

# Introduction to Blood Parasites

It may be a bloody mess, but it is worth knowing

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# Objectives for Learning

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Understand the role of lab testing in blood parasite diagnostics

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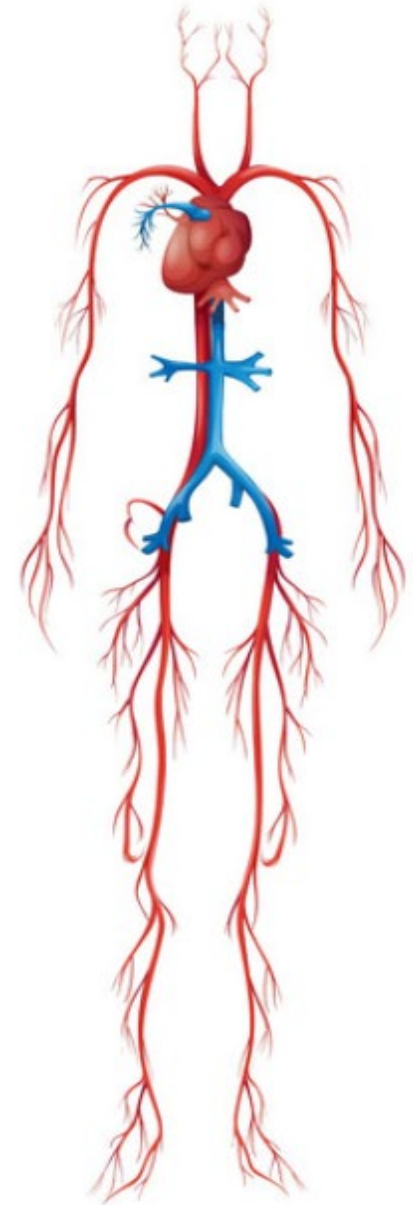
Recognize the major genera of blood parasites

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Describe the clinical associations and syndromes of major blood parasites

# Clinical Parasitology

- Organ systems:
    - » Brain
    - » Skin/Soft tissue
    - » Lungs
    - » Liver
    - » GU
    - » **Blood**
- } See separate video

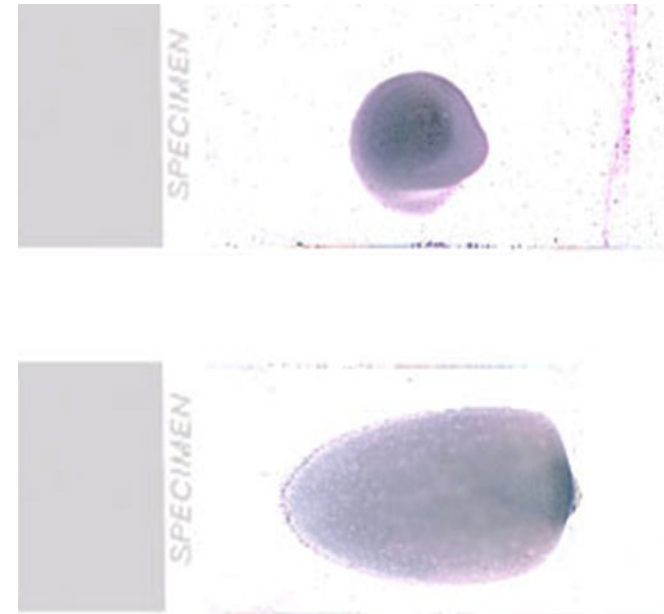


# Blood Parasite testing

- Blood smear overview
- Other methods discussed within organisms

# Blood Smear Exam

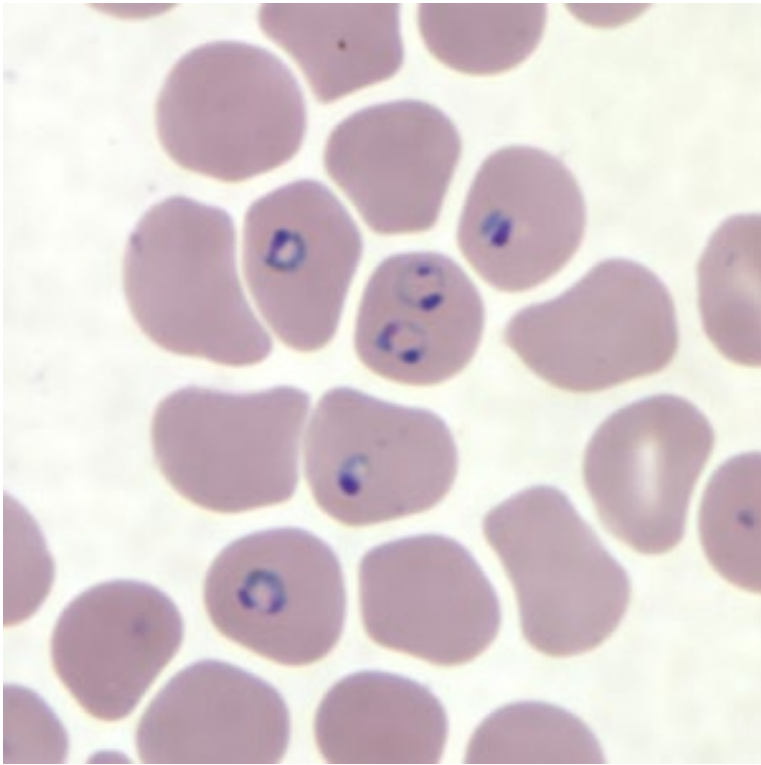
- Collect peripheral or fingerstick blood
- Stain with Giemsa, Wright-Giemsa, or Wright
- Two smears:
  - » Thick
    - Increased sensitivity (more blood examined) & blood is lysed
    - Detect parasites, may not allow full identification
  - » Thin
    - Morphology within in-tact blood cells is maintained
    - Species determination achievable
    - Parasite burden (parasitemia) can be determined



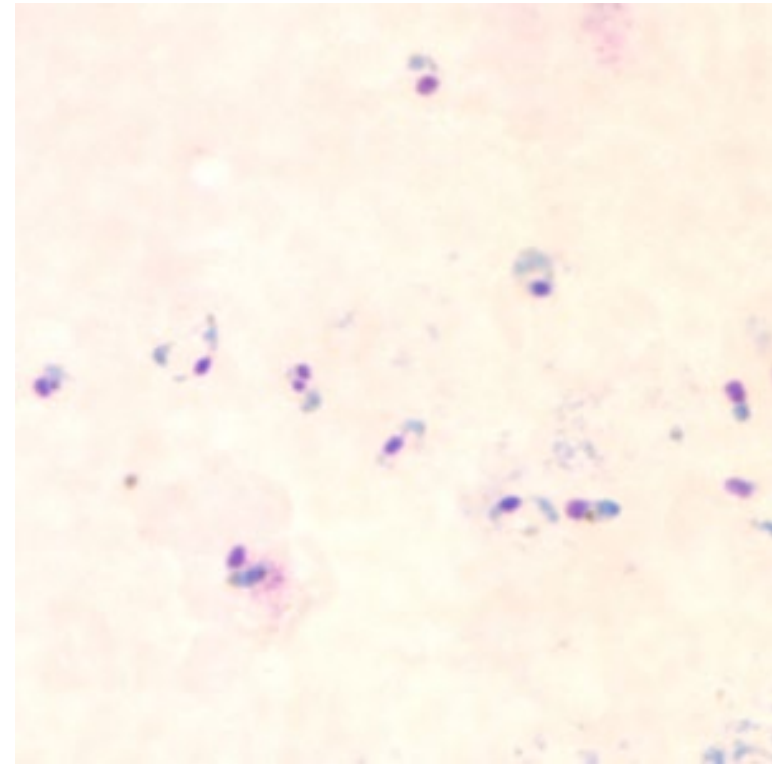


# Blood Smear Exam

- Repeat every 6-8 hrs x3 if first test is negative & high clinical suspicion



*Plasmodium falciparum* thin smear



*Plasmodium falciparum* thick smear

# Major Blood Parasites

- Protozoa
  - » Malaria (*Plasmodium* spp.)
  - » *Babesia*
  - » *Trypanosoma*
- Helminths – filarial nematodes
  - » Lymphatic filariasis – *Wuchereria* & *Brugia* spp.
  - » *Loa loa*
  - » *Mansonella*
- Spirochetes\*
  - \*Not technically parasites

# Malaria – *Plasmodium* spp.

- Protozoan blood parasite >150 species
  - » 4 species are primary human parasites

- *Plasmodium falciparum*
- *Plasmodium vivax*
- *Plasmodium ovale*
- *Plasmodium malariae*

- Symptoms

» Common: fever & chills (cycling)

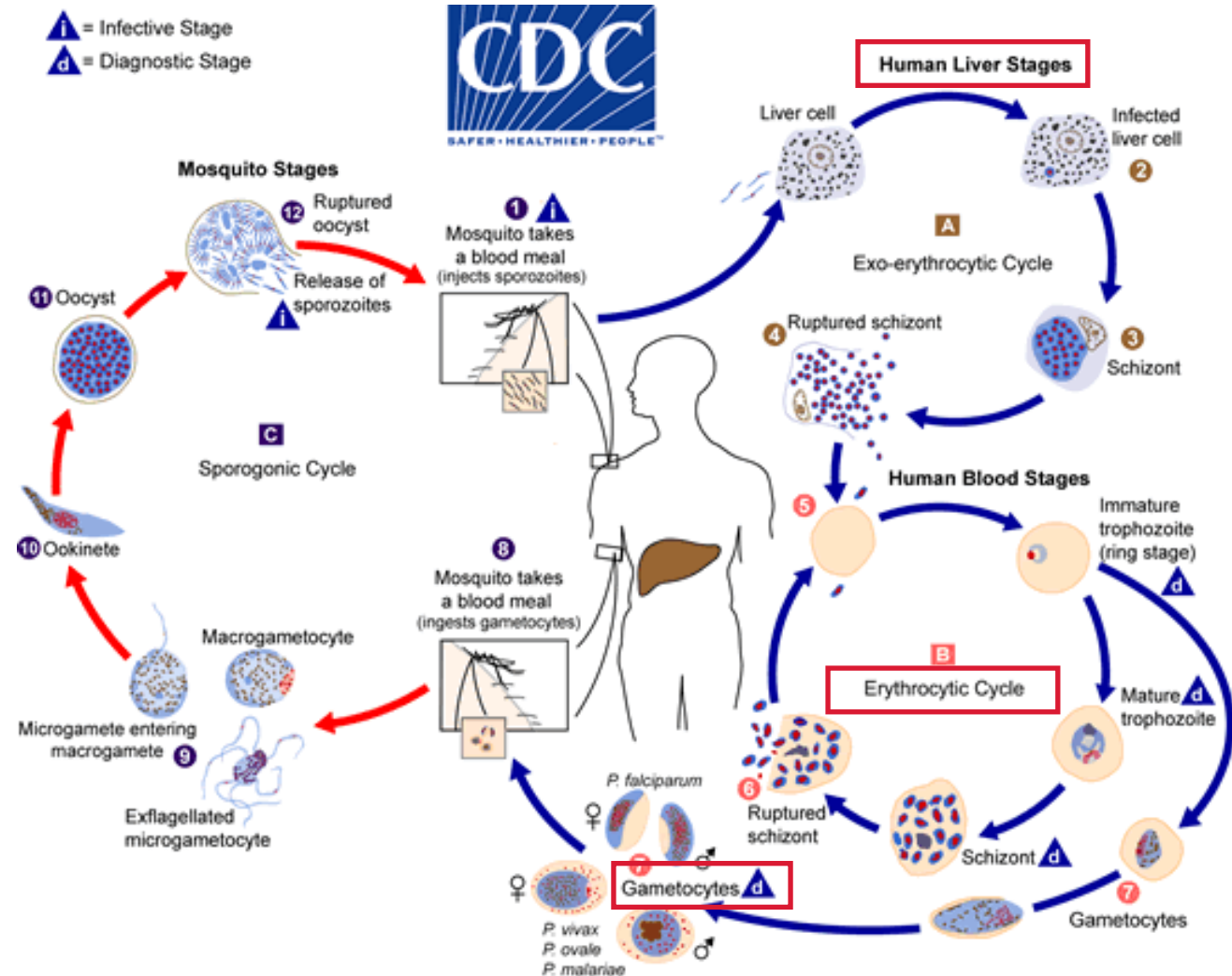
- Can be accompanied by headache, myalgias, arthralgias, weakness, vomiting, & diarrhea.
- Less common: splenomegaly, anemia, thrombocytopenia, hypoglycemia, pulmonary or renal dysfunction, & neurologic changes





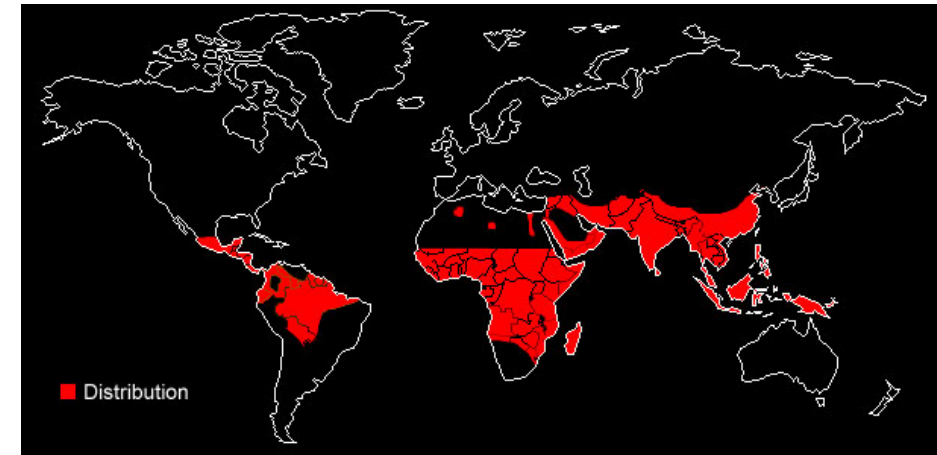
# Plasmodium spp. Lifecycle

- *Anopheles* mosquito vector
- Replicates in liver → blood
- Sexual replication → gametocytes
  - » Transmissible form
- Erythrocytic cycle
  - » Red blood cell replication/ destruction



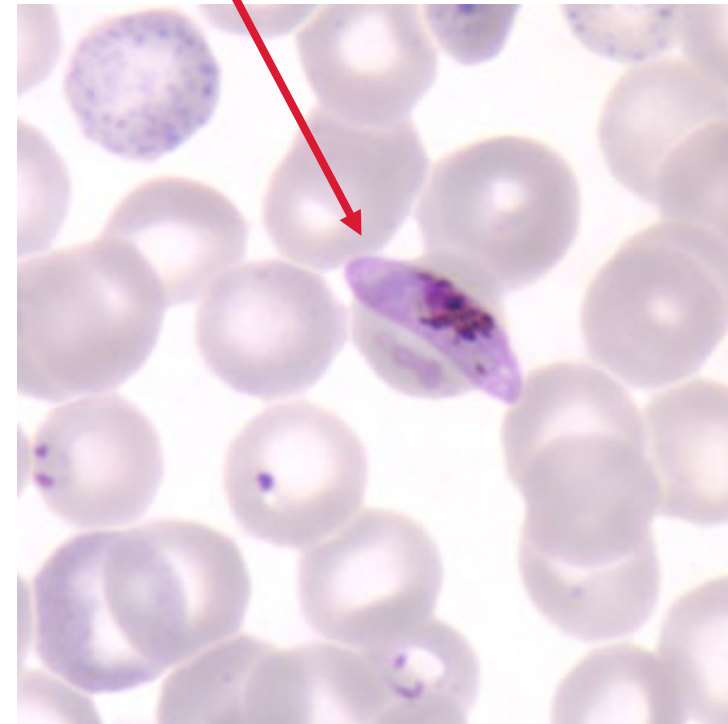
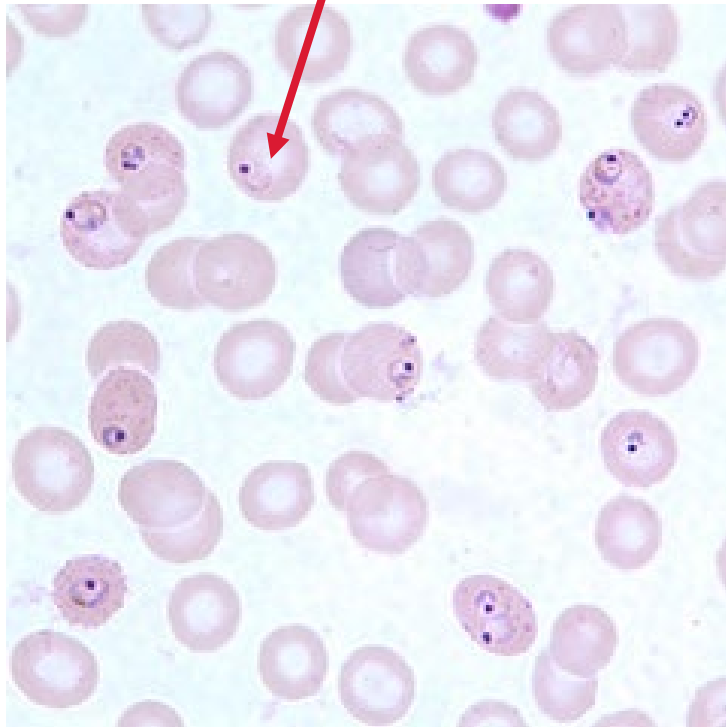
# *Plasmodium falciparum*

- Most dangerous → infects all types of red blood cells
  - » Highest parasitemias
  - » Severe symptoms include cerebral malaria (often fatal in children)
- Most commonly encountered in clinical care
- Most widespread
- Fevers cycle every 24-48 hours
  - » Continuous at high parasitemia

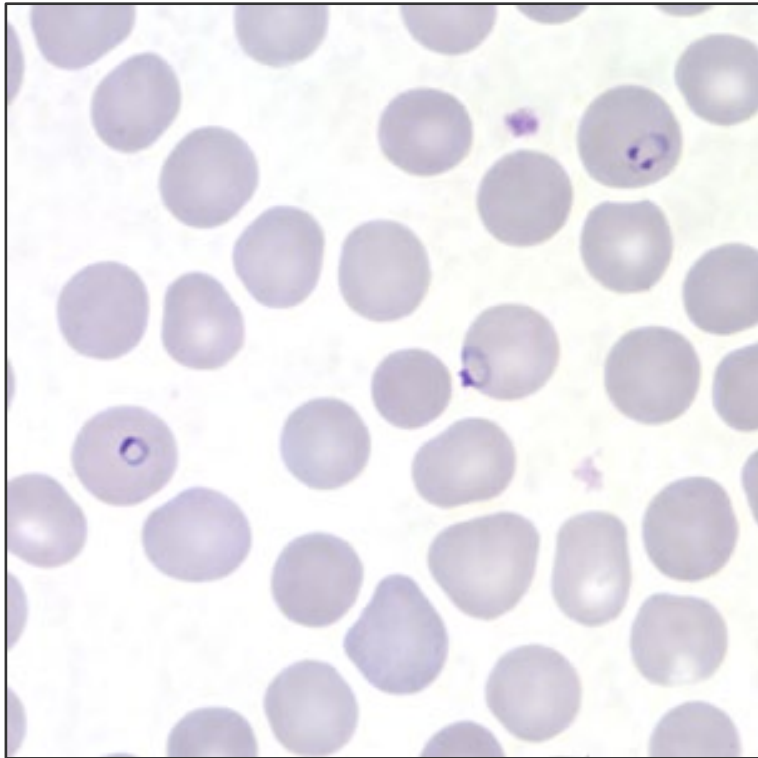


# *Plasmodium falciparum*

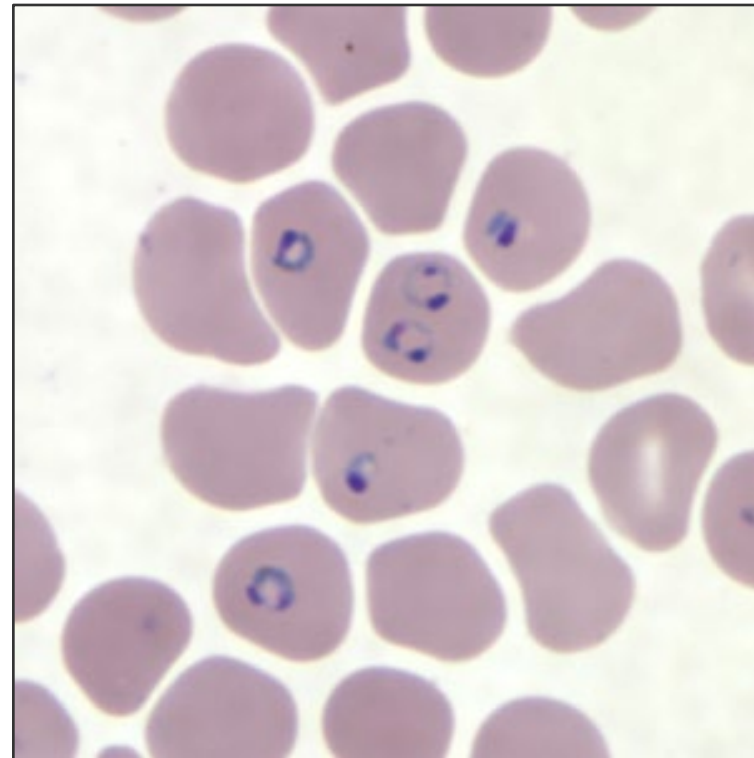
- Microscopy:
  - » Small ring forms and banana-shaped gametocytes



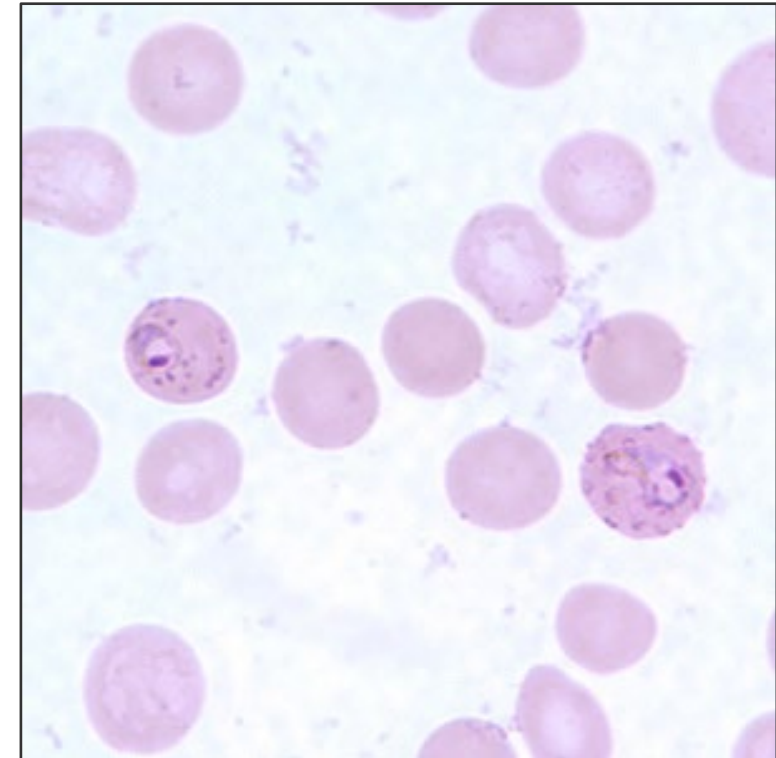
# *Plasmodium falciparum*



Appliqué form



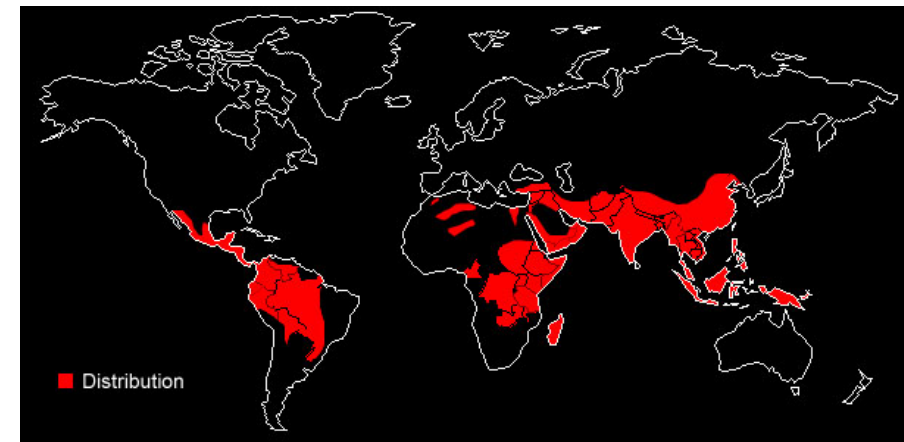
"Headphones"



Maurer's clefts

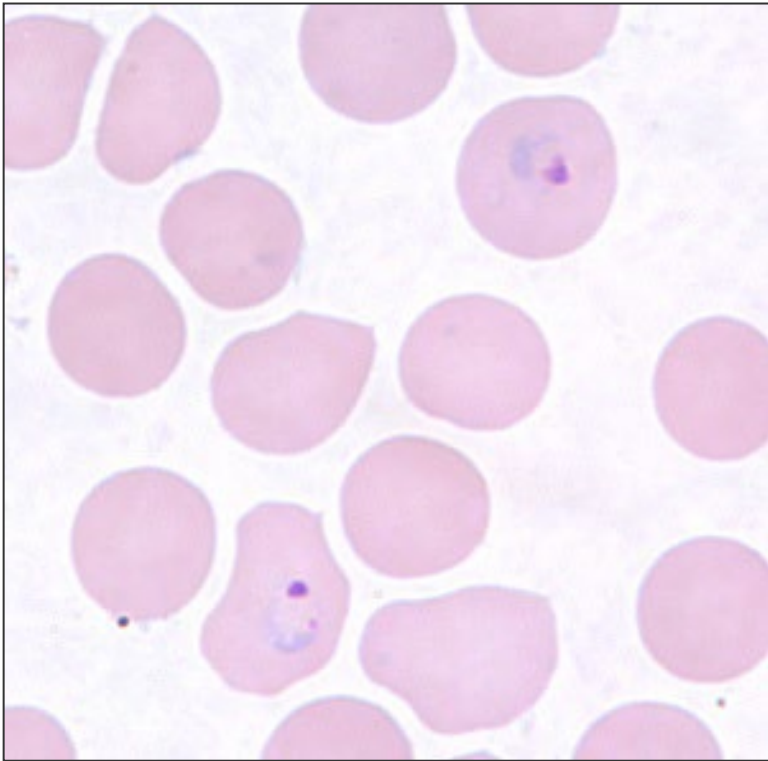
# *Plasmodium vivax*

- Prefers to infect macrocytic (immature) red blood cells
  - » Low parasitemia = restricted host cell availability
    - Rare complication: splenomegaly or splenic rupture
- Second most common species in clinical care
  - » Widespread
- Fevers every ~48 hours
- Liver phase hypnozoites can reactivate months after infection

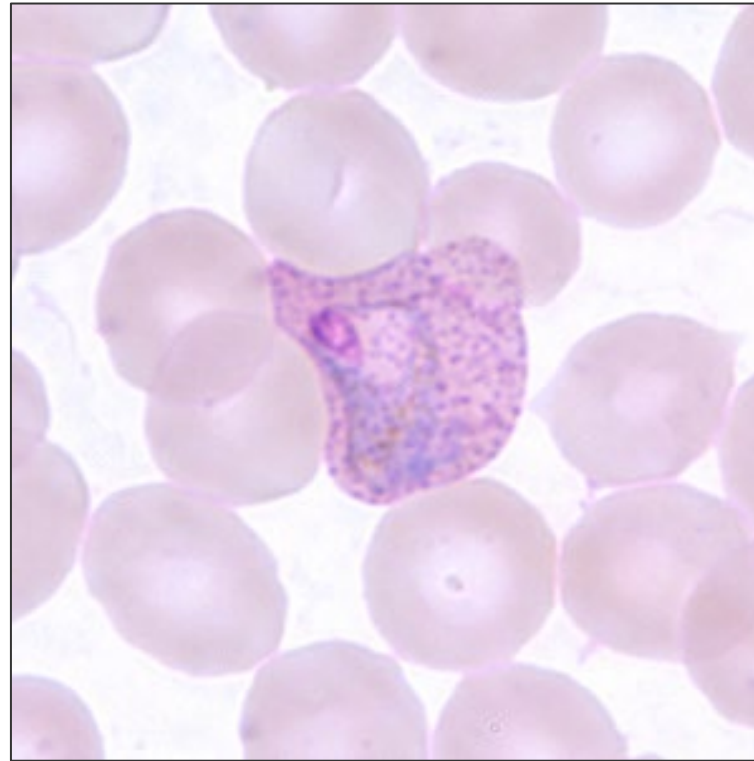




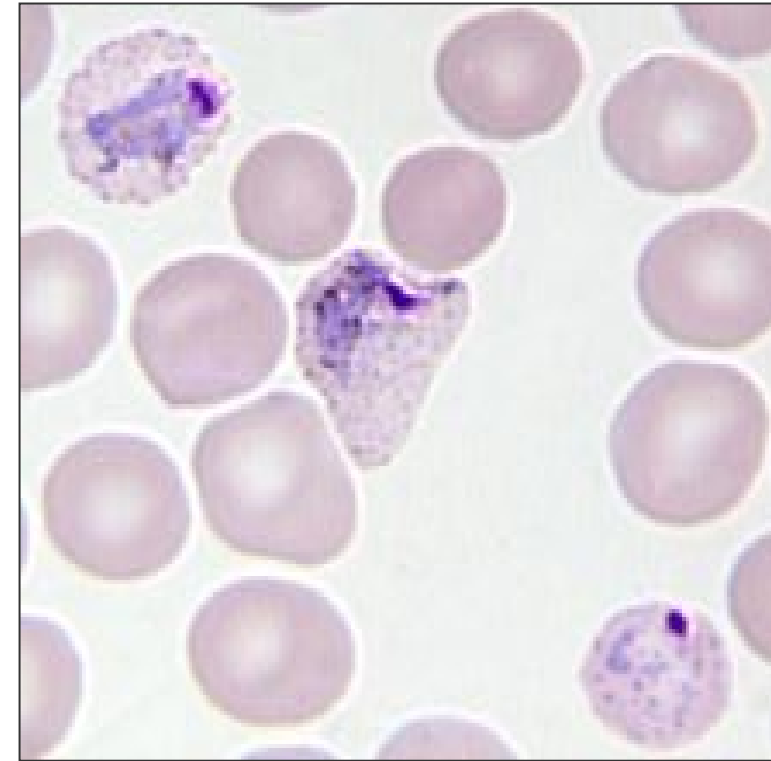
# *Plasmodium vivax*



Ring form trophozoite

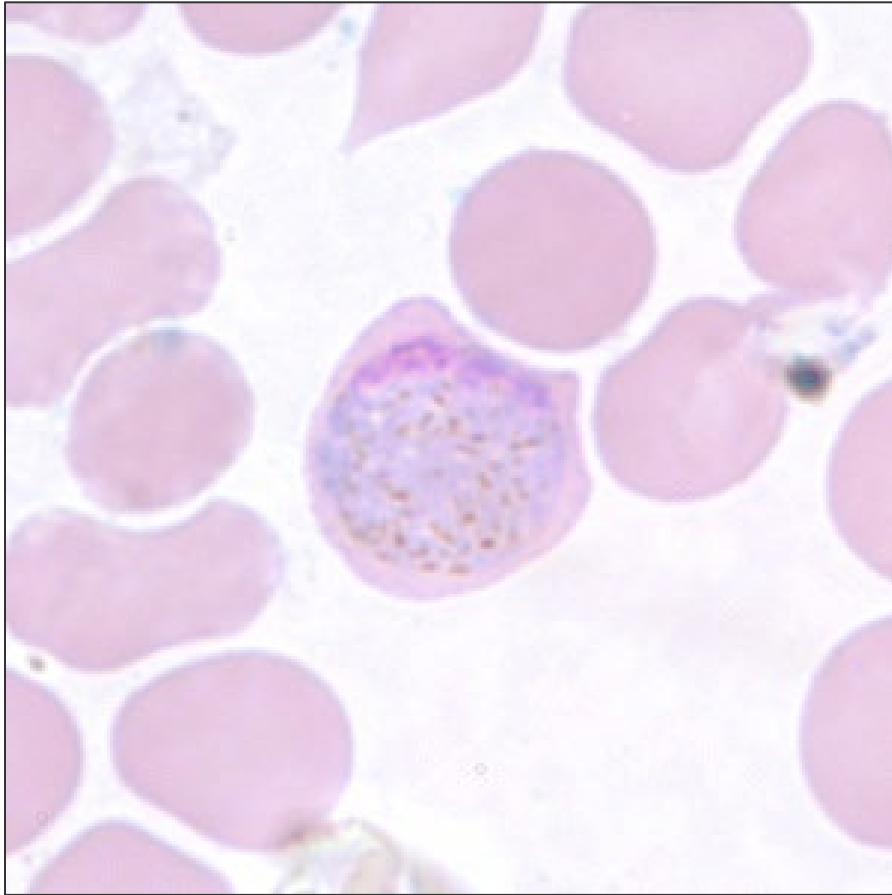


Mature trophozoite w/Schüffner's dots

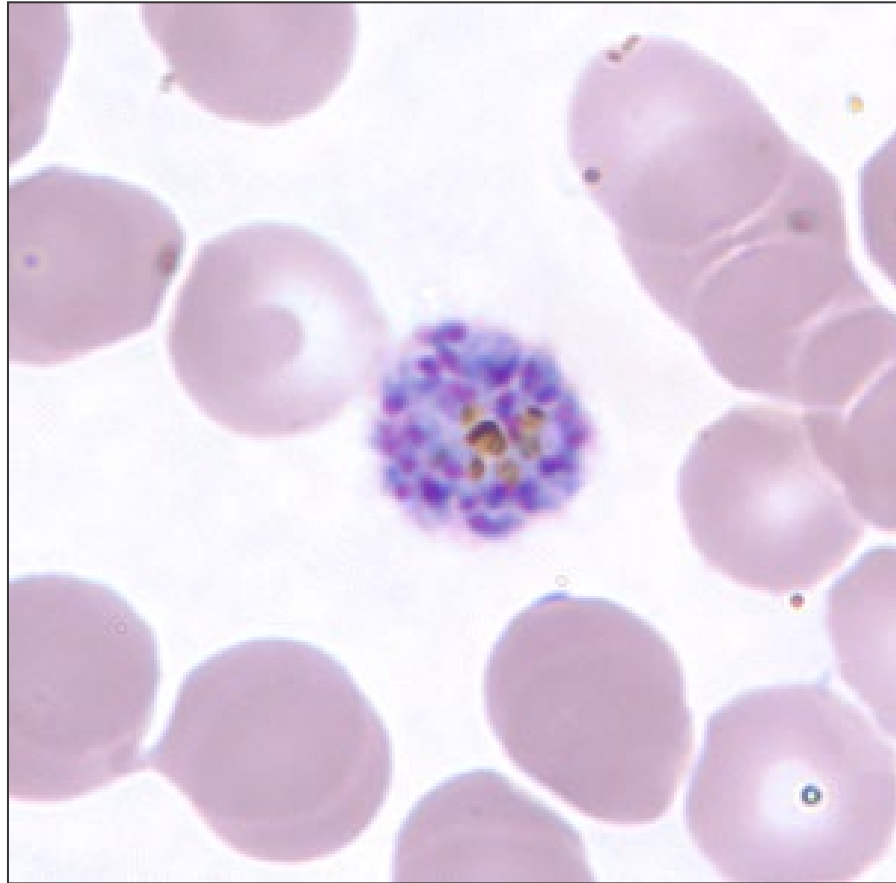




# *Plasmodium vivax*



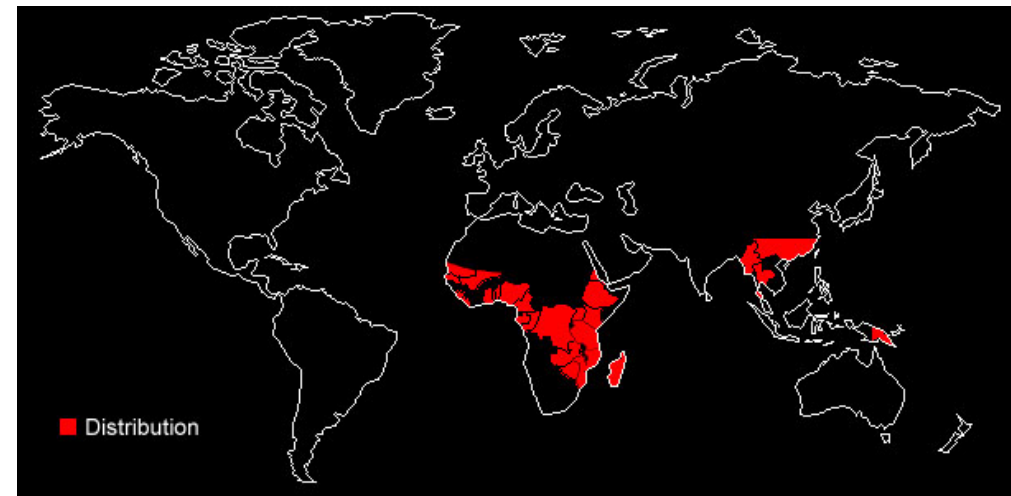
Gametocyte



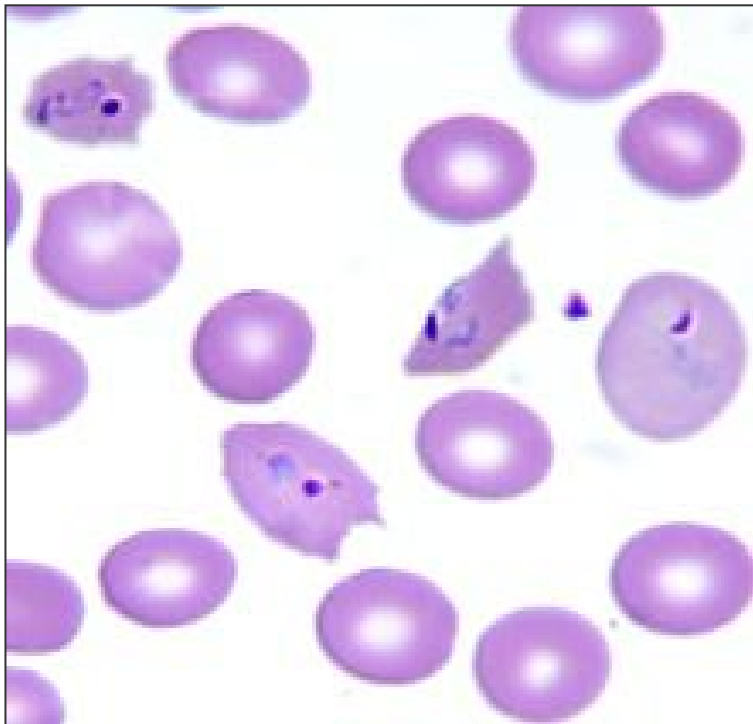
Schizont

# *Plasmodium ovale*

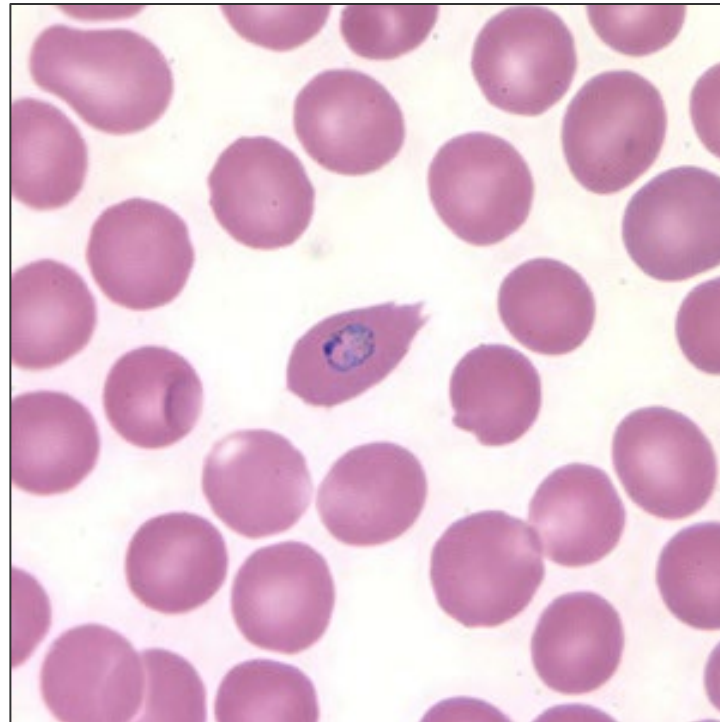
- Prefers to infect macrocytic (immature) red blood cells
  - » Low parasitemia = restricted host cell availability
- Third most common species in clinical care
  - » Most geographically constrained
- Fevers every ~48 hours
- Liver phase hypnozoites can reactivate months after infection



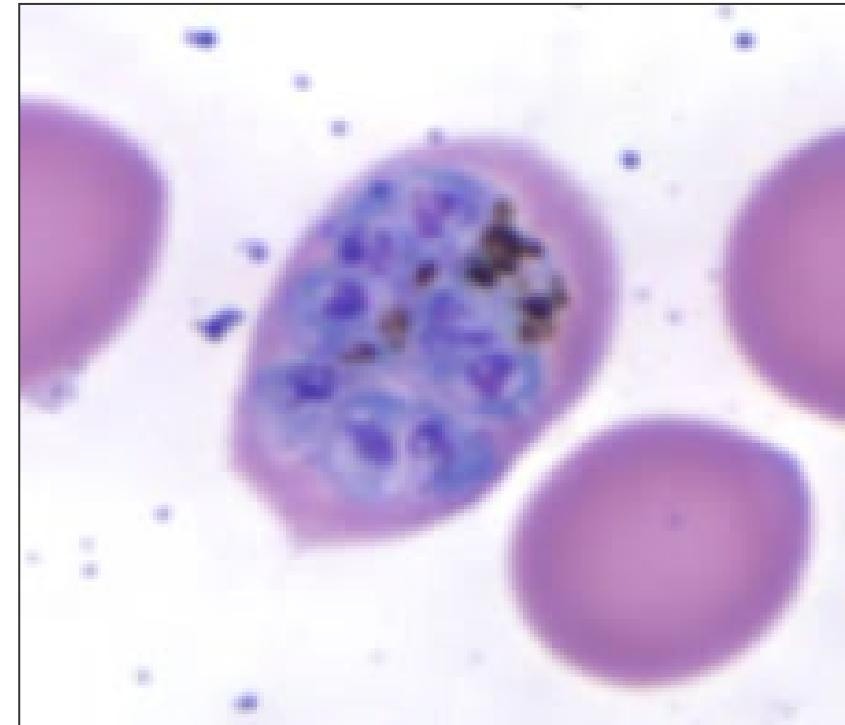
# *Plasmodium ovale*



Trophozoite

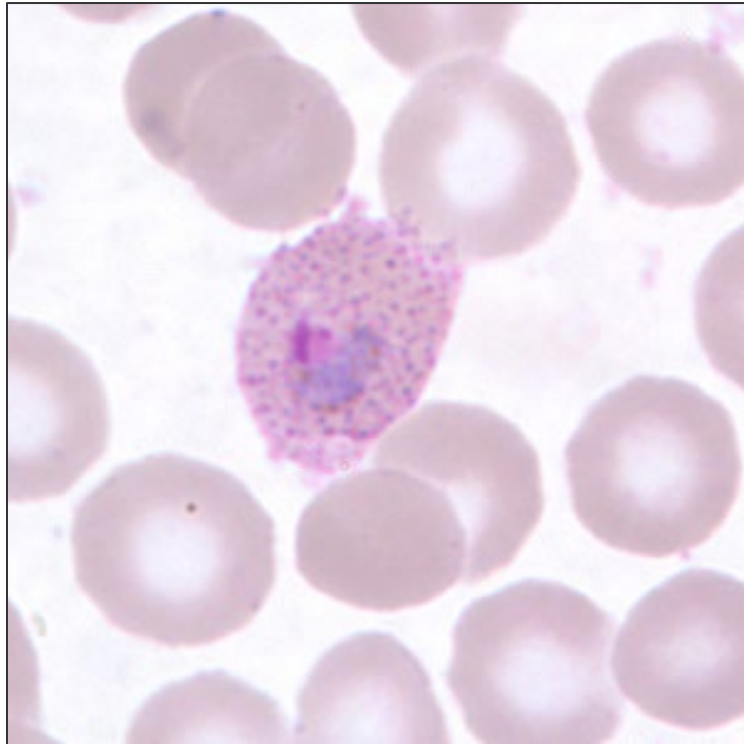


Trophozoite  
w/ fimbriation

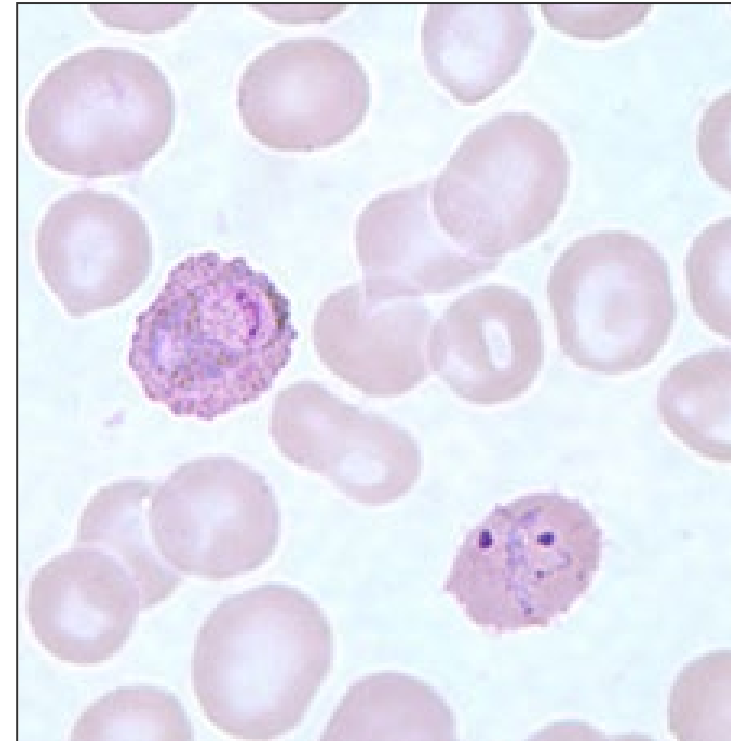


Schizont

# *Plasmodium ovale*



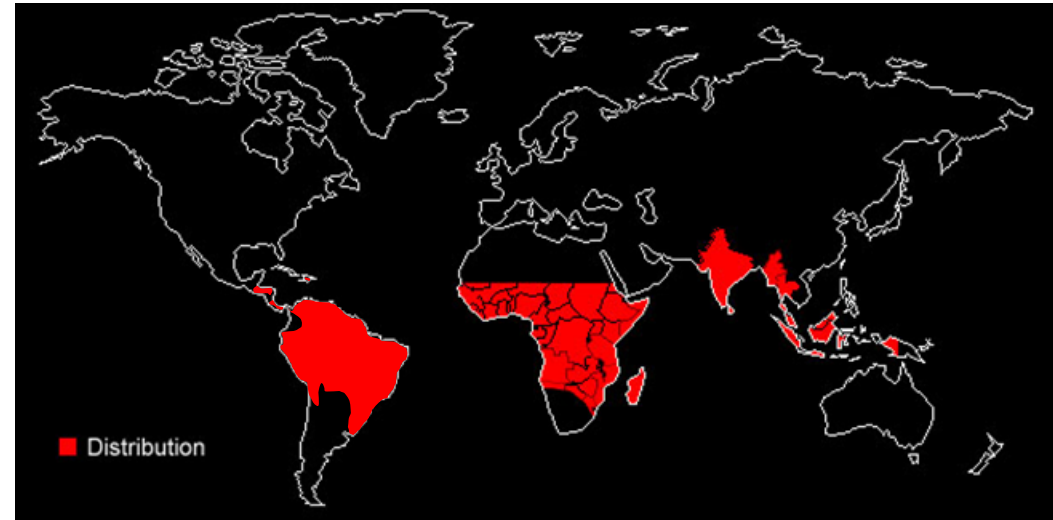
Mature Trophozoite  
w/Schüffner's dots & fimbriation



Mature Trophozoite  
w/Schüffner's dots & fimbriation

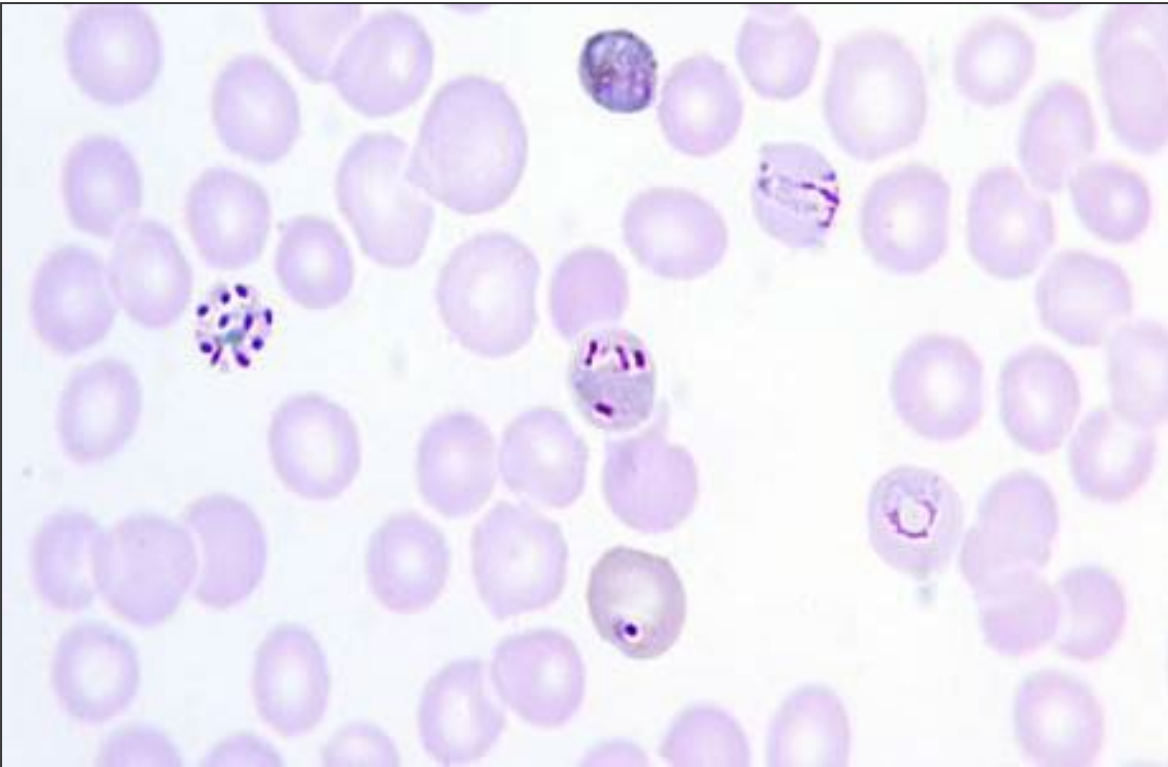
# *Plasmodium malariae*

- Prefers to infect senescent (older) red blood cells
  - » Very low parasitemia = restricted host cell availability
- Fourth most common species in clinical care
  - » Often asymptomatic
  - » Constrained geographically
- Fevers every 72 hours (if any)

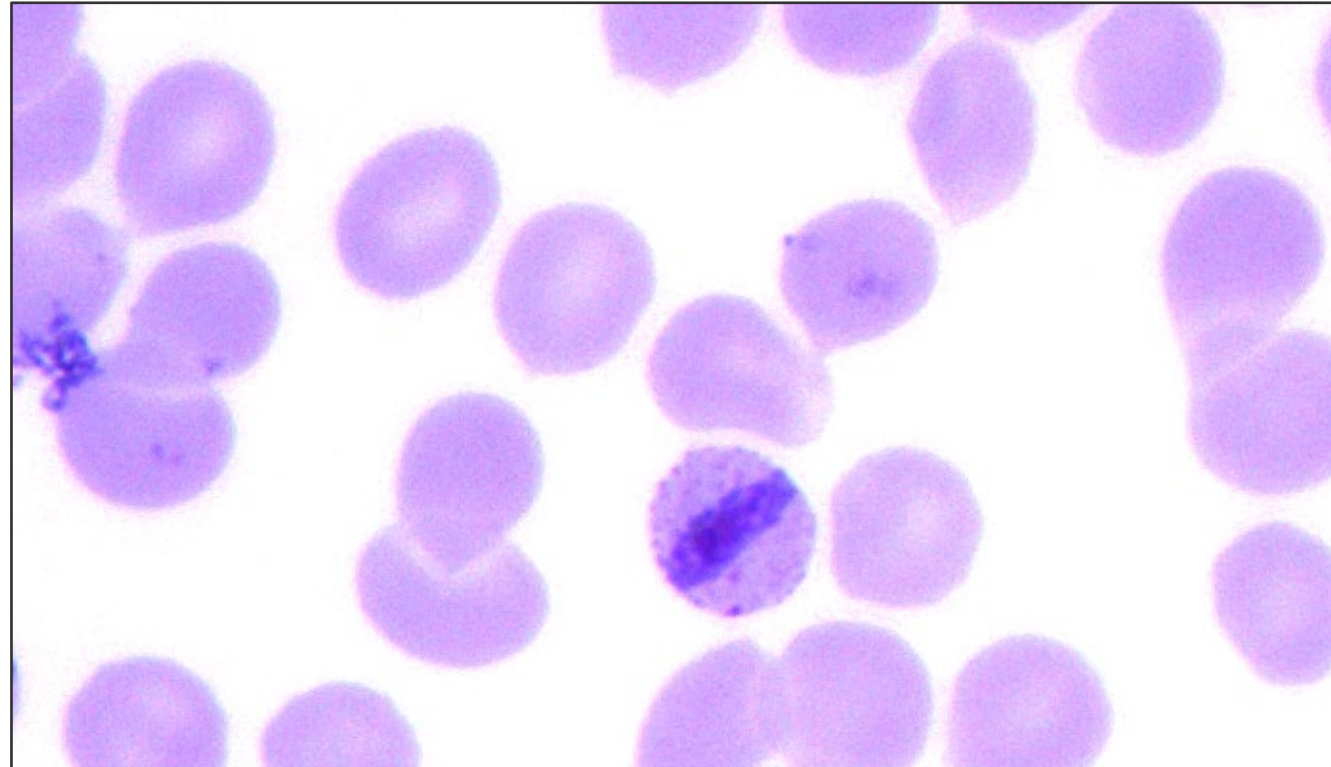




# *Plasmodium malariae*



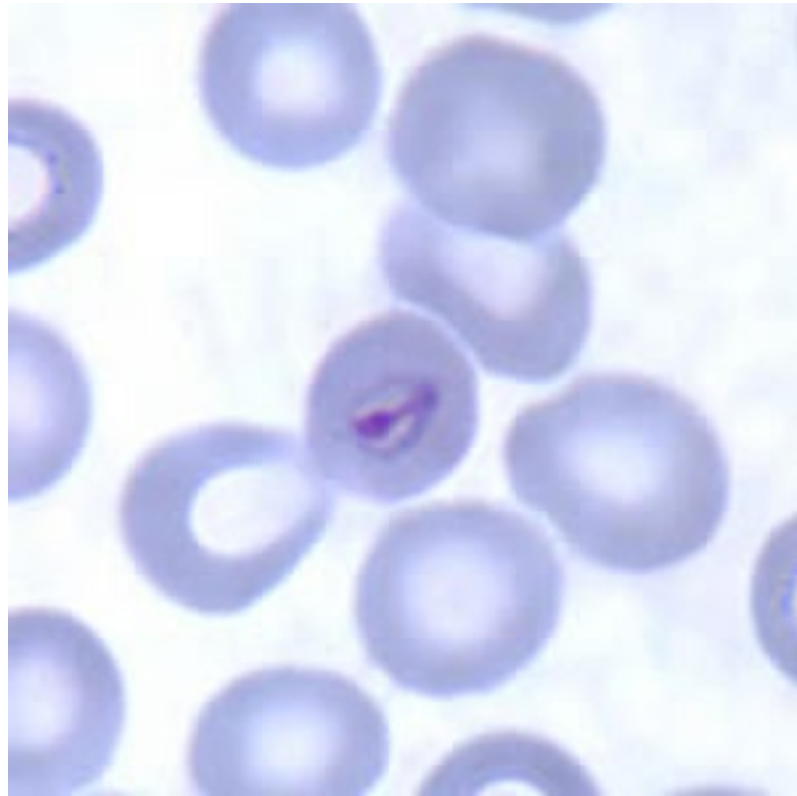
Trophozoite, gametocyte, & schizont



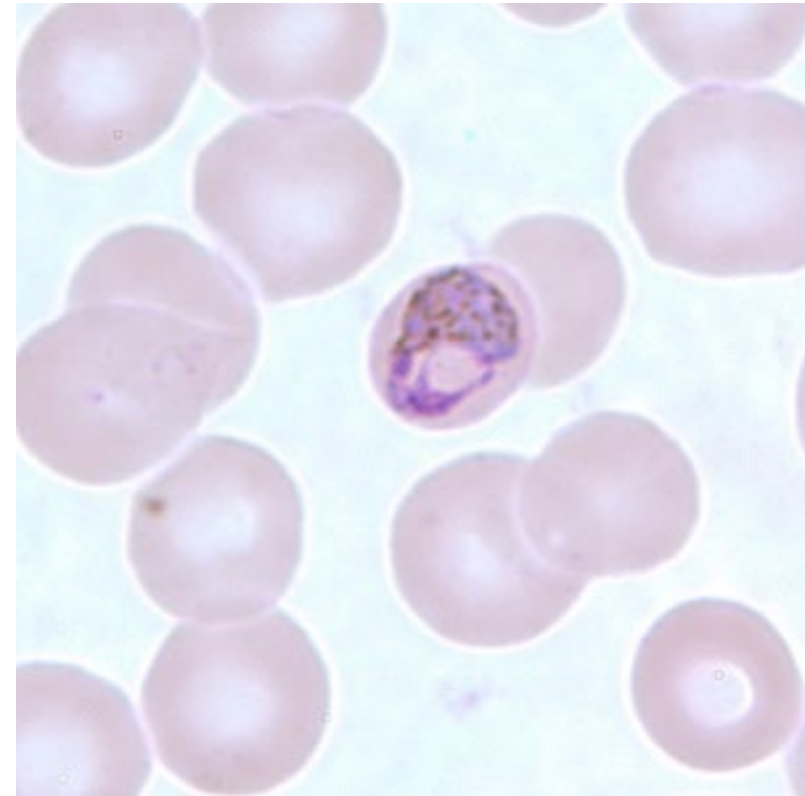
Band form trophozoite



# *Plasmodium malariae*



Bird's eye



Basket form

A blurred background image of a laboratory or hospital setting, showing various pieces of equipment and a window with a view of a building.

■ Regarding “other” *Plasmodium* sp.

Tread carefully with the hyperbole

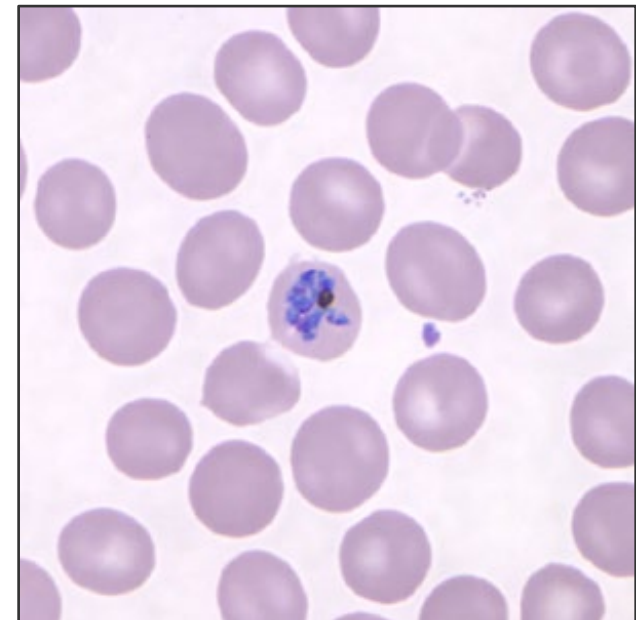
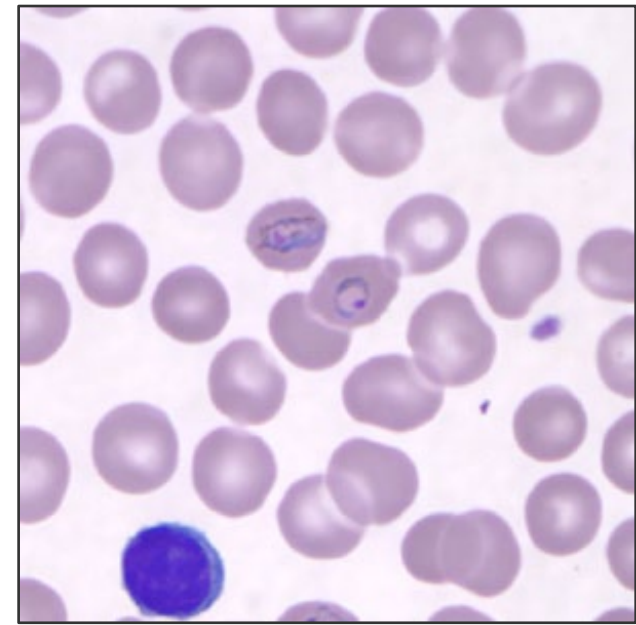
# Simian malaria

- Zoonotic malaria, rarely found in humans:
  - » *Plasmodium knowlesi* - SE Asia/Malaysian peninsula
  - » *Plasmodium cynomolgi* - Peninsular Malaysia
  - » *Plasmodium schwetzi* - Tropical Africa
  - » *Plasmodium coatneyi* - Peninsular Malaysia & Philippines
  - » *Plasmodium inui* - Southeast Asia
  - » *Plasmodium simiovale* - Sri Lanka and Malaysia
  - » *Plasmodium simium* South America
    - Probable *P. vivax* → jumped to monkeys after introduction.
  - » *Plasmodium brasilianum* South America
    - Probable *P. malariae* → jumped to monkeys after introduction.



# *Plasmodium knowlesi*

- Simian malaria: narrow geographic distribution S.E. Asia
  - » Malaysia, Indonesia
- Mimicry:
  - » Clinically → *P. falciparum*
  - » Morphology →
    - › Early, *P. falciparum*
    - › Late, *P. malariae* (but parasitemia too ↑)
  - » NAAT → *P. vivax* if not carefully designed



# *Plasmodium knowlesi* – final note of caution


- Do not default to *P. knowlesi*
  - » RARE → consider common things being common
- Evaluate morphology → Follow the flow
  - » IF, something seems “odd”
  - » THEN, consider other species like *P. knowlesi*
- CONFIRM appropriate geographic exposure
- Consider NAAT



# Malaria Treatment

- Depends on: severity, species, area acquired, previous anti-malarials used
- Resistance is a problem
  - *P. falciparum* & *P. vivax*
    - » See algorithm for detailed decision making: [https://www.cdc.gov/malaria/resources/pdf/treatment\\_algorithm\\_101619.pdf](https://www.cdc.gov/malaria/resources/pdf/treatment_algorithm_101619.pdf)
    - » Acquired in area w/out chloroquine resistance → chloroquine
    - » Acquired in area w/chloroquine resistance →
      - (1) artemether-lumefantrine
      - (2) atovoquone-proguanil
      - (3) quinine + doxycycline
      - (4) mefloquine
- Liver phase hypnozoites also require specific therapy
  - *P. vivax* & *P. ovale* → tafenoquine or primaquine phosphate





# ■ Other Malaria Tests

NAAT & Antigen



# *Plasmodium* antigen from blood

- Rapid Diagnostic Test - Binax Now Malaria (only FDA cleared assay)
  - » Results in < 30 min (good for hospitals unable to do blood smears)
    - But...less sensitive than blood smear examination

- Most sensitive for *P. falciparum*
  - Can detect three remaining human species
  - May cross-react with simian species
- 5000 parasites/ml = 0.125% parasitemia

**SENSITIVITY FOR P.f.**

Parasitemia Level	% Sensitivity	95%CI
> 5000	99.7% (326 / 327)	98 - 100%
1000 – 5000	99.2% (126 / 127)	96 - 100%
500 – 1000	92.6% (25 / 27)	76 - 99%
100 – 500	89.2% (33 / 37)	75 - 97%
0 – 100	53.9% (21 / 39)	37 - 70%
Overall	95.3% (531 / 557)	93 - 97%
	<b>% Specificity</b>	<b>95% CI</b>
	94.2% (3297 / 3500)	93-95%

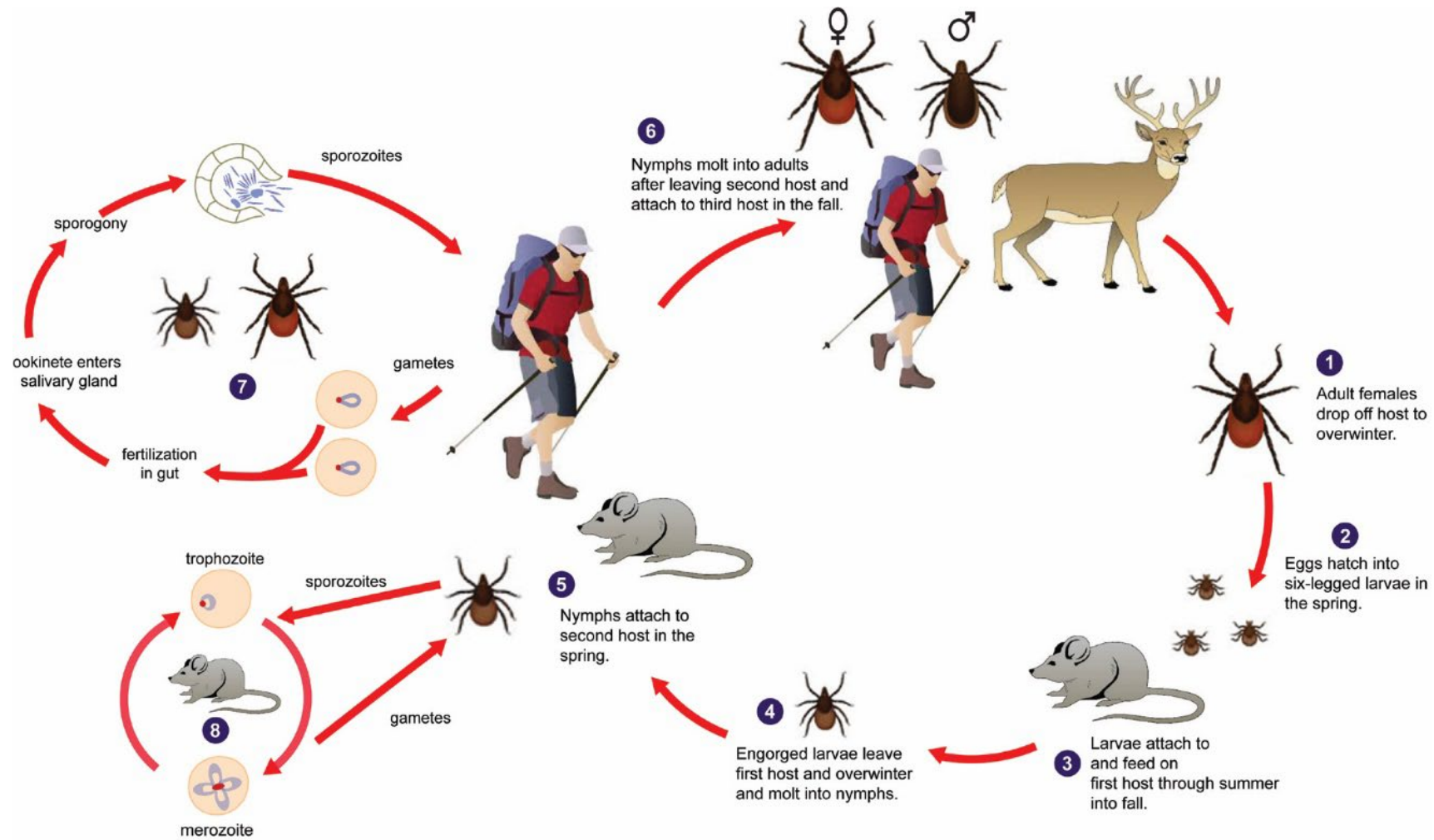
# NAAT for Malaria

- Not standard of care for Dx
- Excellent specificity and sensitivity (design dependent)
- Helpful for:
  - » Possible mixed infections
  - » Very low parasitemia specimens
    - Few organisms to determine *Plasmodium* sp.
    - *Babesia* vs *Plasmodium*
    - *P. knowlesi* rule in/out
- Not truly quantitative, still requires parasitemia by smear

# Babesiosis

- Caused by apicomplexan parasites in the genus *Babesia*.
  - » Primary morphologic differential for malaria
- Transmitted by ticks in the genus *Ixodes*.
- Several species endemic to North America
  - *B. microti*, NE
  - *B. duncani*, West, PNW
  - *Babesia* MO-1, PNW, Missouri River Valley

# Life Cycle of *Babesia microti*



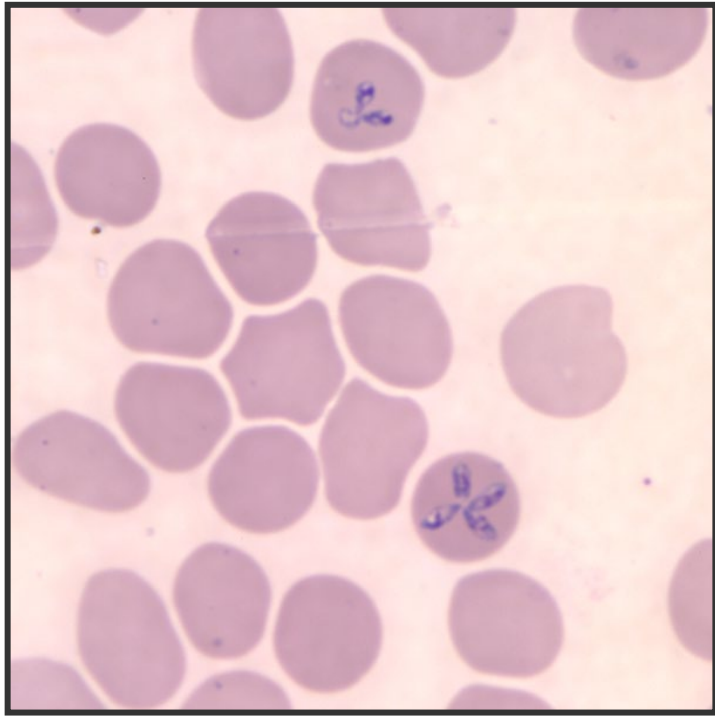
Westblade LF, et al. J Clin Microbiol. 2017. PMID 28747374



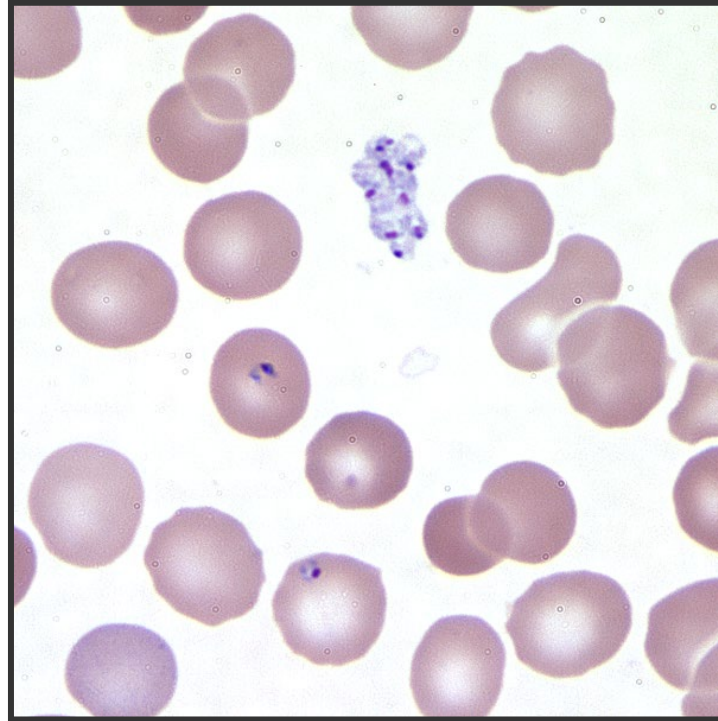
# Babesiosis

- Symptoms – often asymptomatic
  - » When present, usually non-descript (fever, chills, sweating, myalgia, fatigue, hepatosplenomegaly); hemolytic anemia possible.
- Symptoms most severe in immunocompromised, elderly, **asplenic patients**.
- Diagnosis primarily by **blood film examination**
  - » Species cannot be separated morphologically. NAAT or serologic testing needed for species-level ID (epidemiologic data can be helpful).

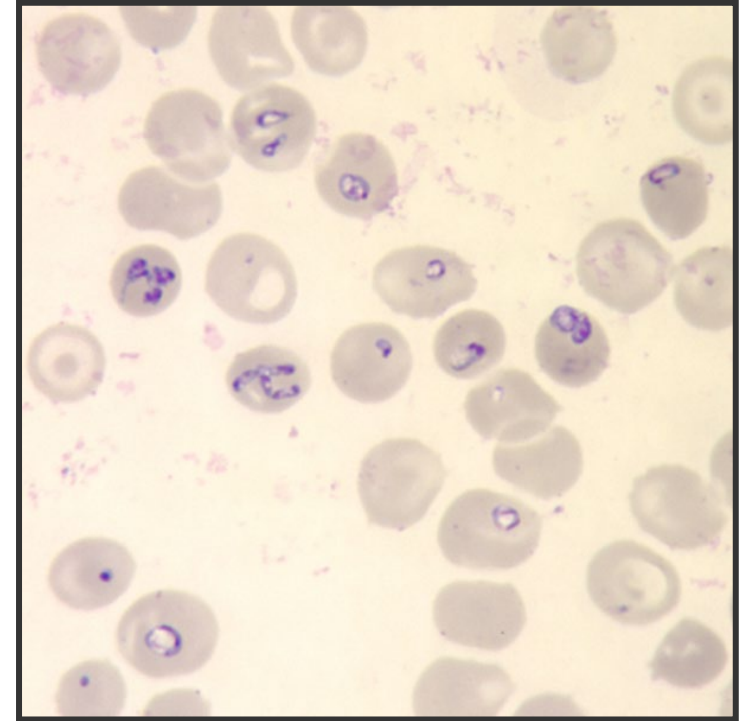
# *Babesia* - Morphology



'Maltese Cross'



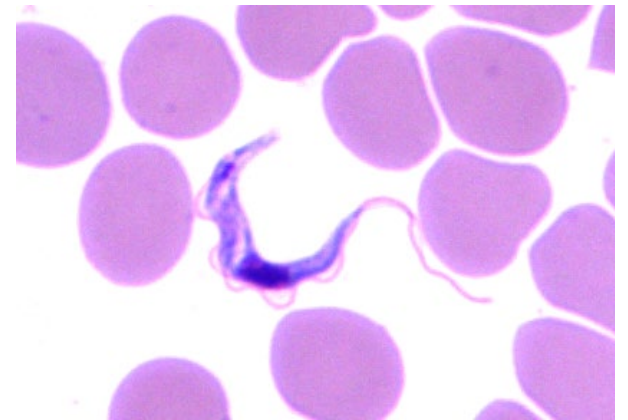
Extracellular forms



Pleomorphic rings

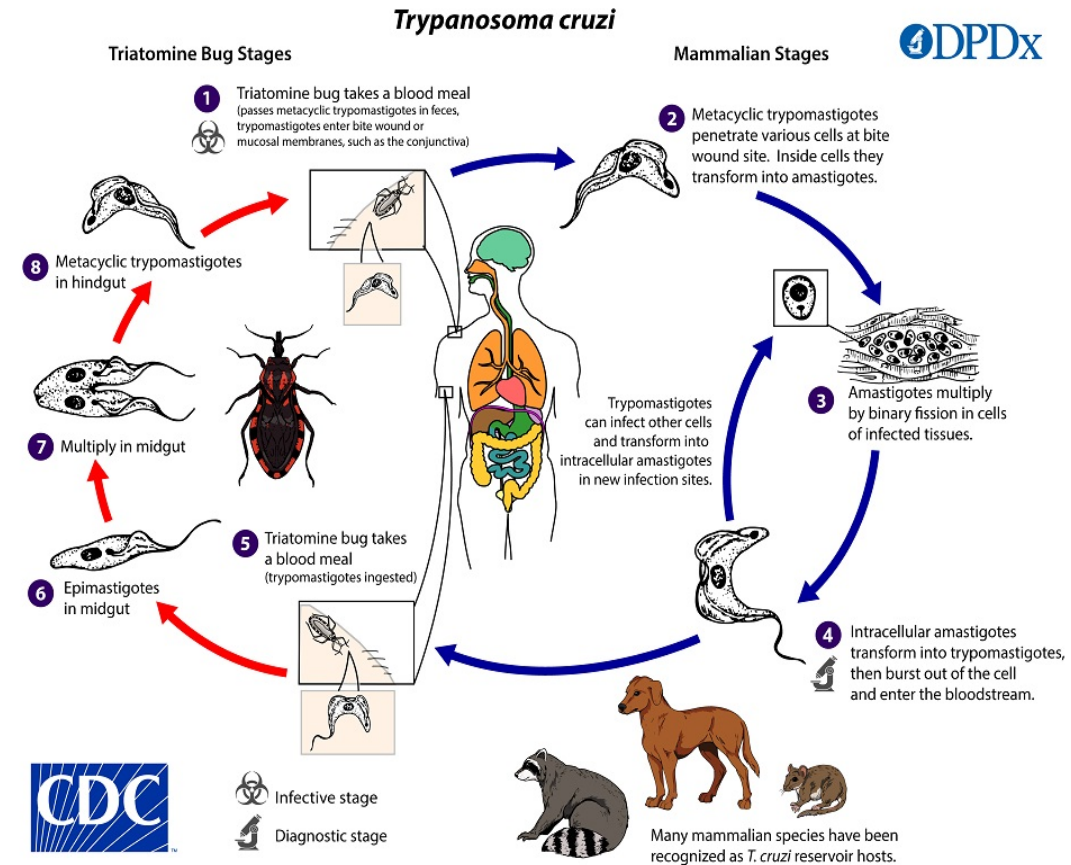
# *Trypanosoma*

- Protozoa (flagellate), two primary human pathogens
  - » *T. cruzi* – causes Chagas disease
  - » *T. brucei* – causes African sleeping sickness



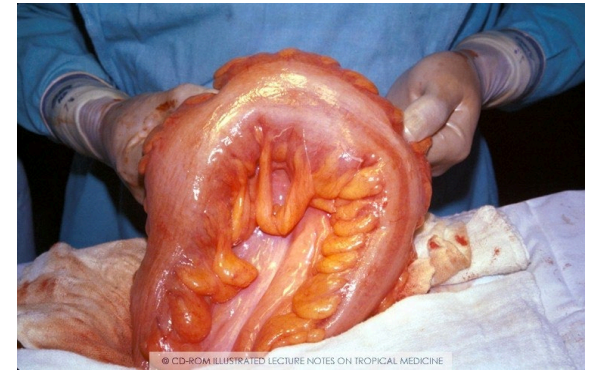
# Trypanosoma cruzi

- Vectored by triatomine bug (**kissing bug**)
  - » Parasite in feces of bug, enters wound or mucus membrane
- Symptoms:
  - » Acute: often asymptomatic, **chagoma** (node or lesion around bite site), **Romaña sign** is swelling around eye (@ bite)
    - +/- fever, malaise
    - Rarely cardiac or CNS involvement



# *Trypanosoma cruzi*

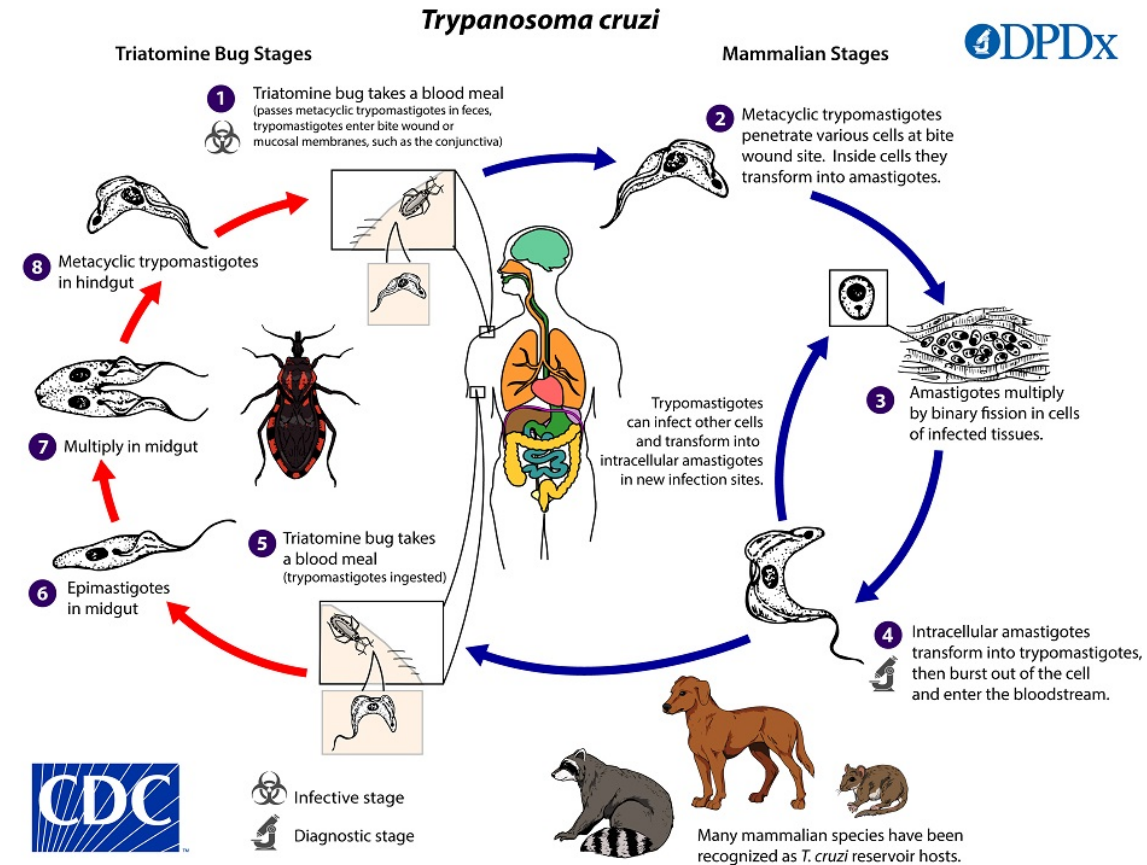
- Symptoms:
  - » Chronic:
    - Cardiac and/or GI involvement
  - » ~70-80% remain chronically infected, asymptomatic for life (Indeterminate form)
  - » 20-30% progress to disease over years to decades (Determinante form)
    - Megacolon
    - Cardiomyopathy
    - Megaesophagus





# Trypanosoma cruzi

- Diagnosis:
  - » Acute → **Microscopy** (blood, CSF, biopsy)  
PCR  
Culture
  - » Chronic → **Serology**
    - Recommend two different IgG serology tests to optimize accuracy
- Treatment: most effective for acute phase
  - » Benznidazole (FDA cleared)
  - » Nifurtimox (via CDC; investigational)



# Trypanosoma brucei

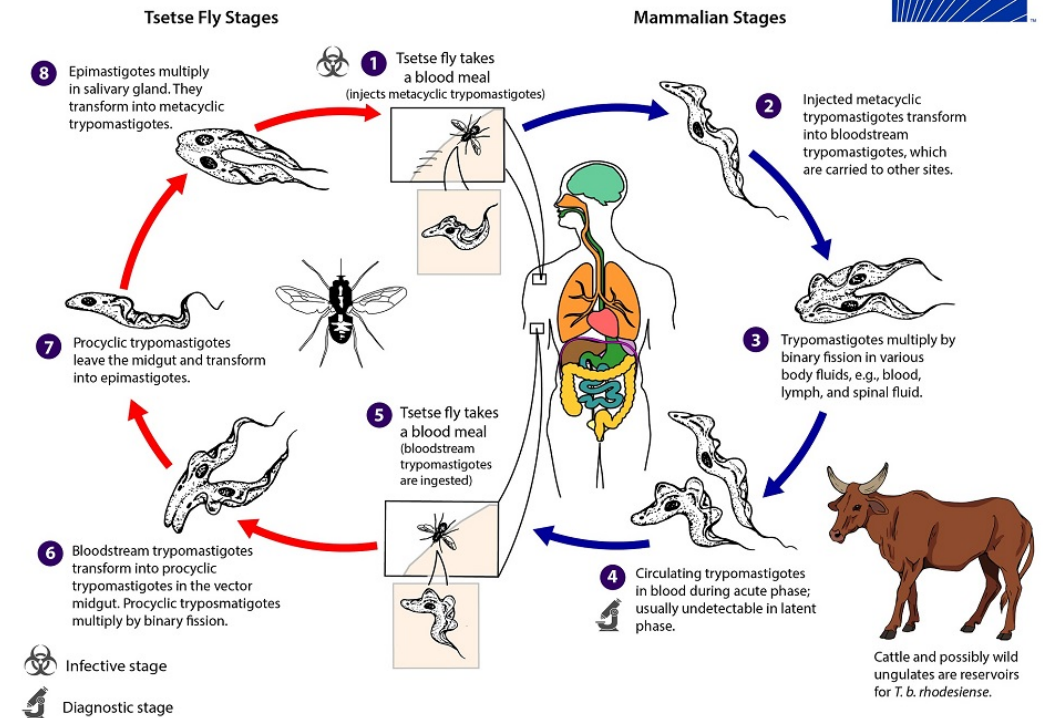
- Vectored by **Tse tse fly** (*Glossina*) bite
- Humans are main reservoir
  - » Occasionally cattle



4DPDx

## African Trypanosomiasis

*Trypanosoma brucei gambiense* & *Trypanosoma brucei rhodesiense*



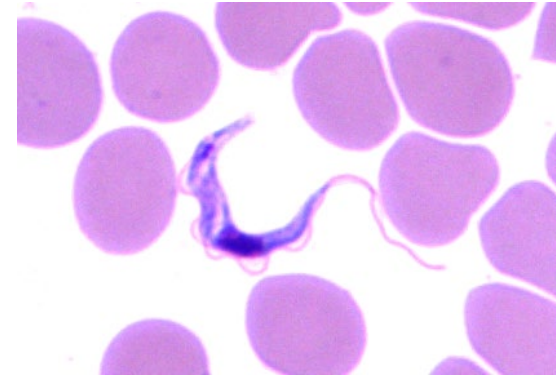
# *Trypanosoma brucei*

- Symptoms:
  - » Early:
    - Hard painful skin ulcer
    - Fever
    - Enlarged lymph nodes
  - » Later:
    - Symptom free (intermediate duration)
  - » Late/end stage disease
    - Somnolence to coma

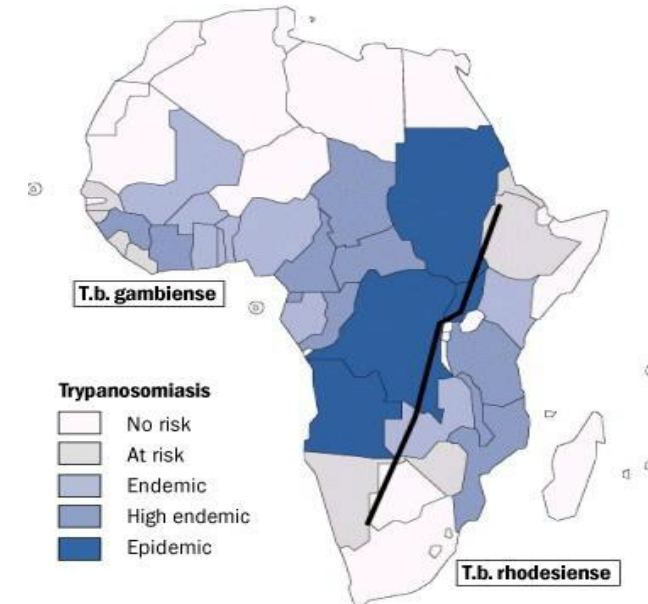


# *Trypanosoma brucei*

- Two subspecies (cannot be distinguished morphologically):
  - » *T.b. gambiense* (Gambling out west)
  - » *T.b. rhodesiense* (Rhode Island is east)



Subspecies	Parasitemia	Severity	CNS tropism	Time to CNS
<i>ssp. gambiense</i>	↓	Less severe	Less tropic	Years
<i>ssp. rhodesiense</i>	↑	More severe	More tropic	<9 months



# *Trypanosoma brucei*

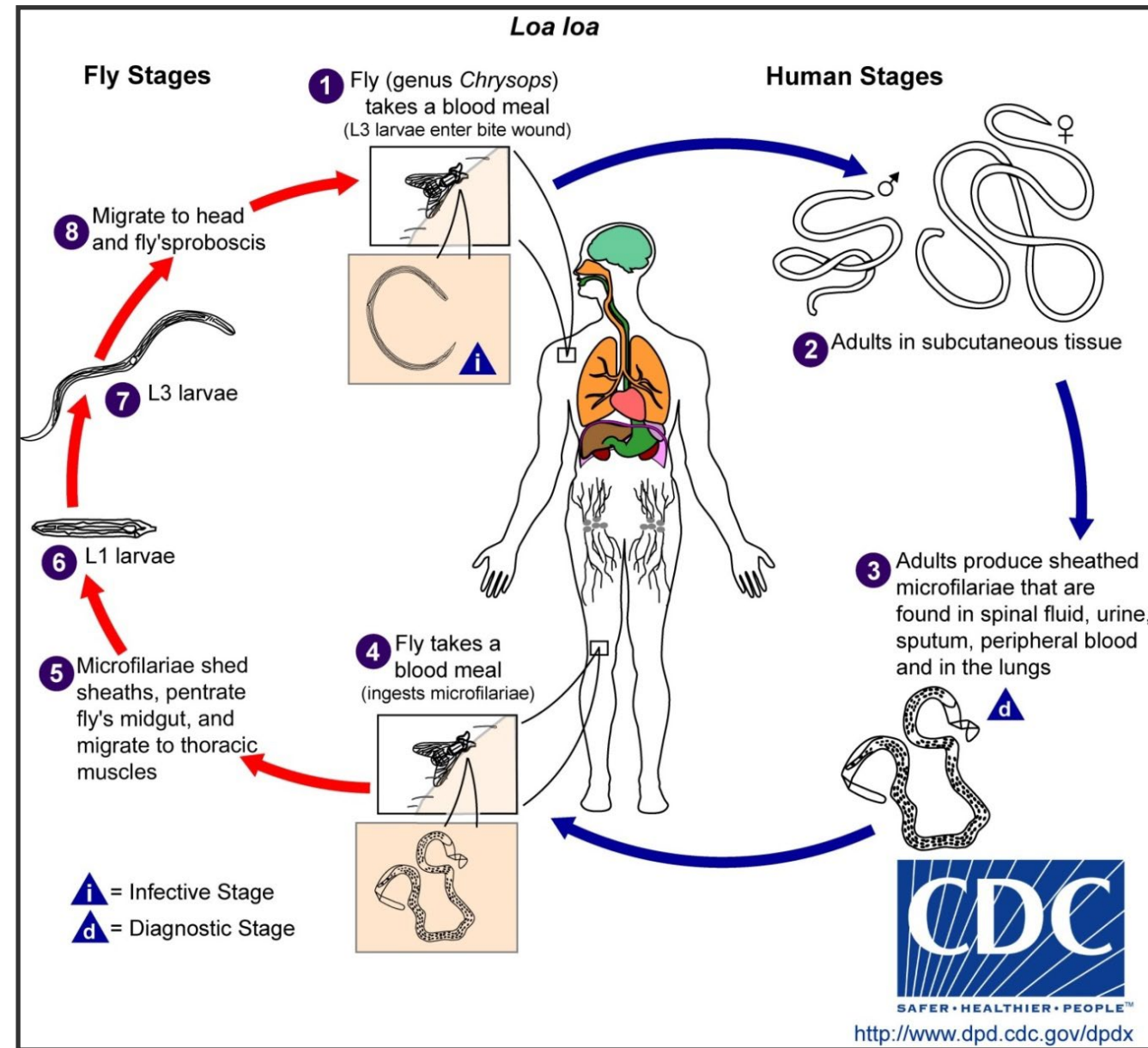
- Diagnosis:
  - » Acute → **Microscopy** (blood, lymph aspirate, chancre fluid, bone marrow)
  - » Chronic → **Microscopy (CSF)**
- Treatment: subspecies and source dependent
  - » *T. b. rhodesiense*
    - Hemolymphatic – Suramin
    - CNS - Melarsoprol
  - » *T. b. gambiense*
    - Hemolymphatic – Pentamidine
    - CNS - Eflornithine

[https://www.cdc.gov/parasites/sleepingsickness/health\\_professionals/index.html#tx](https://www.cdc.gov/parasites/sleepingsickness/health_professionals/index.html#tx)



# Filariases

- Caused by various genera and species of **filarial nematodes**.
- **Vector-borne**
- Adults reside in various locations:
  - » Lymphatic filariasis (lymph tissue)
  - » Loiasis (skin, eye)
  - » Mansonellosis (mesenteries, connective tissue, skin)
- Diagnosis primarily by **detection of microfilariae in blood films**
  - » Serology for lymphatic filariasis



# Lymphatic filariasis

- Caused by *Wuchereria bancrofti* (Circumtropical), *Brugia malayi* and *B. timori* (Southeast Asia)
- Vectors: mosquitos
- Clinical presentation: lymphatic filariasis ('elephantiasis')



Microfilaria of *W. bancrofti* in blood

# Lymphatic filariasis

- Diagnosis:
  - » Microfilariae in blood
  - » Serology
- Treatment: diethylcarbamazine (DEC)
  - » Contraindicated in patients with *Onchocerca* or *Loa*.



Microfilaria of *W. bancrofti* in blood

# Loiasis

- Caused by *Loa loa*, the African eye worm, endemic to west-central Africa
- Vectors: deer flies
- Clinical presentation:
  - » 'Calabar swellings'
  - » ectopic migration to the eye



Adult in eye

<https://www.cdc.gov/dpdx/monthlycasestudies/2011/case301.html>

# Loiasis

- Diagnosis:
  - » *Microfilaria* in blood films
  - » Adults removed from the eye
- Treatment: DEC
  - » Albendazole to lessen worm burden prior to DEC administration



Microfilaria in blood

<https://www.cdc.gov/dpdx/monthlycasestudies/2011/case301.html>



# Mansonellosis

- Three species:
  - » *Mansonella perstans*  
(Africa, Latin America, Caribbean)
  - » *Mansonella ozzardi* (Latin America, Caribbean)
  - » *Mansonella streptocerca* (Africa)
- Vectors: biting midges (all 3), also black flies (*M. ozzardi*)
- Diagnosis: microfilariae in blood [often incidental]
  - » *M. streptocerca* in skin snips
- Treatment: no standards; DEC + mebendazole; also ivermectin

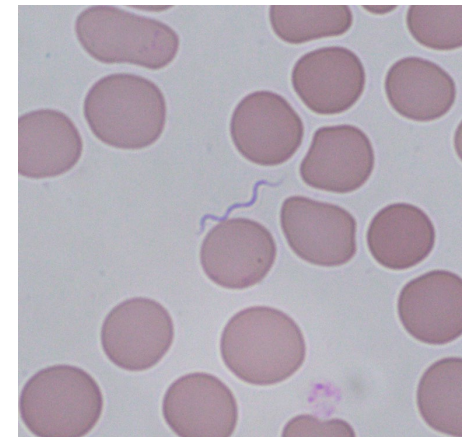


*Mansonella perstans*, thin blood smear

# Relapsing Fever Borreliosis



- Not a parasite: caused by *Borrelia* spp. in the relapsing fever group
  - » Vectored by soft ticks (*Ornithodoros*)
- Detected in blood smears (intentionally or accidental)
- Recurring febrile episodes ~3 days separated by afebrile period ~7 days
  - » 75%: headache, myalgia, chills, nausea
  - » 50%: arthralgia, vomiting
  - » 25%: abdominal pain, dry cough, eye pain, diarrhea, photophobia, neck pain

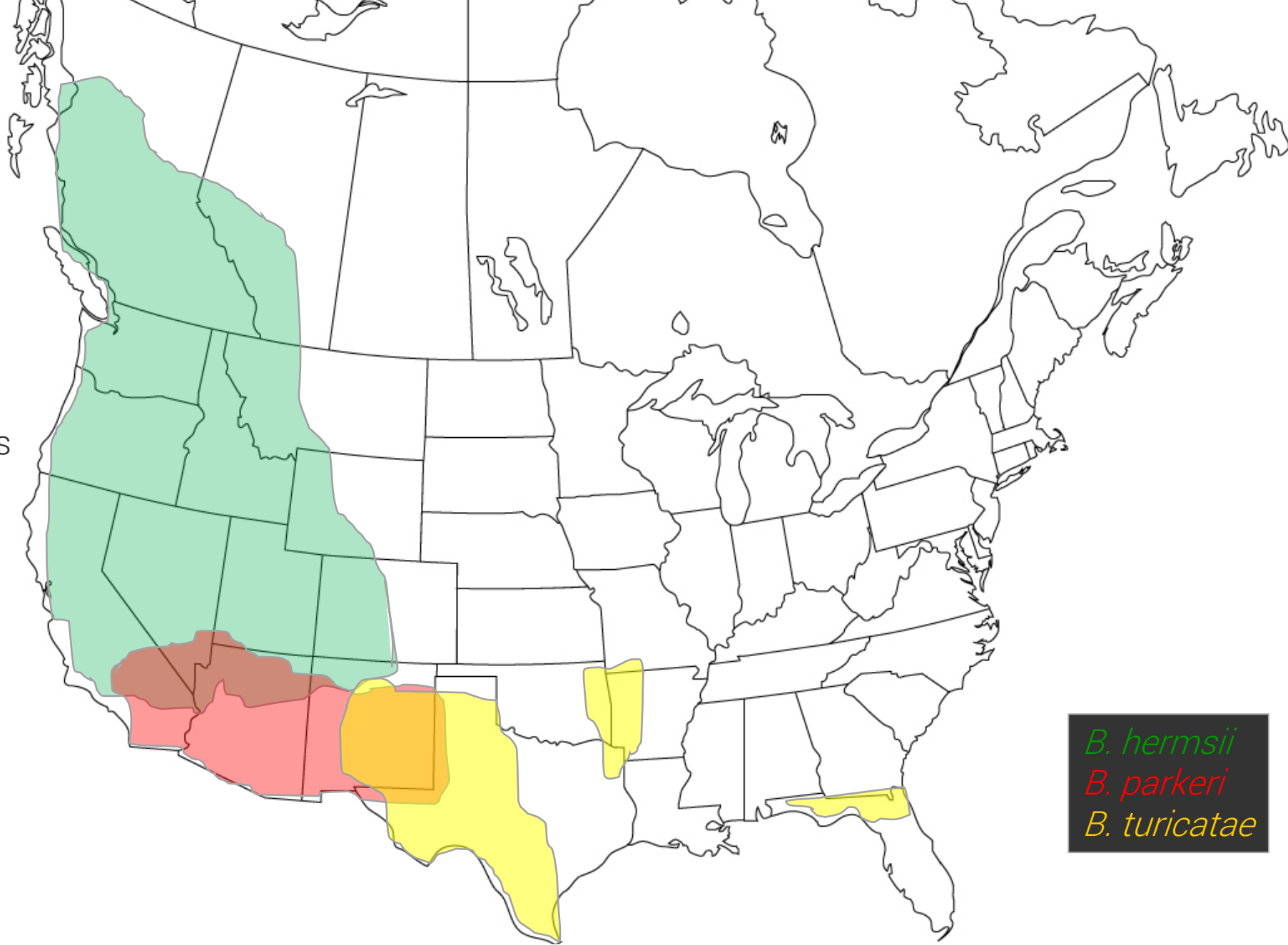


# Relapsing Fever Borreliosis

- Diagnosis:
  - » Blood smear
  - » NAAT (most sensitive)
  - » Serology (retrospective)
- Treatment:
  - » Doxycycline

Approximate geographic ranges  
in the USA

Worldwide distribution for  
other species



*B. hermsii*  
*B. parkeri*  
*B. turicatae*

# Key Points

- Malaria – *Anopheles* mosquitos
  - » *P. falciparum* – most dangerous, most widespread, chloroquine resistance
  - » *P. vivax* – liver phase reactivation, chloroquine resistance
  - » *P. ovale* – liver phase reactivation
  - » *P. malariae* – mild or asymptomatic
- *Babesia* – tick-borne, asplenic patients @ high risk
- *Trypanosoma cruzi* – Chagas disease, Americas, chronic (e.g. cardiomyopathy, megacolon)
- *Trypanosoma brucei* – African sleeping sickness, blood microscopy, mostly fatal if untreated



# Key Points

- Filariasis
  - » *Wuchereria* – lymphatic filariasis and elephantiasis
  - » *Loa loa* – African eye worm, Calabar swellings
  - » *Mansonella* – often an incidental finding when blood films ordered for something else
- Tick-borne Relapsing Fever – soft ticks, widespread, cycling fevers



*A nonprofit enterprise of the University of Utah and its Department of Pathology*