cricetid (cotton rats, hamsters, lemmings), Primates: cebid (capuchins, squirrel monkeys), cercopithecid (baboons, guenons, macaques), hominid (chimpanzees)	small (1.5-2.0)	three-host ticks (*Ixodes muris, I. ricinus, I. scapularis* syn. *dammini, I. persulcatus, I. ovatus*)	Northern Hemisphere (+ lab model worldwide)
B. missirolii	Carnivora: mustelid (European badger)			Europe
B. motasi	Artiodactyla: bovid (sheep, goat)	large (2.5-4.0)	three-host ticks (*Dermacentor silvarum, Haemaphysalis otophila, Ha. punctata*), two-host ticks (*Rhipicephalus bursa*)	Europe, Middle-East, North Africa, Asia
B. mungo	Carnivora: herpestid (Indian grey mongoose)			India
B. muratovi	Rodentia: murid (house mouse, brown rat), sciurid (long-clawed ground squirrel)			Eurasia
B. muris	Rodentia: murid (brown rat, long-tailed field mouse)			Europe
B. musculi	Rodentia: murid (house mouse)			Europe
B. mustelae	Carnivora: mustelid (European polecat)			Eurasia
B. myoxi	Rodentia: glirid (fat dormouse)			Europe
B.	Carnivora: canid (grey wolf)			Europe

ninakohlyakimovae				
B. ninensis	Eulipotyphla: erinaceid (European hedgehog, Algerian hedgehog, long-eared hedgehog), soricid (Eurasian shrew)			Eurasia
B. occultans	Artiodactyla: bovid (cattle)		two-host ticks (*Hyalomma marginatum*)	Africa
B. odocoilei	Artiodactyla: cervid (white-tailed deer)		three-host ticks (*Ixodes scapularis*)	North America
B. ovata	Artiodactyla: bovid (cattle)	large (3)	three-host ticks (*Haemaphysalis longicornis, Ha. punctata*)	Asia
B. ovis	Artiodactyla: bovid (sheep, goat)	small (1.0-2.5)	three-host ticks (*Dermacentor marginatus, D. reticulatus, Haemaphysalis punctata, Ixodes ricinus, I. persulcatus, Rhipicephalus turanicus*), two-host ticks (*Hyalomma anatolicum, Hy. excavatum, R. bursa, R. evertsi*)	Southern and Eastern Europe, North Africa, Middle-East, Asia
B. pantherae	Carnivora: felid (leopard),and experimentally felid (cat)	small (1.5-2.5)		Africa
B. pattoni	Artiodactyla: cervid (spotted deer, sambar)			Asia
B. perodictici	Primates: lorisid (potto)			Africa
B. perroncitoi	Artiodactyla: suid (pig, boar)	small (0.7-3.0)	three-host ticks (*Dermacentor reticulatus, Rhipicephalus appendiculatus, R. sanguineus*)	Southern Europe, West and Central Africa, Vietnam
B. pitheci	Primates: cercopithecid (guenons, mangabeys, baboons)			Africa
B. procyoni	Carnivora: canid (raccoon dog)			Asia
B. propitheci	Primates: indriid (white sifaka)			Madagascar
B. quadrigernina	Rodentia: ctenodactylid (common gundi)			North Africa
B. ratti	Rodentia: murid (Natal multimammate mouse)			Africa
B. rhombomys	Rodentia: murid (great gerbil)			Central Asia
B. rigolleti	Rodentia: glirid (Huet's dormouse)			Africa
B. rodhaini	Rodentia: murid (rats, mice)	small (1.0-2.5)		Europe, Africa (+ lab model worldwide)
B. roubaudi	Carnivora: mustelid (striped polecat)			Africa
B. tachyglossi	Monotremata: tachyglossid (echidna)			Australia
B. talpae	Eulipotyphla: talpid (European mole)			Europe
B. taterae	Rodentia: murid (Indian gerbil)			India
B. taterillae	Rodentia: murid (Emin's gerbil)			Africa
B. taylori	Artiodactyla: bovid (goat)	small (1.5-2.0)	?	Eurasia
B. thomasi	Hyracoidea: procaviid (rock hyrax, bush hyrax)			Africa
B. thylacis	Peramelemorphia: peramelid (southern brown bandicoot), Dasyuromorphia: dasyurid (quolls)			Australia

B. trautmanni	Artiodactyla: suid (pig)	large (2.5-4.0)	one-host ticks (*Rhipicephalus decloratus*), three-host ticks (*Dermacentor reticulatus, R. appendiculatus, R. sanguineus*)	Southern Europe, Africa, Asia
B. tucotucoi	Rodentia: Ctenomyid (tuco-tuco)			South America
B. vanhoofi	Carnivora: herpestid (common dwarf mongoose)			Africa
B. venatorum	Artiodactyla: cervid (European roe deer), occasionally Primates: hominid (human)	small (1.0-3.0)	three-host ticks (*Ixodes ricinus, I. persulcatus*)	Eurasia
B. vespertilionis	Chiroptera: vespertilionid (common noctule)			Eurasia, Africa
B. vesperugina	Chiroptera: vespertilionid (noctule bats, mouse-eared bats, long-eared bats, pipistrelles)			Eurasia, Africa
B. volgensis	Rodentia: sciurid (yellow ground squirrel)			Central Asia
B. vulpes (syn. *B. microti*-like, *Theileria annae*)	Carnivora: canid (dogs, fox)	small (< 2)	three-host ticks (*Dermacentor reticulatus, Ixodes canisuga, I. hexagonus*, *I. ricinus, Rhipicephalus sanguineus*)	North America, Europe
B. wrighti	Rodentia: sciurid (rock squirrel)			North America
B. yakimovi	Rodentia: sciurid (Siberian chipmunk, Chinese rock squirrel)			Asia
B. zolotarevi	Artiodactyla: bovid (bison)			North America
Species in birds				
B. avium (*incertae sedis*)	Galliformes: phasianid (rock partridges)	2		Iran
B. ardea	Pelecaniformes: ardeid (grey heron)	cruciform		Eurasia
B. balearica	Gruiformes: gruid (black-crowned crane)			Africa
B. bennetti	Charadriiformes: larid (yellow-legged gull)	2.9-4.6		Mediterranean
B. emberizica	Passeriformes: emberizid (buntings)			Asia
B. frugilegica	Passeriformes: corvid (rook, house crow, treepie, chough)			Europe, Asia
B. henryi (*nomem nudum* – possibly rickettsias)	Anseriformes: anatid (swan goose, ducks)	< 1.2		Asia
B. kazachstanica	Passeriformes: alaudid (crested lark)			Eurasia
B. kiwiensis	Apterygiformes: apterygid (kiwis)			Australasian
B. krylovi	Bucerotiformes: upupid (hoopoe)			Afro-Eurasia
B. moshkovskii (*species inquirenda* – other records referable to *B. shortti*)	Accipitriformes: accipitrid (bearded vulture)	rings, tetrads, cruciforms (plus schizonts? in leucocytes and RE cells)		Africa, Eurasia
B. mujunkumica (syn. *socius*)	Passeriformes: passerid (Indian sparrow), ploceid (sociable weavers)	1-2.1 x 0.4-0.5		India, Africa
B. necrophorum (*nomen nudum* – tabulation and mis-translation errors)	Passeriformes: corvid (crows, rooks, jays, magpies, nutcracker), Galliformes: phasianid (grouse), Charadriiformes: scolopacid (woodcock, snipe)	-	-	Russia
B. peircei	Sphenisciformes: spheniscid (jackass penguin)	1.5-4.0		Africa
B. poelea	Suliformes: sulid (boobies)	nr		Melanesia

B. rustica	Passeriformes: passerid (barn swallow, red-rumped swallow)			Afro-Eurasia, Americas
B. shortti	Falconiformes: falconid (kestrels, prairie falcon, saker falcon) [pathogenic]	1.6-2.4 x 0.7-1.0		Europe, North America
B. tropicus (*nomem nudum* – confused description)	Galliformes: phasianid (chickens)			India
Species in reptiles				
B. passeritae	Serpentes: colubrid (Malayan green whipsnake)			Malaya

Parasite morphology: The parasites form pyriform (pear-shaped) bodies in the erythrocytes of vertebrates and vermiform (worm-like) bodies in tissues of their tick vectors. In vertebrates, intraerythrocytic stages appear singly as small round, ovoid or elongate trophozoites (1-4 µm), in pairs as pyriform merozoites (hence the common name piroplasm), or in tetrads as cruciform merozoites (sometimes called Maltese cross forms). Babesial stages do not form haemozoin pigment and they do undergo erythrocytic merogony. Erythrocytic stages are usually basophilic with dense chromatin granules, and some stages form large central vacuoles that gives the piroplasm a ring-shape. Blood stages do not cause alterations in red cell morphology nor produce Maurer's clefts, Schuffner's dots or James's dots (as observed for *Plasmodium* spp.). Individual species are often grouped into 'small *Babesia'* (merozoites 1.0-2.5 µm long) or 'large *Babesia'* (merozoites > 2.5 µm long. In very high parasitaemias, merozoites may also be found occasionally as extracellular forms, either singly or as syncytial structures. Merozoites typically lack a conoid, micropores and mitochondria but possess other apical complex organelles (rhoptries, micronemes, polar rings and subpellicular microtubules). In ticks, some ingested parasites (presumably gametocytes) develop unique anterior arrowhead-shaped organelles (called Strahlenkorper or ray-bodies). These parasites pair up and fuse to form motile kinetes which invade tick body tissues before undergoing division to produce vermiform sporozoites (2-3 µm long) in the salivary glands.

Site of infection: In vertebrates, parasites infect host erythrocytes and undergo transformation to form trophozoites which divide by binary merogony (schizogony) and undergo differentiation to form merozoites. The host cell is ultimately lysed and the merozoites infect new cells, repeating the cycle of development. A total of 126 parasite species have been described: 107 parasite species in over 160 mammalian species (belonging to 39 families in 16 orders); 18 parasite species in over 30 bird species (belonging to 12 orders); and one species in a reptile (colubrid snake). In vectors, parasites form ray-bodies in the gut, ookinetes and sporokinetes in tick tissues, and finally sporonts and sporozoites in the salivary glands. A total of 42 species of ixodid ticks have been identified as vectors, including 24 species of 3-host ticks (belonging to 4 genera), 8 species of 2-host ticks (2 genera) and even 10 species of 1-host ticks (3 genera).

Pathogenesis: Many infections remain asymptomatic or subclinical in healthy individuals, but heavy infections by various species may cause mild-severe disease (called babesiosis or piroplasmosis). Infected animals develop a high persistent fever (commonly known as tick fever) becoming dull, listless and anorexic. Piroplasms affect erythrocyte membrane fragility which can lead to extensive intravascular haemolysis (erythrocyte rupture) producing progressive signs of anaemia. Erythrocyte destruction may be as high as 75% in fatal cases and even milder infections produce severe anaemia (macrocytic, hypochromic). Haemoglobin clearance mechanisms become overloaded, resulting in jaundice, hyperbilirubinuria and haemoglobinuria (red discolouration of the urine, 'red-water' in bovine babesiosis). Haemolysis involves the release of many pharmacologically active agents (e.g. proteolytic enzymes) which affect microcirculation (vasodilatation, increased permeability) leading to hypotension and oedema, and affect blood (viscosity, coagulation, cytoadherence) leading to ischaemia (congestion and degenerative changes in tissues/organs). Infected animals may exhibit diarrhoea, nausea, vomiting, pyrexia, tachycardia, tachypnoea (perhaps dyspnoea), abortion if pregnant, myalgia, muscle tremors, cerebral signs (due to sequestration of infected erythrocytes in cerebral capillaries), ataxia, anorexia, lethargy, fatigue, weakness, wasting, coma and death. Chronically infected animals remain weak, thin and out of condition for several weeks before recovery. Animals that recover are usually immune for life, sometimes thought to be due to complete cure (sterile immunity) but more often associated with the persistence of small numbers of parasites (premunitive immunity). There is an inverse age-resistance to infection and disease, with young cattle being less susceptible than older cattle. There is also a genetic component to resistance, with *Bos taurus* cattle being more susceptible than *Bos indicus* (zebu) cattle. Infections in humans have proven severe and fatal in asplenic or otherwise immuno-compromised individuals, with symptoms appearing 10-20 days after tick bite and presenting as a fulminant febrile haemolytic disease over 9 weeks (with subsequent relapses), characterized by general malaise, then fever, shaking chills, sweating, arthralgias, myalgias, fatigue, weakness, occasional hepatosplenomegaly, jaundice and occasionally retinal infarctions, ecchymoses and petechiae, acute respiratory failure, congestive heart failure, disseminated intravascular coagulation, liver and renal failure and splenic rupture.

Developmental cycle and mode of transmission: Infections are transmitted by ixodid (hard-bodied) ticks which may be one-, two- or three-host ticks. After ticks have fed on infected host blood, some parasites are liberated from ingested erythrocytes in the tick gut and form elongate stages (gametocytes?) with unique arrowhead-shaped organelles (ray-bodies or Strahlenkorper). These bodies pair up (syzygy) and fuse (syngamous fertilization?) to produce a nonmotile zygote which uses its spike-like arrowhead organelle upon contact to invade an epithelial cell and transform into a motile ookinete stage. Ookinetes penetrate the gut wall into the body cavity and invade tick tissues where they form more kinetes (sporokinetes). Sporokinetes undergo trans-stadial transmission, thus infections persist during metamorphosis from larvae to nymphs to adults. Kinetes of some *Babesia* species may also invade the tick ovary and penetrate developing eggs where they divide to form small round organisms. These stages facilitate trans-ovarian transmission, so that nearly all the progeny are born already infected (particularly important process for one-host ticks whose developmental stages do not move between different individual hosts). To complete the cycle, some kinetes eventually invade the salivary glands and form polymorphic multinucleate sporonts (or sporoblasts) which produce hundreds of vermiform sporozoites through a budding process. When the tick next feeds, the sporozoites are injected with tick saliva into the vertebrate host. In this host, *Babesia* parasites do not undergo exo-erythrocytic division in host tissues but directly invade host erythrocytes where they undergo cyclic merogony dividing by binary fission to produce 2-4 characteristic piroplasm merozoites. It has been reported that some merozoites grow slowly and fold to form accordion-like structures which may be pre-gametocytes destined to undergo further development in tick vectors. Infections by a few species have occasionally been transmitted between vertebrate hosts by blood transfusions and infrequently by transplacental or perinatal infection.

Differential diagnosis: A history of tick infestation and clinical signs of fever, anaemia and haemoglobinuria are suggestive of babesiosis (tick fever). Congested abdominal organs, watery blood, haemoglobinaemia, jaundice and dark red urine may be observed at necropsy. Confirmation of diagnosis is conventionally afforded by the detection of intraerythrocytic stages in smears of peripheral blood stained with any of the Romanowsky's stains, notably Giemsa. However, once the acute febrile phase has passed, parasites may be difficult to find as they are rapidly removed from the circulation. Some parasites may be cultured *in vivo* by inoculation into susceptible laboratory animals (golden hamsters, jirds, mice) or *in vitro* by inoculation into autologous blood preparations, but considerable variation has been observed in host susceptibility and culture success. Diagnostic recourse is therefore often made to immunoserological tests to detect specific host antibodies against the parasites (fluorescent-antibody tests, enzyme immunoassays and immunoblotting). Molecular biological techniques have also been developed to detect parasite DNA following the polymerase chain reaction (PCR) amplification of specific gene sequences (18S (small subunit) ribosomal RNA (SSU rRNA), internal transcribed spacers (ITS), beta-tubulin).

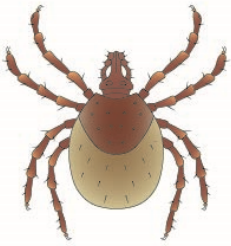
Treatment and control: Timely chemotherapy is generally effective, although the small virulent species (such as *B. bovis*) are usually more difficult to treat than other less aggressive species. One of the first successful treatments for bovine babesiosis was the azonaphthalene dye, trypan blue, but it was not very effective against *B. bovis*. The most commonly used compounds are the diamidines (diminazene diaceturate, imidocarb, amicarbalide), and quinuronium and acridine derivatives. Naphthoquinones (atovaquone), macrolide antibiotics (clindamycin, azithromycin), tetracyclines (oxytetracycline, chlortetracycline) and cinchona alkaloids (quinine) have shown variable effects against human infections, with other interventions including blood exchange transfusion for life-threatening infections, and dialysis in case of renal failure. Cats have been treated with long courses of primaquine, with blood transfusion supplementation if required. Treatment can facilitate recovery, leaving latent infections or complete cure. However, elimination of all parasites may also eliminate premunitive immunity. Because young animals in endemic areas develop infection-immunity (premunition), this has been exploited for immunological control through premunization or chemoimmunization (infect animals then treat them) or vaccination using whole parasites (attenuated strains) or subcellular (subunit) fractions. Several commercially available preparations have proven effective in regional areas, but a universal vaccine is not yet available. Prevention strategies involving tick control programmes (barriers, quarantine, tick treatment, tick-resistant hosts) have been relatively effective in several countries in controlling or eliminating infections in domestic stock. If possible, wild or feral animals acting as reservoir populations for parasites and/or ticks (especially deer populations) should be excluded from farms or treated using medicated foods or acaricidal rubbing posts. Humans at high risk of tick bite (farm workers and hikers) may use long clothing to cover exposed skin and apply repellents to skin or clothing (permethrin, DEET).

Babesia

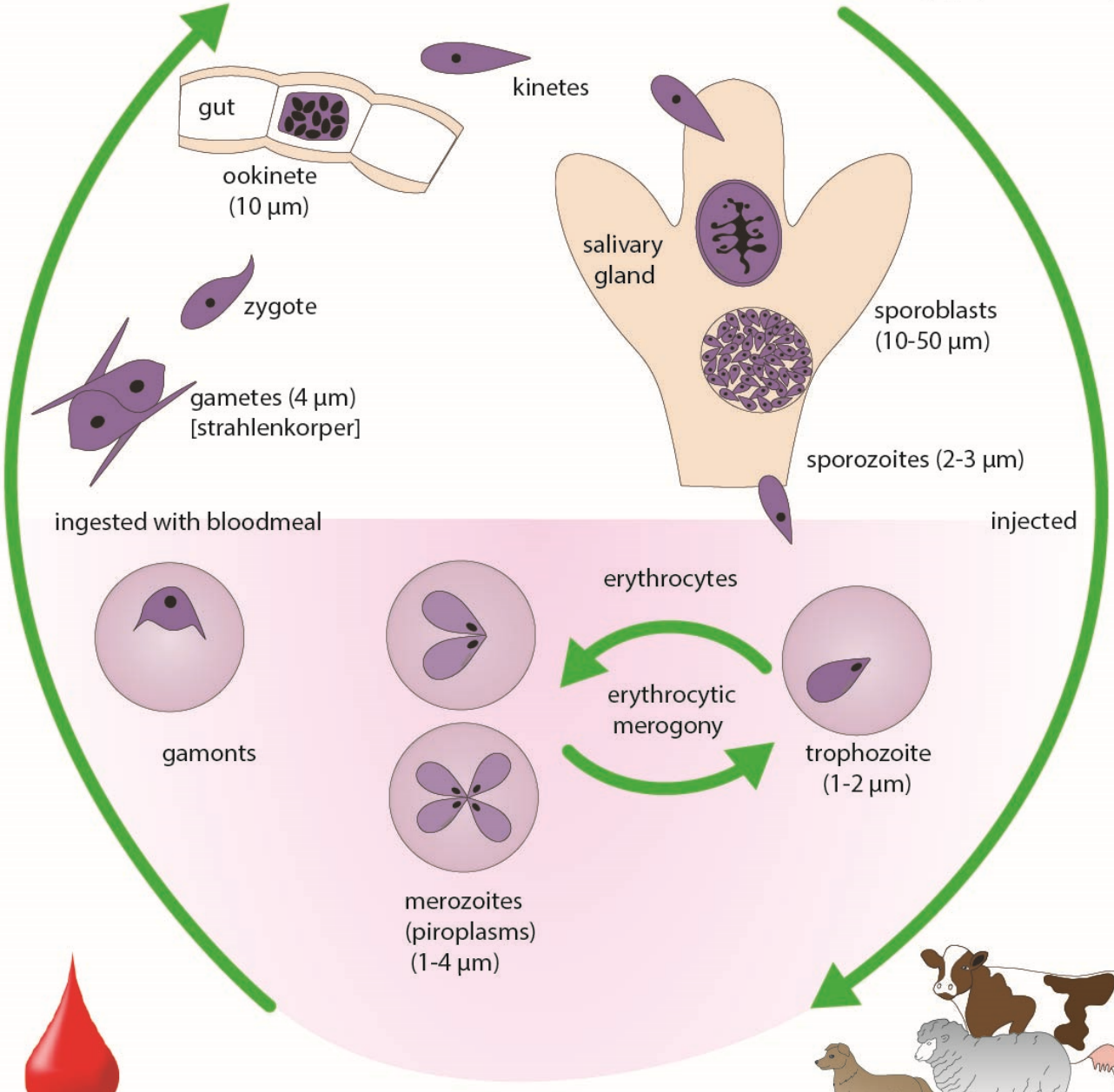
2 major clades:
Babesia s.s.
(forming 2 piroplasms, undergo trans-stadial and trans-ovarian transmission in ticks)
Babesia s.l.
(forming 4 piroplasms, only undergo trans-stadial transmission in ticks)

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

trans-stadial and trans-ovarian transmission may occur within tick developmental stages

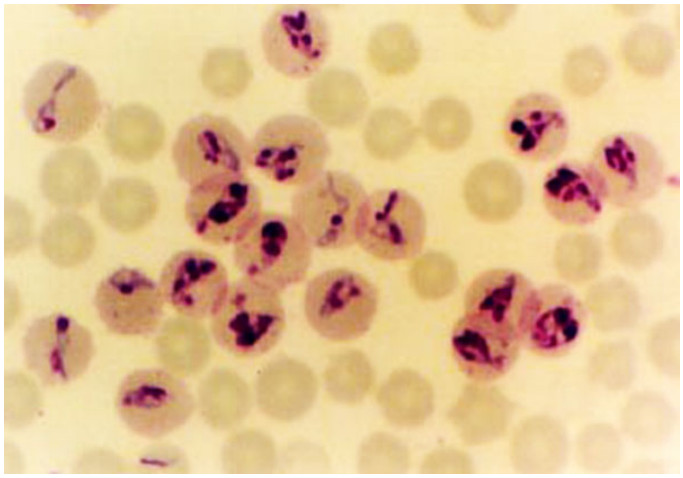


Definitive Hosts (vectors)
(1-, 2-, 3-host ticks)

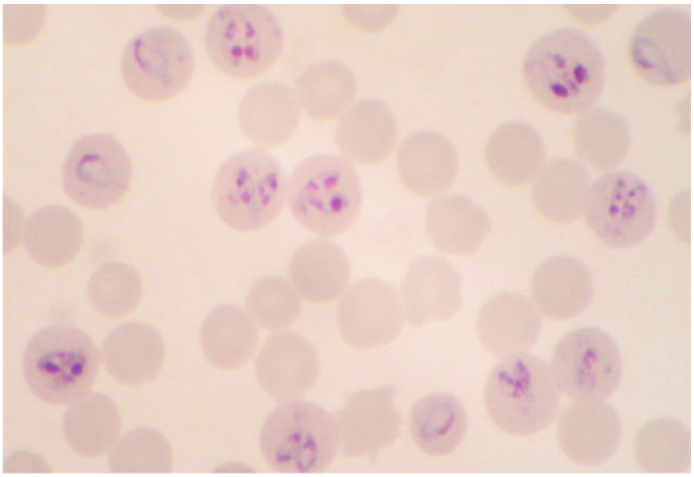


blood cells
(fever, anaemia, jaundice, ischaemia)

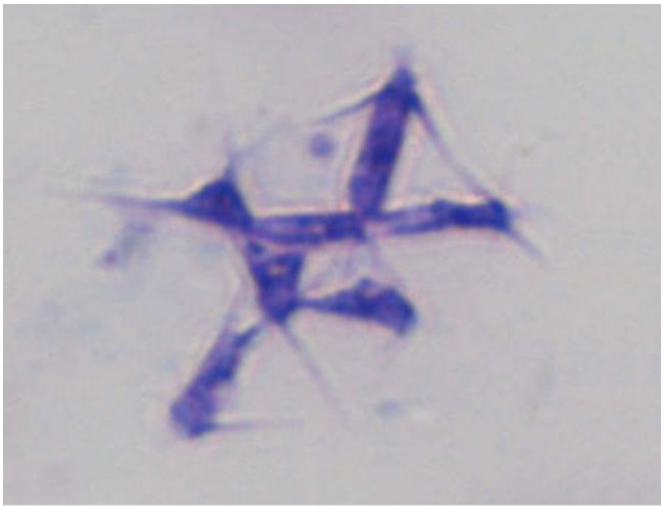
Intermediate Hosts
(mammals, esp. ungulates, carnivores, rodents)



Babesia piroplasms in cow blood



Babesia piroplasms in cow blood



Babesia ray bodies in tick gut

Tick vector for *Babesia*