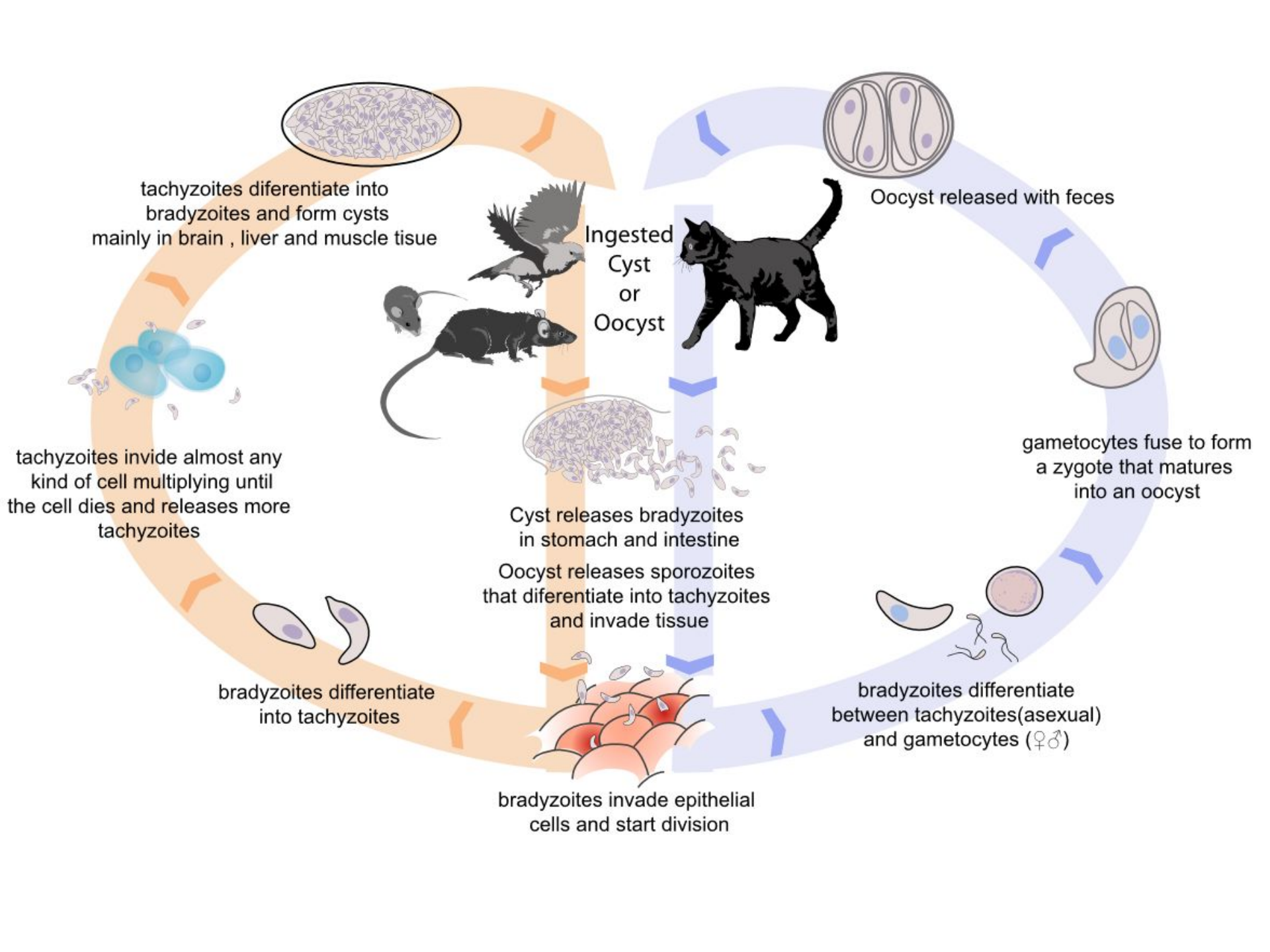
Medical protozoology: Apicomplexa

Toxoplasmosis

- Caused by *Toxoxplasma gondii*
- Worldwide distribution, very common human infection
- Infection of a small rodent in North Africa
- In the U.S., domestic cats serve as definitive host (litter box, outdoor sand box)
  - Shed oocysts
- Birds and mammals intermediate hosts (humans accidental hosts)
- High risk/disease pathology: immunocompromised, pregnant women and their fetuses


tachyzoites diferentiate into bradyzoites and form cysts mainly in brain , liver and muscle tisue
Ingested Cyst or Oocyst
Oocyst released with feces
tachyzoites invide almost any kind of cell multiplying until the cell dies and releases more tachyzoites
Cyst releases bradyzoites in stomach and intestine
gametocytes fuse to form a zygote that matures into an oocyst
Oocyst releases sporozoites that diferentiate into tachyzoites and invade tissue
bradyzoites differentiate into tachyzoites
bradyzoites differentiate between tachyzoites(asexual) and gametocytes (♀♂)
bradyzoites invade epithelial cells and start division

NATURAL CYCLE ACCIDENTAL CYCLE

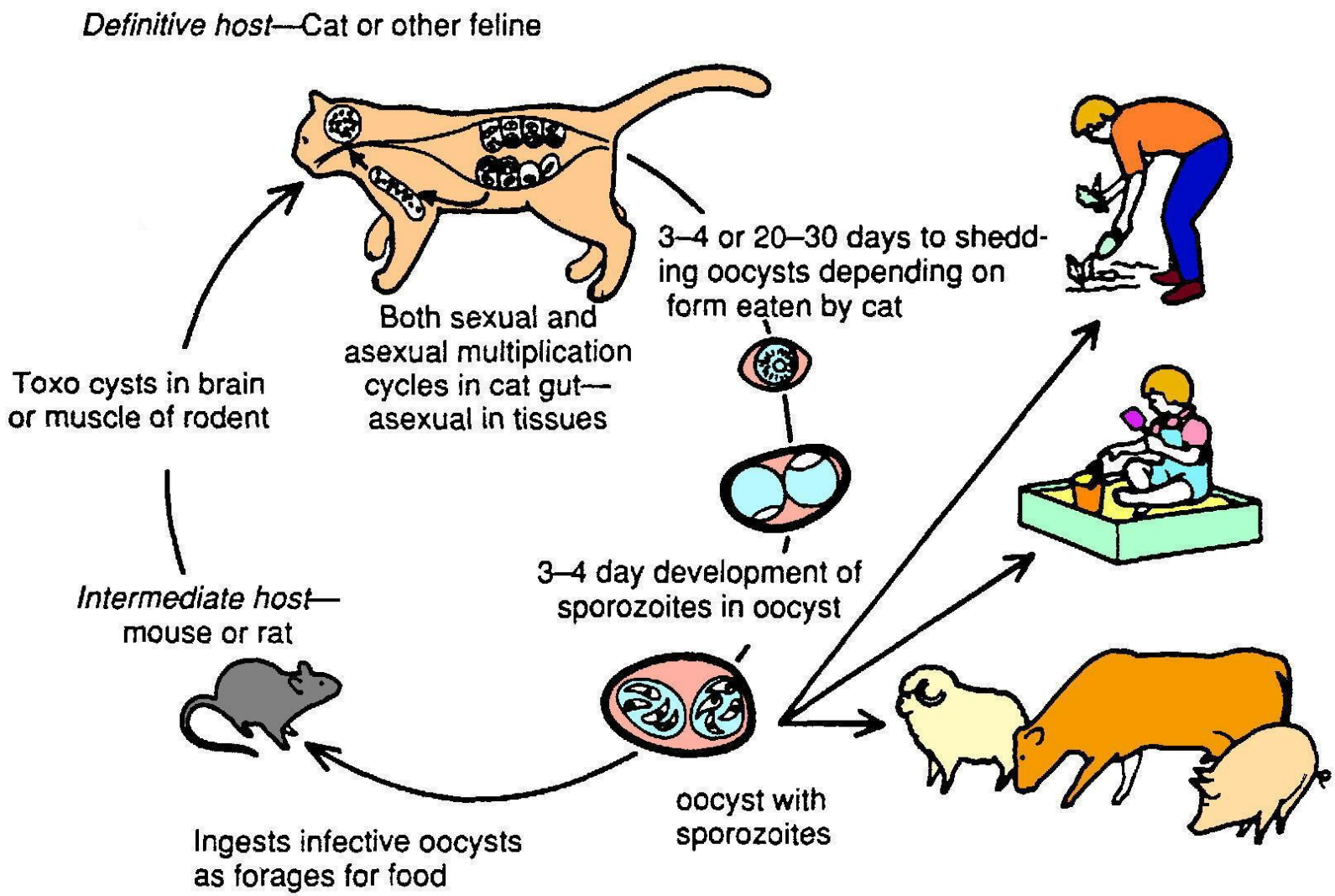
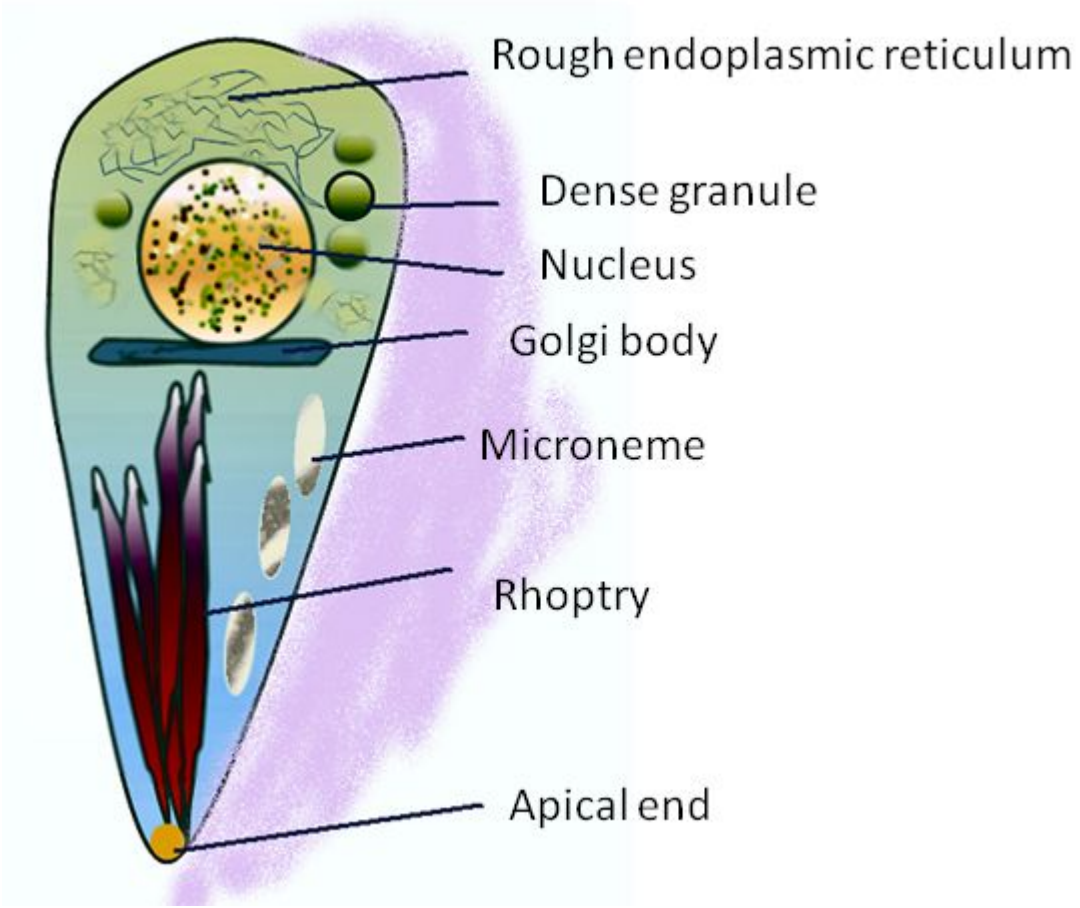
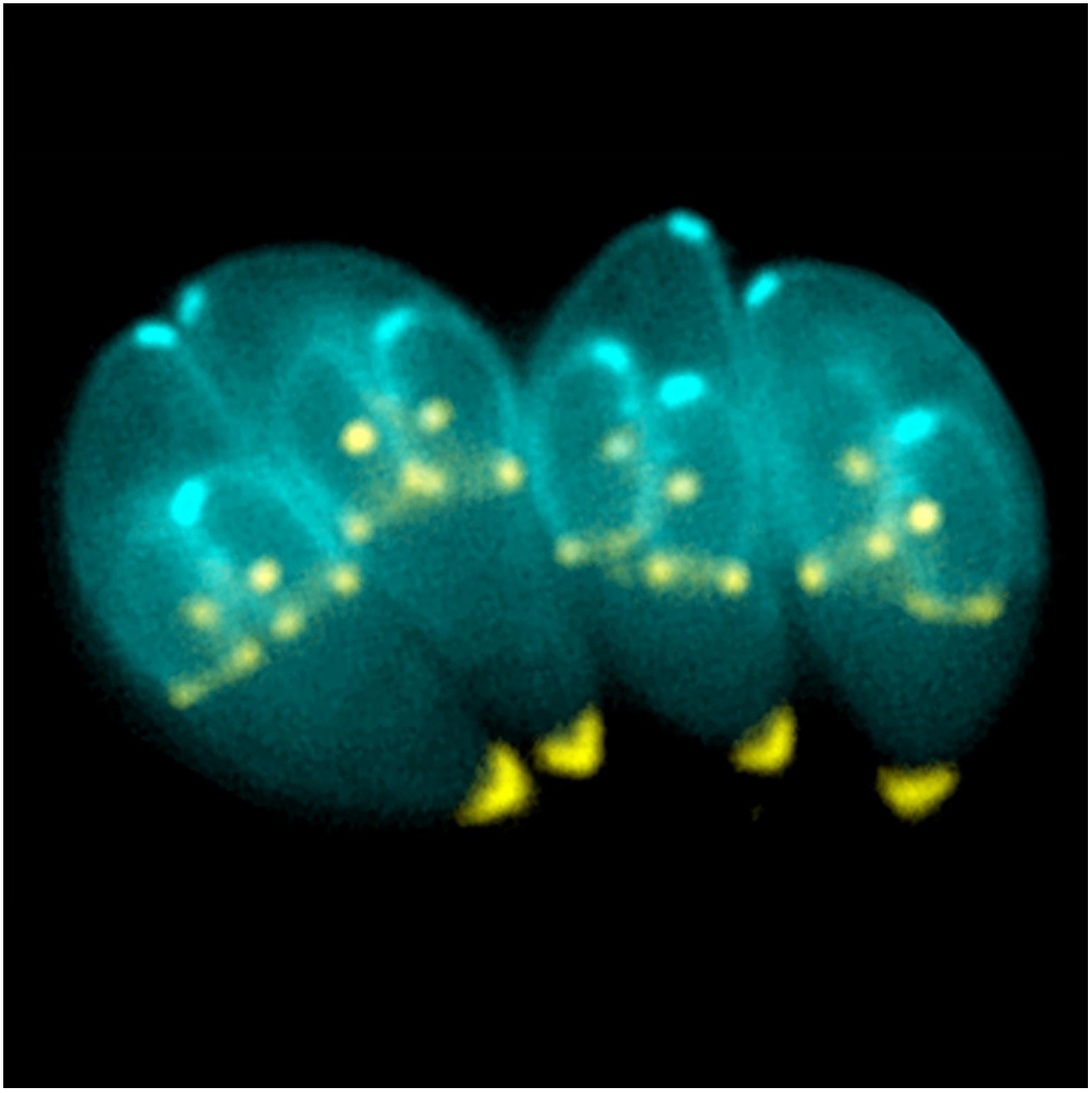


Fig. 26. Transmission life-cycle of Toxoplasma gondii.

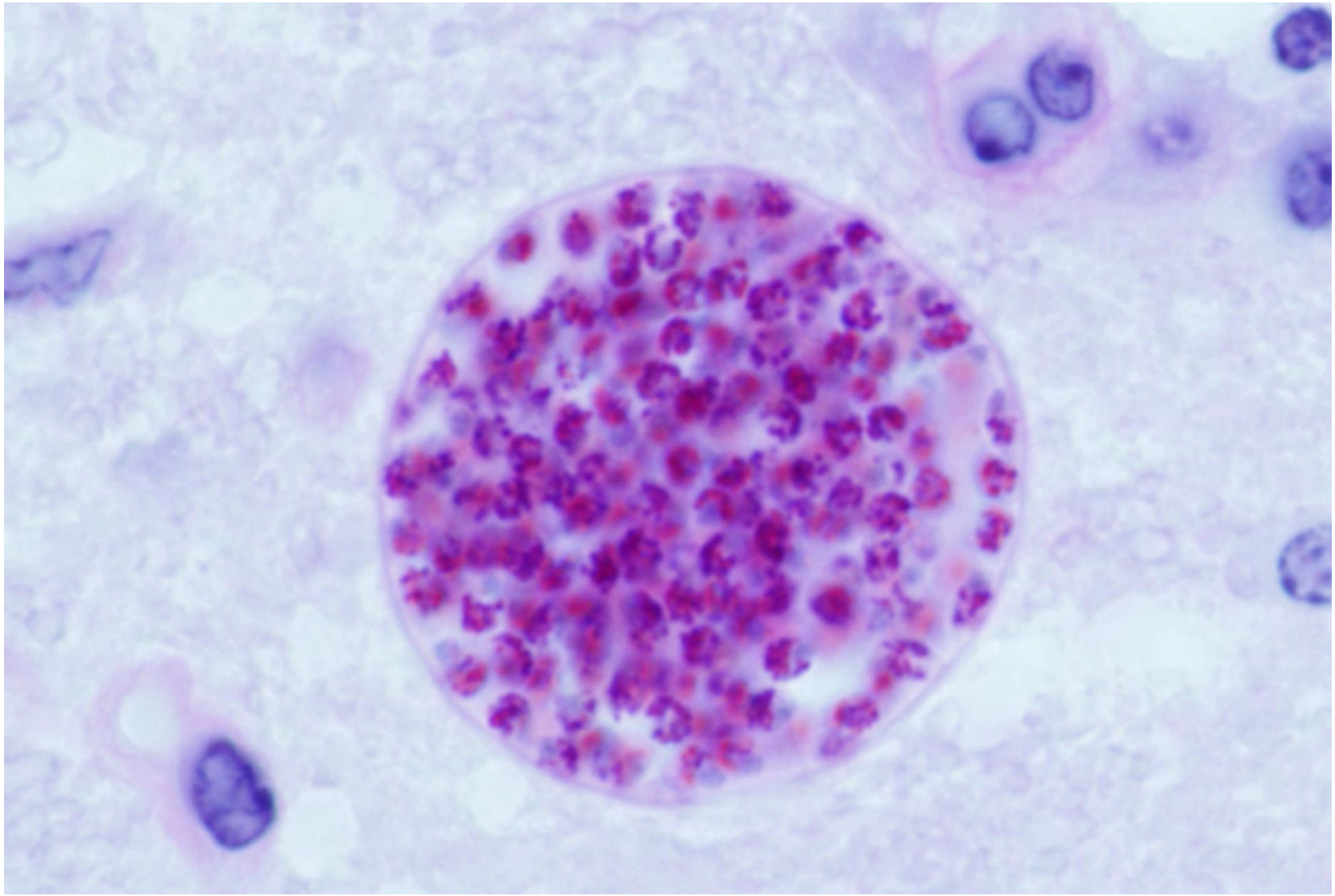
Diagram of *T. gondii* structure





Dividing *T. gondii* parasites

T. gondii tissue cyst in a mouse brain, individual bradyzoites can be seen within



Toxoplasmosis: Human infection

- Only non-intestinal form found in humans
- Early in infection, tachyzoites may be seen as intracellular parasites in Giemsa stained smears of heart, lung, lymph node and CNS tissue (pathology)
- Organisms encysts late in infection
  - Immune system stops attack
- Organism **may reactivate** if patient becomes immunocompromised

Transmission of *T. gondii*

- Human infection with *Toxoplasma gondii* can be acquired by:
  - Fecal-oral of oocysts (pregnancy women should be advised NOT to clean cat litter boxes)
  - Ingestion of raw or undercooked meat containing encysted *T. gondii*
  - Transplacental passage
  - Blood transfusion or organ transplantation

Clinical Features of Toxoplasmosis

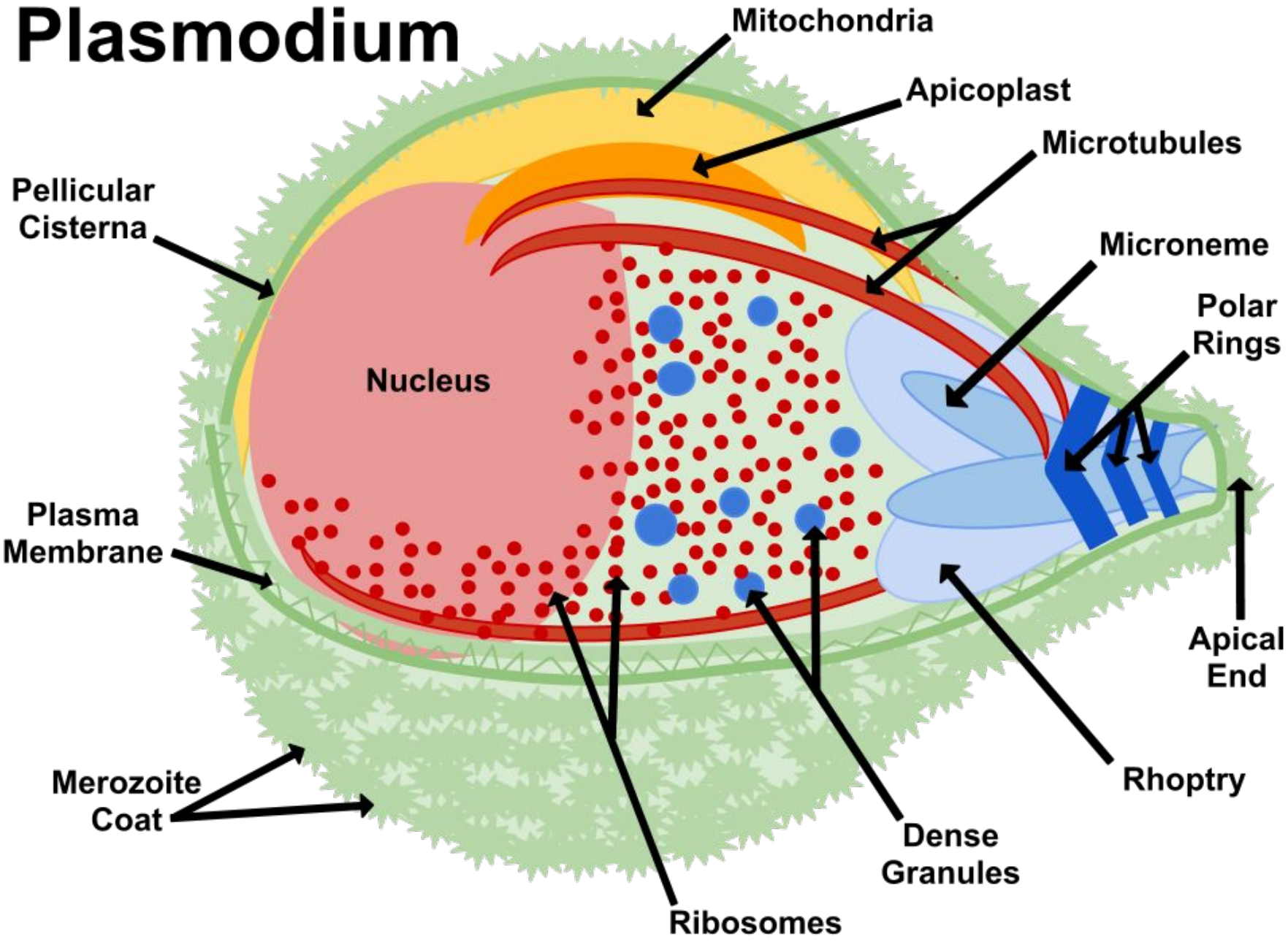
- Majority of human infections are asymptomatic and benign
- Symptoms mimic mononucleosis
- Severe cases: maculopapular rash, myocarditis, hepatitis, encephalomyelitis, retinochroiditis
- Fetal mortality from transplacental passage is 2-6/1000 pregnancies in US
  - First or second trimester greatest consequence

Laboratory Diagnosis of Toxoplasmosis

- Serological testing for antibody response to the infection (EIA)
- In infants, test for IgM isotype only as evidence of congenital infection (can't use IgG since it crosses placenta and could be from mother)
- Histologists may process biopsies for Giemsa stain of organisms

Malaria

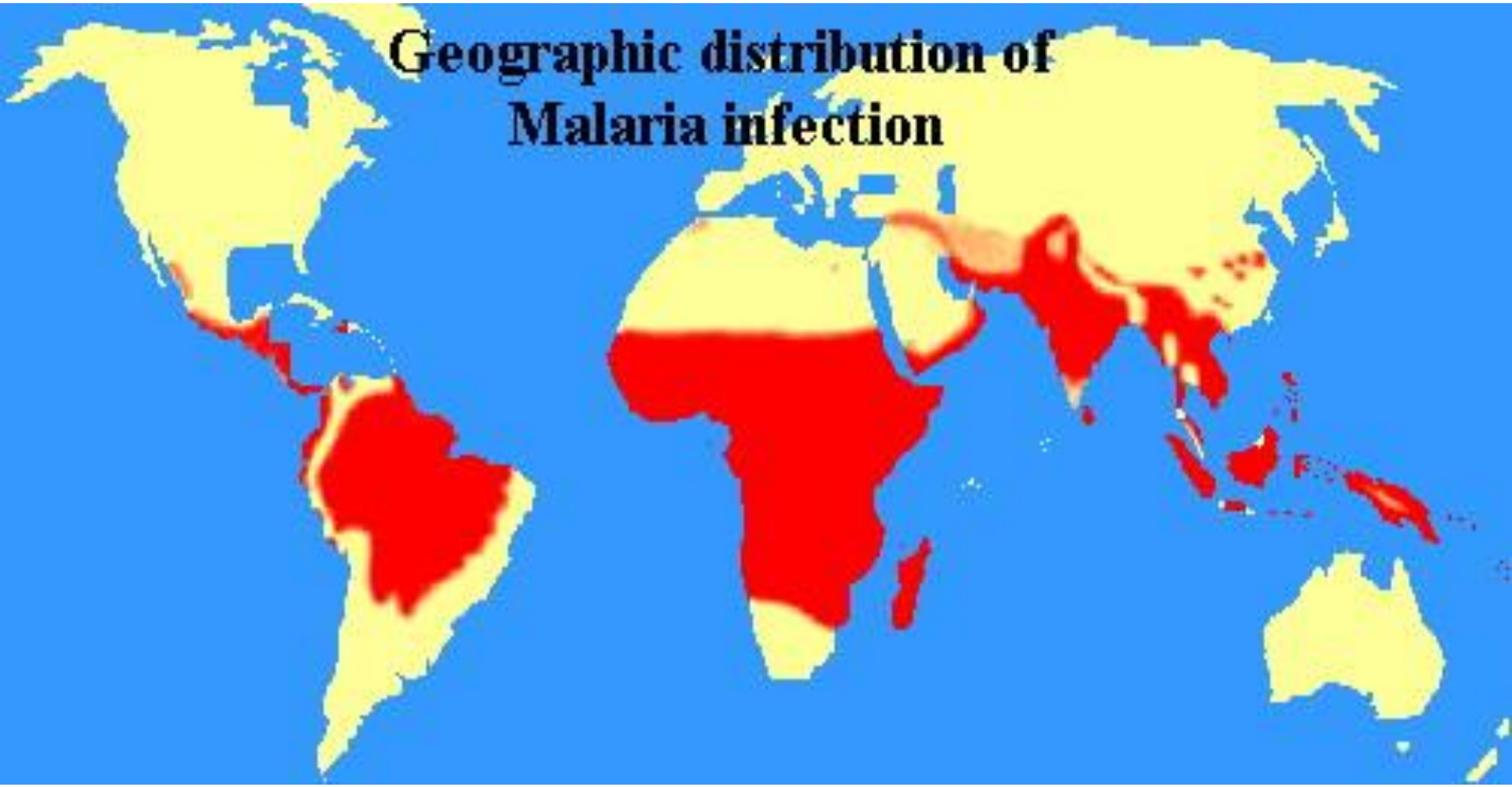
- World's most notorious tropical parasite threatening 2,400 million people (~40% of the world population)
  - People can be reinfected daily and can be infected with multiple species of *Plasmodium* infections
- WHO claims 300-500 million new cases each year, over 1 million deaths (mainly African children)
- The agents of human malaria are four species of the genus *Plasmodium*:
  - *Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, and Plasmodium falciparum*


Plasmodium
Mitochondria
Apicoplast
Microtubules
Pellicular Cisterna
Microneme
Polar Rings
Nucleus
Plasma Membrane
Apical End
Merozoite Coat
Rhoptry
Dense Granules
Ribosomes

Distribution of Malaria

- *P. vivax* account for the majority of malarial infections, parasite is widely distributed and only species that extends through tropical, subtropical and temperate regions
- *P. falciparum* causes falciparum, confined to the tropics and subtropics and is the most lethal form of malaria
  - Not in temperate regions
- *P. ovale* is confined West Africa, South America and Asia
- *P. malariae* is distributed throughout the subtropics and tropics

Distribution of malaria.

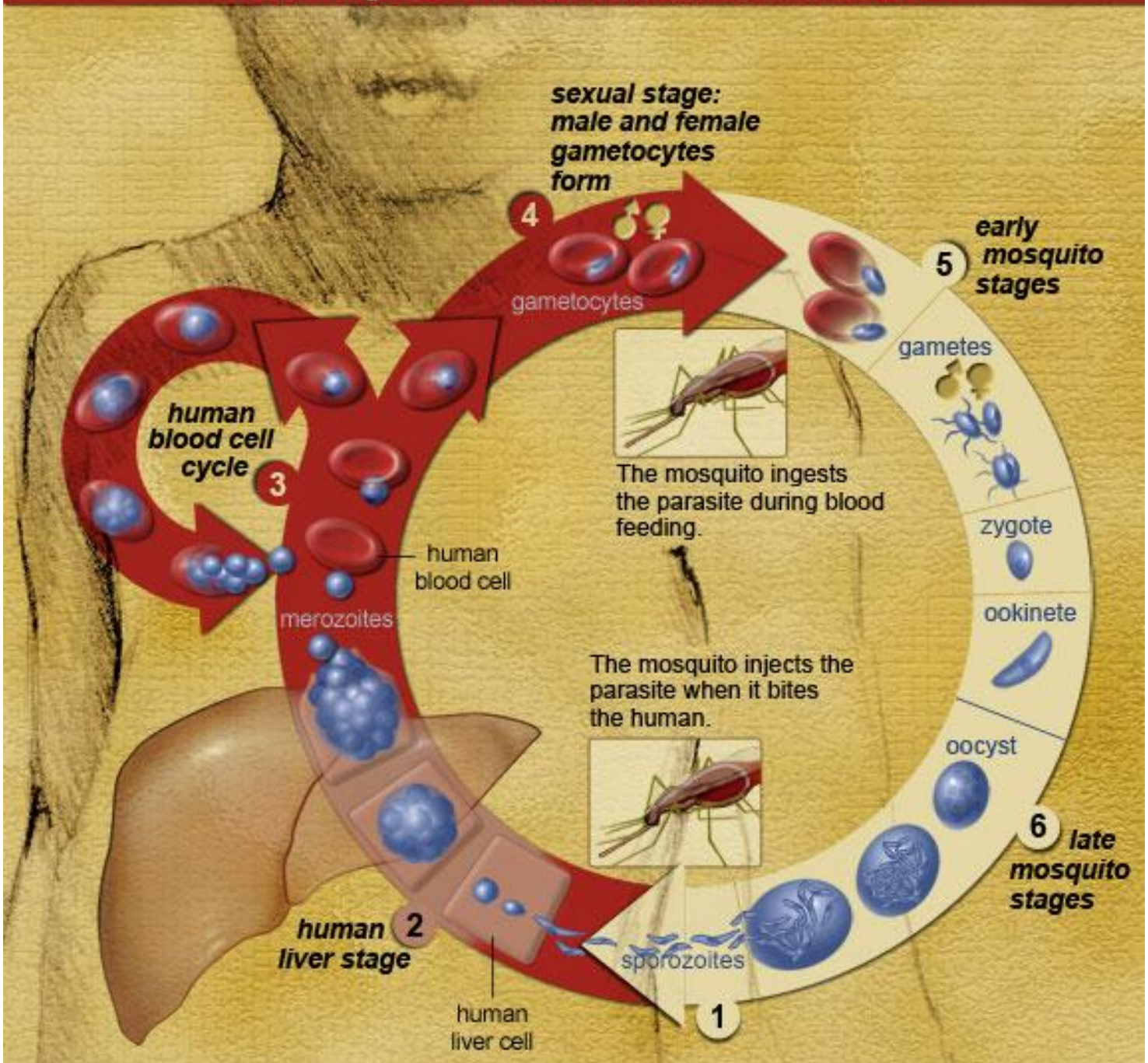


Malaria

- The parasite is transmitted primarily by female Anopheles mosquito
- Malaria cases reported in U.S. primarily due to travelers or immigrants (1,000-2,000/year)
- Malaria may also be contracted by sharing contaminated needles, blood transfusion, congenital transmission, or by the bite of domestic mosquito that has previously bitten an individual with an imported infection
  - Prophylactic medicines available
  - Organism mutates readily so no vaccine is developed

Anopheles mosquito – definitive host of Plasmodium.

Life Cycle of the Malaria Parasite



Malaria Life Cycle

- Two distinct phases of infection:
  - Asexual development = schizogony, which takes place in the human host
  - Sexual development – sporogony, which takes place in the mosquito
- Mosquito is considered definitive host and primary vector, man is intermediate host

Malaria Life cycle cont.

- As mosquito draws blood meal, spindle shaped sporozoites are injected into capillary wound and carried throughout body
- Sporozoites make their way to liver (reside in parenchymal cells), it is here asexual division (schizogony) begins
- The portion of development is called the **exo**erythrocytic cycle, and lasts from 5-6 days depending on species of *Plasmodium*

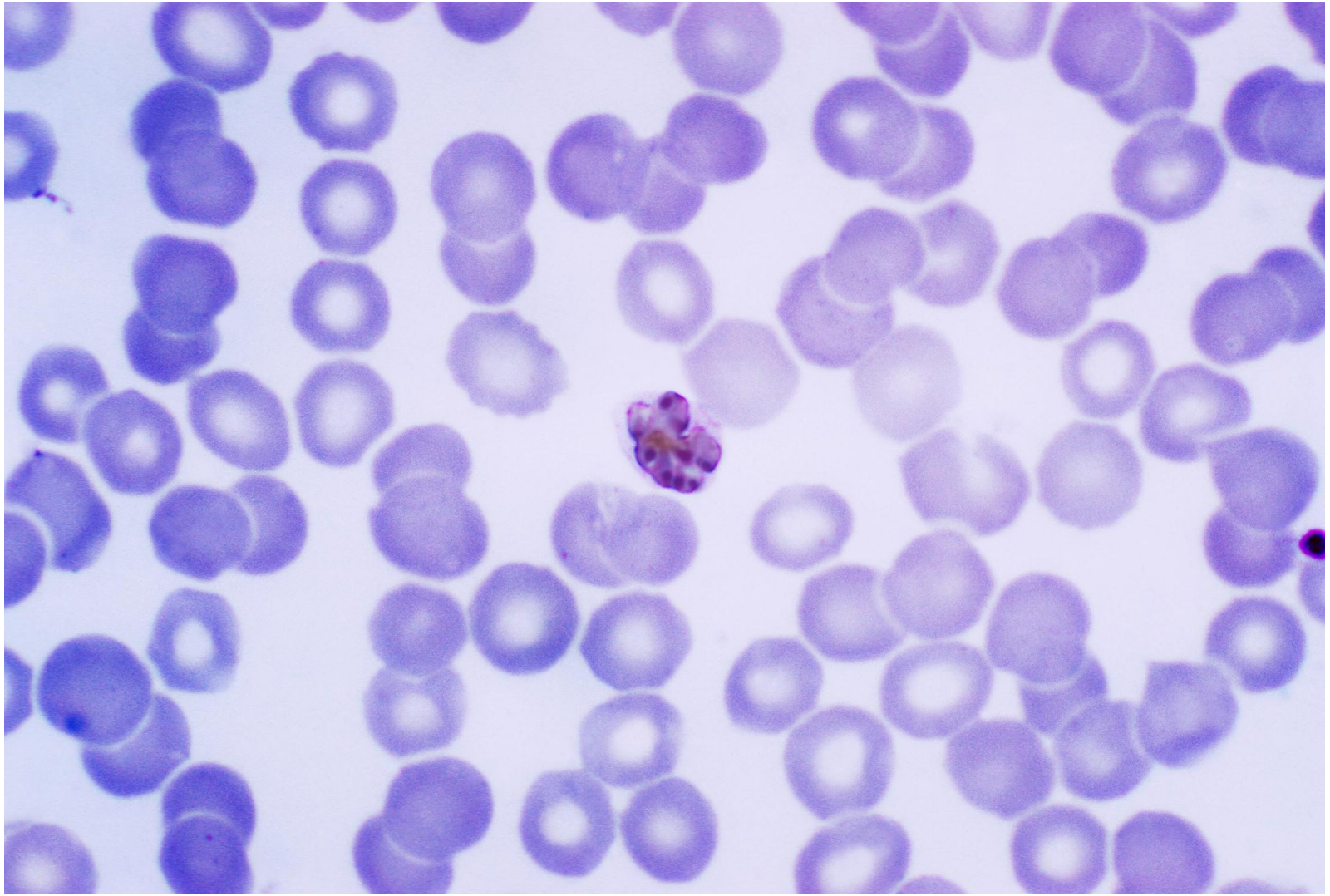
Malaria Life cycle cont.

- Sporozoite division in the liver produces thousands of merozoites
- Infected parenchymal cells rupture, releasing merozoites into the circulation
- All four species of *Plasmodium* undergo asexual multiplication in lever cells
- ** Some sporozoites of *P. vivax* and *P. ovale* can become latent in the liver – reactivation of the latent parasites cause **true clinical relapse**

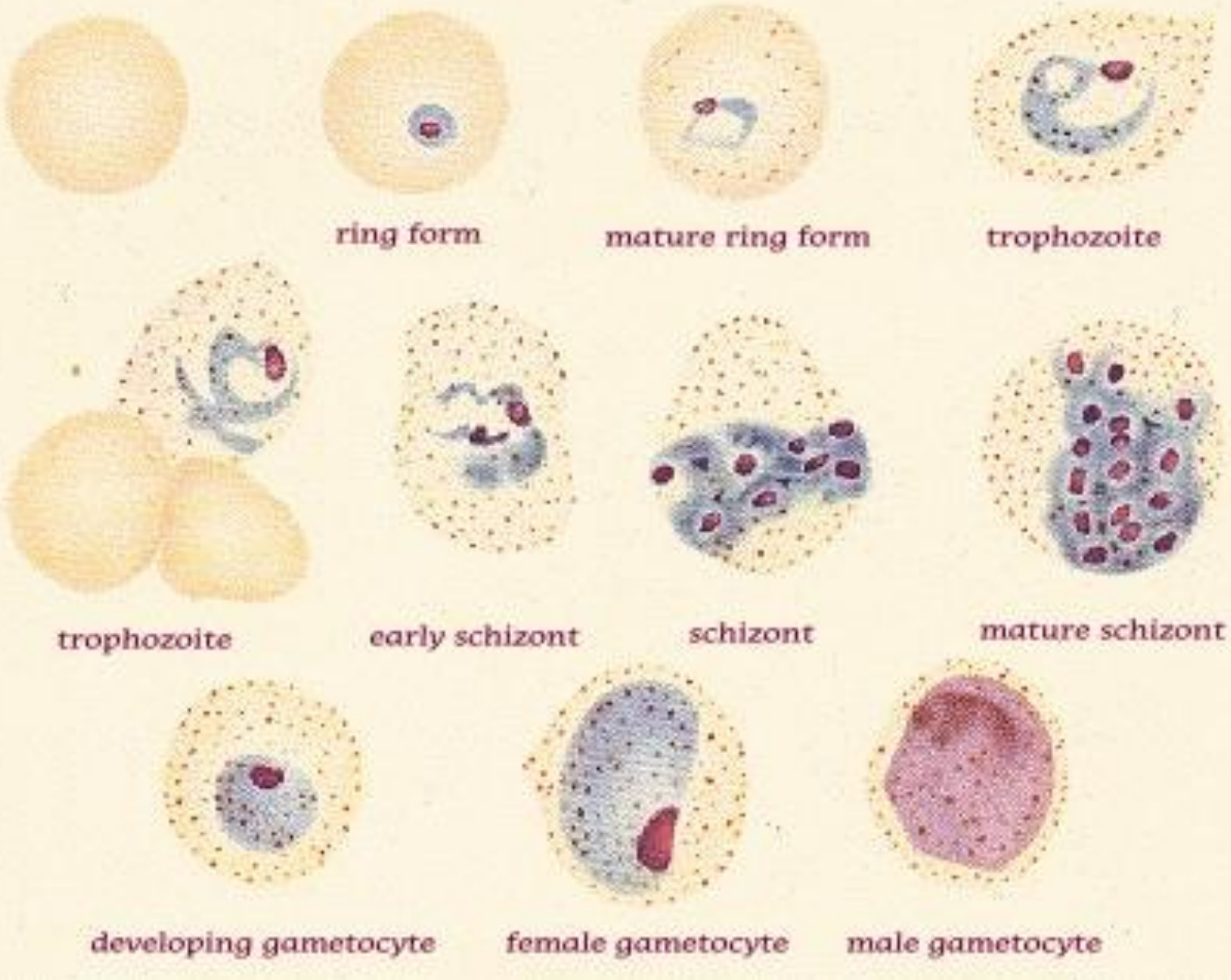
Malaria Life cycle cont.

- Circulating merozoites invade mature RBC's or reticulocytes (immature RBCs) , begin to grow as ring forms (trophozoites), feed on hemoglobin
- Remaining byproducts of hemoglobin metabolism combine to form malarial pigment
- The trophozoite enlarges until it's nucleus begins to divide and then it is called a schizont
- Mature schizont undergoes erythrocytic schizogony, forming multiple merozoites (number of merozoites is species diagnostic)

Giemsa-stained micrograph of a mature *Plasmodium malariae* schizont



P. vivax


ring form
mature ring form
trophozoite
trophozoite
early schizont
schizont
mature schizont
developing gametocyte
female gametocyte
male gametocyte

Malaria Life cycle cont.

- When the infected RBC's rupture, new cells are either infected or merozoites are destroyed by hosts' immune system
- The liberation of the parasite from the RBC's releases waste and toxic debris
- Parasite debris causes the onset of the malarial paroxysm (shaking, fever and chills)

Malaria paroxysm lengths

- P. vivax = 48 hours parosysms (Benign tertian malaria
- P. ovale = 48 hours parosysms (Tertian malaria)
- P. falciparum = 36-48 hour paroxysms (Malignant tertian malaria)
  - Replicates the fastest
- P. malariae = 72 hours paroxysms (Quartan malaria)
  - Longest cycle of replication

Clinical symptoms of malaria

- Paroxysms
- Anemia
- Splenomegaly
- Complications:
  - Tissue hypoxia (RBC debris blocks capillaries)
  - Major organ collapse (kidney)
  - CNS (stroke)

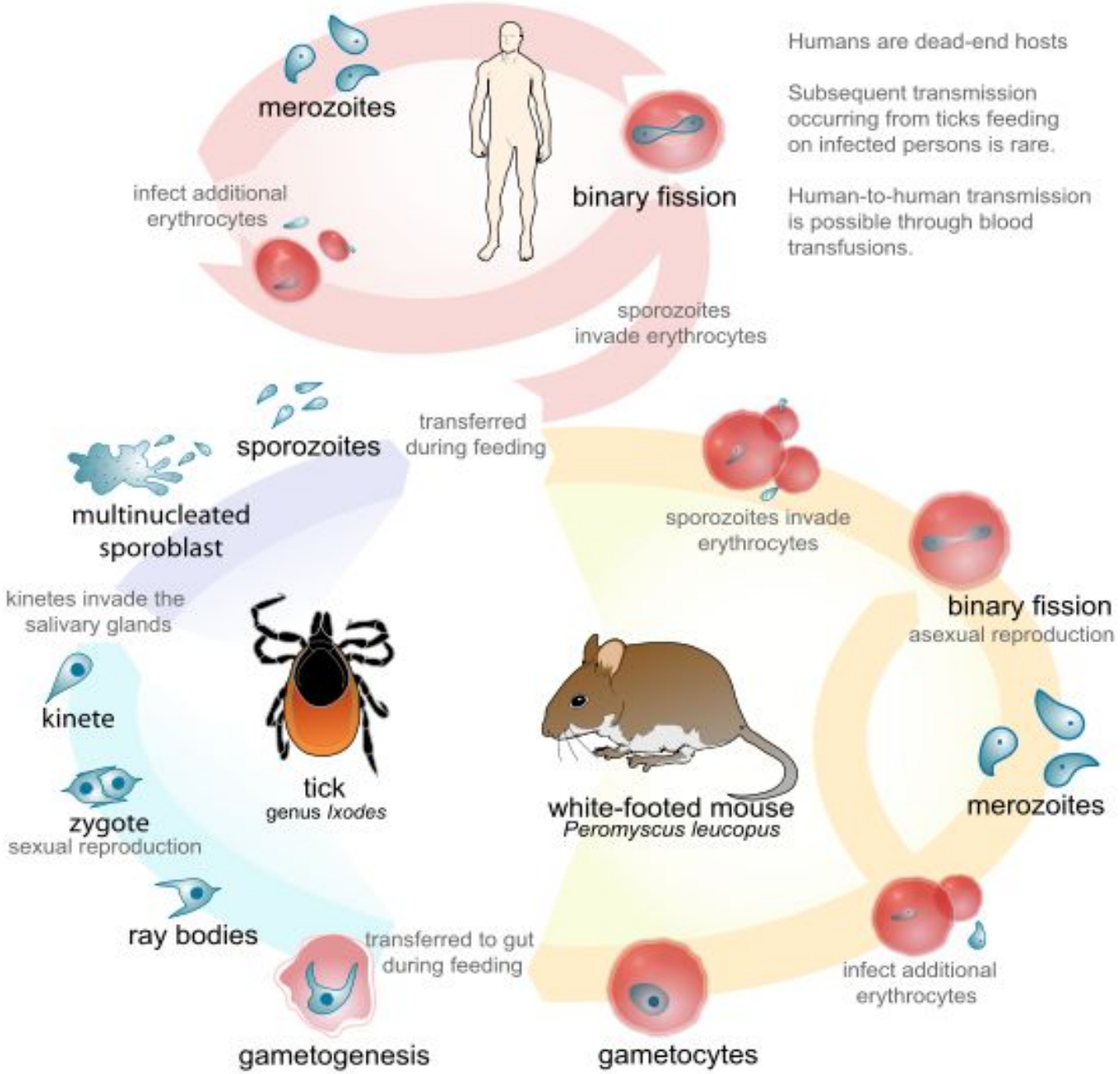
Malaria Diagnosis

- Direct observation of peripheral blood thick and thin smears (Giemsa stain)
- ALWAYS treated as STAT test (life-threatening!)
- Observe characteristics of **parasite** and the **RBC** it infects

Babesiosis

- *Babesia sp.* are tick-borne (*Ixodes sp.* – deer tick) blood parasites passed during blood meal
- Found in domestic animals and wild rodents, humans are accidental hosts
- Causes **Texas cattle fever**, and **malignant jaundice of dogs**
- North America – human Babesiosis caused by *Babesia microti*

Life cycle of *Babesia*



Human Babesiosis

- Babesioisis closely mimics Malaria in morphology, pathology and symptomology
- Incubation period is 1-4 weeks
  - Replicating in liver
- Gradual onset of fever, headache, chills, malaise, **NO periodicity** in fever/chills cycle
- Patients may develop febrile hemolytic anemia, mild hepatosplenomegaly and jaundice
- Self-limited, non-fatal infection, but sometimes treated

Babesia sp. diagnostic morphology

- Intracellular organism in red blood cells
- **Only the ring form is observed in humans** (NO schizonts or gametocytes; asexual reproduction only in humans)
- "Maltese Cross" forms with 4 rings together is diagnostic for *Babesia sp.* but may not be seen
  - No blue cytoplasm around ring forms