PLASMODIUM SPP.

AETIOLOGY

Classification of the causative agent

Plasmodium spp. are apicomplexan parasites in the order *Haemoproteidae* that infect blood and other tissues. Most notably, these are the causative agents of malaria. There are over 250 species that can infect both humans and animals, including nonhuman primates, rodents, and birds. They are spread by several mosquito species, mostly commonly *Aedes*, *Anopheles*, and *Culex* genera. These are zoonotic diseases and humans are at risk for infection with *P. falciparum, P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*.

Resistance to physical and chemical action

Temperature: Stable at 4-30°C

pH: Not well determined

Chemicals/Disinfectants: Susceptible to disinfection with 10% hypochlorite and 70% ethanol

Survival: Unable to survive outside host

EPIDEMIOLOGY

Hosts

Plasmodium spp. are able to infect a wide variety of hosts. This is not an exhaustive list.

- *Plasmodium* spp. of birds
    - *P. gallinaceum*
        - Chickens (*Gallus gallus domesticus*)
        - Guinea fowl (Family *Numididae*)
        - Red jungle fowl (natural host) (*Gallus gallus*)
    - *P. juxtanucleare*
        - Chickens (*Gallus gallus domesticus*)
        - Red jungle fowl (natural host) (*Gallus gallus*)
        - Bamboo partridges (*Bambusicola thoracica*)
        - Grey-winged francolins (*Francolinus africanus*)
    - *P. durae*
        - Domestic turkeys (*Meleagris gallopavo*)
        - Yellow-necked spurfowl (*Francolinus leucoscepus*)
        - Red-winged francolins (*F. levaillantii levaillantii*)
    - *P. relictum*
        - Common greenshanks (*Tringa nebularia*)
        - Great white pelicans (*Pelecanus onocrotalus*)
        - Hawaiian forest birds
            - Extinct: akialoa (Genus *Akialoa*)
            - Extinct: o'o (Genus *Moho*)
            - Apapane (*Himatione sanguinea*)
            - Common amakihi (*Hemignathus virens*)
            - Iiwi (*Vestiaria coccinea*)
            - Omao (*Myadestes obscurus*)
        - Hooded siskins (*Carduelis magellanica*)
        - House wrens (*Troglodytes aedon*)

        - Rufous-collared sparrows (*Zonotrichia capensis*)
- *Plasmodium* spp. of primates
    - Humans (*Homo sapiens*)
        - *P. brasilianum, P. cynomolgi, P. falciparum, P. inui,P. knowlesi, P. malariae*, *P. ovale*, *P. simium*, *P. vivax*
    - Prosimians (namely Gibbons, *Hylobatidae* family)
        - *P. eylesi*, *P. hylobati*, *P. jefferyi*, and *P. youngi*
    - Old World monkeys
        - *P. knowlesi*
            - Cynomolgus macaques (*Macaca fascicularis*) Silvered leaf monkeys (*Trachypithecus cristatus*)
            - Northern and Southern pig-tailed macaques (*Macaca leonina* and *M. nemestrina*)
            - Rhesus macaques (*Macaca mulatta*)
        - *P. cynomolgi*
            - Bonnet macaques (*Macaca radiata*)
            - Pig-tailed macaques (*Macaca nemestrina*)
            - Rhesus macaques (*Macaca mulatta*)
            - Silvered leaf monkey (*Trachypithecus cristatus*)
            - Toque macaques (*Macaca sinica*)
        - *P. gonderi*
            - Drills (*Mandrillus leucophaeus*)
            - Mangabeys (*Cercocebus* spp.)
        - *P. fieldi*
            - Cynomolgus macaques (*Macaca fascicularis*)
            - Pig-tailed macaques (*Macaca nemestrina*)
        - *P. fragile, P. shorti*
            - Bonnet macaques (*Macaca radiata*)
            - Toque macaques (*Macaca sinica*)
        - *P. siminovale*
            - Toque macaques (*Macaca sinica*)
        - *P. coatneyi*
            - Cynomolgus macaques (*Macaca fascicularis*)
        - *P. inui*
            - Celebes black apes (*Macaca nigra*)
            - Cynomolgus macaques (*Macaca fascicularis*)
            - Pig-tailed macaques (*Macaca nemestrina*)
    - New World monkeys
        - *P. simium*, *P. brasilianum*
            - Capuchin monkeys (*Cebus* and *Sapajus* spp.)
            - Howler monkeys (*Alouatta* spp.)
            - Spider monkeys (*Ateles* spp.)
            - Squirrel monkeys (*Saimiri* spp.)
            - Woolly monkeys (*Lagothrix* spp.)
    - Apes
        - *P. rohaini*, *P. reichenowi*, *P. shwetzi*
            - Chimpanzees (*Pan* spp.)
            - Gorillas (*Gorilla* spp.)
        - *P. pitheci*, *P. silvaticum*
            - Orangutans (*Pongo* spp.)
- *P. odocoilei*
    - White-tailed deer (*Odocoileus virginianus*)
- *P. berghei*
    - Rodents
- *Plasmodium* spp. of even-toed ungulates
    - Goats (*Capra aegagrus hircus*)
    - Duiker (*Sylvicapra grimmia*)
    - Marshbuck (*Tragelaphus spekii*)

    - Pampas deer (*Ozotoceros bezoarticus*)
- Multiple *Plasmodium* spp. are known to infect these species
    - Bat spp. (order *Chiroptera*)
    - Raptors
        - Levant sparrowhawk (*Accipiter brevipes*)
        - Common buzzard (*Buteo buteo*)
        - Falcon spp. genus
        - Owl spp. genus
        - Crested Caracara (*Caracara cheriway*)
    - Reptiles

Transmission

- Bite from infectious mosquitoes or midges

Sources

- *P. gallinaceum*
    - *Mansonia crassipes* mosquitoes
    - Other mosquitoes that have been shown to experimentally infect birds include members of the *Anopheles*, *Culex*, *Culiseta*, and *Armigeres* genera
- *P. juxtanucleare*
    - *Culex* spp.
- *P. relictum*
    - *Aedes* and *Culex* spp.
    - *Culicoides* midges
- *P. falciparum, P. vivax*, *P. malariae*, *P. ovale*, *P. knowlesi*
    - *Anopheles* spp.

Occurrence

Plasmodium spp. are found in tropical and subtropical climates worldwide including Southeast Asia, Sri Lanka, Indonesia, India, Malaysia, Borneo, Hawaii, and New Zealand. *P. juxtanucleare* is found in these locations as well as South and Central America, East Africa, South Africa, Japan, Taiwan, and the Philippines. *P. durae* is found in sub-Saharan Africa, including Nigeria, Kenya, ZImbabwe, and South Africa. Several primate-specific species are found in Southeast Asia, including *P. hylobati*, *P. eylesi*, *P. jefferyi*, *P. youngi*, and *P. knowlesi*. *P. coatneyi*, *P. inui*, *P. siminovale*, and *P. shorti* are found in Southeast Asia. *P. brasilianum* is in Mexico, Central America, and South America. Several *Plasmodium* spp. have been found in even-toed ungulates in South America, Southeast Asia, and Africa. Raptors migrating from Africa to Eurasia, such as the Levant sparrowhawk and the common buzzard, have been found to harbour *Plasmodium* spp.

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

The life cycle of *Plasmodium* spp. includes a progression from the mosquito to the host. After an infected mosquito bites a host, sporozoites are injected into the host's bloodstream, where they make their way to liver hepatocytes. About three days after initial infection, the sporozoites transform into schizonts, after which merozoites are formed by the fusion of cytoplasm and nuclei. Subsequently, the schizont and host hepatocyte rupture and release merozoites into the bloodstream. After the merozoites enter the bloodstream, they infect erythrocytes. The digestion of haemoglobin marks the transition of merozoite to trophozoite. Lastly, the trophozoite divides several times and becomes a schizont, which rupture and release merozoites. Some species of *Plasmodium*, such as *P. berghei* and *P. falciparum*, enter a sexual phase of reproduction in the erythrocyte, resulting in microgametocytes (male) and macrogametocytes (female).

The different types of infection caused by *Plasmodium* spp., called quotidian, tertiary, and quartan, result from the schizont and maturation of the merozoite stage that last 24, 48, or 72 hours. Fevers correspond with these different stages of periodicity.

P. juxtanucleare, *P. durae*, and *P. gallinaceum* can be especially pathogenic to domestic avian species such as chickens and turkeys. More specifically, *P. gallinaceum* can cause significant pathology in birds, particularly domestic chickens. Turkey poults are especially affected by *P. durae*, which has a mortality rate of approximately 90%. In wild birds species, *P. relictum* is the most common. Chionophilic species in captivity are especially prone to developing signs of infection, with passerine birds carrying this species asymptomatically. *P. relictum* is thought to be an emerging infectious disease of wild Peruvian birds, such as the rufous-collared sparrow and hooded siskin. *P. relictum* on the Hawaiian Islands, spread by *C. quinquefasciatus*, is thought to be a major cause of population decline of native Hawaiian forest birds, such as the omao and apapane. It is also believed to be the cause of extinction of several other species, such as several species of akialoa and o'o.

Clinical diagnosis

In birds, infections with *Plasmodium* spp. do not usually cause clinical signs. *P. gallinaceum* causes lethargy, diarrhoea, anaemia, and paralysis. Additional signs of birds infected with *P. juxtanucleare* or *P. durae* include ocular haemorrhage, central nervous system signs, coma, and death with heavy parasite burdens. Turkey poults do not present with signs until they develop convulsions, typically followed by death. Adult turkeys may become lethargic and anorexic, with gangrenous wattles and oedematous legs. *P. hylobati*, *P. eylesi*, and *P. youngi* are associated with fever.

Nonhuman primates generally present without clinical signs, but may develop anorexia, jaundice, fever, and anaemia. Reptiles infected with *Plasmodium* spp. may experience erythroblastosis and anaemia, and chelonians may experience haemolytic anaemia. In rodents, *P. berghei* infects reticulocytes and can cause anaemia, hypoglycaemia, and lactic acidosis. *Plasmodium* spp. are not known to cause pathology in bats and do not result in clinical signs in ungulates.

Lesions

- *P. gallinaceum*, *P. juxtanucleare*, and *P. durae*
    - Pale combs
    - Splenomegaly
    - Darkening of viscera of liver, brain, lungs, spleen, and skin
    - Kidneys
        - Hemozoin in macrophages
        - Fatty degeneration of parenchyma
        - Antibody-antigen immune complex glomerulonephritis
    - Lungs
        - Hemozoin in macrophages
        - Pulmonary oedema
        - Blood vessel and lymphatic obstruction
    - Blood
        - *P. gallinaceum*: meronts with many merozoites and round gametocytes that displace host cell nucleus
        - *P. juxtanucleare*: darkly pigmented cells; meronts and gamonts in erythrocytes
            - Can be distinguished from *P. gallinaceum* by elongated gametocytes and meronts clinging to host cell nucleus
        - *P. durae*: small, rounded meronts, elongated gametocytes that do not curve around the host erythrocyte nucleus
- Non-human primates
    - Hepatomegaly
    - Splenomegaly, splenic rupture
    - Nephron necrosis
    - Brain haemorrhage

        - Cerebral oedema
        - Hemozoin in:
            - Kupffer cells of liver
            - Red pulp of spleen
            - Macrophages of bone marrow
- Reptiles
    - Splenomegaly

Differential diagnoses

- Avian
    - *Leucocytozoon* spp.
    - *Haemoproteus* spp.
    - Spirochaetosis
    - Anaemia due to heavy tick burdens
        - *Argas* spp.
        - *Ornithodoros* spp.
- Primates
    - Iron deficiency anaemia
    - *Oesophagostomum* spp.
    - Simian parvovirus (SPV)
    - Simian immunodeficiency virus (SIV)
    - Vitamin C deficiency
- Reptiles
    - Anaemia due heavy tick burdens
        - *Argas* spp.
        - *Ornithodoros* spp.
    - *Hameoproteus* spp.
    - *Saurocytozoon* spp.

Laboratory diagnosis

Samples

For isolation of agent

- Whole blood

Serological tests

- Serum

Procedures

Identification of the agent

- Giemsa stain of peripheral blood smears
- Nonhuman primates
    - Fluorescence microscopy using acridine orange (AO), benzothiocarboxypruine (BCP), or rhodamine-123 dyes
    - Rapid diagnostic tests (RTDs) detecting malarial antigen
    - Polymerase chain reaction (PCR)
        - This test has high sensitivity and specificity
    - Reverse-transcription polymerase chain reaction (RT-PCR) tests have been developed for *P. knowlesi* and *P. inui*

Serological tests

- Immunofluorescent antibody (IFA) and antibody enzyme-linked immunosorbent assays (ELISA) have been developed for use in non-human primates
- There are no commercially available serological tests for use in birds

PREVENTION AND CONTROL

Sanitary prophylaxis

- Use insecticide spray to prevent captive birds from being bitten by mosquitoes or biting midges
    - Keep fowl in screened, vector-proof buildings
- For animals in zoological collections, maintain a low-stress environment by ensuring they are properly fed, provided an environment appropriate to their ecological needs (e.g., temperature), and given adequate space and enrichment
- Humans can take several measures to prevent mosquito bites, including insect repellents, nets, wearing long-sleeved shirts and long pants, and regularly spraying adulticide on property
    - Effective repellents contain permethrin, DEET, picaridin, and oil of lemon eucalyptus (OLE)
- Prevent the establishment of mosquito habitats by applying chemical larvicide to standing water, draining swamps, and clearing areas of trash and tyres
- Fogging or ultra-low volume spraying can be used to kill mosquitoes in the event of a malaria outbreak

Medical prophylaxis

- Several malarial prophylaxis agents have been developed for use in humans, including chloroquine, malarone, doxycycline, and mefloquine

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Humans who live in sub-Saharan Africa and Southeast Asia are at greatest risk for infection with *P. falciparum*, *P. vivax*, or *P. malariae*
    - People without access to medicine and preventive resources are at greatest risk for morbidity and mortality associated with the disease

Risks to agriculture

- Several *Plasmodium* spp. have the ability to infect domestic poultry, resulting in production and economic losses to farmers.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated 2020. Written by Samantha Gieger and Erin Furmaga with assistance from the USGS National Wildlife Health Center.