

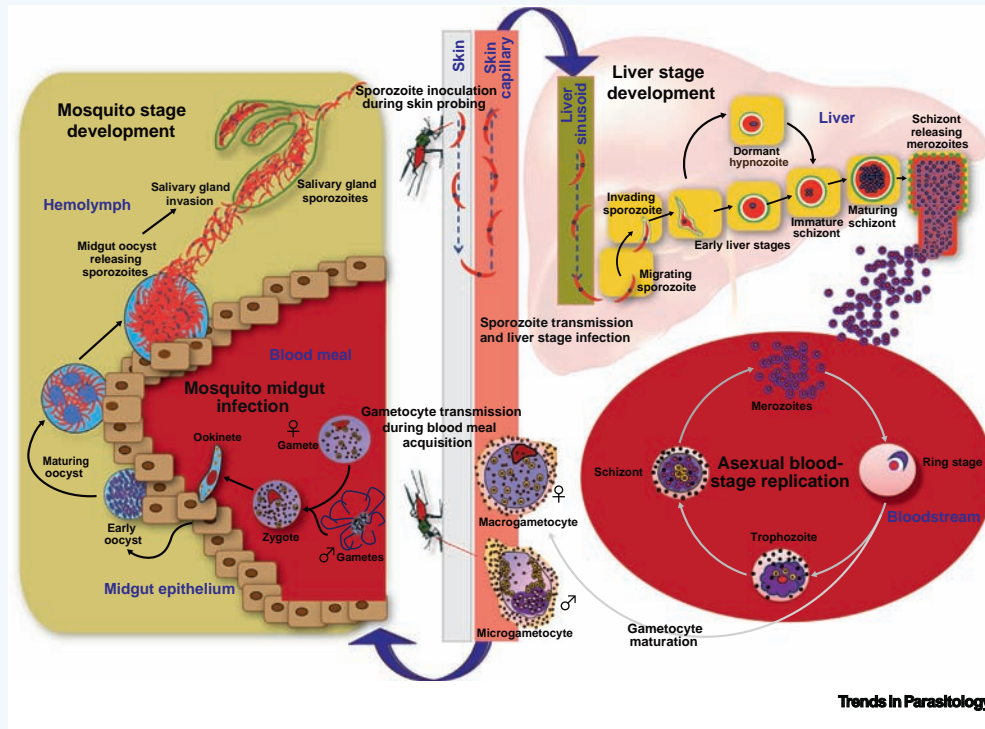
# Plasmodium vivax

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**KEY FACTS:**

Sporozoites of *P. vivax* are injected into the human skin by a mosquito and migrate to the liver, where a clinically silent phase of either parasite multiplication (schizogony) or dormancy occurs per sporozoite. Both forms of the parasite (schizont and hypnozoite) can exist simultaneously in the liver.

The transition from liver stage to blood stage results in asexual parasite expansion in erythrocytes. Sexual-stage gametocytes also develop in erythrocytes and are taken up during a mosquito blood meal, after which mature gametes fuse. Ultimately, midgut oocysts mature, releasing sporozoites that travel to the mosquito's salivary glands.

The nuclear genome is 29 Mb, encoding 6642 genes; the mitochondrial genome is 6 kb; and the apicoplast genome is 29.6 kb.

**DISEASE FACTS:**

Asexual blood-stage reproduction leads to illness involving febrile episodes, anemia, diarrhea, abdominal pain, nausea and vomiting, headache, and muscular pains. Disease consequences include organ failure, respiratory problems, splenomegaly, splenic rupture and occasionally death.

*P. vivax* is a major cause of suffering in resource-poor settings.

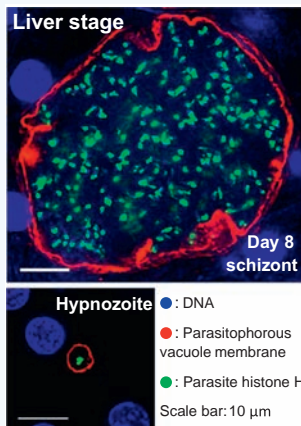
Continuous reinfection or superinfection is frequent, but is usually subclinical.

Patients may experience relapses after weeks to years, because of (presumed) hypnozoite activation.

**TAXONOMY AND CLASSIFICATION:**

- PHYLUM:** Apicomplexa
- CLASS:** Aconoidasida
- ORDER:** Haemosporida
- FAMILY:** Plasmodiidae
- GENUS:** *Plasmodium*
- SPECIES:** *P. vivax*

*Plasmodium vivax* is the most widely distributed of several plasmodial species that cause human malaria, a disease associated with blood-stage parasite replication. About 2.5 billion people are at risk of *P. vivax* infection; they live mainly in Southeast Asia and the Americas, where *P. vivax* accounts for approximately 72% of malaria cases. In Africa, widespread lack of the Duffy antigen constrains transmission. The dormant liver form of the parasite, the hypnozoite, which can reactivate long after the primary infection and give rise to a relapsing blood-stage infection, complicates eradication. In fact, hypnozoites are the origin of most blood-stage infections. Primaquine and tafenoquine are the only drugs that prevent relapse. However, neither is used during pregnancy or by people with glucose-6-phosphate dehydrogenase deficiency; and tafenoquine is not yet approved for treating children. Thus, this species of malaria-causing parasite is a unique challenge in eradication campaigns.



Key biological and epidemiological differences		
Species	<i>Plasmodium vivax</i>	<i>Plasmodium falciparum</i>
Infective gametocytes in bloodstream	Present earlier (leads to earlier transmission)	Transmission occurs later
Sporogony in mosquito	Duration shorter (facilitates transmission)	Longer duration
Development in mosquito	Can occur in temperate regions, thus widespread geographically	Higher temperatures required and therefore less widespread
Parasite density in peripheral blood	Low (infection very easily overlooked)	Can be very high
Parasite population genetic diversity	High global diversity	Less diverse
Hypnozoite stage in liver	Yes	Not known to occur
Mortality	Infrequent	Frequent
Immunity	Acquired quickly	Acquired slowly

Trends in Parasitology

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## Resources

[www.malariaeradication.org/](http://www.malariaeradication.org/)  
[www.who.int/malaria/en/](http://www.who.int/malaria/en/)  
[www.cdc.gov/malaria/](http://www.cdc.gov/malaria/)  
[www.plasmodb.org](http://www.plasmodb.org)  
[www.mmv.org](http://www.mmv.org)

## Literature

1. Campo, B. *et al.* (2015) Killing the hypnozoite – drug discovery approaches to prevent relapse in *Plasmodium vivax*. *Pathog. Glob. Health* 109, 107–122
2. Adekunle, A.I. *et al.* (2015) Modeling the dynamics of *Plasmodium vivax* infection and hypnozoite reactivation *in vivo*. *PLoS Negl. Trop. Dis.* 9, e0003595
3. Auburn, S. *et al.* (2016) A new *Plasmodium vivax* reference sequence with improved assembly of the subtelomeres reveals an abundance of *pir* genes. *Wellcome Open Res.* 1, 4
4. Markus, M.B. (2018) Biological concepts in recurrent *Plasmodium vivax* malaria. *Parasitology* 145, 1765–1771
5. Vale, N. *et al.* (2009) Primaquine revisited six decades after its discovery. *Eur. J. Med. Chem.* 44, 937–953
6. Gualdrón-López, M. *et al.* (2018) Characterization of *Plasmodium vivax* proteins in plasma-derived exosomes from malaria-infected liver-chimeric humanized mice. *Front. Microbiol.* 9, 1271
7. Popovici, J. *et al.* (2018) Genomic analyses reveal the common occurrence and complexity of *Plasmodium vivax* relapses in Cambodia. *mBio* 9, e01888-17
8. Longley, R.J. *et al.* (2016) Insights into the naturally acquired immune response to *Plasmodium vivax* malaria. *Parasitology* 143, 154–170
9. Pfeffer, D.A. *et al.* (2018) *MalariaAtlas*: an R interface to global malariometric data hosted by the Malaria Atlas Project. *Malar. J.* 17, 352
10. Price, R.N. *et al.* (2007) *Vivax* malaria: neglected and not benign. *Am. J. Trop. Med. Hyg.* 77 (6, Suppl.), 79–87