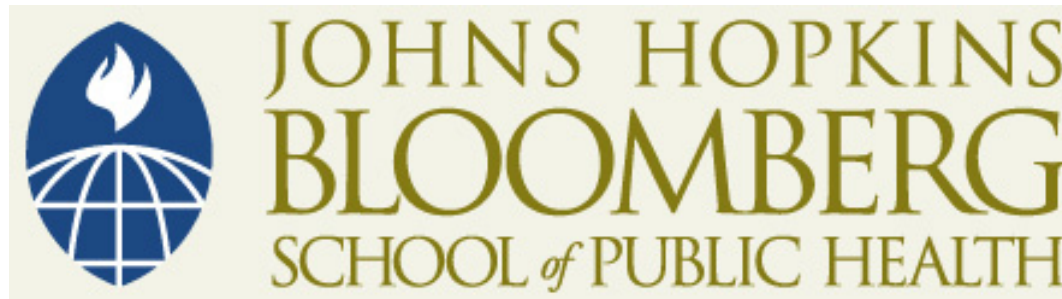


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Malariology: Biology of the Parasite

Nirbhay Kumar, PhD

Impact

- Worldwide
 - >2.3 **billions** people at risk
 - 300 to 500 million cases annually
 - 1.5 to 2.7 million deaths annually

One death every 20 to 30 seconds,
somewhere in the world

Malaria: *Plasmodium* Species of Human Disease

- *P. falciparum* (malignant, TERTIAN)
- *P. vivax* (benign, TERTIAN)
- *P. ovale* (TERTIAN)
- *P. malariae* (QUARTAN)

Malaria parasites are highly species specific. No animal reservoir for human malaria parasites.

**The Infective stage (SPOROZOITE) transmitted
by female anopheline mosquito**



Source: Nirbhay Kumar

- Sporozoites invade hepatocytes
 - ($t_{1/2} < 30$ minutes)
- Undergo asexual development over the next 7-10 days
- Results in 20,000 – 30,000 fold increase in parasite numbers
- Merozoites released then invade RBCs (erythrocytes)
- *P. vivax* and *P. ovale* parasites produce hypnozoites (dormant parasites) which are responsible for relapse of malaria

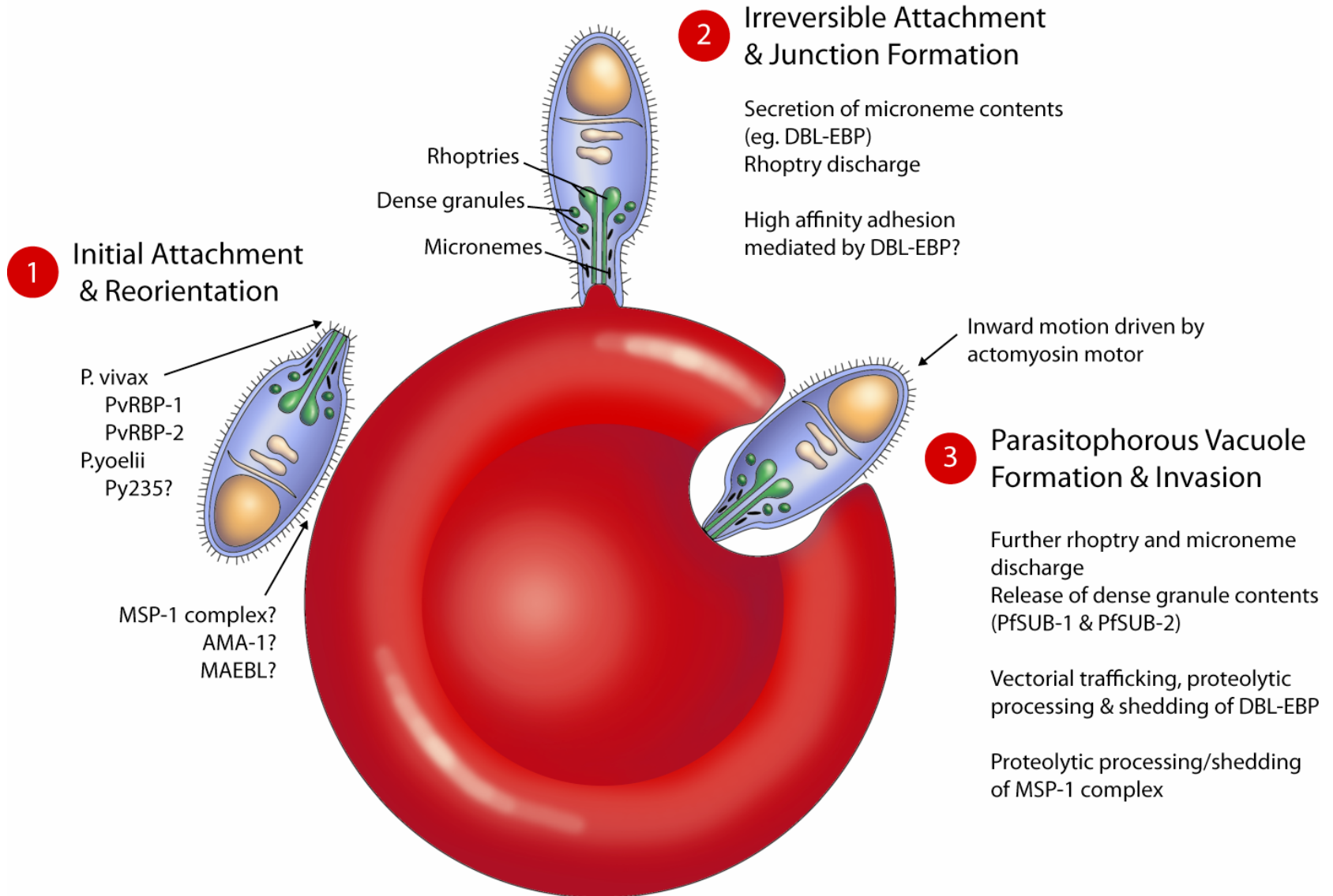
Relapse versus Recrudescence

- **Relapse:** (*P. vivax* and *P. ovale*)
 - Presence of dormant hypnozoites in the liver
- **Recrudescence:** (All 4 species)
 - Reappearance of blood forms of parasites (drug resistance)

A Typical Asexual Cycle

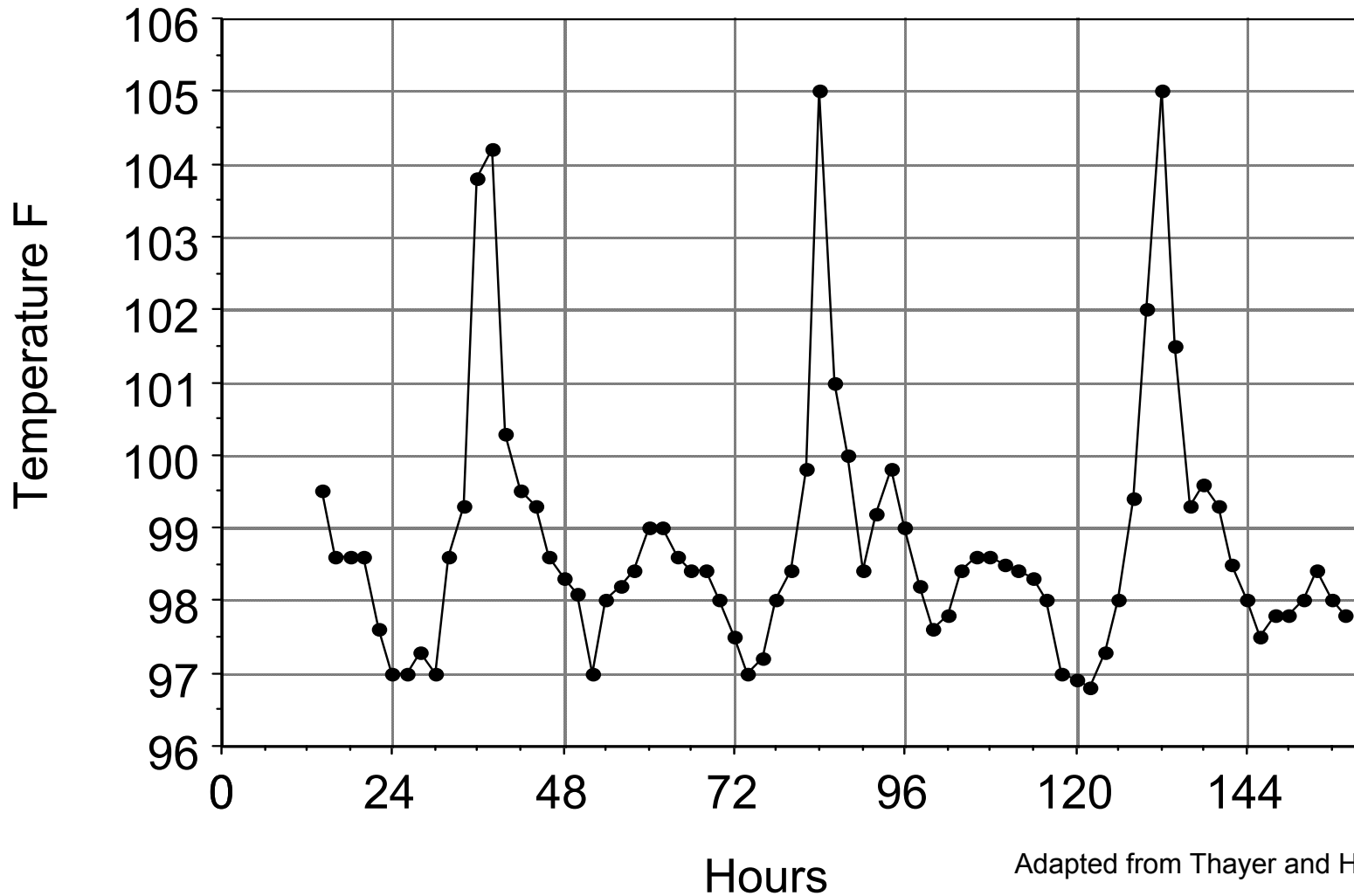
- Merozoites attach to rbc, orient to apical end, invaginate into RBC by forming rbc membrane pocket called parasitophorous vacuole.
- Merozoites invade RBCs and develop into 'RING' forms
- Rings develop into TROPHOZOITES (contain microscopic heme crystal)
- Trophozoites replicate nuclear material to form SCHIZONTS (form with more than one nucleus)
- RBCs are lysed and Merozoites (12-32) released continue the RBC cycle
- (Tertian malaria – 48 hour cycle for Pf, Pv, Po), and (Quartan malaria–72 hour cycle for Pm)

Early Stages of Red Blood Cell Invasion by the Malaria Merozoite



Classic Every Other Day Malaria Fevers

“Tertian” *P. vivax*



Adapted from Thayer and Hewetson

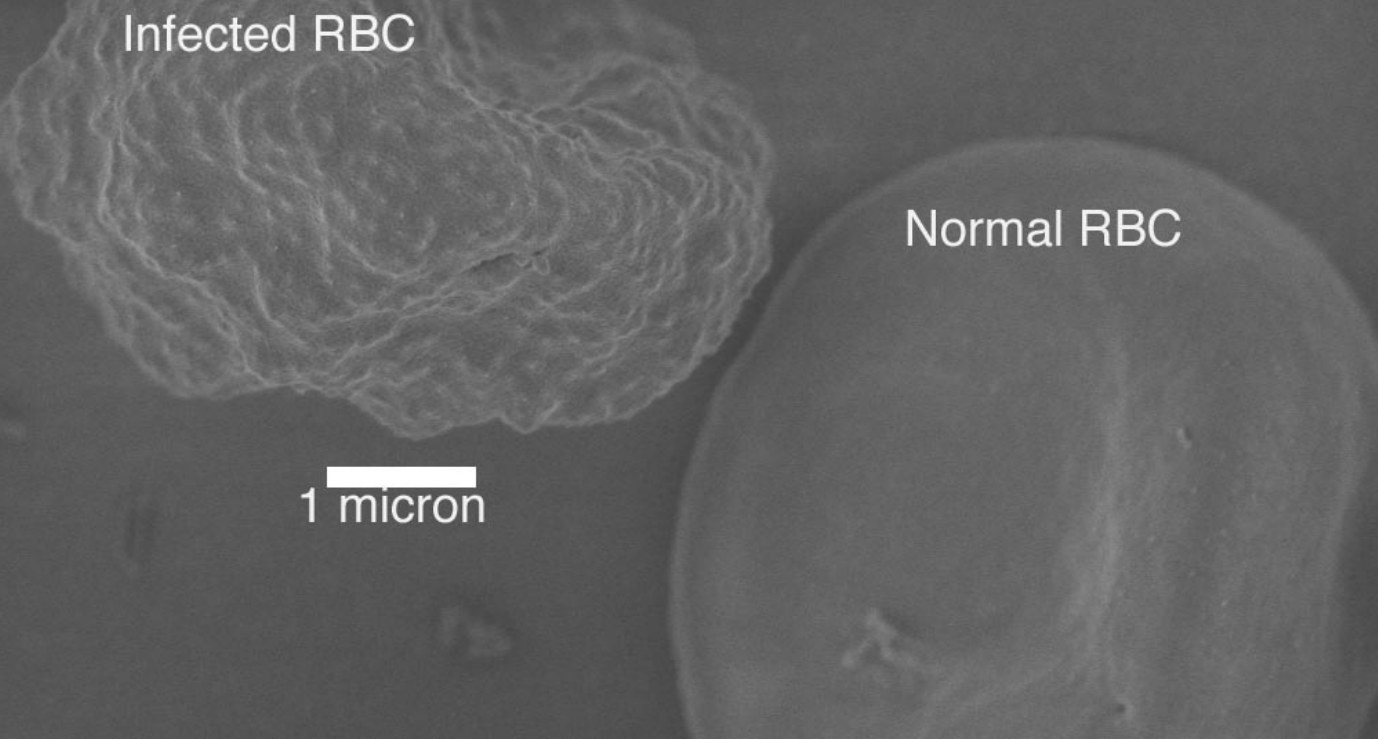
Johns Hopkins Hosp Reports V 1895 p. 3-224

Typical Malaria Paroxysms

- Three stages
 - **COLD**: Chilly feeling followed by rising body temperature (headache/nausea/vomit)
 - **HOT**: High temperature 39 to 40.5 C
 - **SWEATING**: Falling temperature is accompanied by sweating (fatigue and weakness)

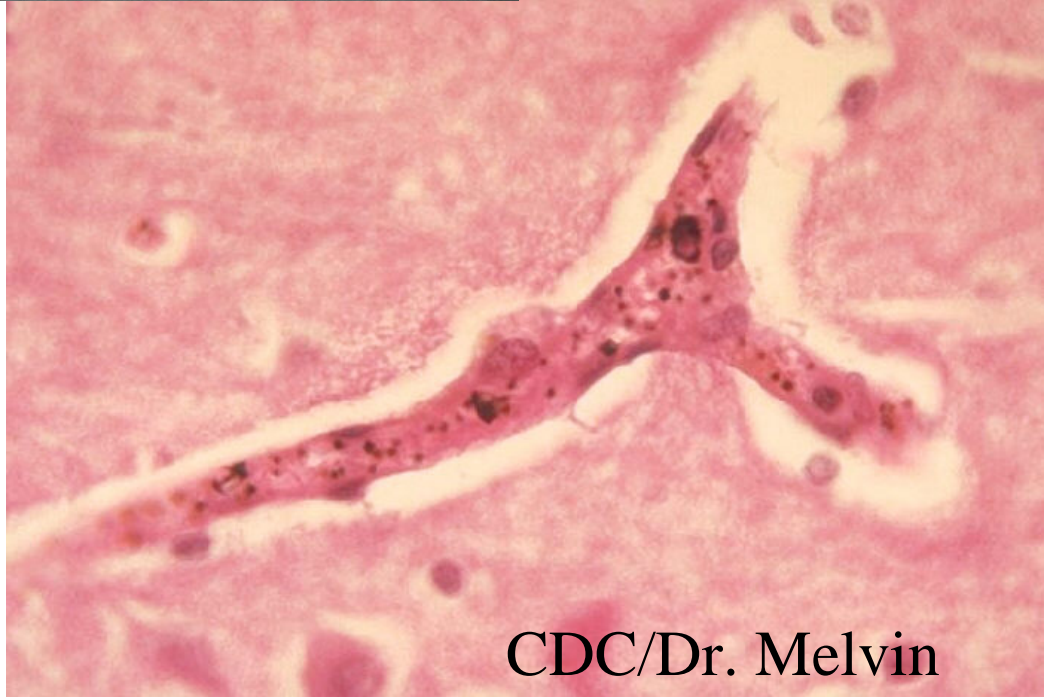
Pathological Complications of *P. falciparum* Malaria

- **Uncomplicated**
 - Fever
 - Parasitemia
 - Anemia
- **Complicated (severe) malaria**
 - Cerebral malaria (coma)
 - Severe anemia
 - Hypoglycemia
 - Renal failure
 - Electrolyte disturbances
 - Jaundice
 - Lactic acidosis
 - Etc. Etc.



Knobs on surface

Adherent parasites in brain



CDC/Dr. Melvin

Cytoadherence (Sequestration)

- Binding of **TROPHOZOITE & SCHIZONT** infected RBCs to endothelial cells in post-capillary venuels in the deep tissues.
- The binding is thought to be mediated by parasite proteins in the electron-dense structures defined as **KNOBS**

Rosetting

- Binding of RBCs containing parasites (**mixed stages**) with uninfected RBCs

Malaria Parasites Use Two Hosts

- A **human** where it causes the disease malaria
- A **mosquito** which it uses as a vector

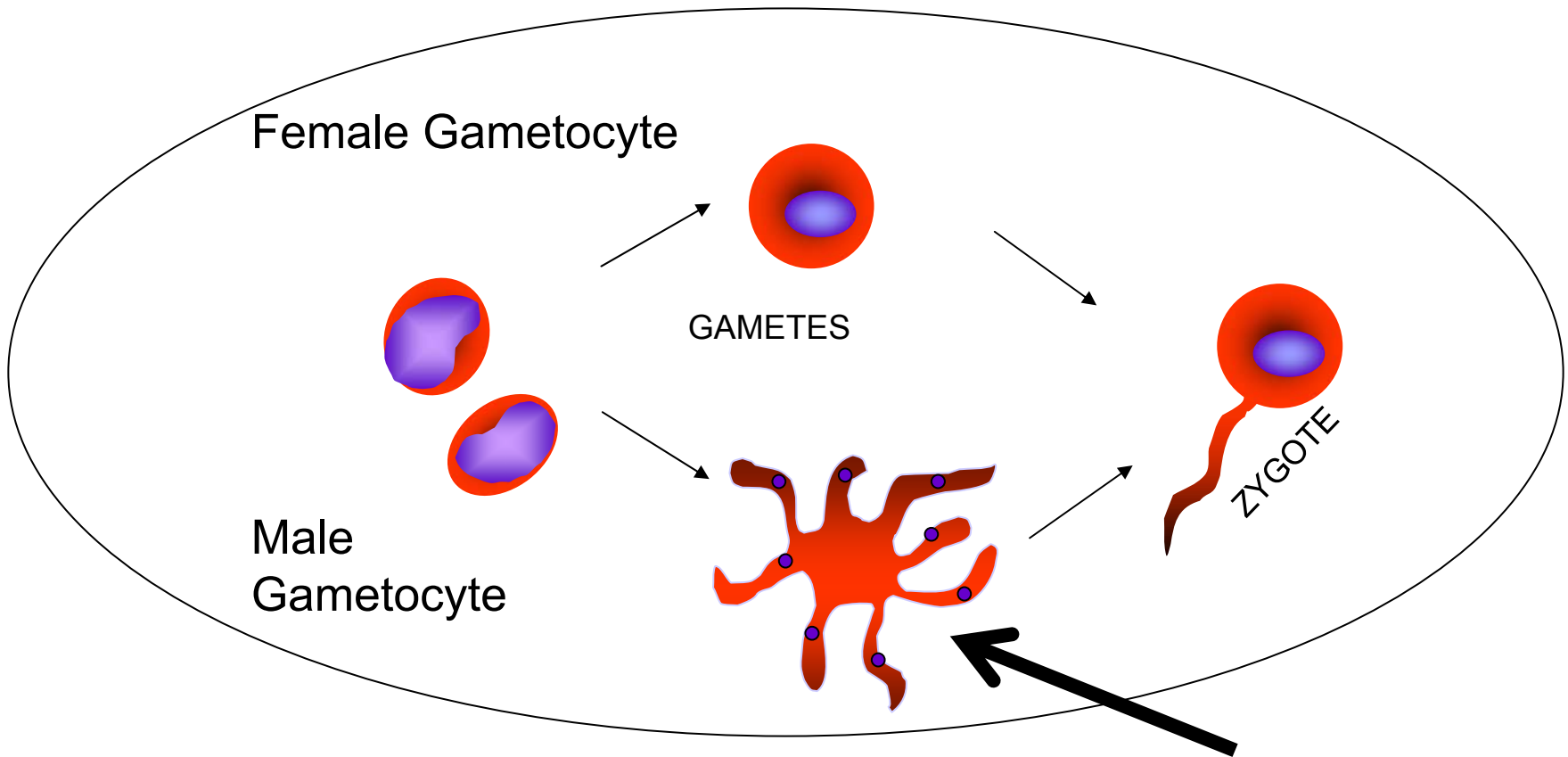
Sexual Development

?

Asexual Stages  Sexual Stages

Gametocyte (male and female sexual stages) development is crucial to transmission

Exflagellation (Emergence of Male Gametes)



8 male gametes from a single gametocytes in <10 min
(XANTHURENIC ACID – exflagellation factor)

Innate Resistance Mechanisms (Nonimmunological Mechanisms of Refractoriness)

Hemoglobinopathies (>300 in humans, most due to a single amino acid change in the hemoglobin molecule)

- Hbs (sickle cell Hb), Autosomal recessive (β -6 GLU to VAL)
- HbC (β -6 GLU to LYS)
- HbE (β -26 GLU to LYS)
- HbF (α/γ as compared to α/β in normal Hb)
- The Thalessemias (imbalance of α and β globin chains)

Cont. . .

Innate Resistance Mechanisms (Nonimmunological Mechanisms of Refractoriness)

RBC enzyme deficiency

- Glucose-6-phosphate dehydrogenase (G6PD)

RBC surface components

- Glycophorins (*P. falciparum*)
- Duffy blood group (*P. vivax*) (West Africans are Duffy -ve)

RBC Cytoskeleton abnormality

- (abnormal Band 3 protein)
- Ovalocytosis (elliptical red cells, PNG)

Cont. . .

Innate Resistance Mechanisms (Nonimmunological Mechanisms of Refractoriness)

Sickle-cell hemoglobin (HbS)

- SC – trait in heterozygotes (AS)
- SC- anemia in homozygotes (SS) (Fatal prior to reproductive age)
- Gene frequency of AS is $\gg 20\%$ in Nigerian population and $\sim 10\%$ in Afro-Americans

PARASITES DIE DUE TO LACK OF OXYGEN
and OTHER CAUSES