

# \* Plasmodium Life Cycle

Italian *mala aria* which means “bad or evil air” because it was originally thought that this disease was caused by foul air, and particularly by vapors given off by swamps. It was also called “swamp fever”, and it is one of the most ancient infections known to humans.

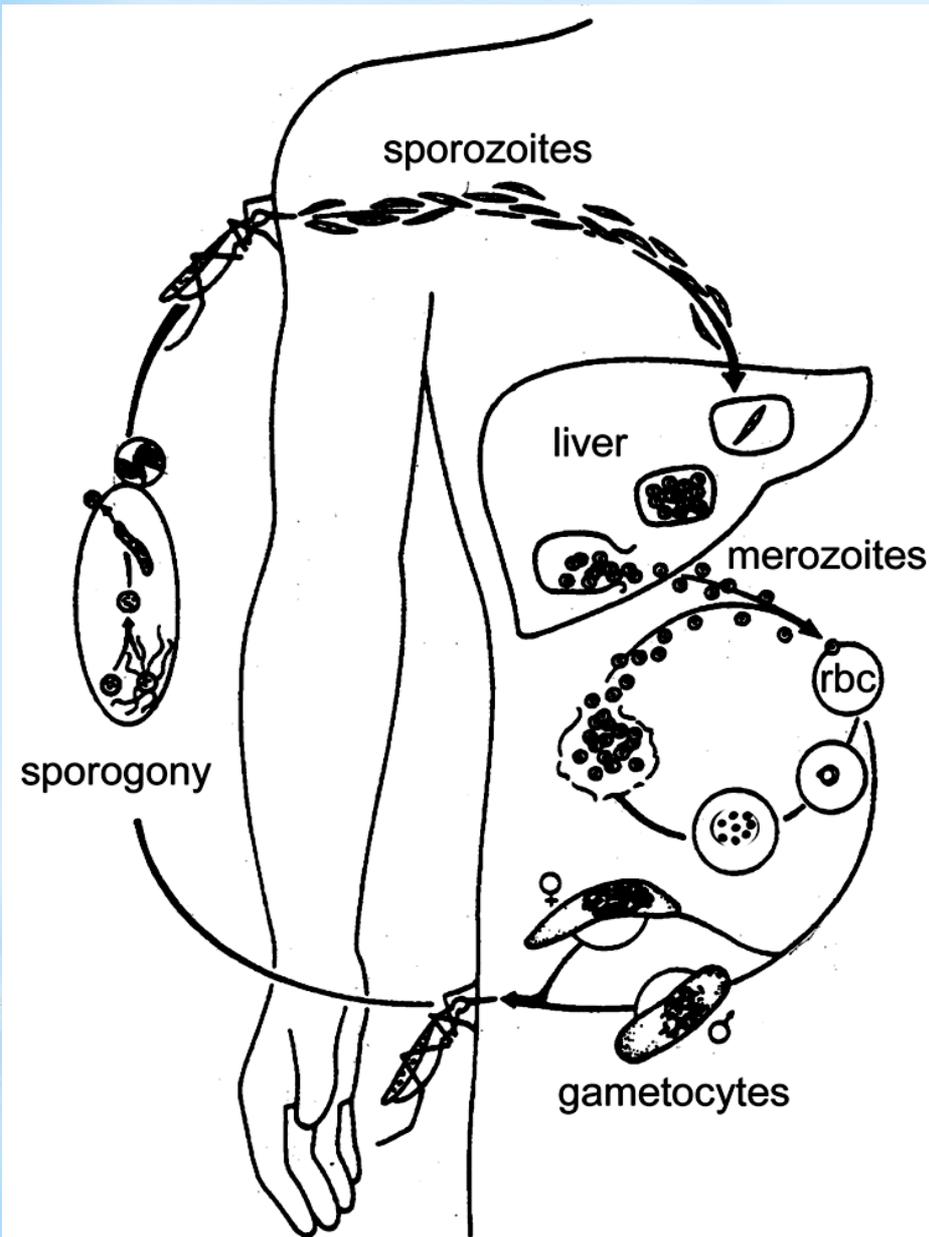
# MALARIA

- 40% of the world's population lives in endemic areas
- 3-500 million clinical cases per year
- 1.5-2.7 million deaths (90% Africa)
- increasing problem (re-emerging disease)
  - resurgence in some areas
  - drug resistance (↑ mortality)
- causative agent = *Plasmodium* species
  - protozoan parasite
  - member of Apicomplexa
  - 4 species infecting humans
- transmitted by anopheline mosquitoes

- *P. falciparum*
- *P. vivax*
- *P. malariae*
- *P. ovale*

# Life Cycle

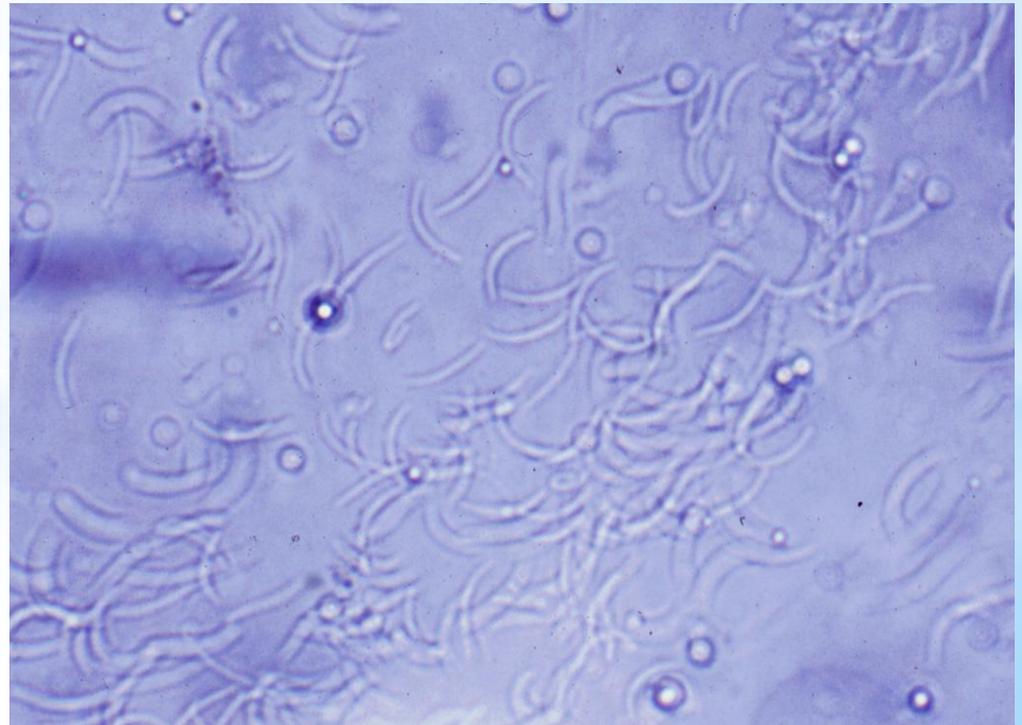
- sporozoites injected during mosquito feeding
- invade liver cells
- exoerythrocytic schizogony (merozoites)
- merozoites invade RBCs
- repeated erythrocytic schizogony cycles
- gametocytes infective for mosquito
- fusion of gametes in gut
- sporogony on gut wall in hemocoel
- sporozoites invade salivary glands



# Transmission

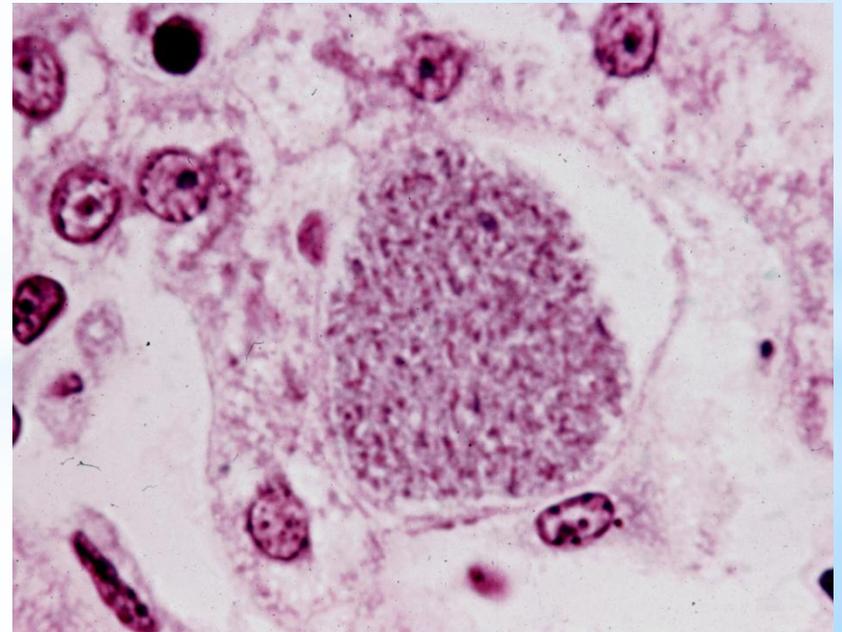
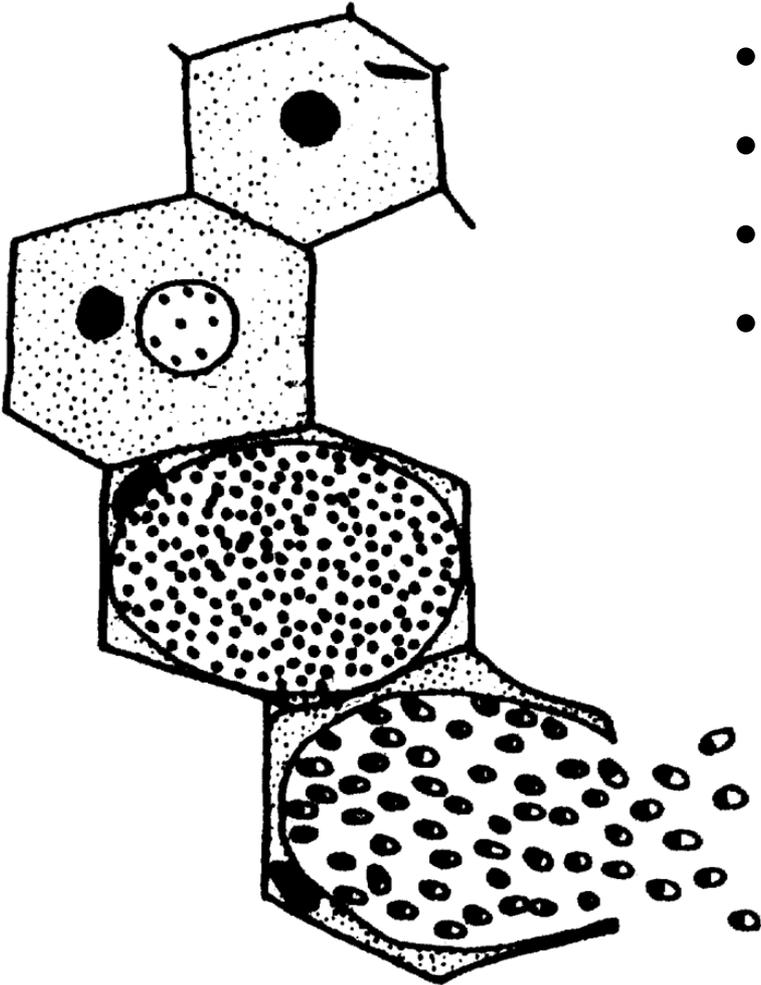
- sporozoites injected with saliva
- enter circulation
- trapped by liver (receptor-ligand)

*Anopheles*



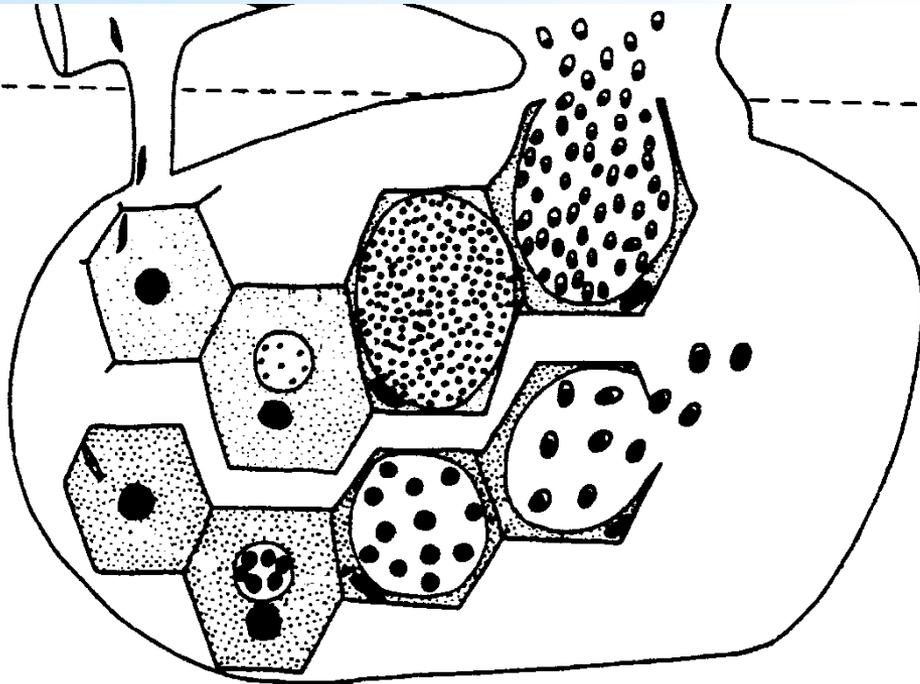
# Exoerythrocytic Schizogony

- hepatocyte invasion
- asexual replication
- 6-15 days
- 1000-10,000 merozoites
- no overt pathology



# Hyponozoite Forms

- some EE forms exhibit delayed replication (ie, dormant)
- merozoites produced months after initial infection
- only *P. vivax* and *P. ovale*

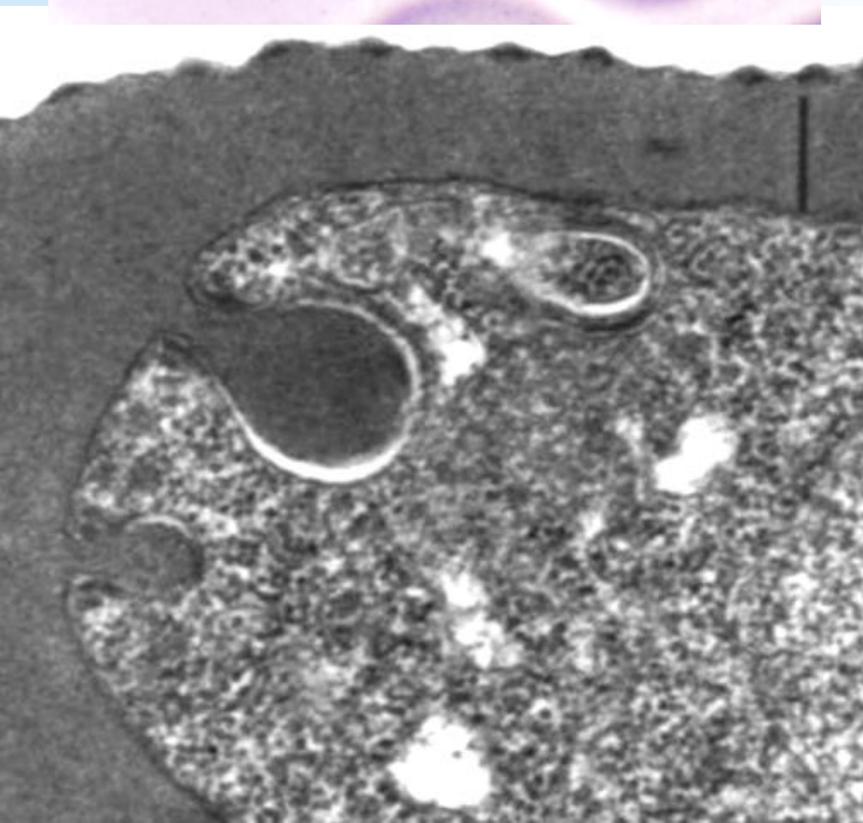
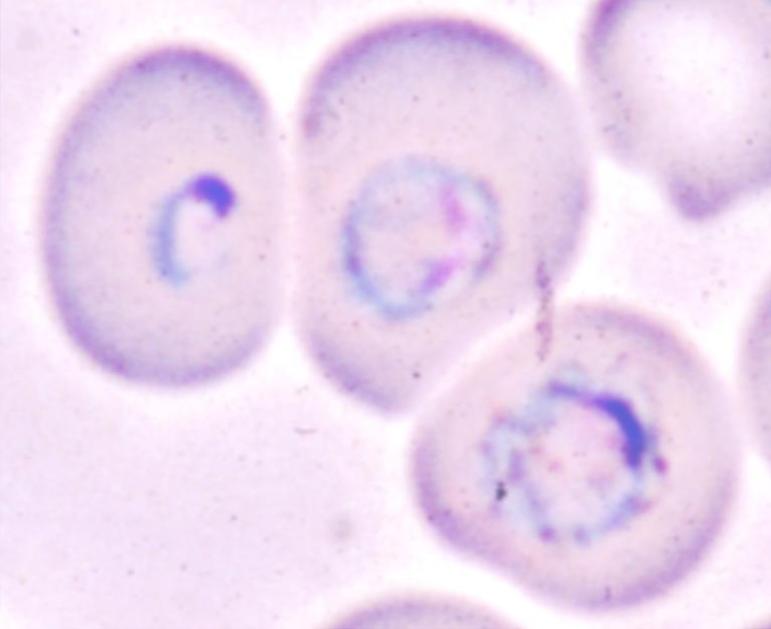


relapse = hypnozoite

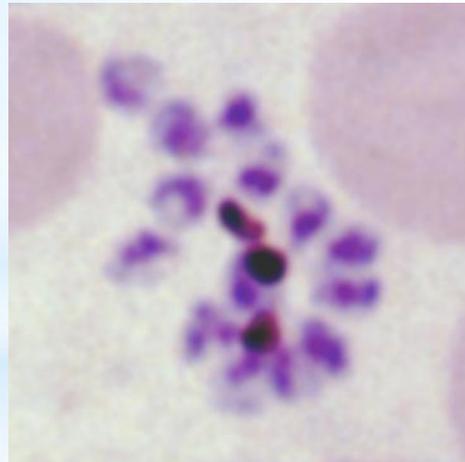
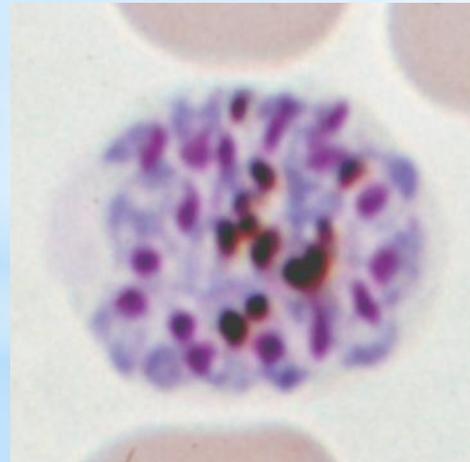
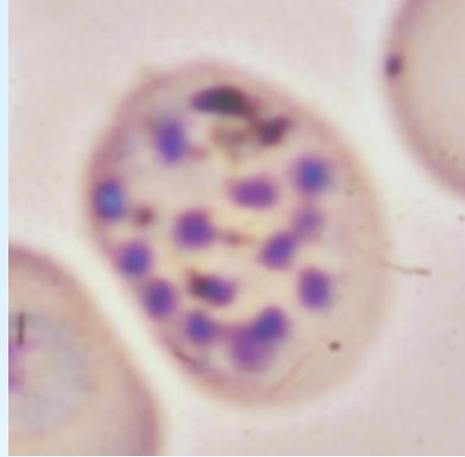
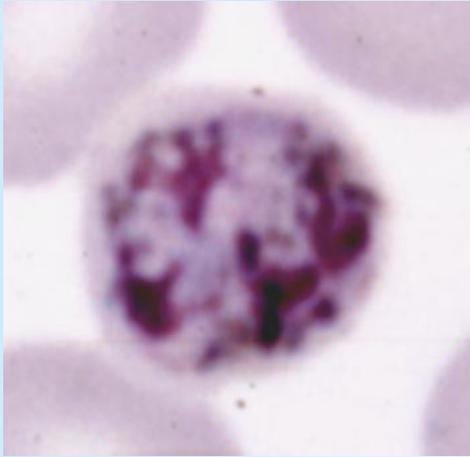
recrudescence = subpatent

# Erythrocytic Stage

- intracellular parasite undergoes trophic phase
- young trophozoite called 'ring form'
- ingests host hemoglobin
  - cytostome
  - food vacuole
  - hemozoin (malarial pigment)



# Erythrocytic Schizogony



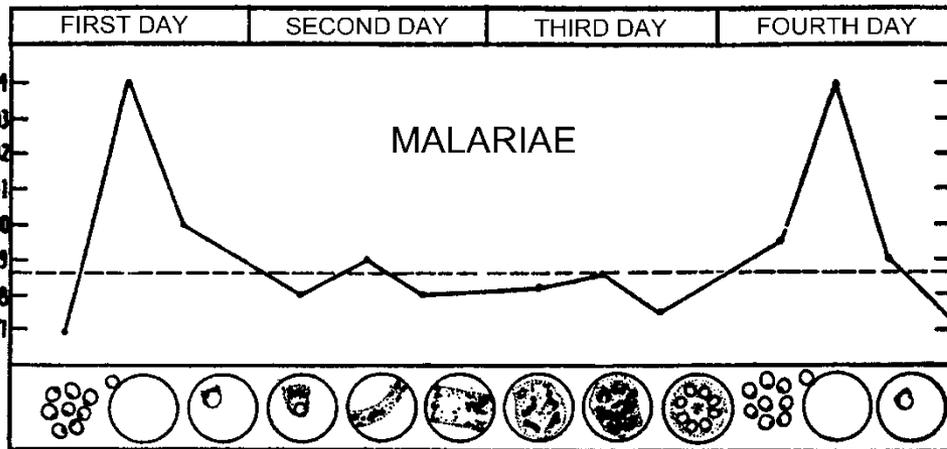
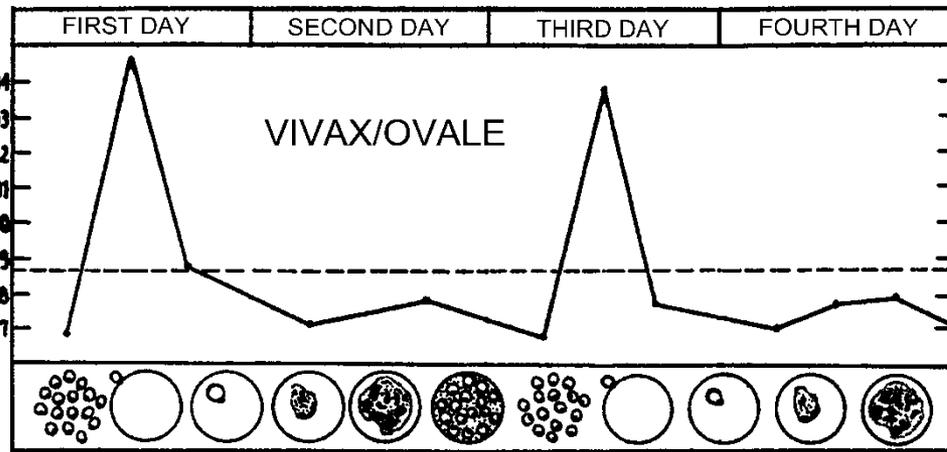
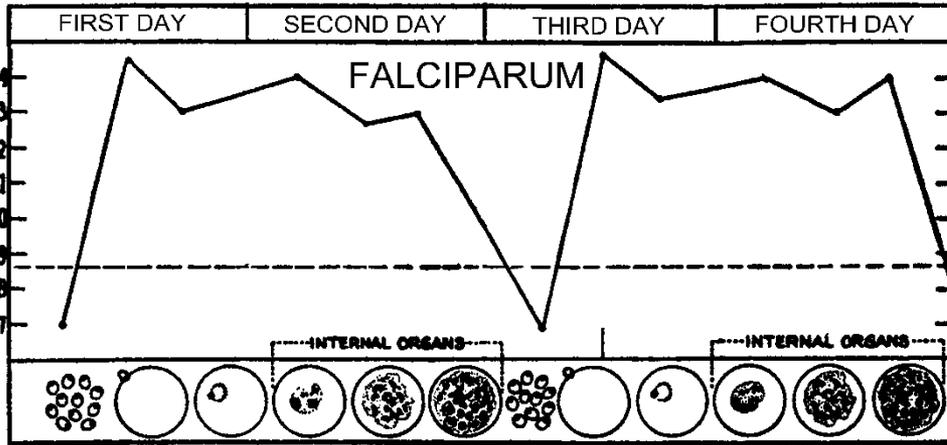
- nuclear division = begin schizont stage
- 6-40 nuclei
- budding merozoites = segmenter
- erythrocyte rupture releases merozoites
- blood stage results in disease symptoms

# Clinical Features

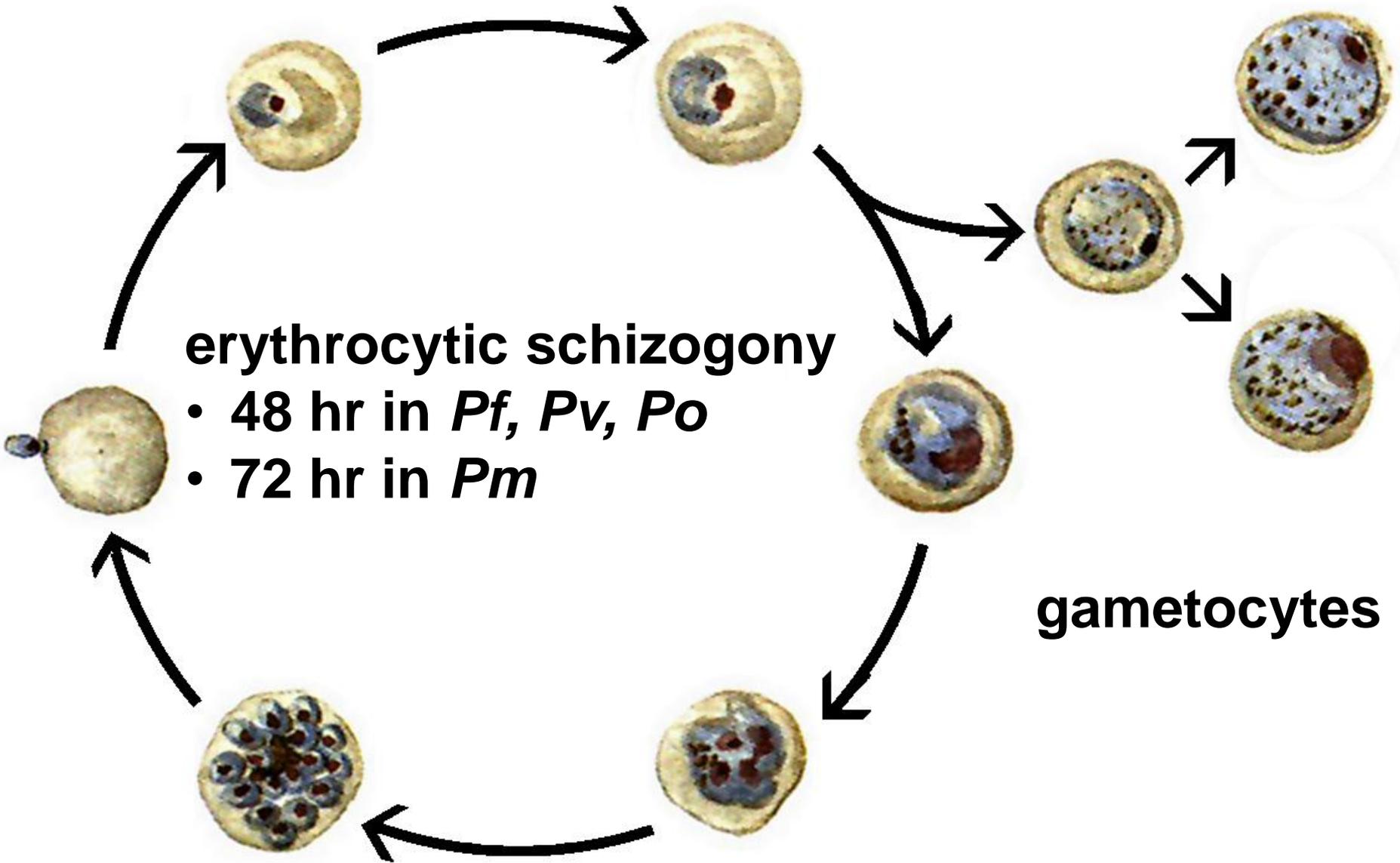
- **characterized by acute febrile attacks (malaria paroxysms)**
  - **periodic episodes of fever alternating with symptom-free periods**
- **manifestations and severity depend on species and host status**
  - **immunity, general health, nutritional state, genetics**
- **recrudescences and relapses can occur over months or years**
- **can develop severe complications (especially *P. falciparum*)**

# Malaria Paroxysm

- paroxysms associated with synchrony of merozoite release
- between paroxysms temperature is normal and patient feels well
- falciparum may not exhibit classic paroxysms (continuous fever)



tertian malaria  
quartan malaria

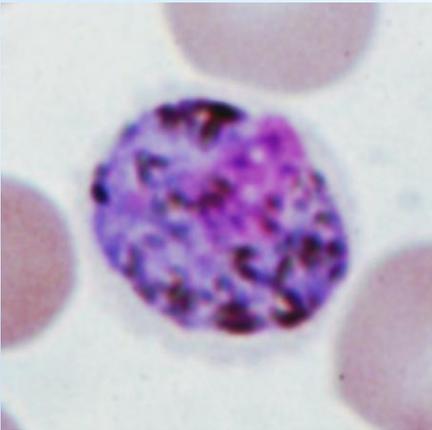
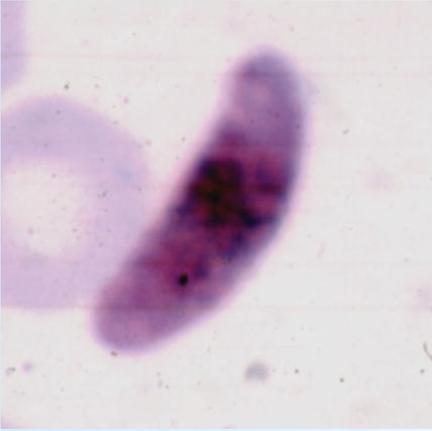


**erythrocytic schizogony**

- 48 hr in *Pf*, *Pv*, *Po*
- 72 hr in *Pm*

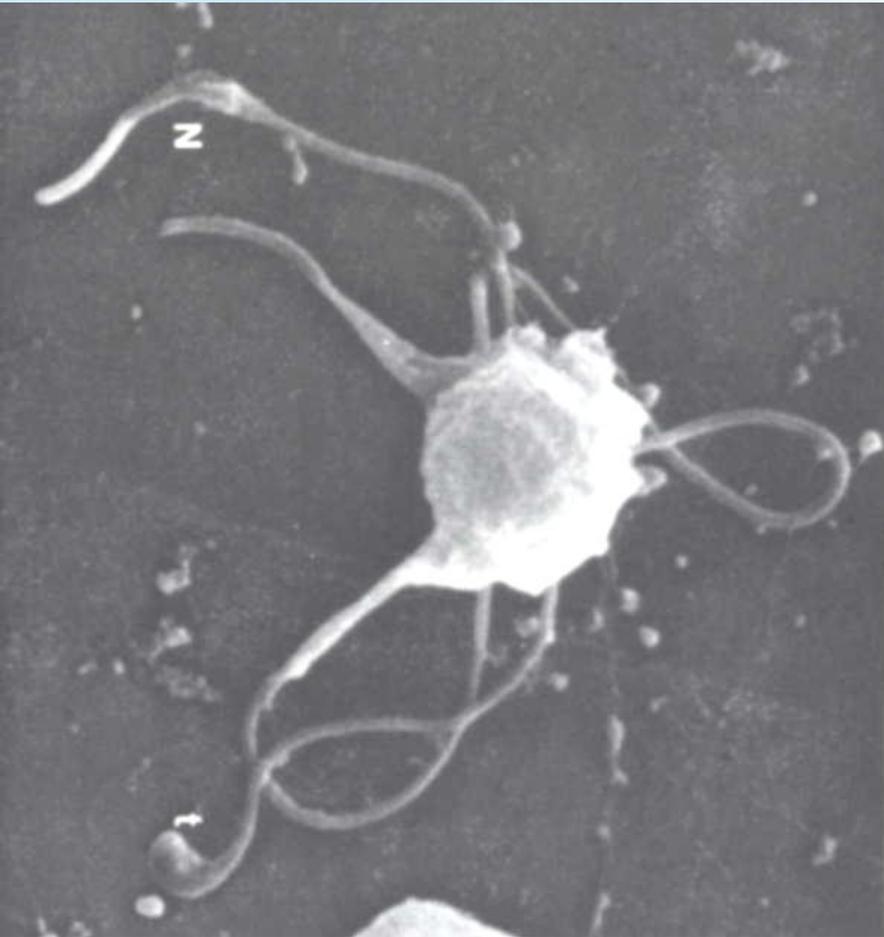
**gametocytes**

# Gametocytogenesis



- alternative to asexual replication
- induction factors not known
  - drug treatment  $\uparrow$  #'s
  - immune response  $\uparrow$  #'s
- ring  $\rightarrow$  gametocyte
  - *Pf* : ~10 days
  - others: ~same as schizogony
- sexual dimorphism
  - microgametocytes
  - macrogametocytes
- no pathology
- infective stage for mosquito

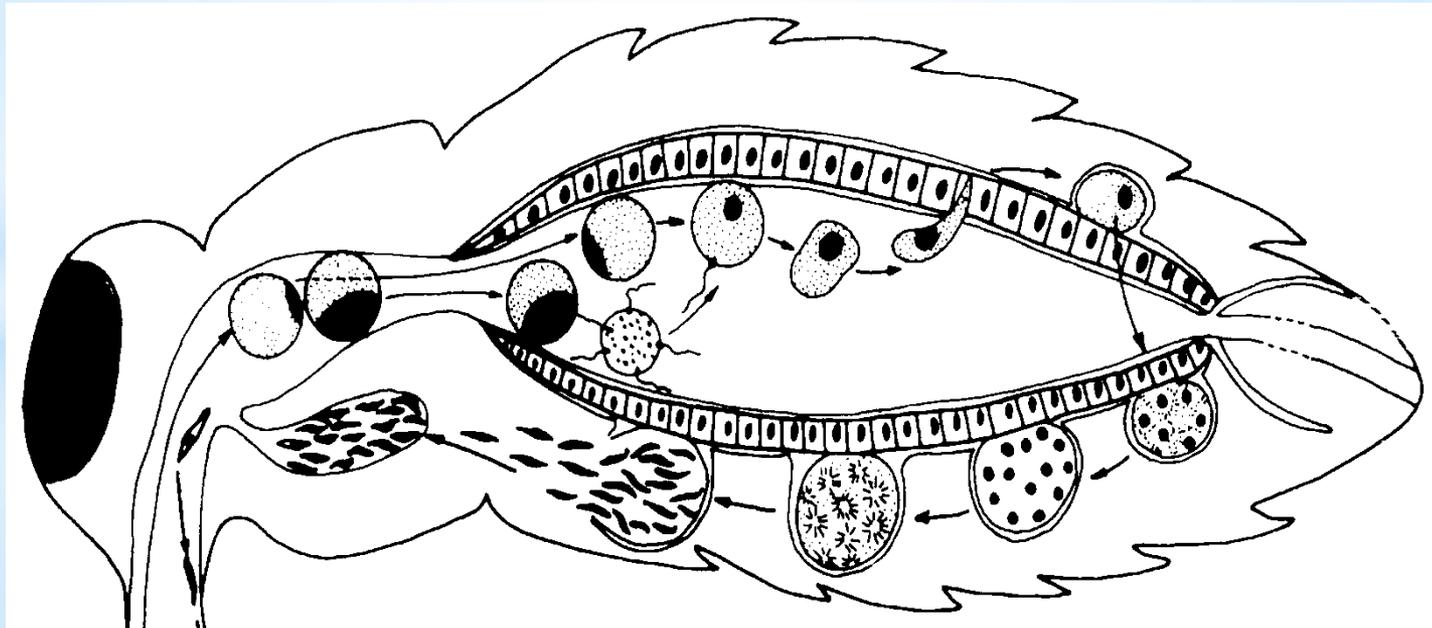
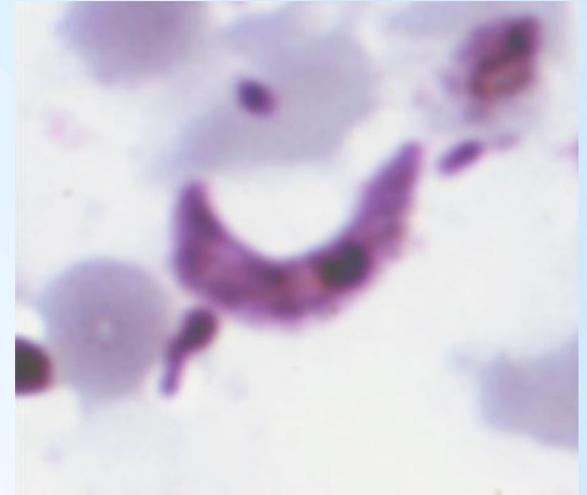
# Gametogenesis



- occurs in mosquito gut
- ‘exflagellation’ most obvious
  - 3X nuclear replication
  - 8 microgametes formed
- exposure to air induces
  - ↓ temperature (2-3°C)
  - ↑ pH (8-8.3)
  - result of ↓ pCO<sub>2</sub>
- gametocyte activating factor in mosquito
  - xanthurenic acid

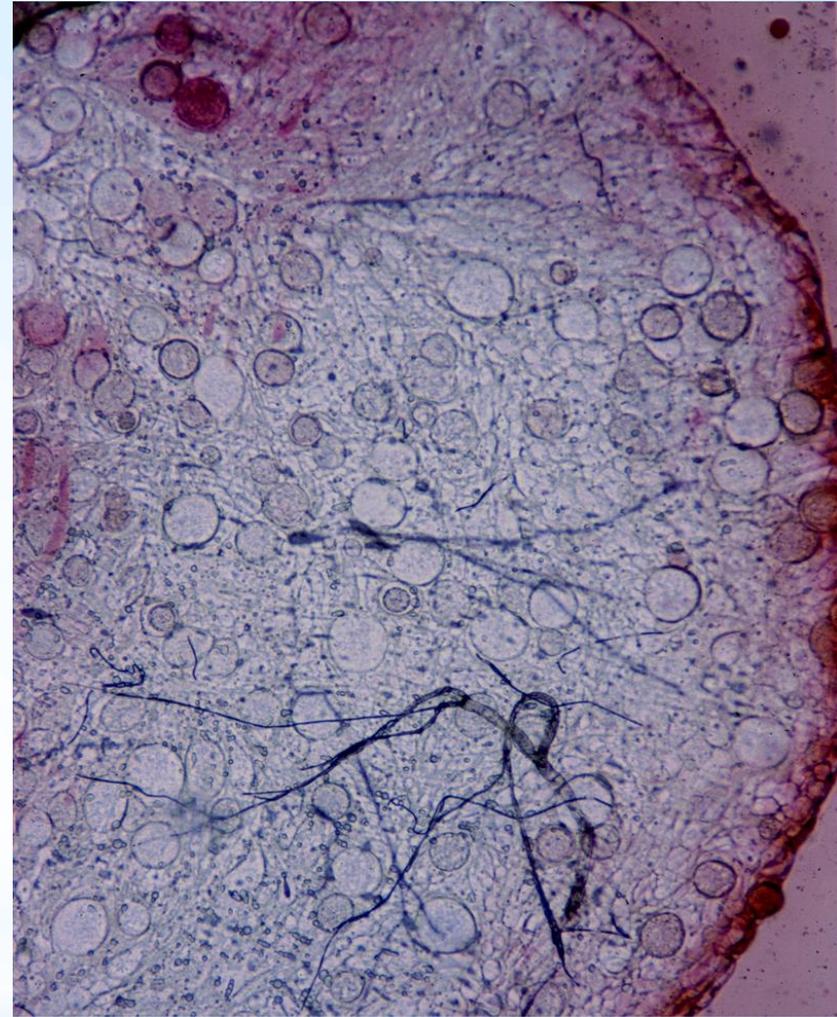
# Sporogony

- occurs in mosquito (9-21 d)
- fusion of micro- and macrogametes
- zygote → ookinete (~24 hr)
- ookinete transverses gut epithelium ('trans-invasion')



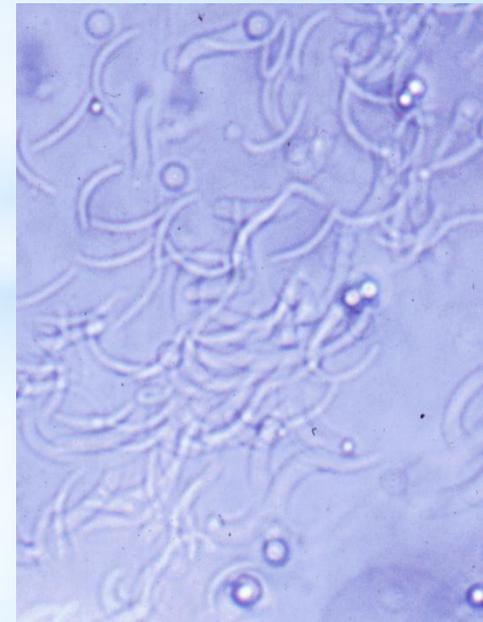
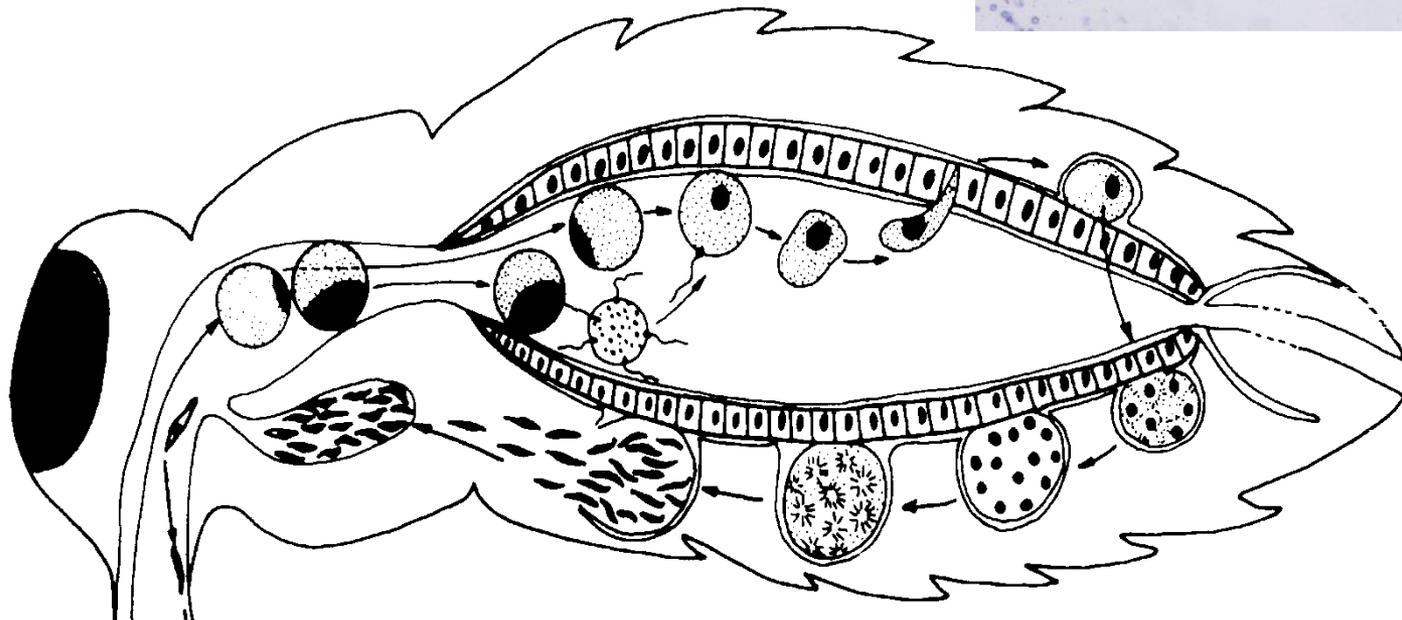
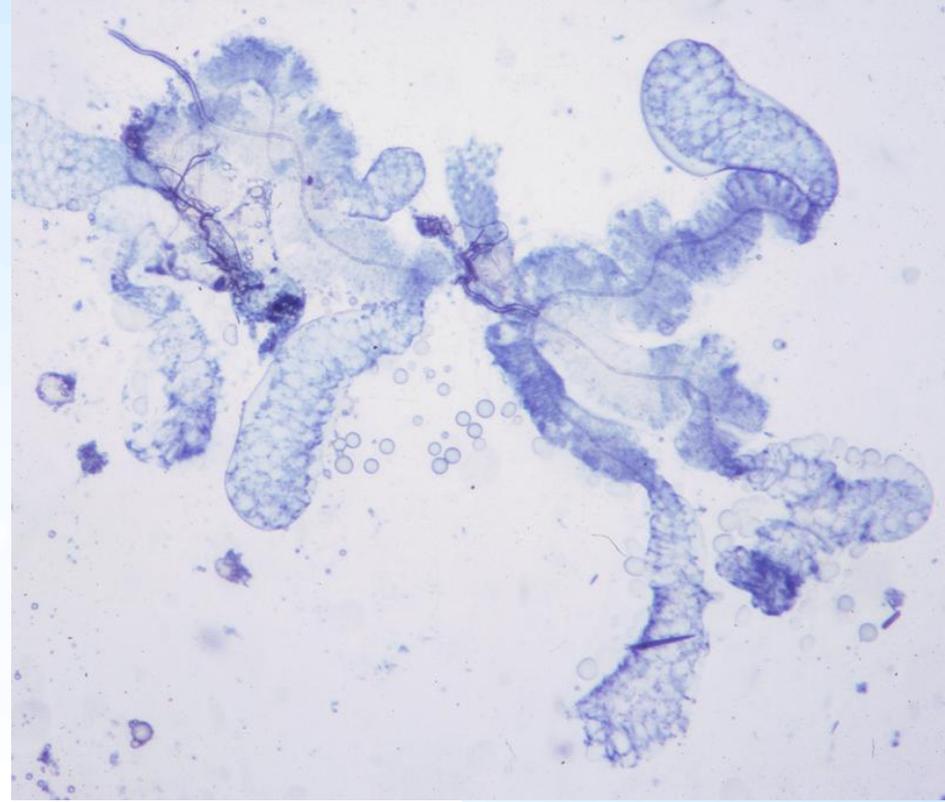
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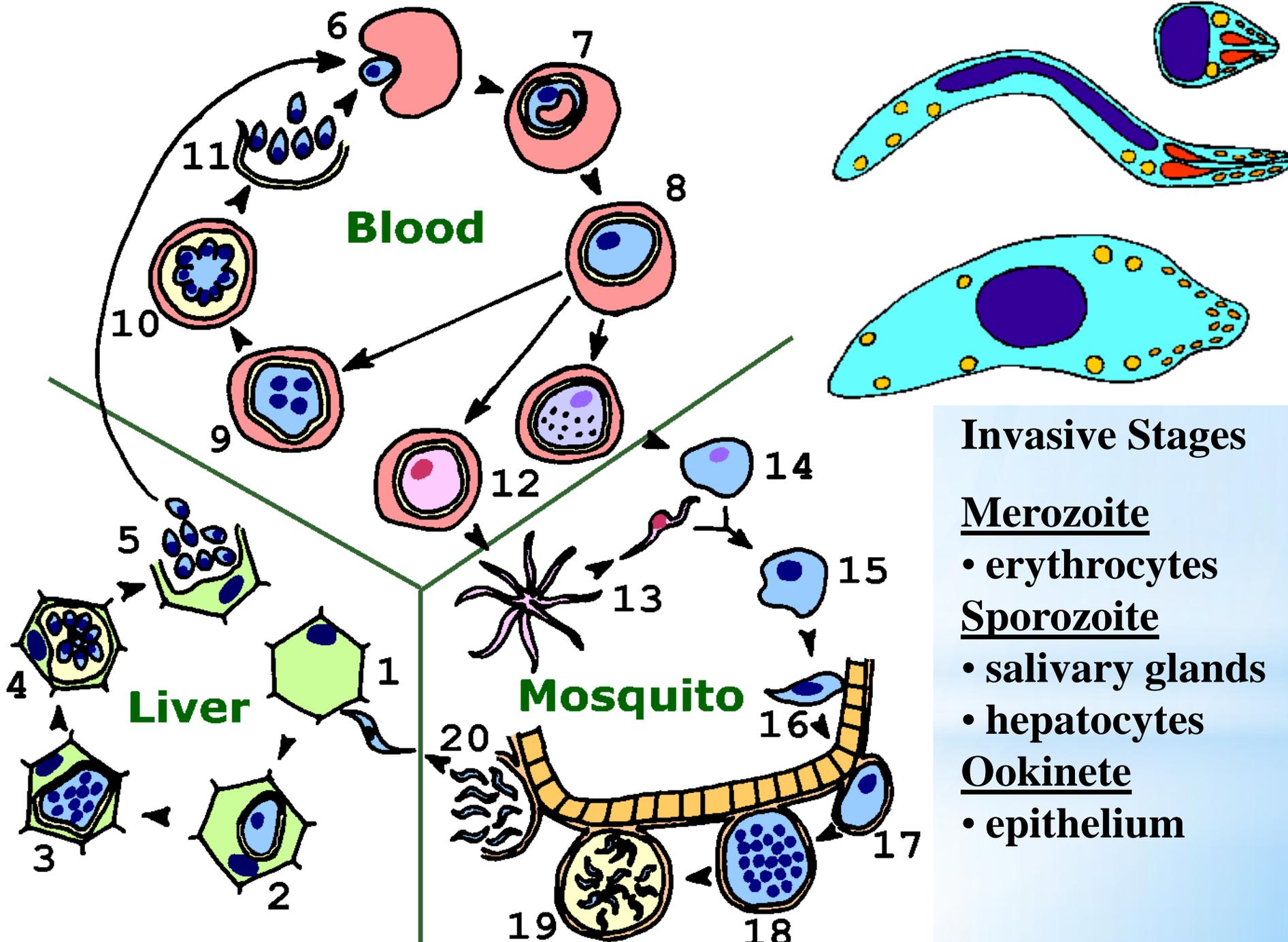
- ookinete → oocyst
  - between epithelium and basal lamina
- asexual replication → sporozoites
- sporozoites released



# Sporogony

- sporozoites migrate through hemocoel
- sporozoites 'invade' salivary glands





**Invasive Stages**

**Merozoite**

- erythrocytes

**Sporozoite**

- salivary glands
- hepatocytes

**Ookinete**

- epithelium

