

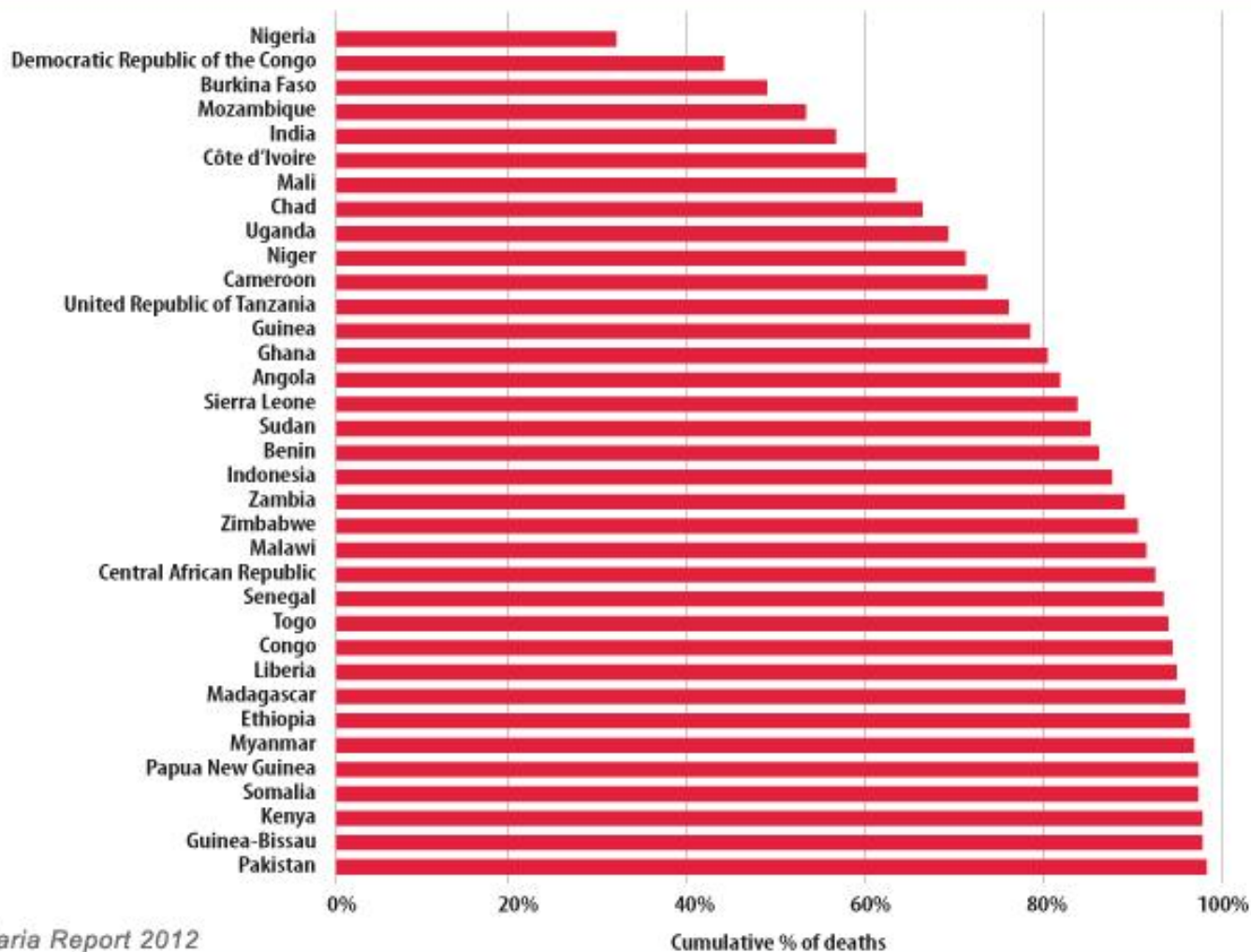
# Malaria

2014

# WHO – World Health Report of 2002 – Leading Causes of Death

Infectious & parasitic disease deaths – total	10.9 million
● Acute respiratory infections	3.96 million
● HIV/AIDS	2.77 million
● Gastroenteritis	1.79 million
● Tuberculosis	1.56 million
● Malaria	1.27 million*
● Measles	0.61 million
● Bordetella pertussis	0.29 million
● Tetanus	0.21 million
● Dengue fever	0.18 million
● Meningitis	0.17 million
● STD' s	0.17 million
● Intestinal parasites	0.11 million
● Hepatitis B	0.10 million

\*\*\* 2013 now down to 207 million cases and 627,000 deaths per year.



Source: WHO *World Malaria Report 2012*

# Malaria in Ghana

Malaria data from Ghana Health Service Report, 2011

Outpatient visits	40.2%
Hospital admissions	35.2%
Percent of Deaths	18.1%
Percent of Deaths <5YO	29.5%
Case fatality <5YO	1.20%





# History of Malaria

The Greeks drained swamps to stop “periodic fevers and splenomegaly”

1700 – bark --quina-quina (cinchona) tree used for treatment

Mid-1800's quinine is the active alkaloid for treatment

1891 – mosquitoes noted as part of the life cycle

1902 – Ross describes malaria life cycle and wins Nobel Prize

1948 – liver as site for exoerythrocytic development

1955 – WHO eradication program initiated

- DDT to kill mosquitoes

- Decrease mosquito reproduction by draining swamps and covering water with oil

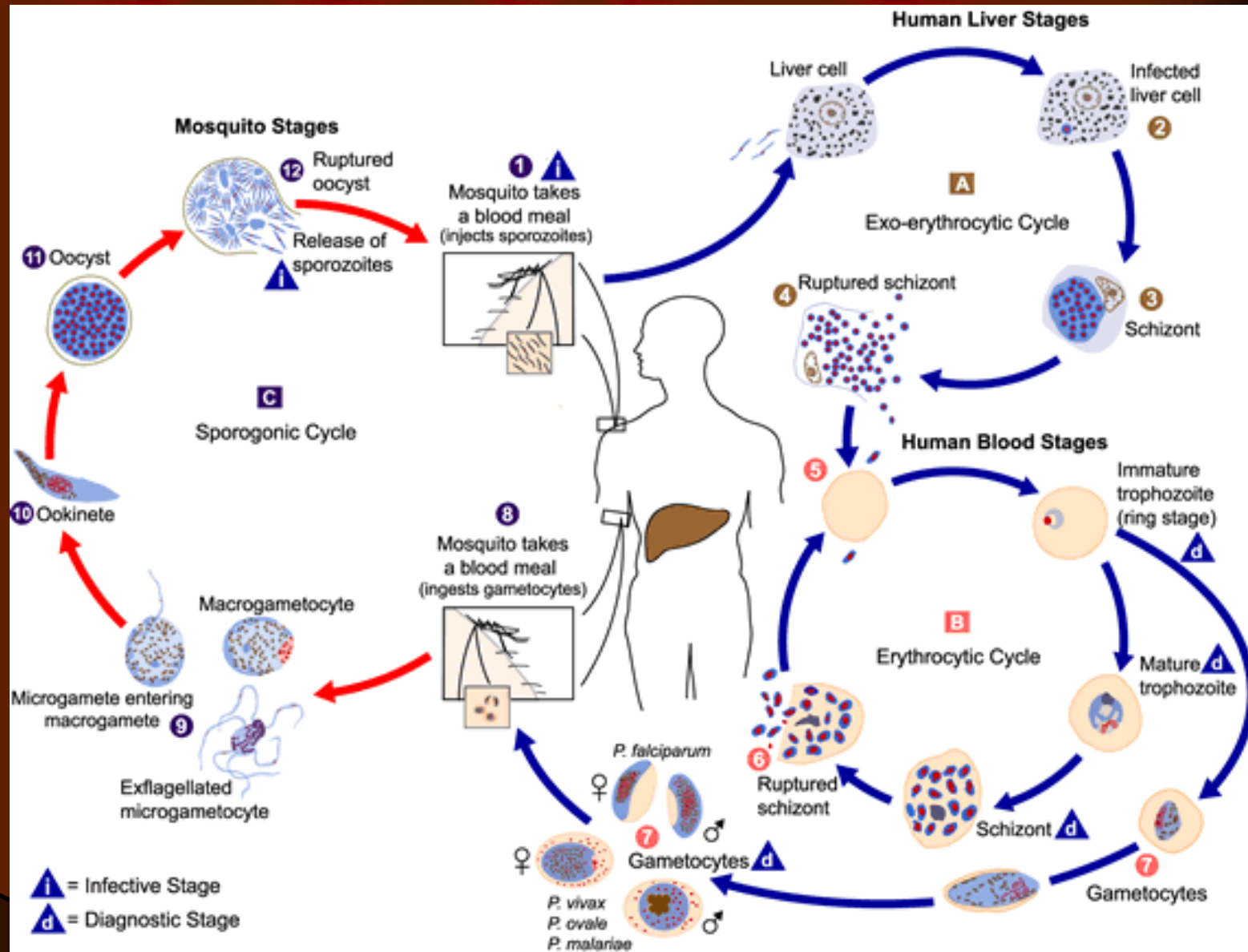
- Chloroquine prophylaxis and treatment

1976 – WHO eradication program declared failure

# Classification of Malaria

- Kingdom – Protista
- Class – Sporozoa
- Genus – Plasmodium
- Species – falciparum, vivax, ovale, malariae
- Definitive host – Anopheles mosquito
- Intermediate host – Humans (monkeys, rodents, birds, reptiles and have own species)

# Life Cycle of *Plasmodium*





# Case #1 – *Falciparum* Malaria

## A Medical Emergency

A 52-year-old male – 3 weeks in Ghana, Africa – no prophylaxis  
One week after arriving back home, flu-like symptoms of chills, fever, sweating, muscle aching and headache.

He called his physician who phoned in a prescription for an antibiotic.

Two days – found unresponsive in his room.

One hour after arriving at SLC Hospital blood smear positive – parasitemia 30% with *P. falciparum* malaria.

Started on malaria medication, and received an exchange transfusion with 12 units of blood and his parasitemia decreased to 10%.

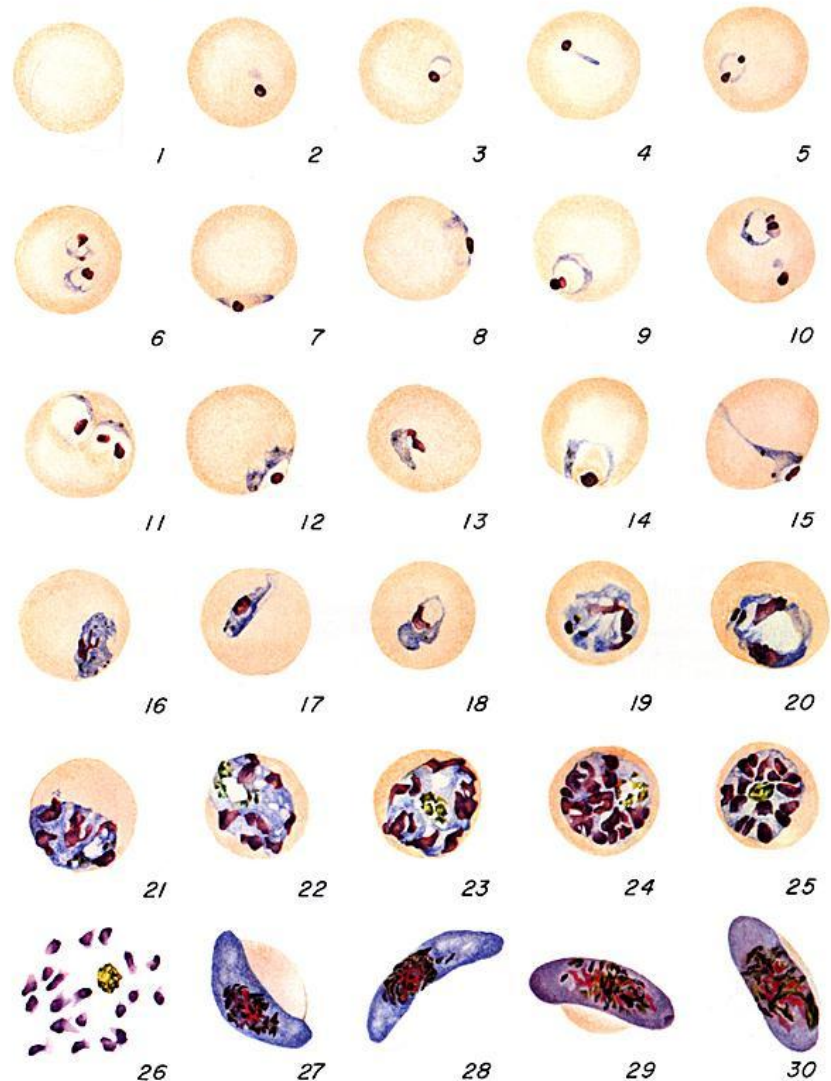
48 hours later and a 2nd exchange transfusion his parasitemia was less than 1%.

End organ damage resulted in treatment for a coma for two weeks, mechanical ventilation for three weeks and renal dialysis for 6 weeks.

# Virulence Factors for *P. falciparum*

- May invade all stages of red blood cells can result in high level parasitemia
- Cyto-adherence -- Produces “knobs”
  - Erythrocyte membrane adhesive protein (PfEMP1)
  - Protein receptors on venules and capillary endothelium
- Rosetting – adhere to non-infected RBC’ s
- Agglutination – adhere to infected RBC’ s

# *Plasmodium falciparum*: Blood Stage Parasites

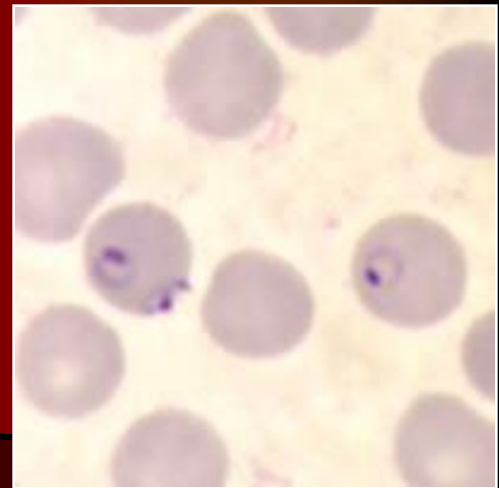
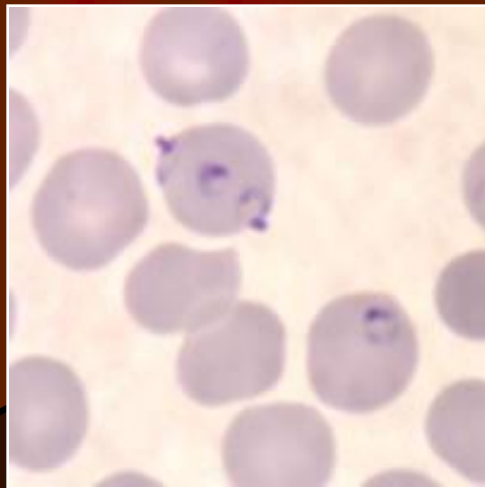
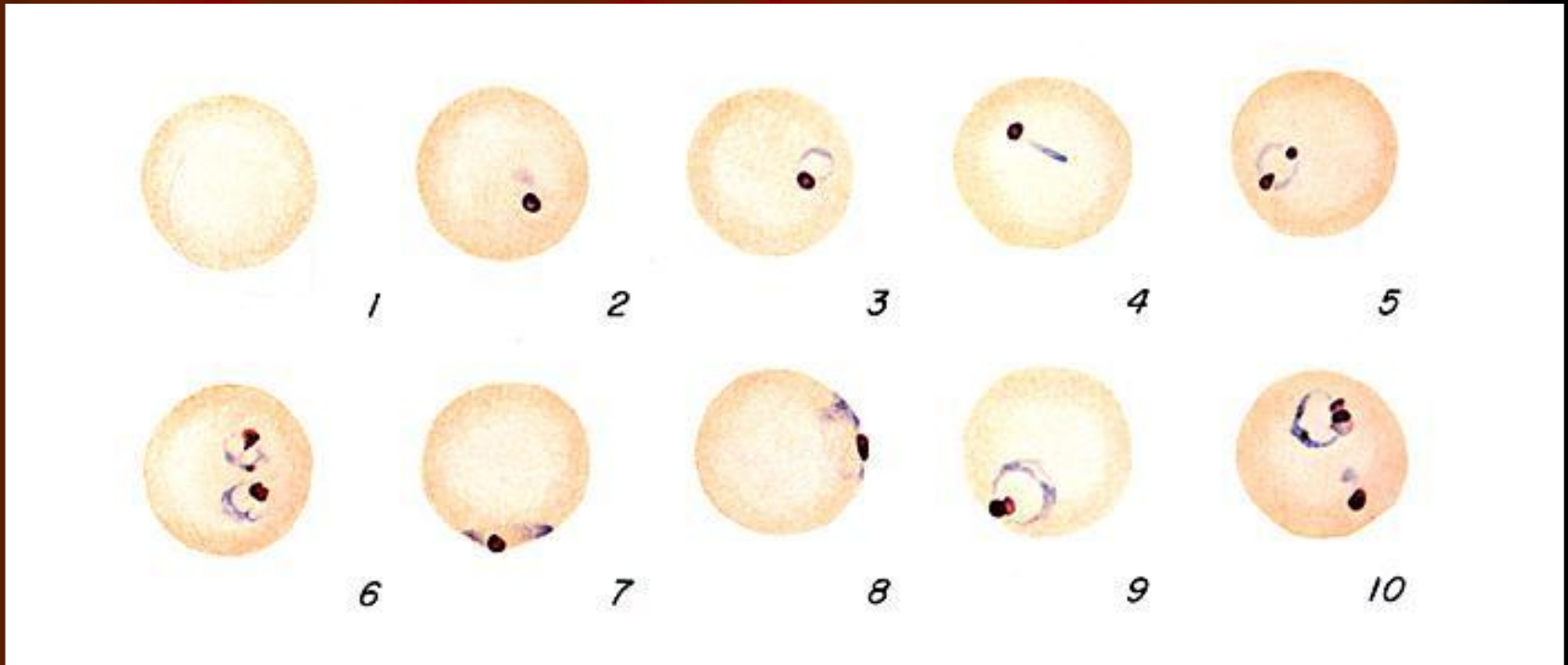


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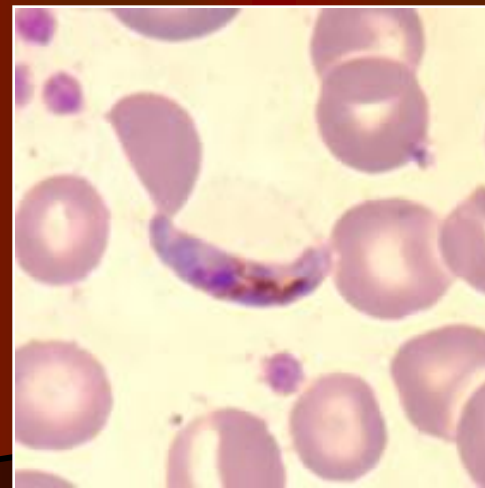
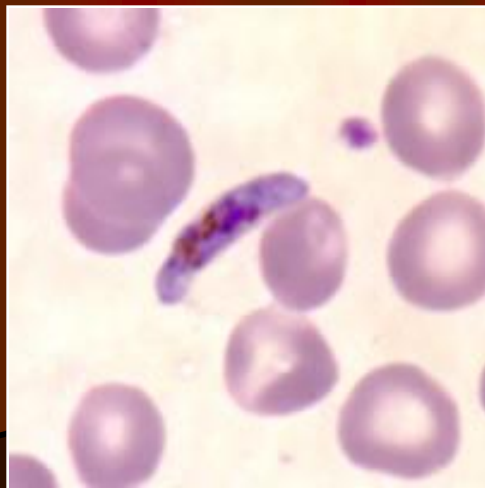
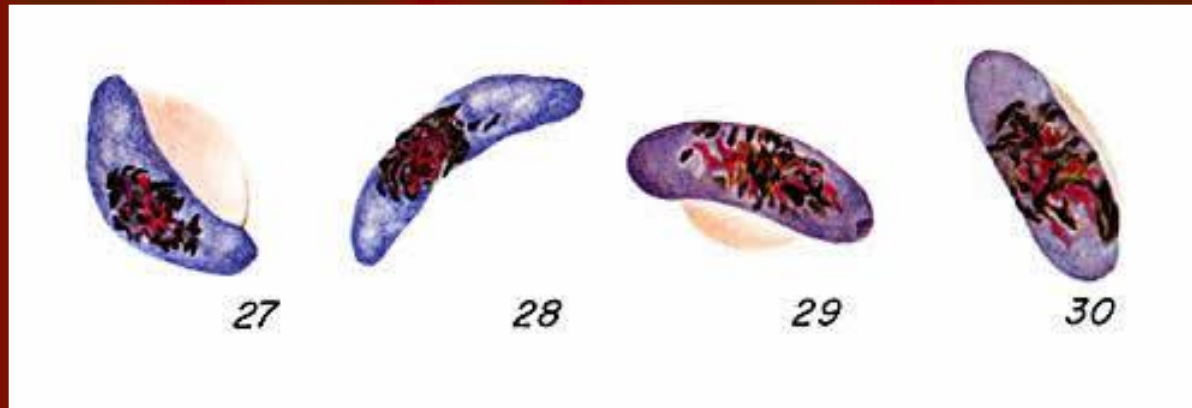
*PLASMODIUM FALCIPARUM*

*J.H. Nicholson*

# *Plasmodium falciparum*: Ring Stage Parasites



# *Plasmodium falciparum*: **Gametocytes**





## Case #2: *Vivax* or *Ovale* Malaria

A 22 yo female -- humanitarian group to Kenya to build schools.  
Used insect precautions and faithfully took preventive medication during travel and for four weeks after travel.

Twelve weeks later -- chills, fever, profuse sweating, muscle aching and headache.

Emergency room and told the doctor that she might have malaria. He laughed and said that it was not possible, but was wise enough to order a malaria smear.

Malaria smear positive with 1% parasitemia.

RBC's larger than the non-infected cells

Stippling consistent with Schüffner's dots

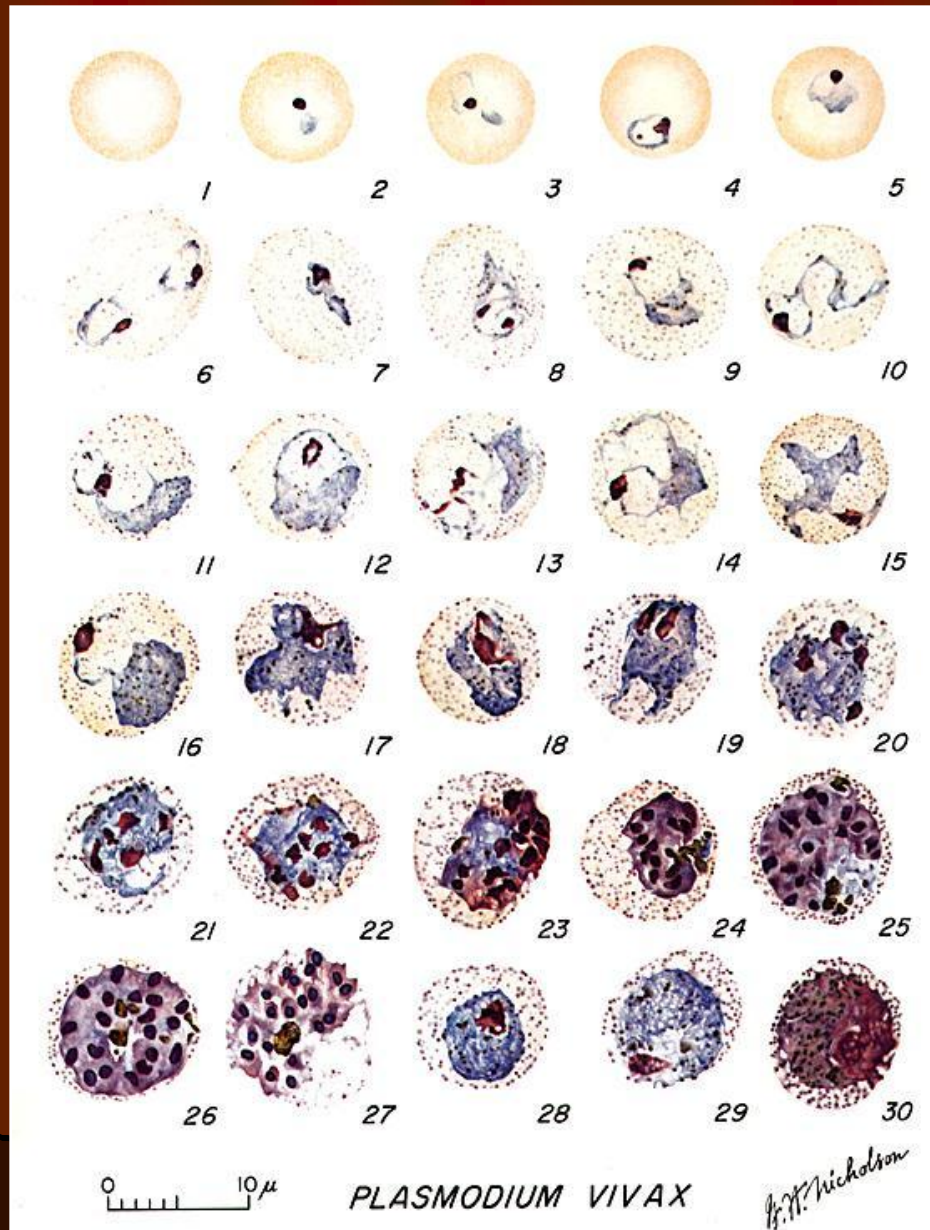
All forms of the RBC life cycle were visualize.

Treated

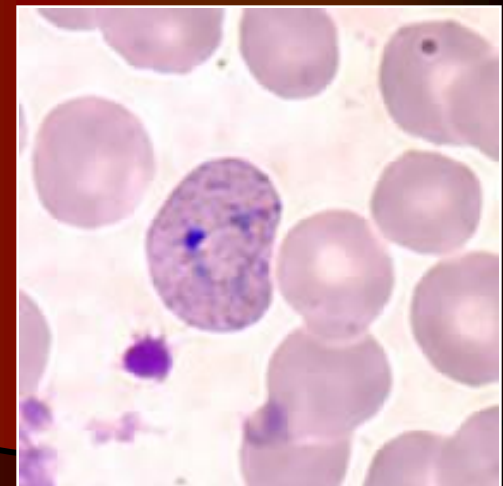
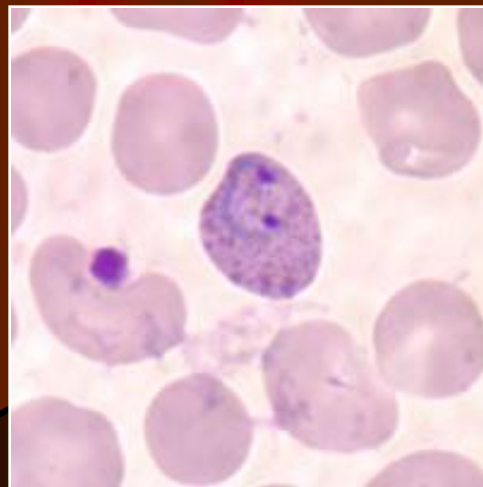
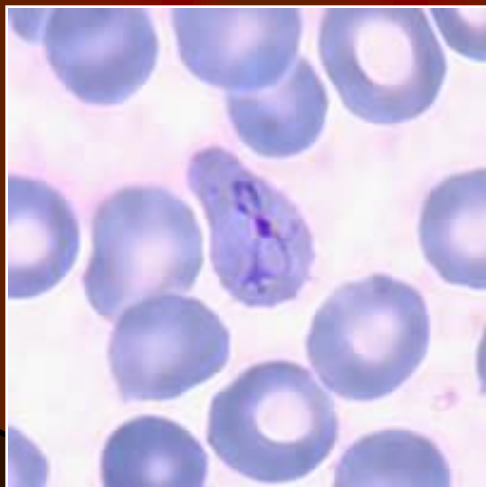
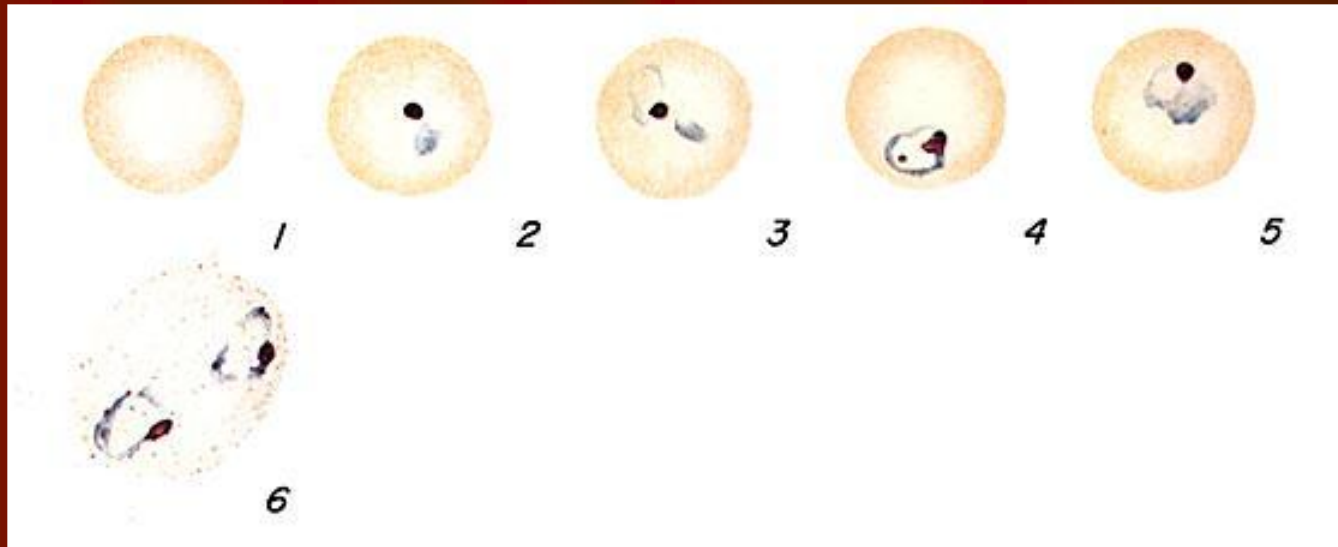
outpatient with Chloroquine for the RBC phase

followed by Primaquine to treat liver "hypnozoites"

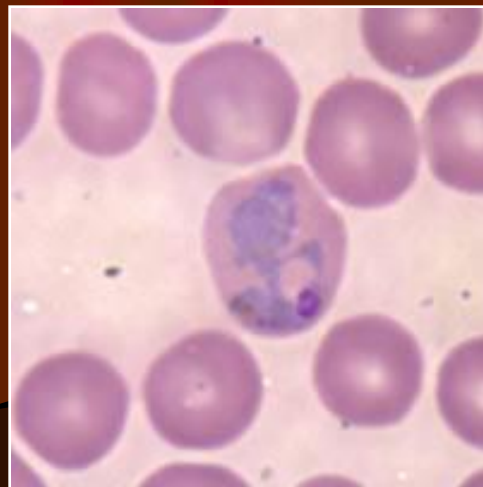
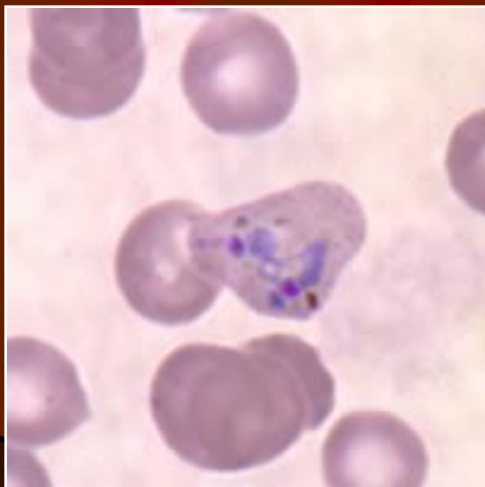
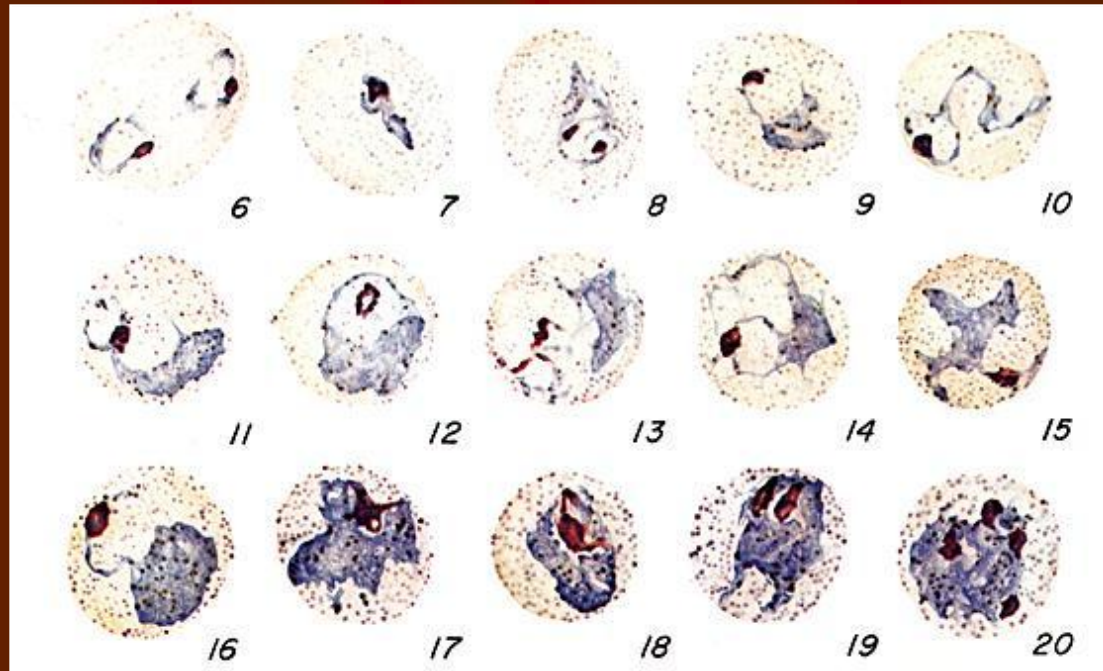
# *Plasmodium vivax*: Blood Stage Parasites



# *Plasmodium vivax*: Ring Stage Parasites

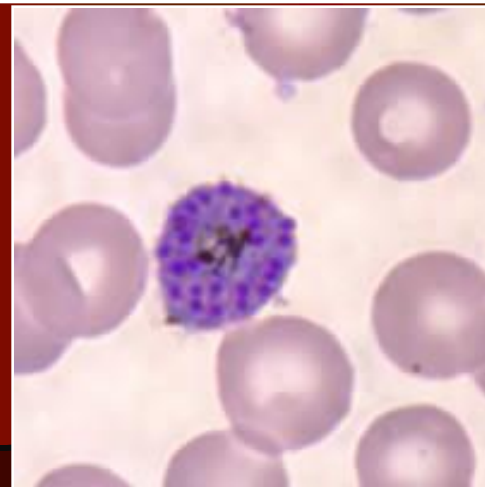
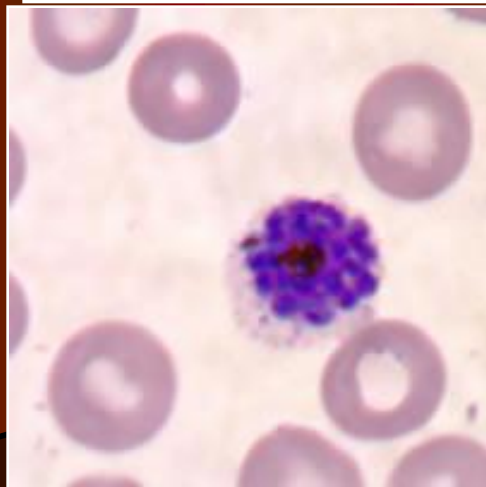
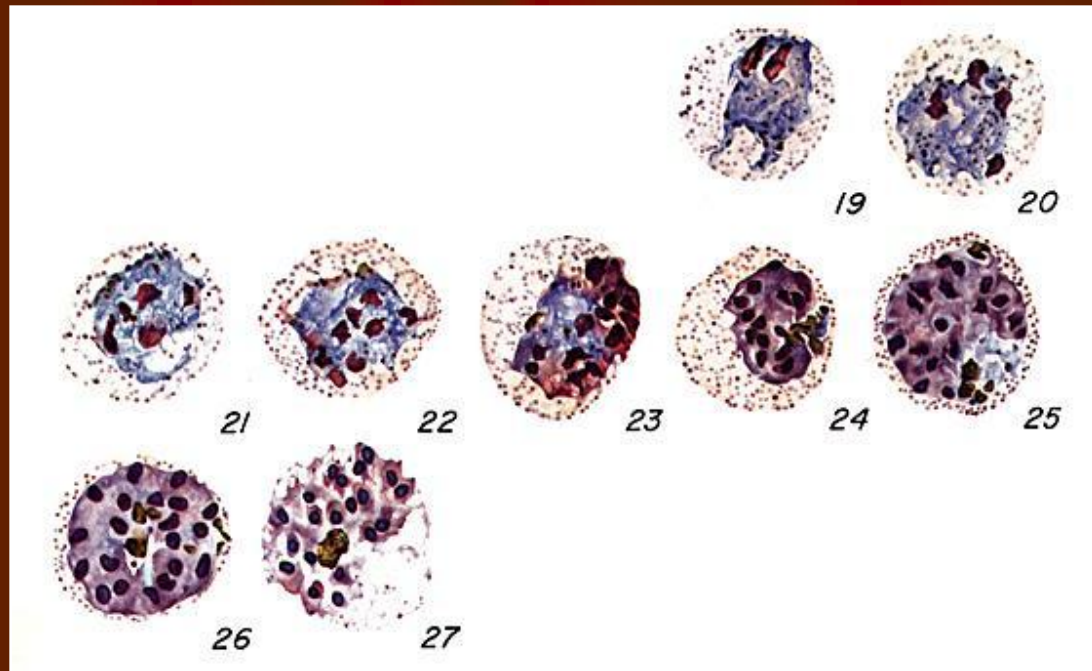


# *Plasmodium vivax*: Trophozoites



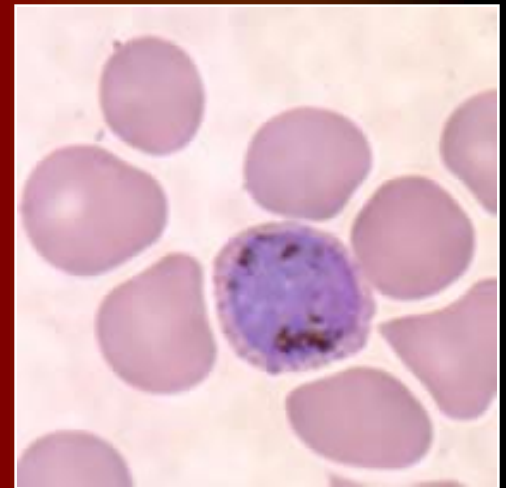
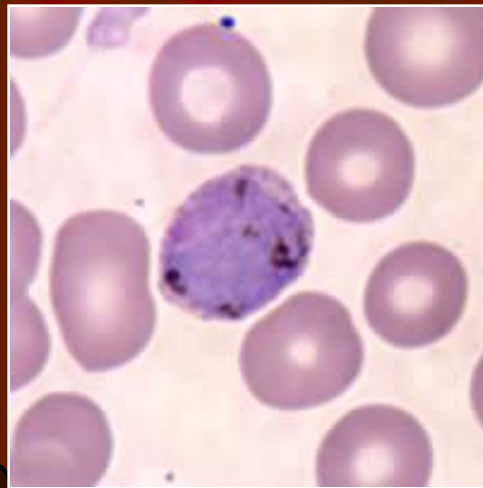
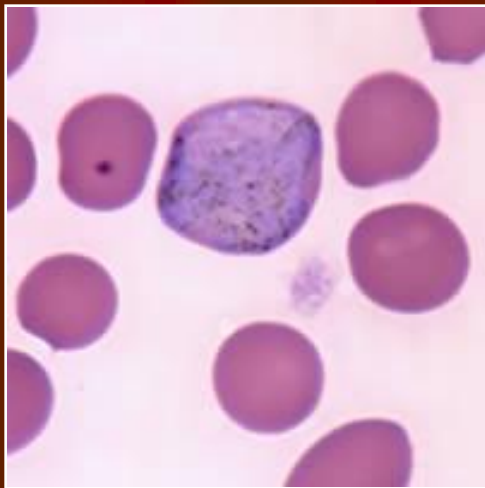
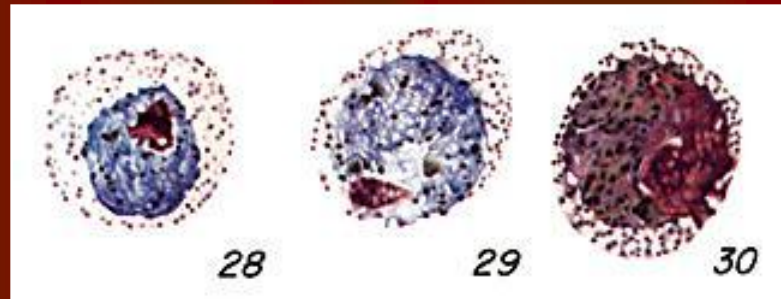


# *Plasmodium vivax*: Schizonts





# *Plasmodium vivax*: **Gametocytes**



# Case #3: Chronic Malaria with *Plasmodium malariae*

74 yo female born and lived in Greece

Healthy life – **no** acute chills, fever and sweating.

1995 -- found to have an enlarged spleen.

Dx with lymphoma, started on methotrexate and developed fever and chills about every 72 h

Antibody was present and reverse-transcription

Southern Blot was positive for *P. malariae*

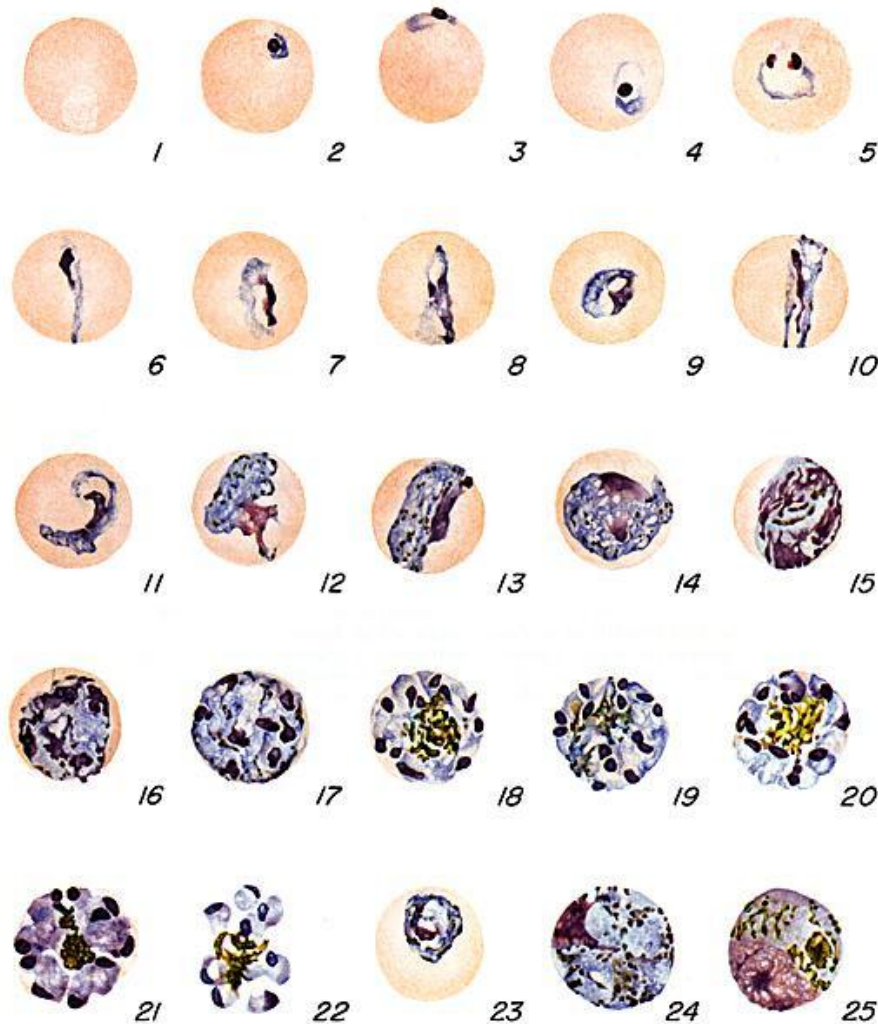
Proteinuria

Treated with Chloroquine for malaria,

Splenomegaly resolved

No evidence of lymphoma

# *Plasmodium malariae*: Blood Stage Parasites

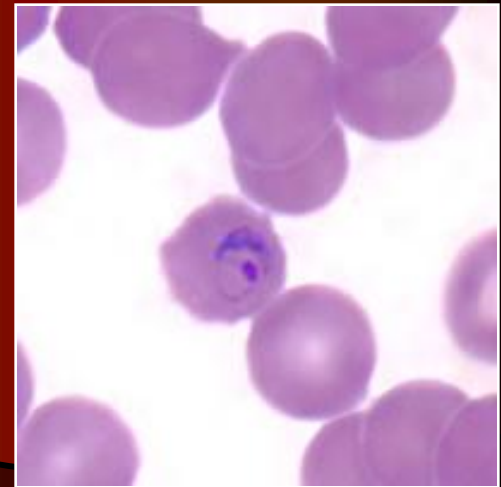
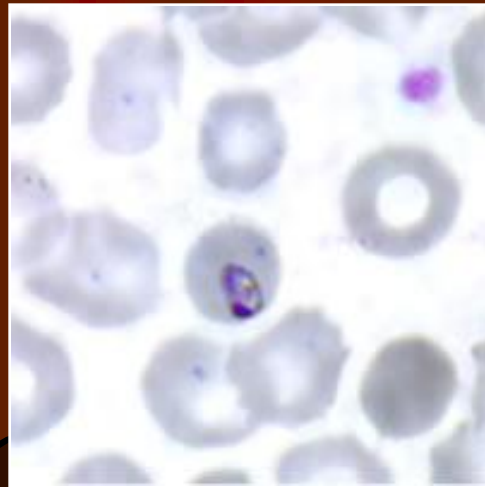
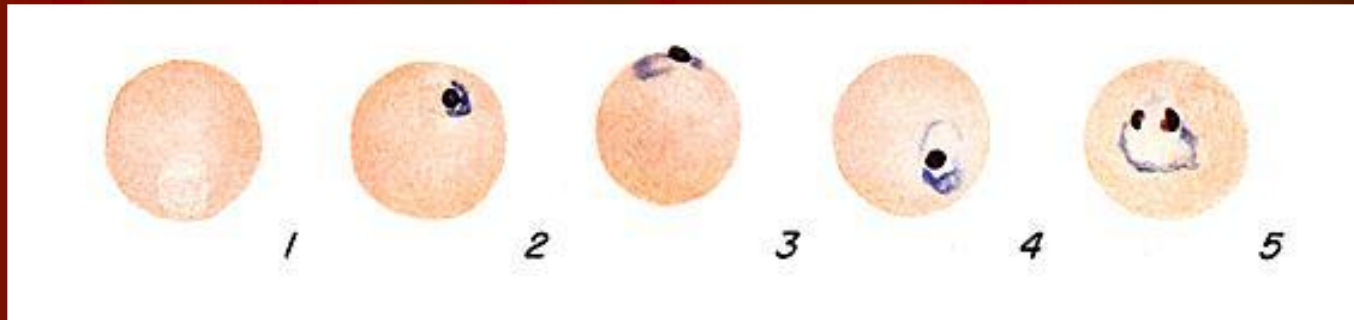


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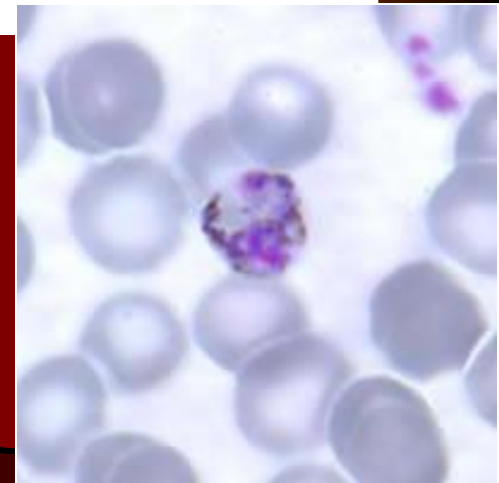
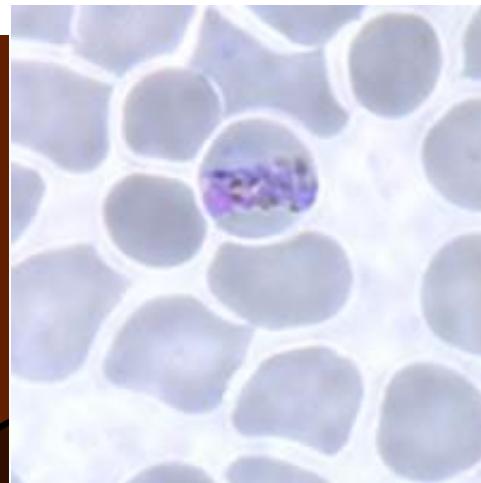
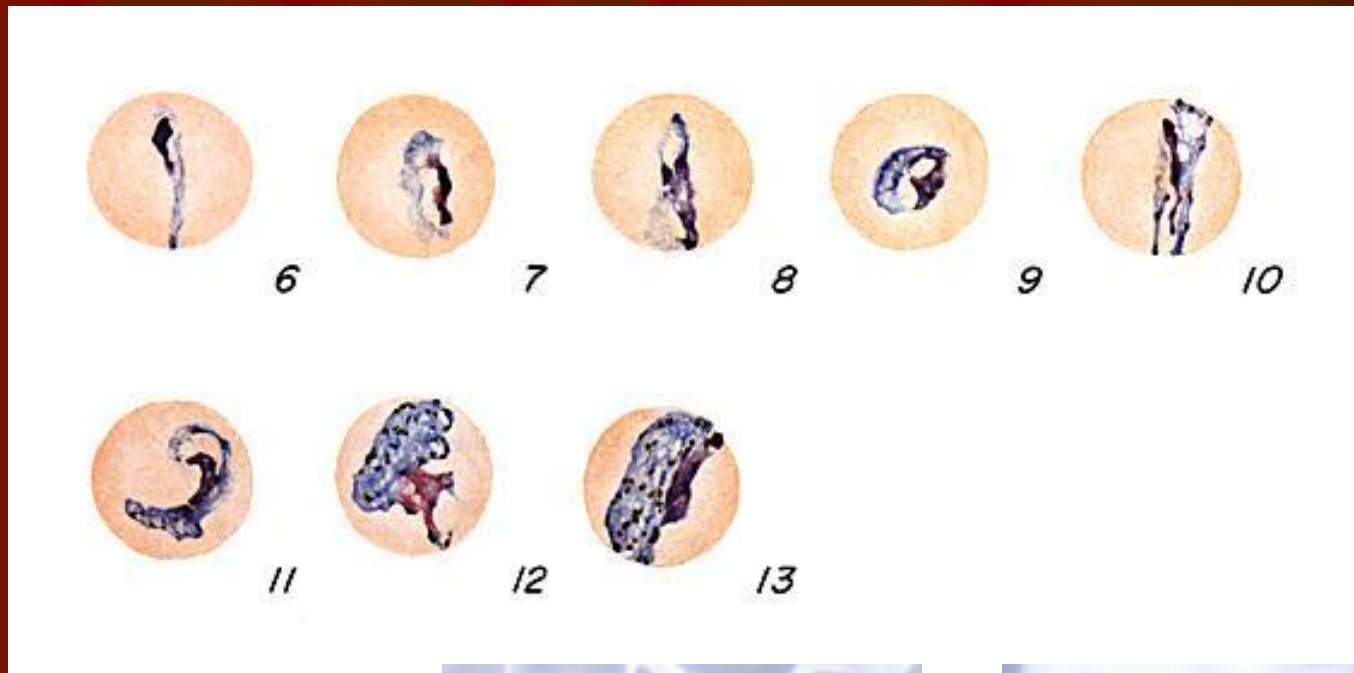
PLASMODIUM MALARIAE

*S. H. Nicholson*

# *Plasmodium malariae*: Ring Stage Parasites

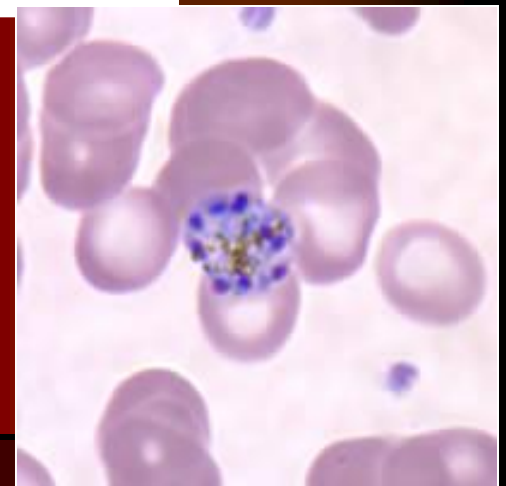
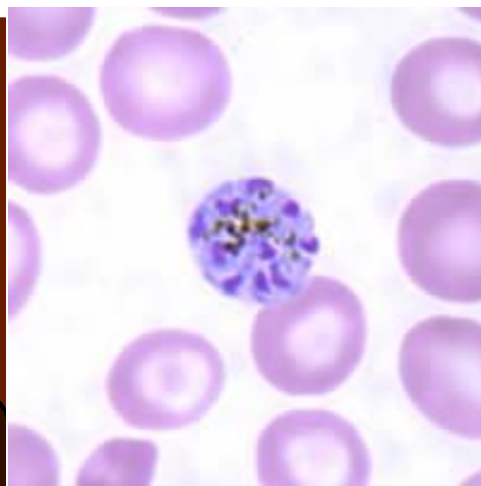
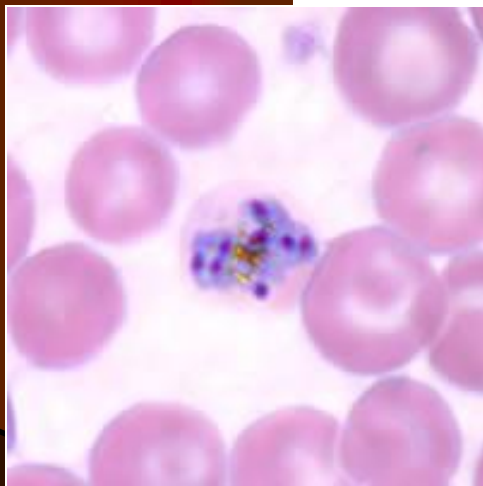
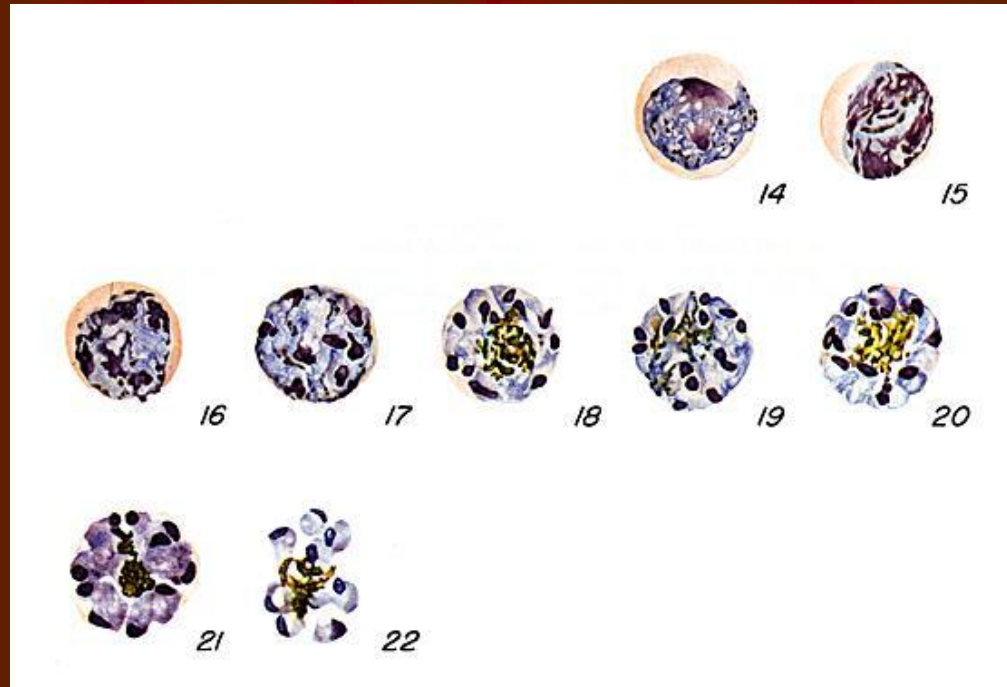


# *Plasmodium malariae*: Trophozoites

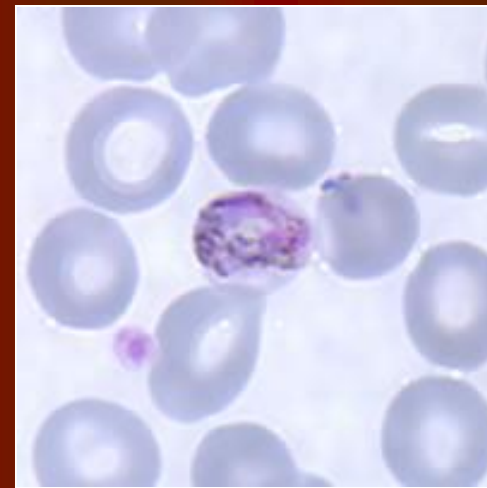
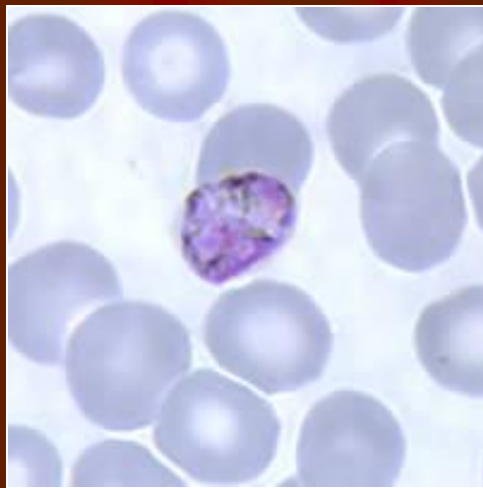




# *Plasmodium malariae*: **Schizonts**



# *Plasmodium malariae*: **Gametocytes**



# Characteristics of *Plasmodium* Species

	<i>falciparum</i>	<i>vivax</i>	<i>ovale</i>	<i>malariae</i>
Distribution	Tropics	Tropics, subtropics	Africa	Subtropics
Host resistance	Sickle cell Hgb C,D,E Thalassemia G6PD Pyridoxine kinase deficiency	Duffy antigen receptor neg		
Host RBC's	All RBC's	Young RBC's (reticulocytes)		Old RBC's
Incubation	2 weeks <25% 1 mo	2 weeks > 25% 6 mo	2 weeks >25% 6 mo	2 weeks Chronic
Avg # merozoite in liver schizont	40,000	10,000	15,000	2,000
Avg # merozoite/RBC 8-24		12-24	8-12	6-12
Periodicity	48 hours	48 hours	48 hours	72 hours
Severity of attack	++++	+++	+++	+

# Characteristics of *Plasmodium* Species

	<i>falciparum</i>	<i>vivax</i>	<i>ovale</i>	<i>malariae</i>
Mortality	1-5%	Rare	Rare	Very rare
Latent infection	No	Yes	Yes	No
Chronic persistence	No	No	No	Yes
Large RBC's	No	Yes	Yes	No
Schüffner's dots	No	Yes	Yes	No
All forms of life cycle in peripheral bloo	No	Yes	Yes	Yes
Gametocyte	Banana shaped	Amoeboid	Amoeboid	Amoeboid

# Diagnosis

- Clinical symptoms – chills, fever, sweats, headache, muscle aches
- Thick blood smear –
  - Inexpensive
  - Sensitive (0.001% parasitemia)
  - Less accurate parasitemia
  - More difficult to speciate
  - Delay for smear to dry
  - Requires an experience observer
  - Artifacts may result in false positive



# Diagnosis

- Thin Smear
  - Rapid (Wright's vs. Giemsa stain)
  - More accurate speciation
  - Red cell morphology
  - Inexpensive
  - Less sensitive ( $<0.05\%$  parasitemia)
  - Better quantitation (except for *falciparum*)
  - Requires an experienced observer

# Diagnosis

- PCR testing
  - Sensitive
  - Expensive
  - Excellent speciation
  - Mixed infections
- Rapid Diagnostic Test (RDT)
  - Histidine-rich protein 2 (PfHRP2) antigen
  - LDH antigen – less sensitive
  - Sensitive
  - Simple
  - Relatively inexpensive
  - May remain positive after infection
  - Poor quantitation

# Prevention

Vaccination – not available but recent optimism

Insect precautions:

- Screened-in housing
- Mosquito netting over the beds
- Clothing
- Insect repellent – DEET
- Insecticides – Permethrin

Prophylactic medication

- Atovaquone/proguanil (Malarone)
- Mefloquine (Lariam)
- Doxycycline
- Chloroquine

# Malaria Treatment

- Oral medication
  - Chloroquine
  - Artesunate/Lumefantrine
  - Atovaquone/proguanil
  - Mefloquine
- IV medication
  - Artesunate
  - Quinine (Quinidine)
- Treatment of hypnozoites in the liver for *P. vivax/ovale*
  - Primaquine

# Medications

Agent	Prevent Treatment Preg			
	Latent			
● Chloroquine	Y	Y	Y	N
● Quinine	N	Y	Y	N
● Mefloquine	Y	Y	Y	N
● Artesunate	N	Y	Y	N
● Lumefantrine	N	Y	Y	N
● Doxycycline	Y	Y	N	N
● Atovaquone/ ● Proguanil	Y	Y	N	N
● Primaquine	Y	N	N	Y



# Medications

- Chloroquine – Resistance so used only in central Am, middle East and Caribbean, Hypotension, cardio-toxicity, retinopathy,
- Quinine/Quinidine – Cinchonism, QT prolongation,
- Mefloquine – psychedelic dreams, seizures, psychosis
- Artemisinin – WHO drug of choice, kills marginated malaria of Pf, relatively safe, rapidly excreted, frequent relapse if not used with a second agent.
- Lumefantrine – Second agent with artesunate, acts rapidly, minor toxicity
- Doxycycline – gastric irritation, photosensitivity, bone and tooth deposit in children, weak anti-malarial.
- Atovaquone/proguanil – well tolerated, causal prophylaxis, contraindicated in renal failure
- Primaquine – eradicates hepatic forms, massive hemolysis if patient has G6PD so must test before prescribing, nausea, vomiting, diarrhea, methemoglobinemia