***Plasmodium* spp. (reptilian species)**
(protist: apicomplexan)

Overview

Protists are single-celled organisms with membrane-bound nuclei (eukaryotes). One protistan supergroup known as SAR comprises the Stramenopiles (with heterokont flagella), Alveolata (with cortical alveoli) and Rhizaria (with fine pseudopodia). Three major alveolate groups are recognized: ciliates, apicomplexans and dinoflagellates. Apicomplexan cells possess a distinctive apical complex of organelles, comprising a conoid, polar ring, rhoptries, micronemes and subpellicular microtubules, which facilitate entry into host cells as they are obligate intracellular parasites for most of their life-cycles. There are three main apicomplexan groups: gregarines, coccidia and haematozoa. Haematozoa are small blood-borne parasites which undergo merogony (= schizogony) and gamogony (gamete formation) in vertebrates and sporogony (sporozoite formation) in blood-sucking invertebrate vectors. Two main groups are recognised in terrestrial vertebrates: haemosporidia with insect vectors; and piroplasms with arachnid vectors. Haemosporidian parasites multiply in the tissues of vertebrates before forming gamonts in blood cells (*Plasmodium* spp. also undergo cyclic merogony in erythrocytes). Most species produce haemozoin pigment granules as a byproduct of haemoglobin metabolism. Gametes ingested by insect vectors undergo fertilization in the gut forming motile zygotes (ookinetes) which form oocysts and then thousands of sporozoites which invade the salivary glands. Infections by *Plasmodium* spp. are transmitted by mosquitoes and numerous species have been described in mammals, birds and reptiles; most causing no apparent harm, except those infecting humans causing one of the worst fever scourges of mankind, the disease malaria.

Classification:

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

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.

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

Four haemosporidian families are recognized mainly on the basis of their developmental cycles and whether haemozoin pigment is produced: namely, Plasmodiidae (merogony in tissues then cyclic in erythrocytes, pigment present); Haemoproteidae (merogony in tissues only, pigment present); Leucocytozoidae (merogony in tissues, pigment absent) and Garniidae (merogony in leucocytes, pigment absent). Vertebrates act as intermediate hosts in which the parasites undergo asexual multiplication within tissues and/or blood cells. Even though parasites begin gamete formation in vertebrates, sexual multiplication is not completed until after they are transmitted to their haematophagous invertebrate vectors, which therefore act as definitive hosts. Some 11 genera are recognized in the family Plasmodiidae on the basis of multiple biological characters (including morphology, development, host specificity and range): *Plasmodium* in mammals, birds and reptiles; *Hepatocystis, Polychromophilus, Nycteria, Biguetiella, Bioccala* and *Dionisia* in bats, *Rayella* in flying squirrels, *Billbraya* and *Haemocystidium* (including *Simondia*) in reptiles, and *Mesnilium* in fish.

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

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

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

Over 225 *Plasmodium* species have been classified in 14 subgenera on the basis of parasite morphology, development and host occurrence. Three subgenera contain species in mammals, five subgenera contain those in birds, and six contain those in reptiles:

- *P.* (*Plasmodium*), with large erythrocytic schizonts and round gametocytes, in primates;
- *P.* (*Lavernia*), with large erythrocytic schizonts and crescentic gametocytes, in primates;
- *P.* (*Vinckeia*), with small erythrocytic schizonts and round gametocytes, in antelopes, rodents and other mammals (except primates);

- *P.* (*Haemamoeba*), with large erythrocytic schizonts and round gametocytes, in birds;
- *P.* (*Bennettinia*), with small erythrocytic schizonts and round gametocytes, in birds;
- *P.* (*Huffia*), with large schizonts and elongate gametocytes mostly in immature erythrocytes, in birds;
- *P.* (*Giovannolaia*), with large erythrocytic schizonts and elongate gametocytes, in birds;
- *P.* (*Novyella*), with small erythrocytic schizonts and elongate-oval gametocytes, in birds;

- *P.* (*Sauramoeba*), with large erythrocytic schizonts and large gametocytes, in lizards*;
- *P.* (*Lacertamoeba*), with medium erythrocytic schizonts and medium gametocytes, in lizards;
- *P.* (*Paraplasmodium*), with medium erythrocytic schizonts and large gametocytes, in lizards;
- *P.* (*Carinamoeba*), with small erythrocytic schizonts and small gametocytes, in lizards;
- *P.* (*Asiamoeba*), with small erythrocytic schizonts and large gametocytes, in lizards; and
- *P.* (*Ophidiella*), with large erythrocytic meronts and small elongate gametocytes, in snakes.

*Another 2 subgenera from lizards, *P.* (*Garnia*) and *P.* (*Fallisia*), have been afforded generic status and allocated to the genera *Garnia* and *Fallisia* in the family Garniidae because their developmental stages do not produce haemozoin pigment in host erythrocytes (*Garnia*) or leucocytes (*Fallisia*). Confoundingly, recent molecular studies have shown that several *Plasmodium* spp. from lizards comprised co-infections with cryptic species whose development was confined to white blood cells rather than red blood cells. Further studies are required to determine the validity of the family Garniidae and its constituent genera.

Around 90 *Plasmodium* spp. have been described in reptiles, mostly in semiaquatic and terrestrial lizards, and occasionally in snakes. The parasites varied in their host specificity and geographic range, with most species being found in one or a few closely-related hosts predominantly in tropical and subtropical regions (only a few had broad ranges). In contrast, sexual development and transmission is accomplished in a greater range of blood-sucking dipteran insects, including Culicidae (mosquitoes), Ceratopogonidae (midges) and Phlebotomidae (sand flies). A total of 6 *Plasmodium* subgenera have been identified from reptiles: with 17 *P.* (*Sauramoeba*) spp. found in 10 lizard families mainly from the Southern hemisphere; 39 *P.* (*Lacertamoeba*) spp. from 12 lizard families around the world; 3 *P.* (*Paraplasmodium*) spp. from 2 lizard families in the Americas; 10 *P.* (*Carinamoeba*) spp. in 8 lizard families mainly from the Southern hemisphere; 6 *P.* (*Asiamoeba*) spp. from 4 lizard families from Asia; and 7 *P.* (*Ophidiella*) spp. from 4 snake families from South America and Africa. Reptilian *Plasmodium* spp. are morphologically and biologically (hence taxonomically) diverse, possibly due to the more restricted or isolated habitats of their vertebrate hosts, their lower vagility (dispersal), and their broader vector specificity. Most *Plasmodium* spp. in reptiles undergo hepatic merogony followed by erythrocytic merogony culminating in the formation of gametocytes. During the course of infection, asexual meronts may be found in circulating cells as well as fixed cells in various organs, including erythrocytes, lymphocytes, monocytes, thrombocytes, granulocytes, endothelial and connective tissue cells. Infections in reptiles are generally not associated with clinical disease, with most being chronic or latent as the parasites seem to persist in the larger erythrocytes found in reptiles.

***Plasmodium* species**	**Intermediate hosts**	**Gametocyte shape (pathogenicity)**	**Definitive hosts (vectors)**	**Geographic distribution**
Subgenus: *Sauramoeba* (large erythrocytic schizonts, large gametocytes, in lizards (Sauria))				
P. (*S.*) *achiotense*	corytophanid (common basilisk)	ovoid		Central America
P. (*S.*) *acuminatum*	chamaeleonid (Fischer's chameleon)	elongate and acuminate		East African
P. (*S.*) *agamae*	agamid (common agama, Atlas agama)	ovoid-elongate (mildly pathogenic)	Diptera: ceratopogonid (*Culicoides nubeculosus*)	East, Central and West African
P. (*S.*) *australis*	agamid (bearded dragon)	ovoid		Australia
P. (*S.*) *balli*	dactyloid (lion anole, slender anole, dappled anole)	elongate		Central and South America
P. (*S.*) *beltrani*	phrynosomatid (teapen rosebelly lizard)	elongate, or bulky		North America
P. (*S.*) *caucasica*	agamid (rock agama)	ovoid-elongate		southern

				Asia
P. (*S.*) *cnemidophori*	teiid (rainbow whiptail, giant whiptail)	elongate, or bulky		South America
P. (*S.*) *diploglossi* (type species)	diploglossid (banded galliwasp), scincid (greater Martinique skink)	ovoid-lentiform		South America
P. (*S.*) *egerniae*	scincid (land mullet)	ovoid		Australia
P. (*S.*) *giganteum*	agamid (common agama, blue-bellied ridgeback agama)	round-elongate, or bulky	Diptera: culicid (*Aedes aegypti*)	West African
P. (*S.*) *guyannense*	trophidurid (collared tree runner)	ovoid		South America
P. (*S.*) *heischi*	scincid (African striped skink)	spindle		East African
P. (*S.*) *kentropyxi*	teiid (striped forest whiptail)	elongate		South America
P. (*S.*) *lacertiliae*	scincid (Indonesian brown skink)	ovoid		New Guinea
P. (*S.*) *michikoa*	chamaeleonid (Matschie's dwarf chameleon)	elongate		East African
P. (*S.*) *robinsoni*	chamaeleonid (short-horned chameleon)	oval-elongate, or bulky		Madagascar
Subgenus: *Lacertamoeba* (medium erythrocytic schizonts, medium gametocytes, in lizards (Sauria))				
P. (*L.*) *arachniformis*	chamaeleonid (Werner's three-horned chameleon)	elongate		East African
P. (*L.*) *aurulentum*	dactyloid (slender anole), phyllodactylid (turniptail gecko)	ovoid-lentiform		Central America
P. (*L.*) *basilisci*	corytophanid (common basilisk)	ovoid		North, Central and South America
P. (*L.*) *beebei*	sphaerodactylid (Estado Aragua gecko)	ovoid		South America
P. (*L.*) *billbraya*	gekkonid (marbled gecko)	ovoid (pronounced anaemia)		Australia
P. (*L.*) *brumpti*	phrynosomatid (horrible spiny lizard)	ovoid-elongate		North America
P. (*L.*) *brygooi*	chamaeleonid (short-horned chameleon)	oval-elongate		Madagascar
P. (*L.*) *circularis*	scincid (Gidgee spiny-tailed skink)	ovoid		Australia
P. (*L.*) *cnemaspi*	gekkonid (African gecko)	elongate		East African
P. (*L.*) *colombiense*	dactyloid (grass anole)	ovoid-elongate		South America
P. (*L.*) *draconis*	agamid (common flying dragon)	ovoid		Philippines, Malaysia
P. (*L.*) *fairchildi* (incl. subspp. *fairchildi, hispaniolae*)	dactyloid (slender anole, bark anole)	ovoid-elongate		Central and South America
P. (*L.*) *fischeri*	chamaeleonid (Fischer's chameleon)	oblong-elongate		East African
P. (*L.*) *floridense*	dactyloid (yellow-chinned anole, slender anole, giant green anole, lichen anole, bridled anole, brown anole, humble anole, lion anole, great scaly anole, ghost anole, large-headed anole, bark anole, Jeremie anole, snake anole, Jamaican anole, stripefoot anole, Graham's anole, Bluefield's anole, Grand Cayman anole, Isla San Andres anole, Anguilla anole, Saban anole, panther anole, Plymouth anole, Dominican anole, green anole), phrynosomatid (fence lizard, rosebelly lizard), iguanid (emerald swift); plus exptl infection in iguanid (common collared lizard), crotaphytid (longnose leopard lizard), phrynosomatid (Texas spiny lizard, Florida scrub lizard)	ovoid-elongate	Diptera: culicid (*Aedes aegypti, Culex erraticus, quinquefasciatus, territans*)	North and Central America, Caribbean

P. (*L.*) *gologoloense*	chamaeleonid (Matschie's dwarf chameleon)	ovoid		East African
P. (*L.*) *holaspi*	lacertid (sawtail lizard)	elongate		East African
P. (*L.*) *iguanae*	iguanid (green iguana)	ovoid		South America
P. (*L.*) *intabazwe*	cordylid (highveld crag lizard)	reniform		South African
P. (*L.*) *josephinae*	teiid (rainbow ameiva)	ellipsoidal		North America
P. (*L.*) *lepidoptiformis*	teiid (striped forest whiptail)	elongate		South America
P. (*L.*) *loveridgei*	gekkonid (painted dwarf gecko)	elongate		East African
P. (*L.*) *mackerrasae*	scincid (Cunningham's skink)	elongate		Australia
P. (*L.*) *maculilabre*	skink (speckle-lipped mabuya)	ovoid-elongate		West African
P. (*L.*) *mossambica*	agamid (Mozambique agama)	elongate		East African
P. (*L.*) *pelaezi*	phrynosomatid (tropical tree lizard)	ovoid-elongate		North America
P. (*L.*) *pitmani*	scincid (speckle-lipped mabuya, African striped mabuya)	ovoid		Central and West African
P. (*L.*) *rhacodactyli*	diplodactylid (New Caledonian giant gecko)	ovoid		New Caledonia
P. (*L.*) *sasai*	lacertid (oriental racers)	ovoid-elongate		Japan, Thailand
P. (*L.*) *tanzaniae*	chamaeleonid (Werner's three-horned chameleon)	elongate		East African
P. (*L.*) *telfordi*	teiid (giant whiptail)	ovoid-elongate		South America
P. (*L.*) *torrealbai*	dactyloid (anole)	ovoid-elongate		South America
P. (*L.*) *tropiduri* (incl. subspp. *aquaticum, caribbense, panamense, tropiduri*)	tropidurid (Amazon lava lizard, Peter's lava lizard, calango), dactyloid (large-headed anole, stripefoot anole, Neotropical green anole, lichen anole, lion anole, dappled anole), scincid (Greater Martinique skink), gekkonid (tropical house gecko)	ovoid		Central and South America, Caribbean
P. (*L.*) *tribolonoti*	scincid (red-eyed crocodile skink)	ovoid		Indonesia
P. (*L.*) *uluguruense*	gekkonid (boabab gecko)	ovoid		East African
P. (*L.*) *uncinatum*	tropidurid (collared tree runner)	elongate		South America
P. (*L.*) *uzungwiense*	chamaeleonid (Werner's three-horned chameleon)	elongate		East African
P. (*L.*) *vacuolatum*	tropidurid (blue-lipped tree lizard)	ovoid		South America
P. (*L.*) *vautieri*	leiosaurid (Brazilian Steppe iguana)	ovoid		South America
P. (*L.*) *zonuriae*	cordylid (common girdled lizard), gerrhosaurid (giant plated lizard)	elongate		South African
Subgenus: *Paraplasmodium* (medium erythrocytic schizonts, large gametocytes, in lizards (Sauria))				
P. (*P.*) *chiricahuae*	phrynosomatid (Clark's spiny lizard, Yarrow's spiny lizard, desert spiny lizard)	ovoid-elongate		North America
P. (*P.*) *mexicanum*	phrynosomatid (crevice swift, fence lizards, sagebrush lizard, mesquite lizard), iguanid (spiny-tailed iguana), anguid (alligator lizard), plus exptl. infection in phrynosomatid (spiny lizards, horned lizards), iguanid (eastern collared lizard)	ovoid-elongate (mildly pathogenic)	Diptera: psychodid (*Lutzomyia vexator, stewarti*)	North America
P. (*P.*) *pifanoi*	teiid (giant ameiva)	elongate		South

				America
Subgenus: *Carinamoeba* (small erythrocytic schizonts, small gametocytes, in lizards (Sauria))				
P. (*C.*) *attenuatum*	teiid (giant ameiva)	elongate		South America
P. (*C.*) *auffenbergi*	varanid (peacock monitor)	ovoid		Philippines
P. (*C.*) *cordyli*	cordylid (dwarf sungazer, girdled lizard)	ovoid		East and South African
P. (*C.*) *gracilis*	scincid (red-eyed crocodile skink)	ovoid		Indonesia
P. (*C.*) *mabuiae*	scincid (African five-lined skink)	elongate		East African
P. (*C.*) *marginatum*	dactyloid (bridled anole)	ovoid		Central America
P. (*C.*) *minasense* (type species) (incl. subspp. *anolisi, calcaratae, capitoi, carinii, diminutivum, minasense, plicae, tegui*)	scincid (Greater Martinique skink), iguanid (green iguana), polychrotid (Brazilian bush anole), dactyloid (slender anole, large-headed anole, bark anole, Jeremie anole, bighead anole), tropidurid (harlequin racerunners), teiid (gold tegu, giant ameiva, striped forest whiptail)	ovoid-elongate		South and Central America, Caribbean, Malaysia
P. (*C.*) *rhadinurum*	iguanid (green iguana, black iguana, prairie lizard)	ovoid		North America
P. (*C.*) *sceloporі*	phrynosomatid (rosebelly lizards)	ovoid		Central America
P. (*C.*) *volans*	agamid (flying lizard)	ovoid-elongate		Philippines, Malaysia
Subgenus: *Asiamoeba* (small erythrocytic schizonts, large gametocytes, in lizards (Sauria))				
P. (*A.*) *clelandi*	varanid (Indian monitor)	encircle host nucleus		Sri Lamka
P. (*A.*) *lionatum*	gekkonid (smooth-backed gliding gecko)	elongate		Thailand
P. (*A.*) *lygosomae*	scincid (Moco skink, Chatham Islands skink)	ovoid-reniform		New Zealand
P. (*A.*) *nucleoversans*	scincid (copper-tailed skink, green-blooded skink)	elongate		Solomon Islands
P. (*A.*) *saurocaudatum*	scincid (common sun skink)	ovoid		Singapore, Thailand
P. (*A.*) *vastator*	agamid (common flying dragon)	reniform-elongate, or bulky		Malaysia, Philippines
Subgenus: *Ophidiella* (large erythrocytic meronts, small elongate gametocytes, in snakes (Serpentes))				
P. (*O.*) *bitis*	viperid (puff adders)	ovoid-elongate		South African
P. (*O.*) *causi* (*species inquirenda,* possibly stages of *Dactylosoma*)	viperid (African night adder)			African
P. (*O.*) *melanoleuca*	elapid (forest cobra)	ovoid		East African
P. (*O.*) *pessoai*	colubrid (caninana), viperid (Atlantic forest bush master)	elongate		Central America
P. (*O.*) *pythonis*	pythonid (African rock python)	elongate		South African
P. (*O.*) *tomodoni*	colubrid (pampas snake)	ovoid		South America
P. (*O.*) *wenyoni* [type species]	colubrid (Amazon coastal house snake)	ovoid		South America
Unplaced				
P. ouropretensis (separated from *P.* (*L.*) *tropiduri* by occurrence in white blood cells and molecular studies)	tropidurid (Amazon lava lizard, Peter's lava lizard)	ovoid		South America

Parasite morphology: Reptilian *Plasmodium* spp. form similar developmental stages to avian species, except that various stages may become dormant allowing parasites to survive for long periods and cause relapses. In reptiles, the parasites may undergo 3 types of asexual exo-erythrocytic merogony (forming cryptozoic, metacryptozoic and phanerozoic meronts, sometimes enigmatically referred to simply as cryptozoites, metacryptozoites and phanerozoites, even though all produce merozoites) as well as erythrocytic merogony (trophozoites forming meronts, merozoites and gametocytes). Some sporozoites invading the liver may become inactive inside host cells forming uninucleate dormant hypnozoites (2-5 µm) located within membrane-bound parasitophorous vacuoles. First-generation cryptozoic meronts appear as round-oval basophilic bodies (6-15 x 4-8 µm) that become multinucleate as they divide internally to produce numerous (12-45, sometimes more) merozoites containing golden pigment granules. Some of these cryptozoic merozoites may also become inactive inside host cells. Second-generation metacryptozoic meronts appear as similar rounded basophilic bodies (19-27 µm) that produce numerous merozoites. Erythrocytic merogony involves a cyclic process where pleomorphic (plasmodial) trophozoites (1-4 µm) evident as signet-ring structures or focal packets form meronts (3-6 x 2-5 µm) that are usually fan-shaped (sometimes rosette, cruciform, oval or morulum (spherical mass)) with scattered or clumped dark pigment granules. The meronts produce variable numbers (4-28, rarely more) of merozoites that may be round, oval, elongate or lentiform in shape. Eventually gametocytes appear in erythrocytes as ovoid-elongate (6-18 x 4-10 µm) stages that exhibit sexual dimorphism: with female macrogametocytes being more elongate with a basophilic cytoplasm (due to abundant ribosomes) and compact nucleus; and male microgametocytes being shorter with a pale eosinophilic cytoplasm and a large pale nucleus (giving rise to the paradoxical adage 'blue for girls, pink for boys' when stained with Giemsa). Gametocytes vary in their location within the erythrocyte cytoplasm, being polar, lateral, lateropolar, dumbbell-shaped or halteridial (halter-shaped). Merozoites produced in erythrocytes may also infect white blood cells where they undergo para-erythrocytic merogony, or endothelia and connective tissues in various organs where they undergo a third type of exo-erythrocytic development (phanerozoic merogony), possibly for several generations. Phanerozoic meronts appear as larger ovoid-elongate basophilic bodies (7-28 x 4-16 µm) that become multinucleate as they produce variable numbers (16-210) of merozoites. These merozoites may infect red or white blood cells in the circulation or fixed cells in organs, with some becoming encysted in tissues as dormant stages (termed chronozoites) responsible for relapses. In dipteran vectors, the parasites complete sexual development (gamete formation and fertilization) producing zygotes that mature to oocysts producing numerous sporozoites (sporogony). Male microgametocytes undergo exflagellation producing thin slender microgametes (15 µm long) which fertilize rounded female macrogametes (10 x 7 µm) to produce ookinetes (motile zygotes). Ookinetes are elongate stages (14-20 x 2-5 µm) that mature to form rounded membrane-bound oocysts (22-54 µm) that undergo internal sporulation to form numerous slender sporozoites (7-22 x 1-2 µm).

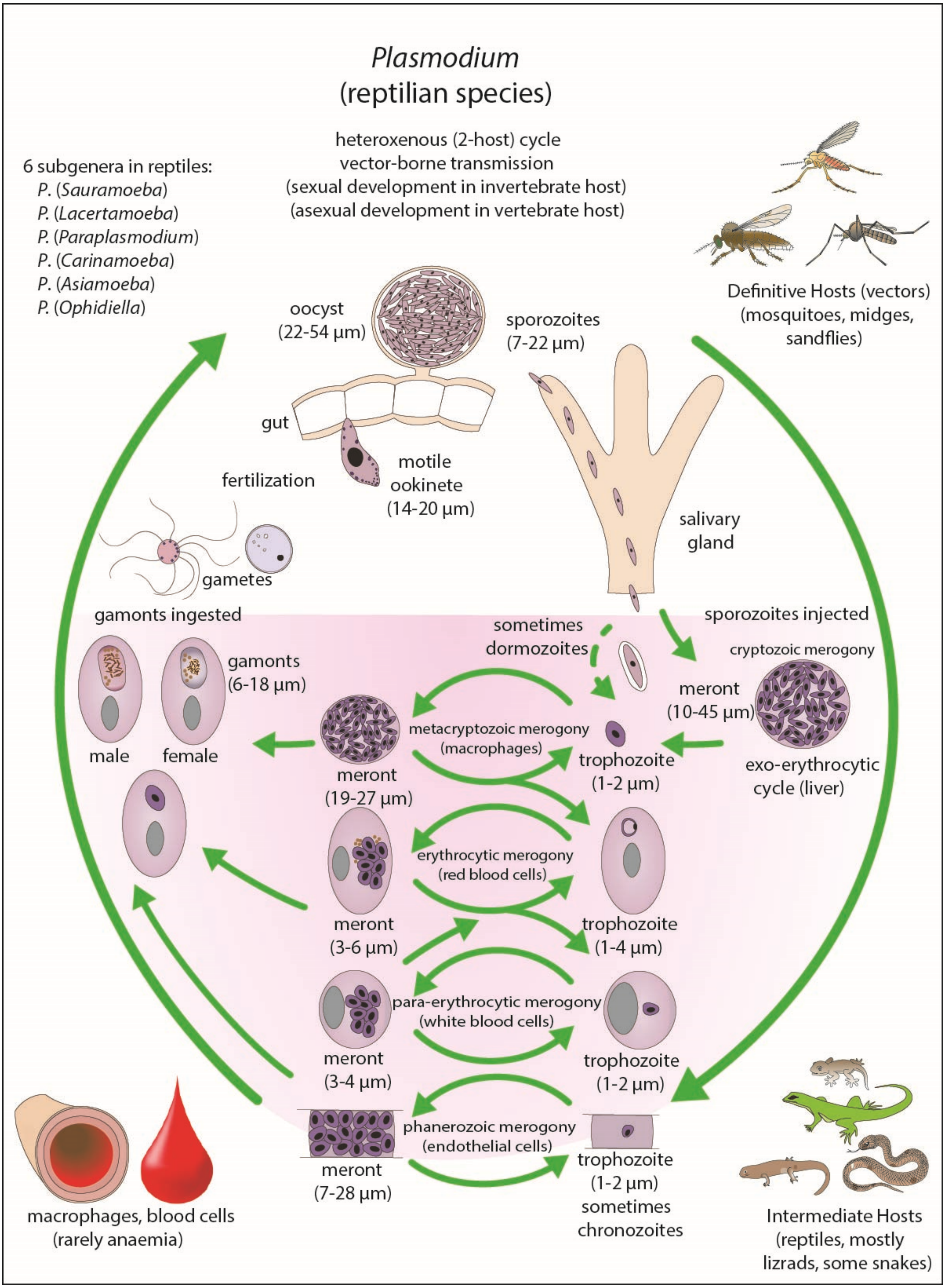
Site of infection: Exo-erythrocytic proliferation occurs in different sites within reptilian hosts: first-generation cryptozoic meronts developing in hepatic parenchymal cells; second-generation metacryptozoic meronts in macrophages (prominent in hepatic sinuses); and third-generation phanerozoic meronts forming in endothelial and connective tissue cells in various organs (including the heart, lungs, muscles, brain, and testes). Erythrocytic merogony occurs in nucleated red blood cells (especially immature cells), and para-erythrocytic merogony occurs in other circulating cells (lymphocytes, monocytes, thrombocytes and sometimes granulocytes). A total of 83 parasite species have been described in reptiles: including 76 parasite species in 117 lizard species (belonging to 22 families); and another 7 parasite species in 8 snake species (from 4 families). Gamete formation and fertilization occurs in the gut lumen of dipteran vectors, while the motile ookinete penetrates the gut wall to form an encapsulated oocyst. Mature oocysts release sporozoites into the haemocoel where they invade the salivary glands. A small number of vectors have been found for reptilian *Plasmodium* spp.: including 4 species of culicid mosquitoes, 2 species of psychodid sandflies and one species of ceratopogonid biting midges.

Pathogenesis: Infections in most reptiles are asymptomatic during the acute and chronic phases of infection, with intra-erythrocytic gametocytes often the only stages detected. Some natural infections have been associated with mild anaemia, lethargy, anorexia, dehydration and stomatitis in several lizard species, and an un-named species has been associated with fatal haemolytic anaemia in star tortoises. Several parasite species are thought to cause seasonal mortalities due to progressive damage caused by pernicious tissue meronts. Experimental infections have sometimes caused severe anaemia and thrombosis in capillary beds, with occasional mortalities. Post-mortem pathological observations have included anaemia, hepatomegaly and splenomegaly with pigment deposits found throughout visceral organs. Haematological perturbations have included erythrocytic distortions in size, shape and nuclear position with reductions in haematocrit, haemoglobin levels and increased numbers of immature red cells (polychromatophils). Several physiological studies have also linked infections to impaired oxygen consumption by lizards (exercise physiology), reduced running activity, slower tail repair (after loss due to predation), alterations in coloration, reduced fat storage, decreased clutch sizes, and reduced competitiveness in males with decreased testis size and testosterone levels. Chronic infections in reptiles are thought to persist for years and possibly for the lifespan of the host.

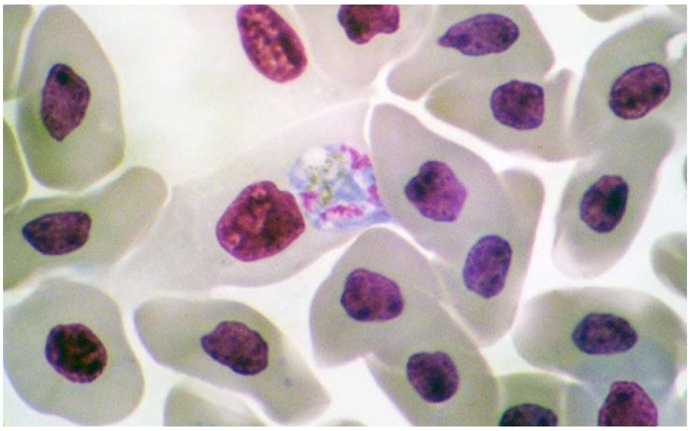
Developmental cycle and mode of transmission: Reptilian *Plasmodium* spp. have obligatory heteroxenous (2-host) life-cycles involving parasite asexual development in lizards and some snakes (acting as intermediate hosts) and sexual development in dipteran vectors (by definition, acting as definitive hosts). Transmission occurs by vector bite, with gametocytes taken up by vectors when feeding on blood and sporozoites injected during feeding (inoculative transmission). In reptiles, sporozoites invade the liver and undergo at least 2 generations of pre-erythrocytic merogony, first forming cryptozoic meronts and then metacryptozoic meronts. After a relatively long prepatent period (5-45 days), merozoites invade red and white blood cells where they undergo erythrocytic or para-erythrocytic merogony respectively. Merogony involves the transformation of invading trophozoites into meronts which produce numerous merozoites. Eventually, merozoites invading erythrocytes form sexually-dimorphic gametocytes, which may be transitory or persistent stages which vary in morphology according to the phase of infection (more rounded in chronic infections). Merozoites may also infect capillary endothelia and connective tissues in various organs and undergo cyclic exo-erythrocytic phanerozoic merogony. Parasitaemias may reach peaks as high as 20% over 35-96 days. The acute phase of infection may last for 15-183 days before becoming chronic and persisting for months to years. Several developmental stages have been observed to become inactive in host tissues forming dormant encysted stages, including sporozoites forming hypnozoites, cryptozoic merozoites and phanerozoic merozoites forming relapsing stages called chronozoites. Dormant stages facilitate chronic infections of long duration, frequent relapses and allow parasites to overwinter in hibernating hosts. While most life-cycles are not known, transmission studies on a few parasite species have found vectors to include members of several diverse and ancient groups of blood-sucking dipteran insects, including Culicidae (mosquitoes), Ceratopogonidae (midges) and Phlebotomidae (sand flies). Ingested gametocytes complete gamete formation in the vector gut with fertilization occurring through gamete fusion. The resultant motile ookinete migrates into the gut wall and forms an oocyst extracellularly between intestinal epithelial cells near the outer wall. The oocysts undergo internal sporulation producing hundreds of sporozoites which are released into the haemocoel to invade the salivary glands. Sporozoites are inoculated into new reptilian hosts when the vector next feeds. Once infected, vectors are thought to remain infected for their entire lives.

Differential diagnosis: Infections are usually diagnosed by the direct microscopic detection of parasite stages in fixed blood smears following staining with Giemsa. Multiple sequential samples may need to be examined to detect low or intermittent parasitaemias. Observations can be made on parasite morphology (size, shape, appearance, pigmentation) and any effects on host cells (hypertrophy, distortions, nuclear displacement). Histological sections of host tissues and organs collected at post-mortem may be examined for merogonous developmental stages. Dipteran vectors may also be examined for endogenous stages by examining squash preparations (especially of the salivary glands) or histological sections. Molecular biological techniques have been used to detect and characterize parasites by the polymerase chain reaction (PCR) amplification of nuclear (small subunit (18S) ribosomal DNA) or mitochondrial (cytochrome b) gene sequences.

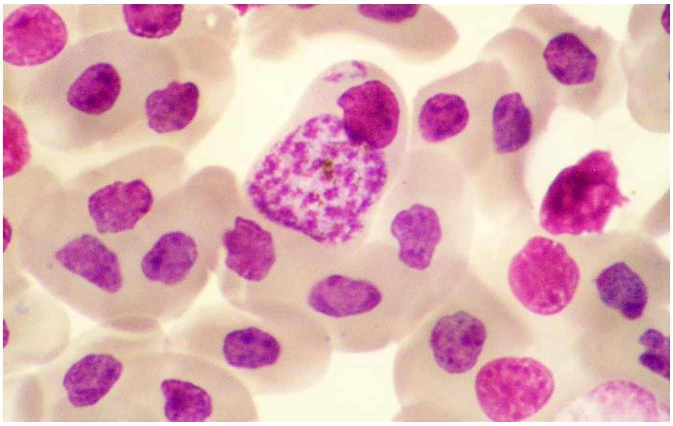
Treatment and control: Several attempts to treat clinical infections in reptiles have yielded encouraging results, with several antimalarial drugs (quinine, mepacrine, sulphamethoxazole-trimethoprim, chloroquine-primaquine) leading to the resolution of clinical signs and/or the elimination of parasitaemia in lizards and tortoises. Preventive measures adopted by professional herpetaria or hobbyists have revolved around vector control by installing screens around holding facilities, applying chemical insecticides either to animals or fomites, and eliminating local breeding grounds for dipteran vectors (water disinfection and/or vegetation clearance).



Plasmodium
(reptilian species)
heteroxenous (2-host) cycle
vector-borne transmission
(sexual development in invertebrate host)
(asexual development in vertebrate host)
6 subgenera in reptiles:
P. (Sauramoeba)
P. (Lacertamoeba)
P. (Paraplasmodium)
P. (Carinamoeba)
P. (Asiamoeba)
P. (Ophidiella)
Definitive Hosts (vectors)
(mosquitoes, midges, sandflies)
oocyst
(22-54 µm)
sporozoites
(7-22 µm)
gut
motile
ookinete
(14-20 µm)
fertilization
salivary
gland
gametes
gamonts ingested
sporozoites injected
sometimes
dormozoites
cryptozoic merogony
gamonts
(6-18 µm)
meront
(10-45 µm)
male
female
metacryptozoic merogony
(macrophages)
trophozoite
(1-2 µm)
exo-erythrocytic
cycle (liver)
meront
(19-27 µm)
erythrocytic merogony
(red blood cells)
meront
(3-6 µm)
trophozoite
(1-4 µm)
para-erythrocytic merogony
(white blood cells)
meront
(3-4 µm)
trophozoite
(1-2 µm)
phanerozoic merogony
(endothelial cells)
meront
(7-28 µm)
trophozoite
(1-2 µm)
sometimes
chronozoites
macrophages, blood cells
(rarely anaemia)
Intermediate Hosts
(reptiles, mostly
lizrads, some snakes)



Plasmodium intraerythrocytic stage in lizard blood



Plasmodium developmental stage in lizard blood