



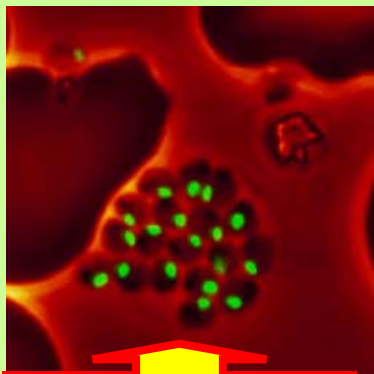
There is a Plant inside Malaria ! (secondary endosymbiosis)

Malaria -Plasmodium- contains a broken down old chloroplast (an **Apicoplast**) that doesn't do any photosynthesizing. The Apicoplast is however, needed for the parasite to invade new cells. Even more fascinating- common herbicides that are generally pretty non-toxic to humans seem to stop the Apicoplast from working.

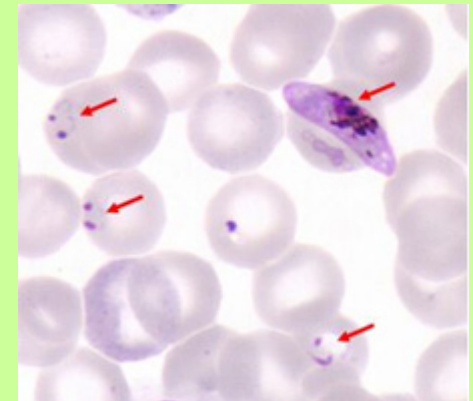
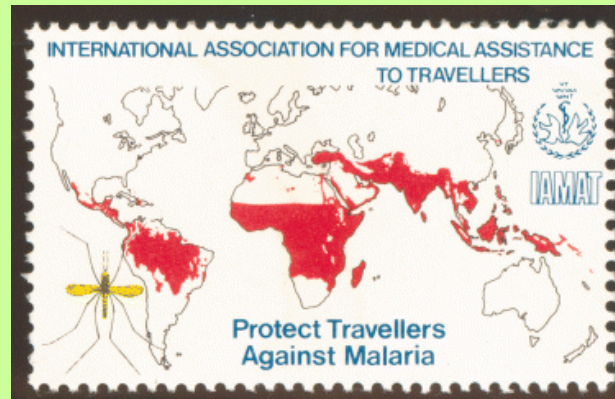


Malaria 2010

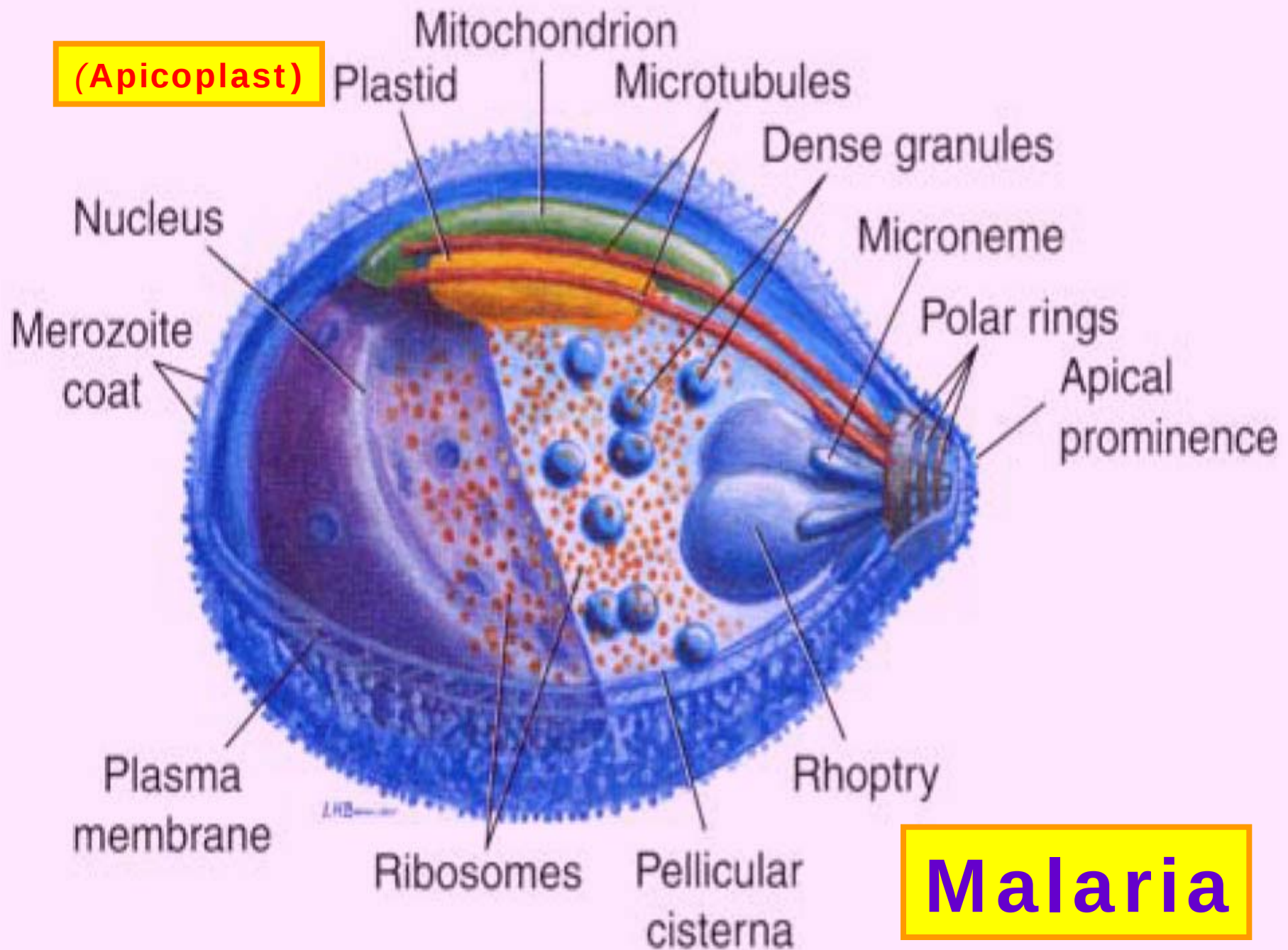
Dr. Lai Kang Yiu
Intensive Care Unit
Queen Elizabeth Hospital



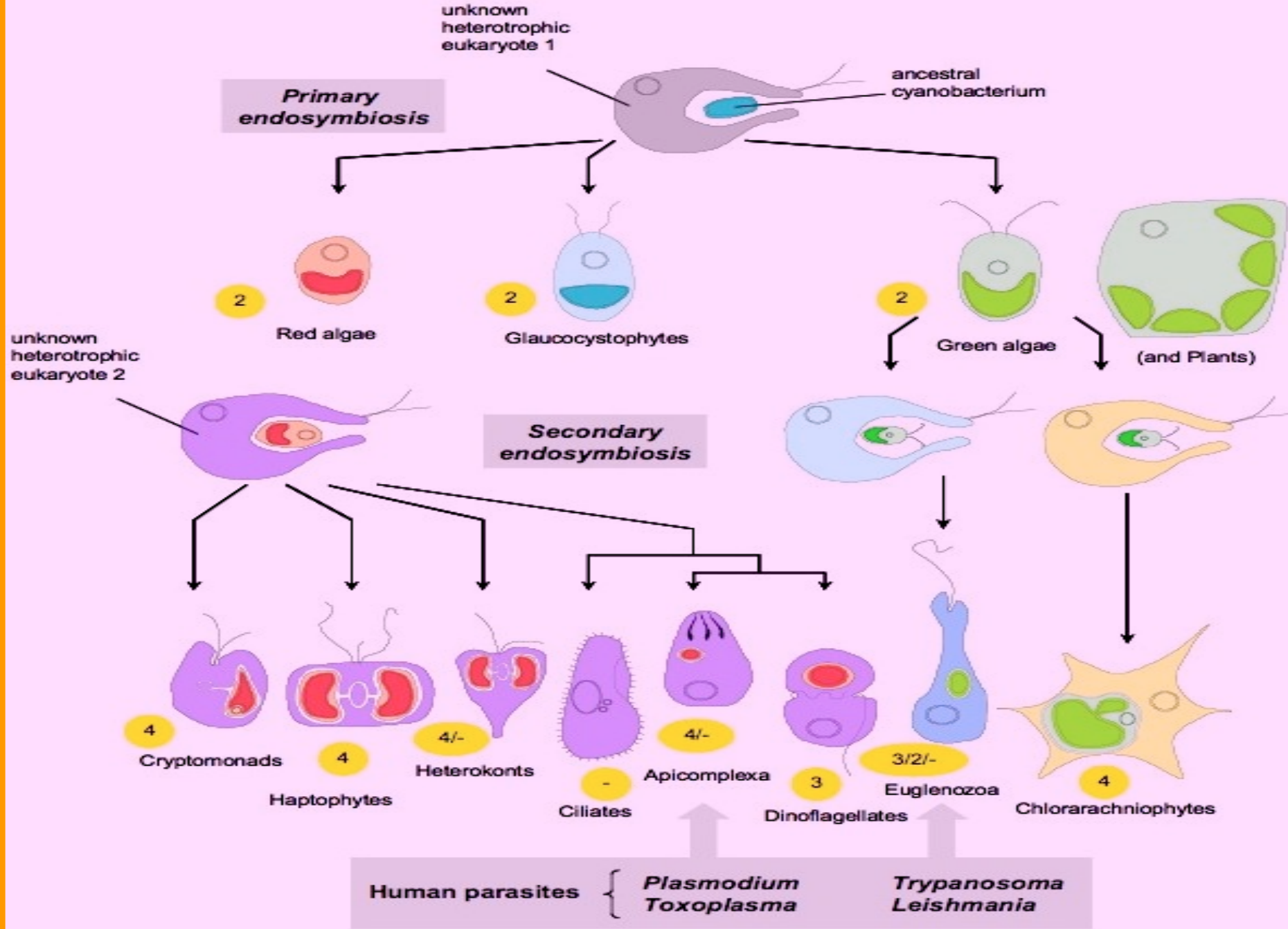
O = Apicoplast



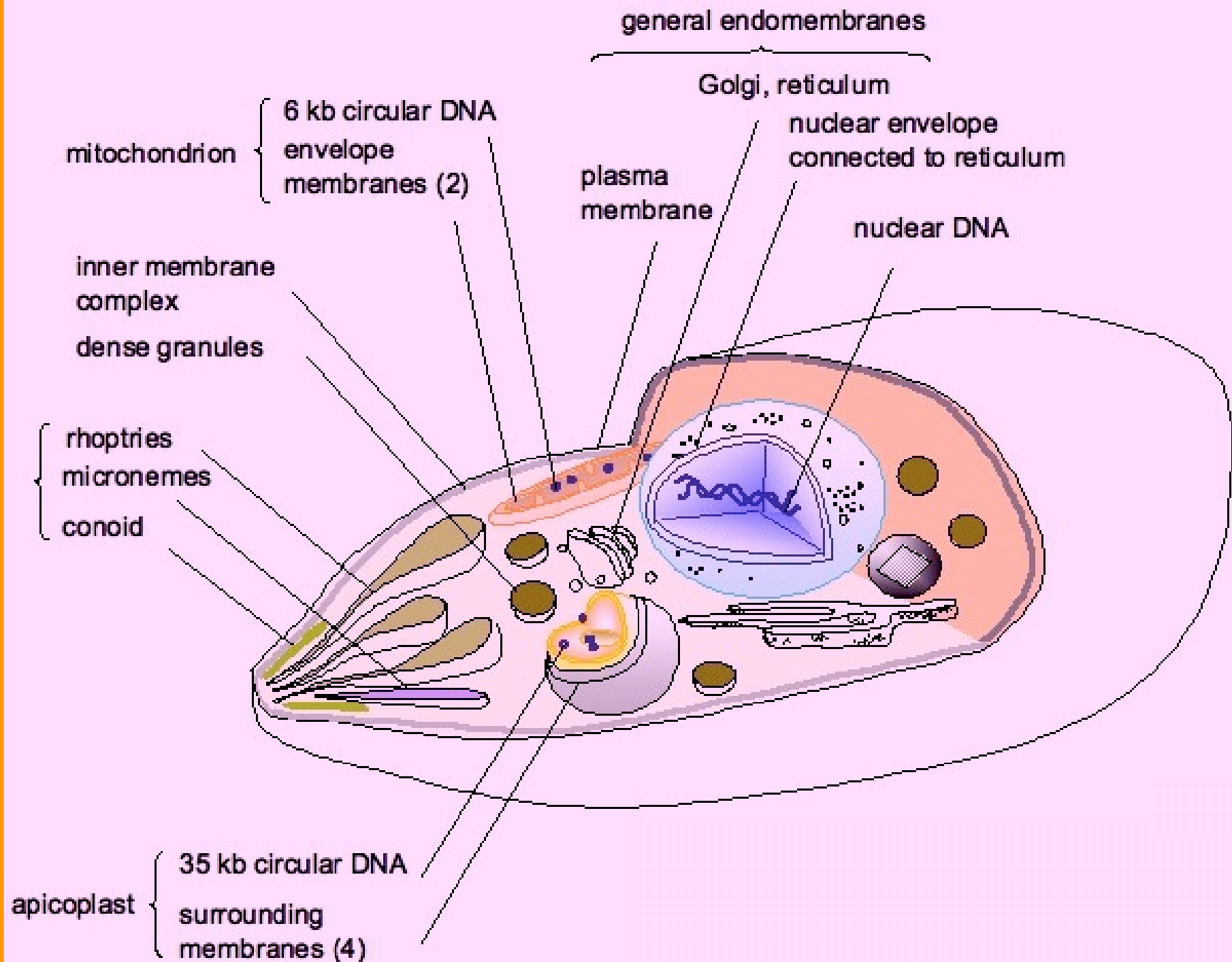
Plasmodium falciparum



Malaria



x = number of membranes limiting the plastids



Apicoplast (the green dots inside the round malaria parasites) is responsible for metabolic pathways for type II fatty acid synthesis, non-mevalonate isoprenoid synthesis and a portion of heme synthesis. It contains an independent genome, encoding prokaryotelike RNA polymerase subunits, 70S ribosomal subunits, tRNAs, and a small number of proteins

Fosmidomycin is an antibiotic that specifically inhibits **DXP reductoisomerase**, a key enzyme in the non-mevalonate pathway and is synergistic with clindamycin against malaria.



Foth, B.J. et al. Dissecting apicoplast targeting in the malaria parasite *Plasmodium falciparum*. *Science* 299, 705-708 (January 31, 2003).

Missinou, M.A. et al. Fosmidomycin for Malaria. *The Lancet* 360, 1941-1942.

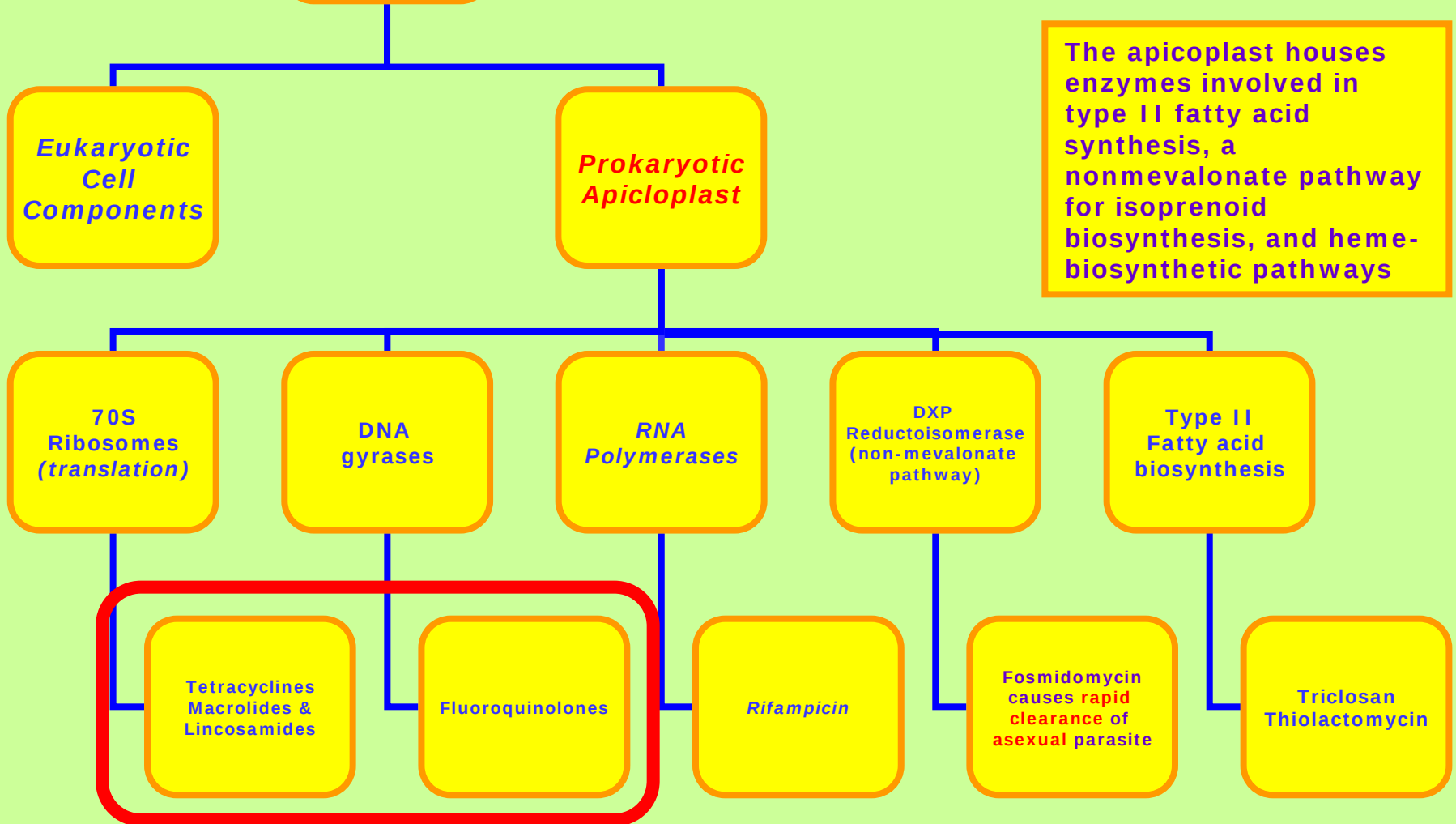
Jomaa, H. et al. Inhibitors of the Nonmevalonate Pathway of Isoprenoid Biosynthesis as Antimalarial Drugs. *Science* 285, 1573-1576.



Antibiotics' targets on Plasmodium

Multiple Antibiotics Exert Delayed Effects against the Plasmodium falciparum Apicoplast

Erica L. Dahl and Philip J. Rosenthal *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*, Oct. 2007, p. 3485-3490



The apicoplast houses enzymes involved in type II fatty acid synthesis, a nonmevalonate pathway for isoprenoid biosynthesis, and heme-biosynthetic pathways

Block expression of the apicoplast genome, resulting in the distribution of nonfunctional apicoplasts into daughter merozoites leading to delayed cell death

Rifampin killed parasites quickly, preventing them from initiating cell division.

Factors favoring spread:

- ➡ At low altitudes
- ➡ During hot seasons
- ➡ In places where the Anopheles mosquito is able to breed in fresh water

Malaria



90 % cases

72 species of anopheles mosquito (♀)

Plasmodium Falciparum

Plasmodium vivax

Plasmodium Ovale

Plasmodium Malariae

**95 %
malarial
Death**

⊙ Malaria is the most common life-threatening infection

- ➡ **1 million deaths/yr**
- ➡ **300-500 million infections/yr**
- ➡ **1 child dies of malaria every 30 seconds**

⊙ ~90% of these deaths occur in sub-Saharan Africa

⊙ Most victims are **children <5 yrs** due to immunity built up in older population (Older people are susceptible when they move from one area and return outside of 6 months)

⊙ **Pregnant women** are also especially vulnerable.

黄帝内经素问

中医古籍名著丛书

黃帝內經素問第十卷內有《瘧論篇》和《刺論篇》等專篇論述瘧疾的病因、症狀和療法，並從發作規律上分為“日作”、“間日作”與“三日作”。

中医古籍出版社



- 2700 B.C. in China, Huang Di Nei Jing has described 瘧 (Nüe) as one form of intermittent fever recurring every one, two or three days.
- Effective treatment of malaria using Qinghao (青蒿 from *Artemisia annua*) was introduced in China by Ge Hong in Jin Dynasty.



Ge Hong 284–363 肘後備急方

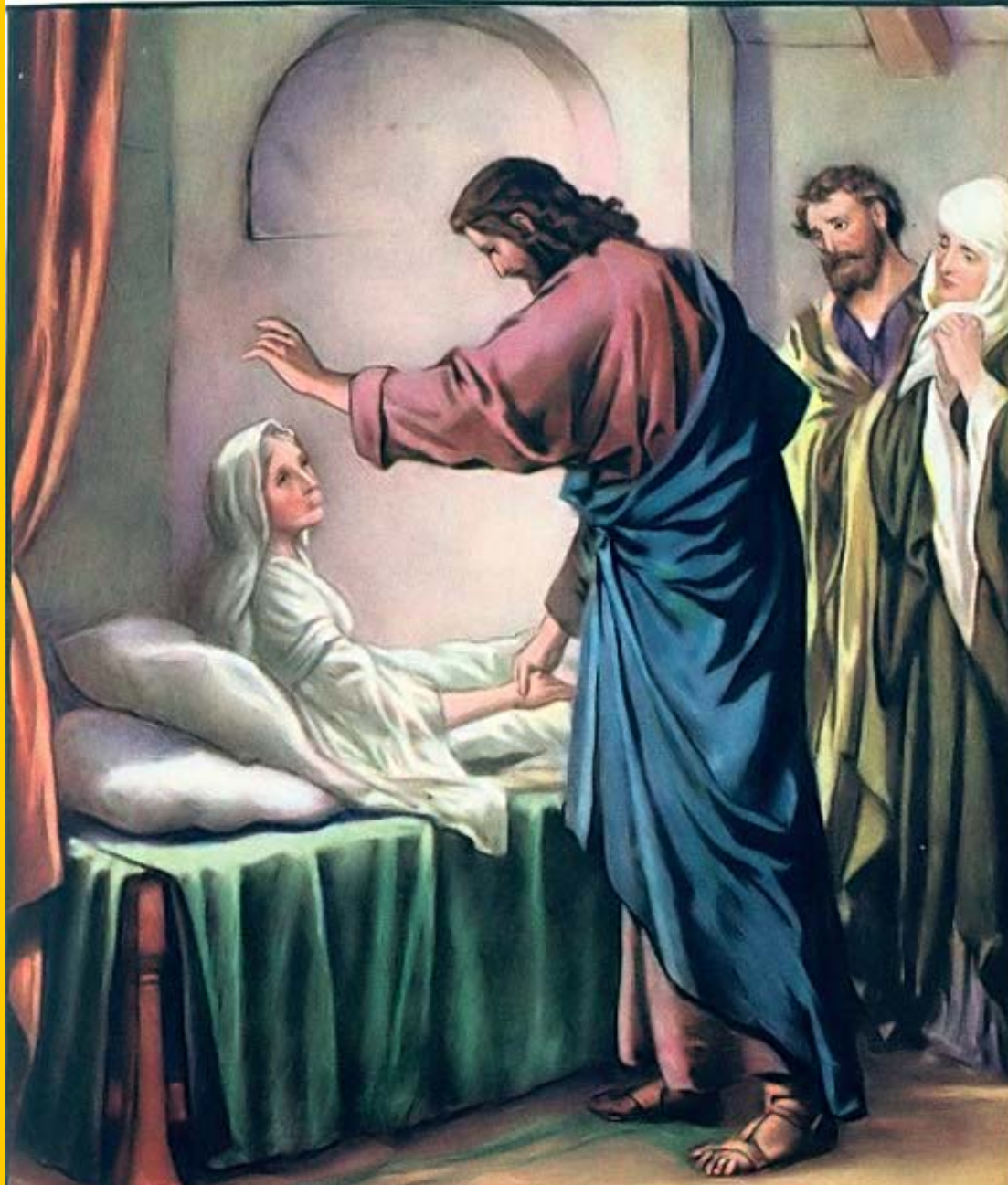


Hippocratic corpus (400 B.C.) distinguished the intermittent malarial fever from the continuous fever of other infectious diseases, and also noted the daily, every-other-day, and every-third-day temperature rise and described the splenomegaly of malaria.

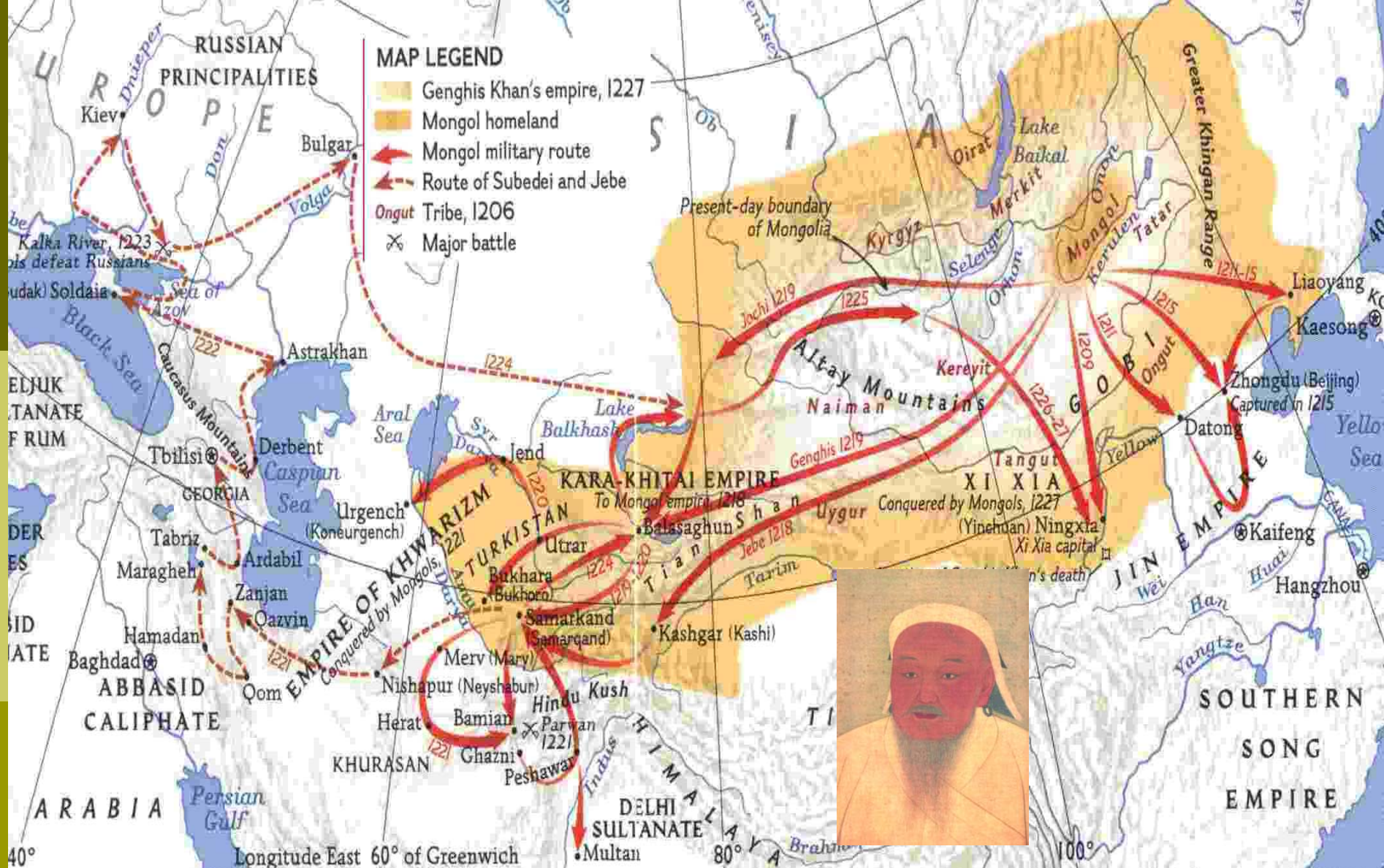
Alexander's Campaigns of Conquest

336-323 B.C.





Matthew (8:14-15) "Peter's mother-in-law was lying sick of a fever"
Malaria is common around the swampy ground around the Lake of Galilee.



Genghis Khan, the Mongol overlord of the 13th Century who set up the largest land empire ever known, is believed to have suffered from a malaria like illness in the spring of 1227, even as he was nursing his injuries. After several months of sickness, the Great Khan died at age 60.



King Charles I, (1600-1649) was beheaded on 30/1/1649



- Oliver Cromwell, Lord Protector, England's first and only dictator died of malaria in 1658

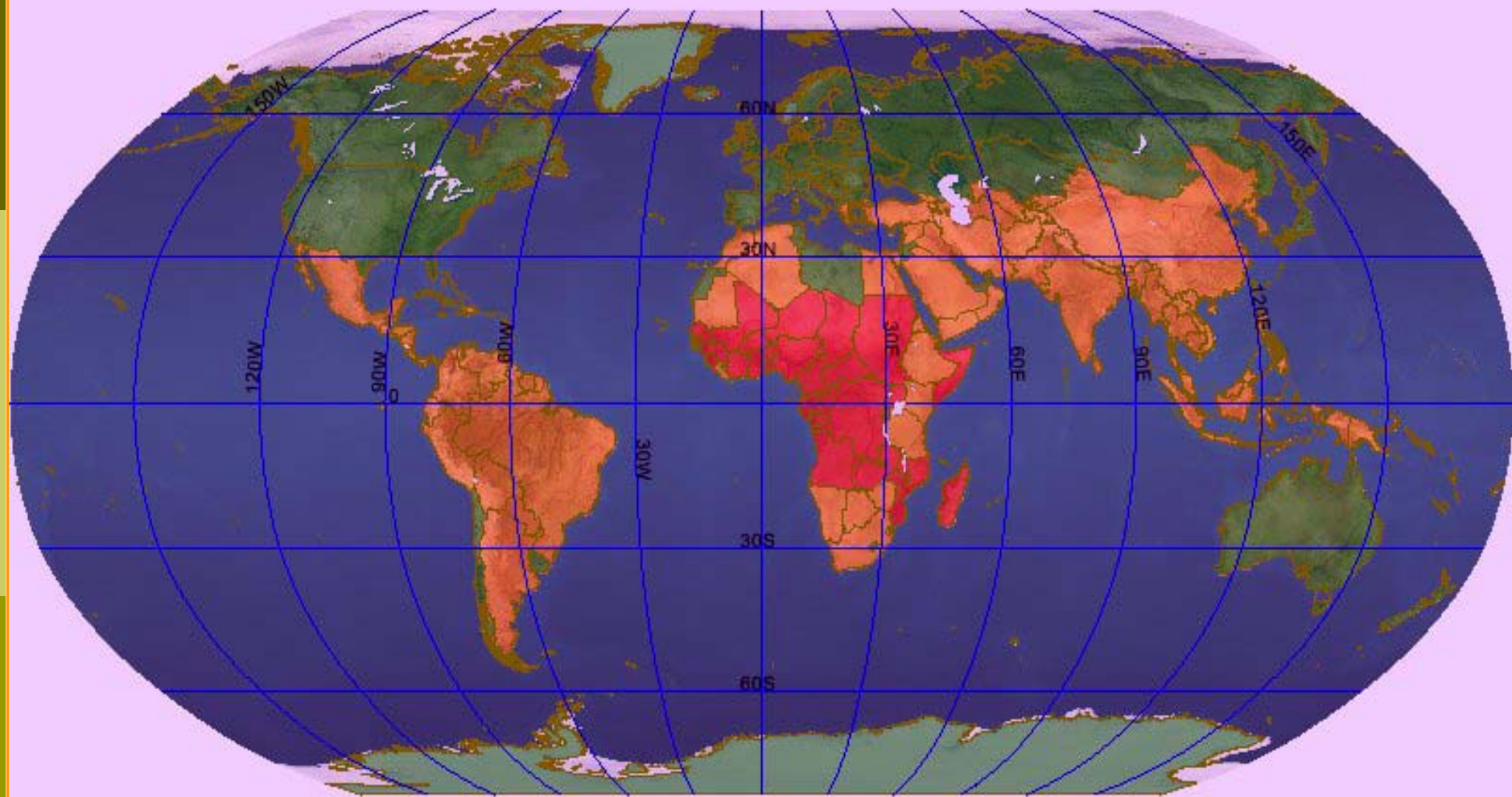
*King John, Constance—lamenting the fate of her son—says
But now will canker-sorrow eat my bud
And chase the native beauty from his cheek
And he will look as hollow as a ghost,
As dim and meagre as an **ague's** fit.”*



*William Shakespeare (1564–1616 mentioned **ague** (malaria) in eight of his plays.
Malaria was an important cause of illness and death in several parts of England.*

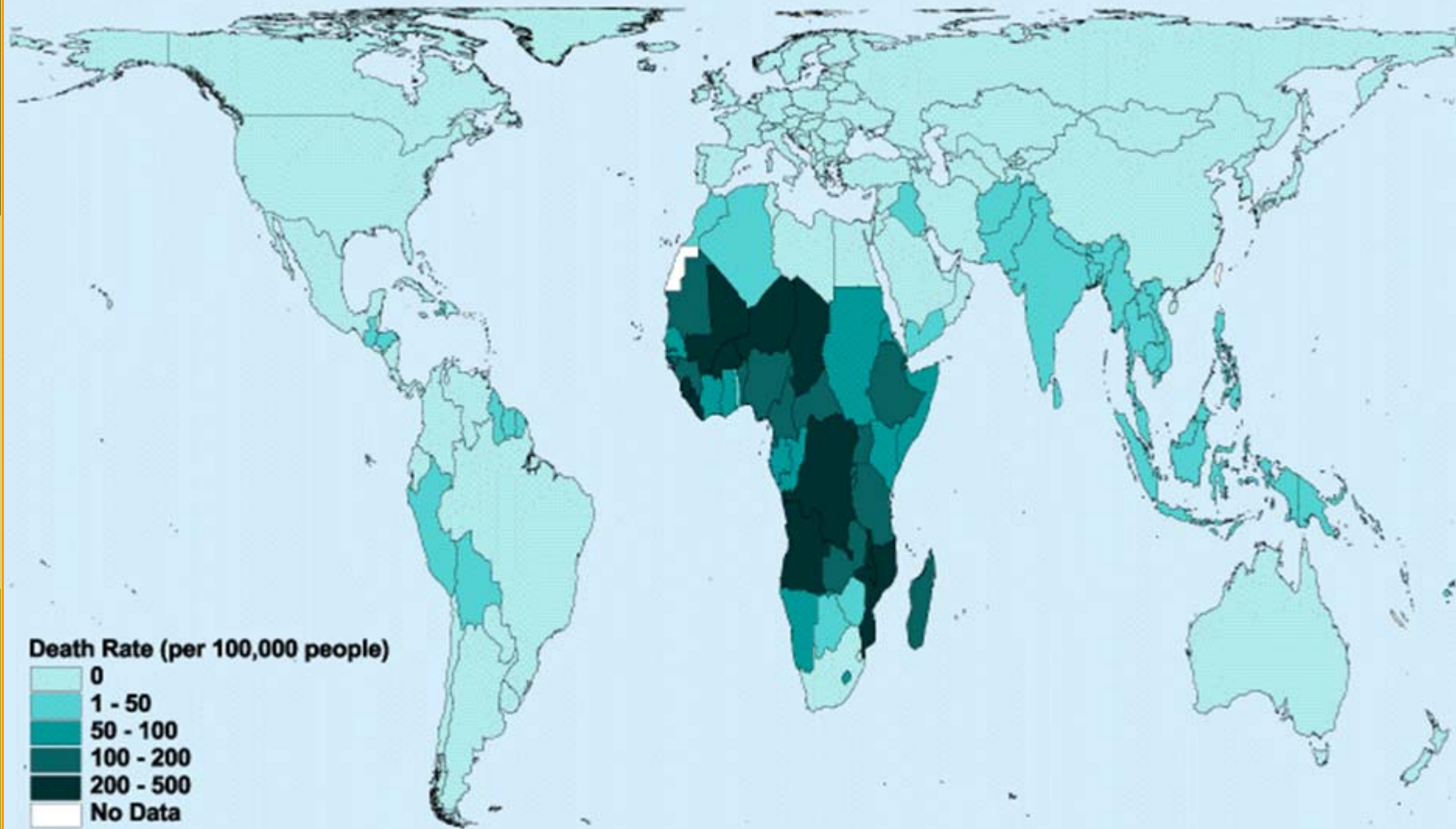
From Shakespeare to Defoe: Malaria in England in the Little Ice Age Paul Reiter Centers for Disease Control and Prevention, San Juan, Puerto Rico

Malaria Worldwide



Green- No known malaria risk
Yellow – Varied malaria risk
Red – Malaria risk throughout country

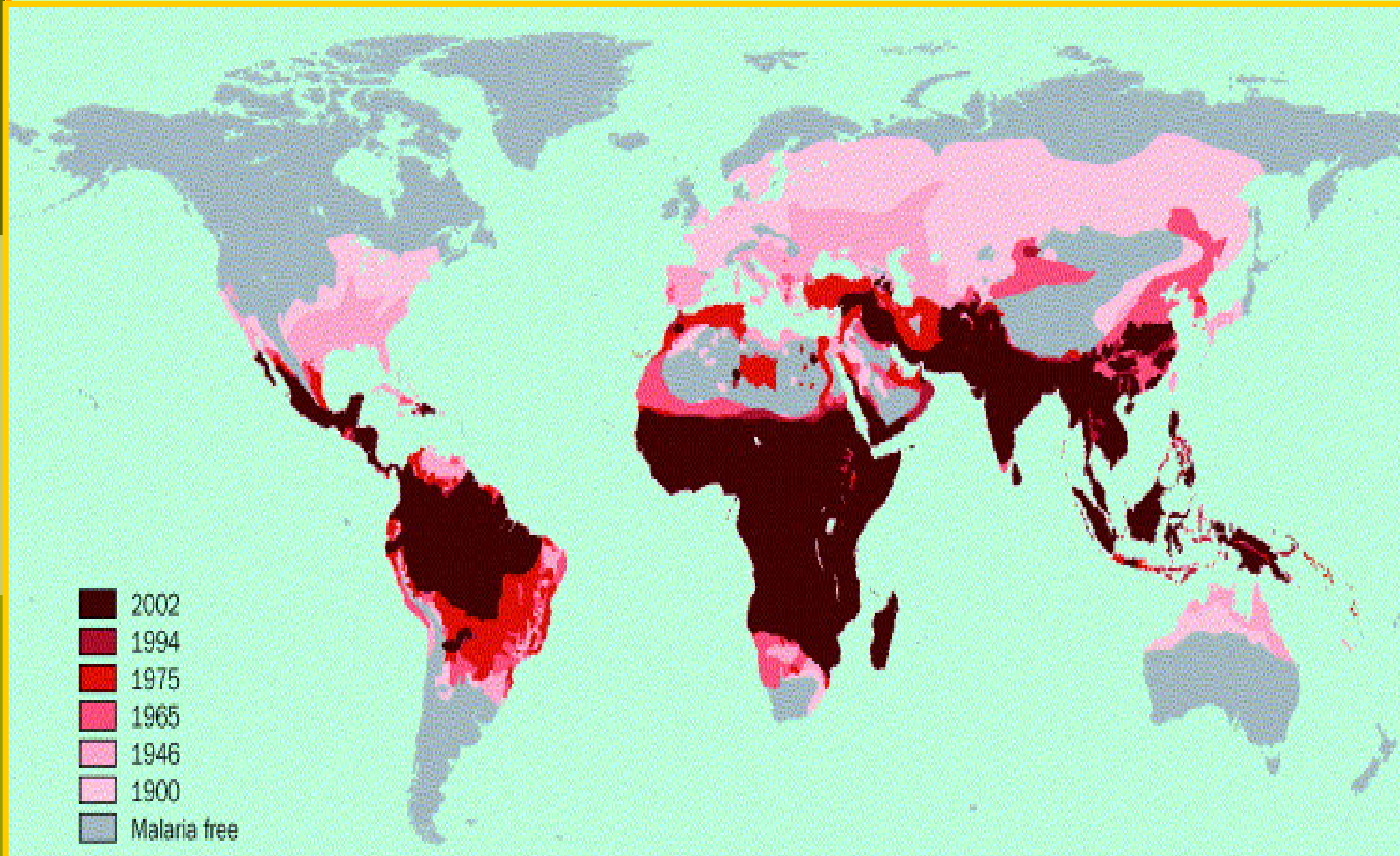
2000: Incidence of Death due to Malaria



UC Atlas of Global Inequality
<http://www2.ucsc.edu/atlas/>
Created 9 April 2003

Data Source: World Health Organization
www3.who.int/whosis

The Contraction of Malarial Zone due to Human Intervention



The global distribution of malaria since preintervention (~1900–2002)

[Hay SI, Guerra CA, Tatem AJ, *et al.* The global distribution and population at risk of malaria: past, present, and future. *Lancet Infect Dis* 2004;4 (6):327–36.]

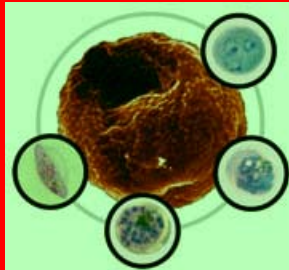
At present, 45 percent of the world has conditions that permit malaria transmission.



15%

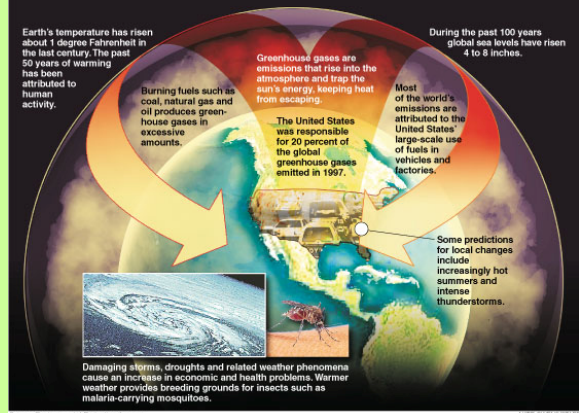
The Intergovernmental Panel on Climate Change estimates that warming of 3° to 5°C could expand the zone of potential transmission to include 60 percent of the globe.

45%



40%

Global warming: Causes and effects



Variations of the Earth's surface temperature: year 1000 to year 2100

Departures in temperature in °C (from the 1990 value)

Observations, Northern Hemisphere, proxy data

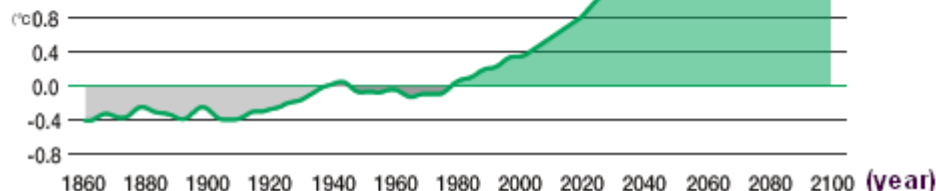
Global
instrumental
observations

Projections

Several models
all SRES envelope

Average Global Temperature Changes
in the Past 140 Years and the Future Forecast

5.8°C



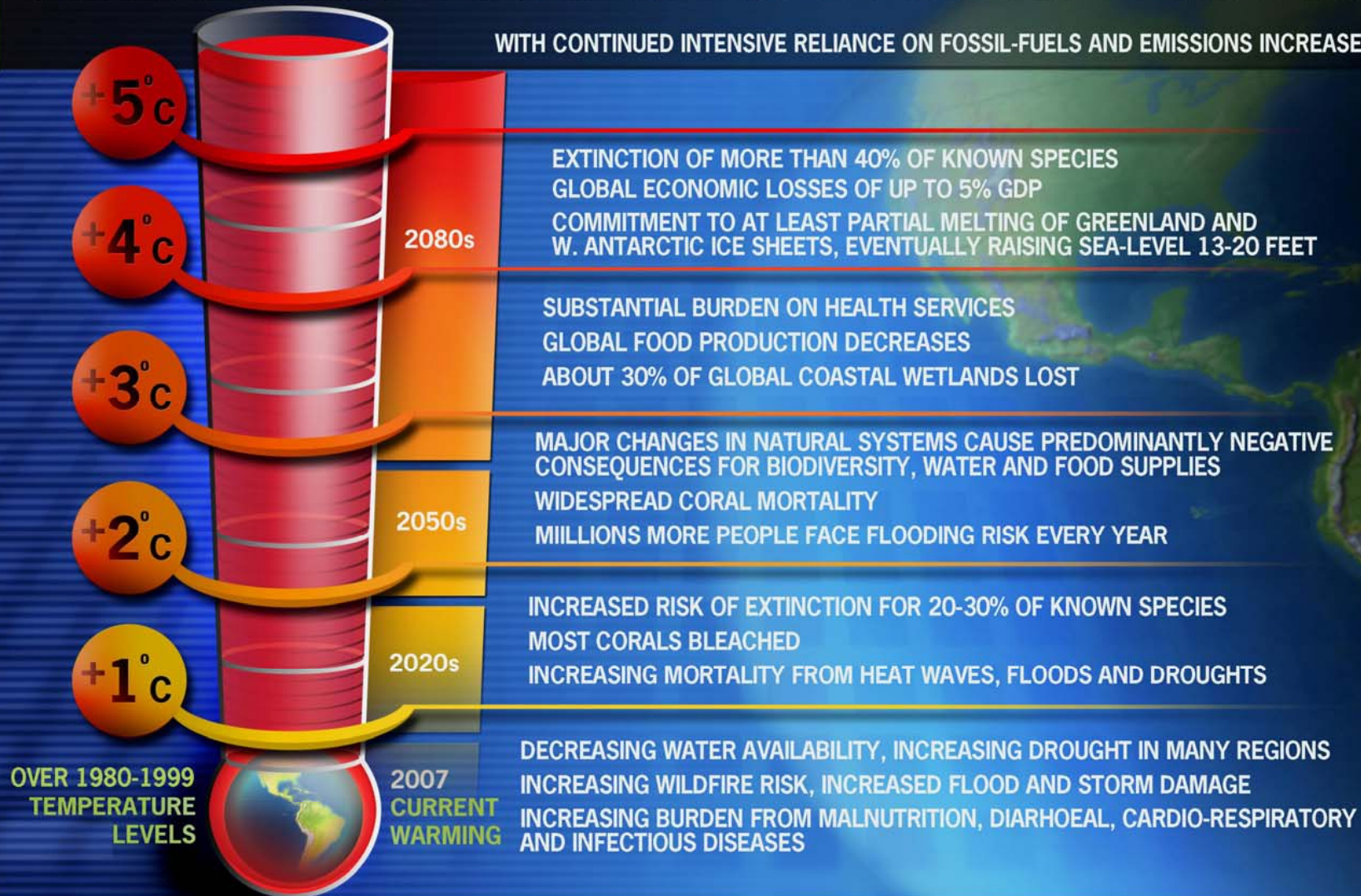
Bars show the
range in year 2100
produced by
several models

Scenarios

- A1B
- - - A1T
- A1FI
- A2
- B1
- B2
- IS92a

RIISING IMPACTS OF GLOBAL WARMING

WITH CONTINUED INTENSIVE RELIANCE ON FOSSIL-FUELS AND EMISSIONS INCREASES

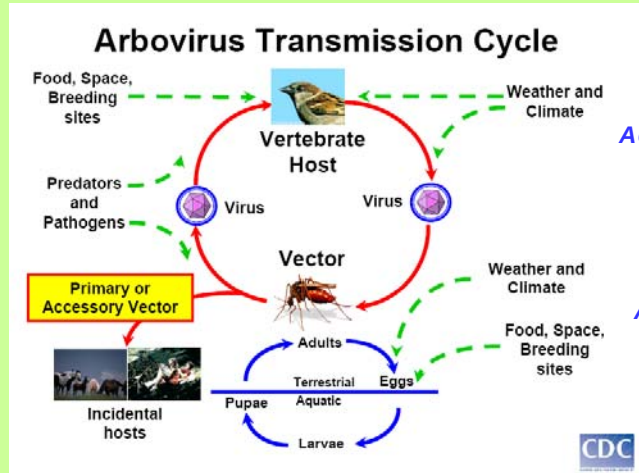


MAJOR VECTORBORNE TROPICAL DISEASES

Impact of Global Warming

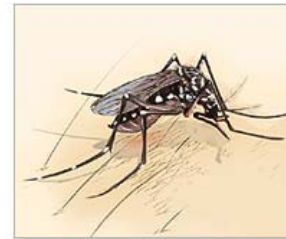
DISEASE	NUMBER OF PEOPLE NOW INFECTED (millions)	POSSIBILITY THAT CLIMATE CHANGE WILL ALTER DISTRIBUTION
Malaria	300-500	Extremely likley
Schistosomiasis	200	Very likley
Lymphatic filariasis	117	Likley
Leishmaniasis	12	Likley
Onchoceriasis (river blindness)	17.5	Very likley
American trypanosomiasis (Chagas' disease)	18	Likley
Dengue	10-30 new cases per year	Very likley
Yellow Fever	<0.005 new cases per year	Very likley

Among diseases that **mosquitoes** spread are West Nile virus, **malaria**, yellow fever, dengue fever, and Arboviral Encephalitides such as Eastern and Western equine encephalitis, St. Louis encephalitis, and La Crosse fever.



Dengue fever is characterized by:

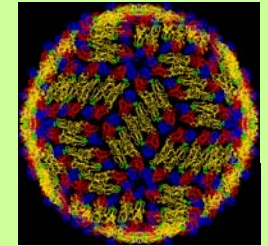
Fever
Rash
Muscle and joint pains



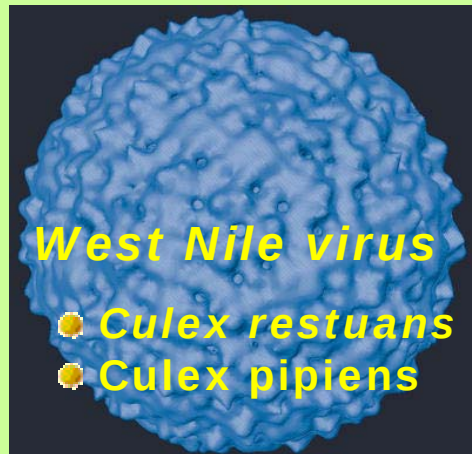
Aedes aegypti mosquito



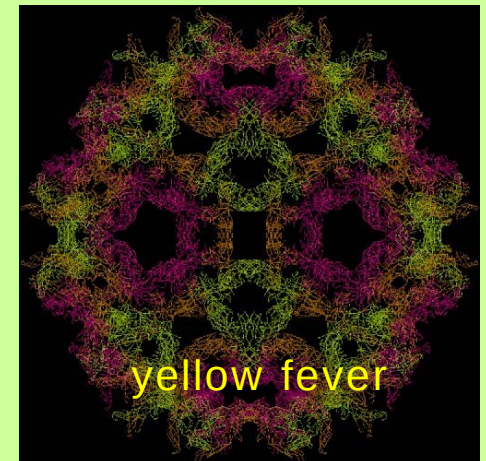
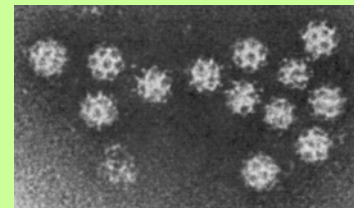
ADAM.



Culex restuans infects primarily birds, but not people, and is dominant in the spring and early summer



Culex pipiens
 $T > 81^{\circ}\text{F}$ (27°C)
Bird $\rightarrow$ human
transmission in
U.S.A.



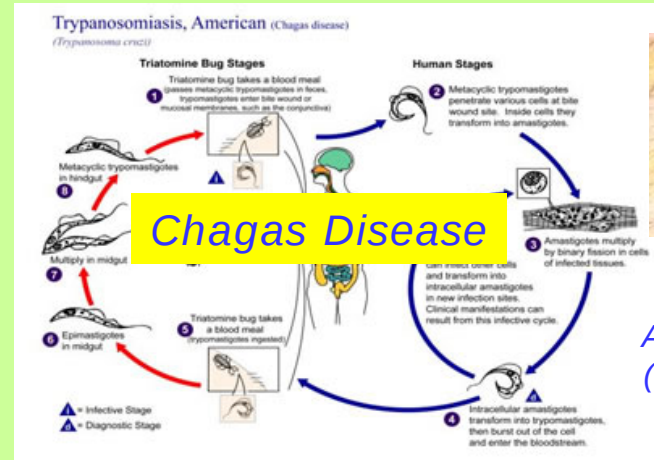
Tropical and temperate regions
Birds $\rightarrow$ humans, horses, and some other mammals

Aedes aegypti

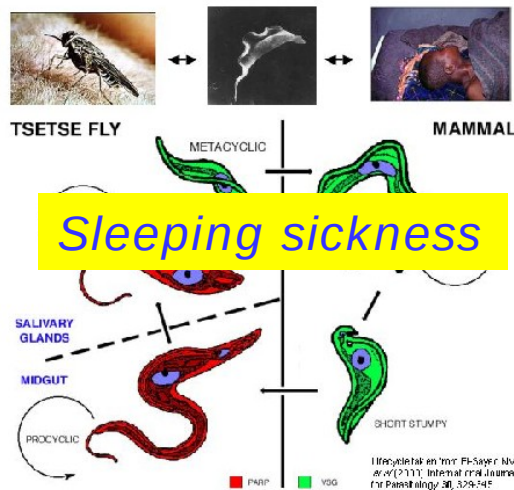
Diseases Due to Global Warming



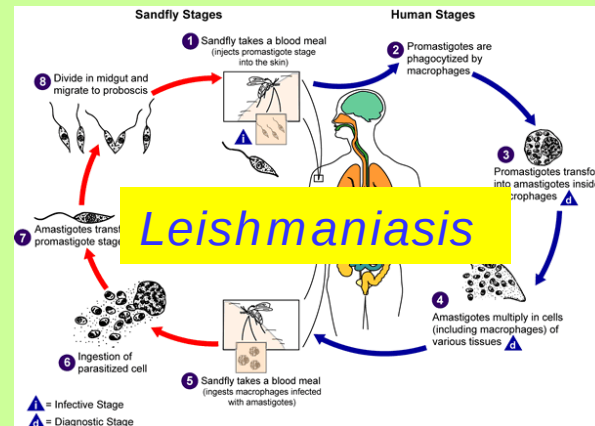
Copepod
繞足動物



Assassin bugs
(or kissing bugs)



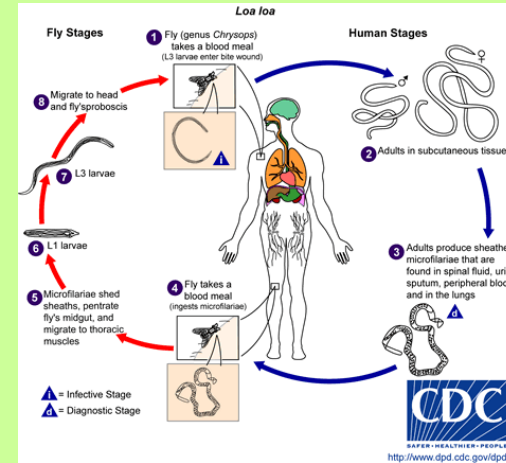
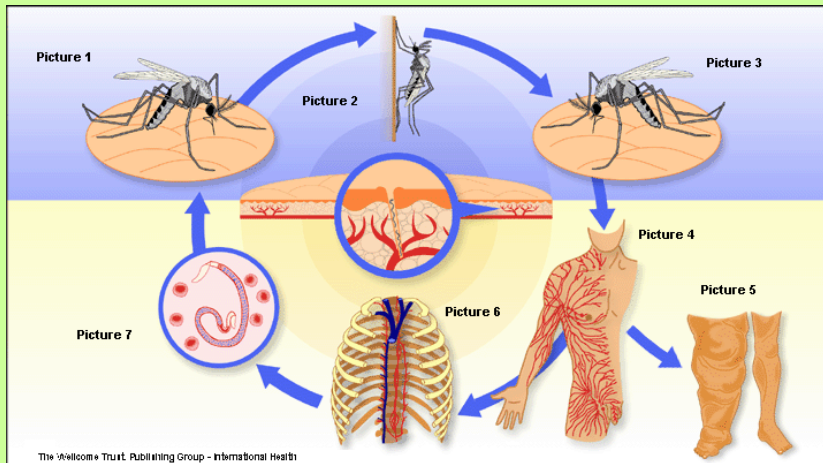
tsetse fly



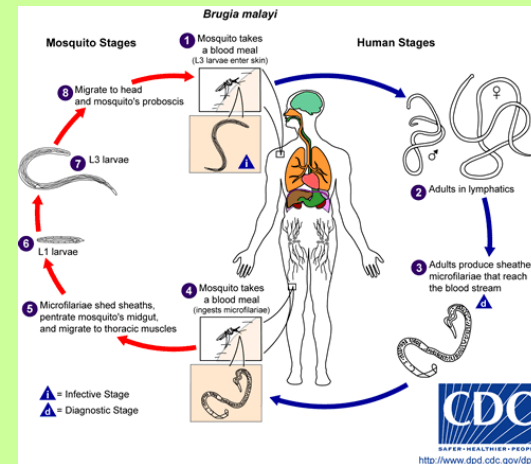
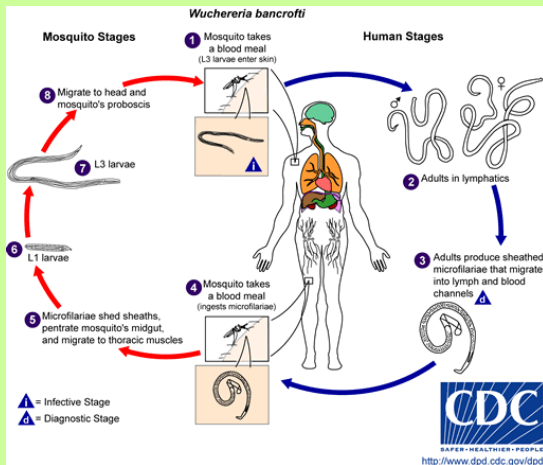
***Phlebotomus dubosci*, a sand fly
WHO/TDR/Stammers**

sand flies

Filariasis



Deer fly



Schistosomiasis 血吸蟲症

Dr.Theodor Bilharz discovered the parasite in 1851 in Cairo

One-sixth of the world's population is at risk
Endemic in 74 countries
200 million persons are infected
Highest prevalence and severity in children

Intestinal 腸道 Schistosomiasis

- ***Schistosoma mansoni*** 曼氏血吸蟲
- ***Schistosoma intercalatum*** 間插血吸蟲
- ***Schistosoma japonicum*** 日本血吸蟲
- ***Schistosoma mekongi*** 湄公血吸蟲

Urinary 尿道 Schistosomiasis

- ***Schistosoma haematobium*** 埃及血吸蟲





2010

towards a malaria-free world



www.rollbackmalaria.org

Photo by Bonnie Gillespie, Johns Hopkins University

Season's greetings!

عيد سعيد!

Felices fiestas!

С НОВЫМ ГОДОМ!

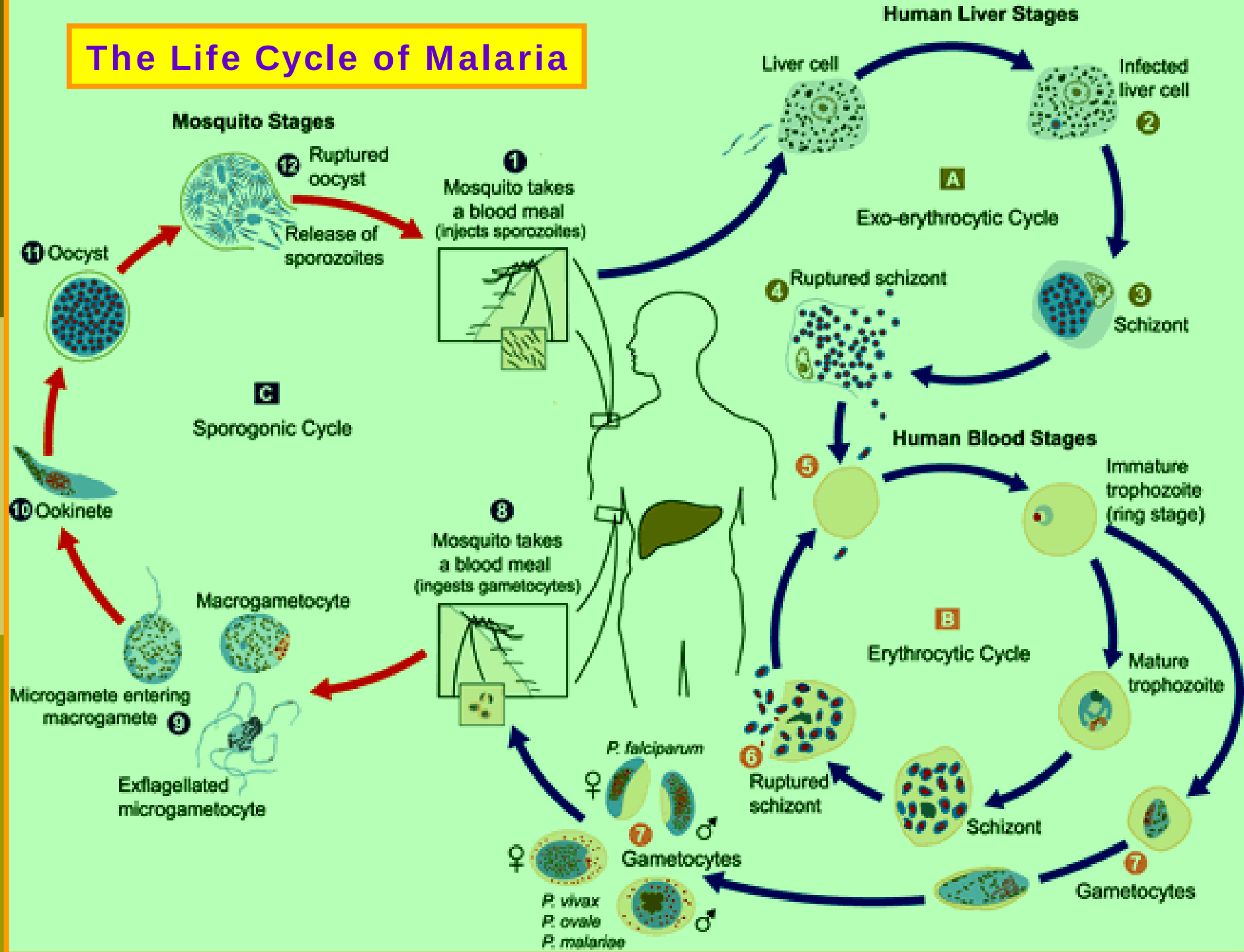
Frohe Festtage!

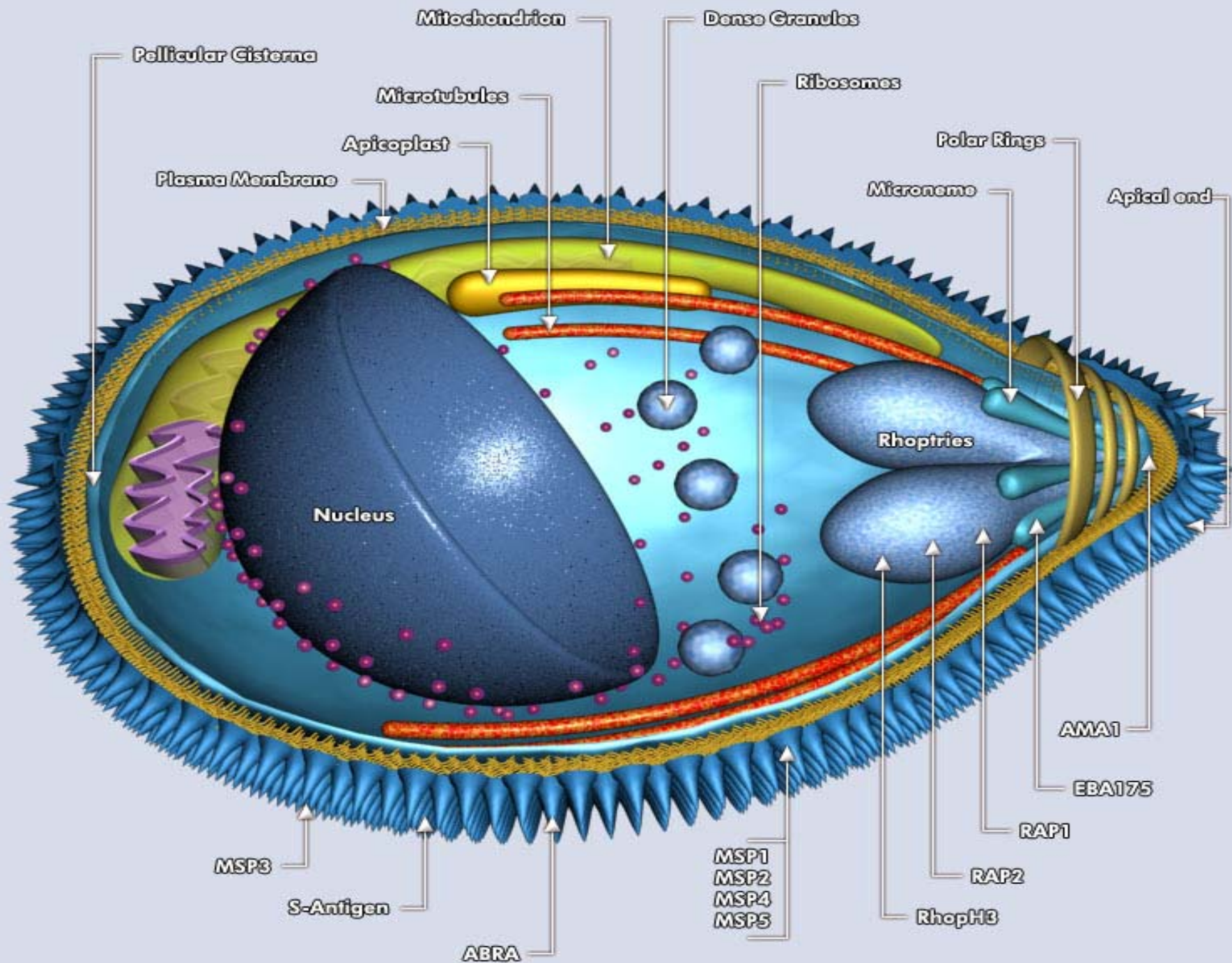
Boas Festas!

Meilleurs vœux !

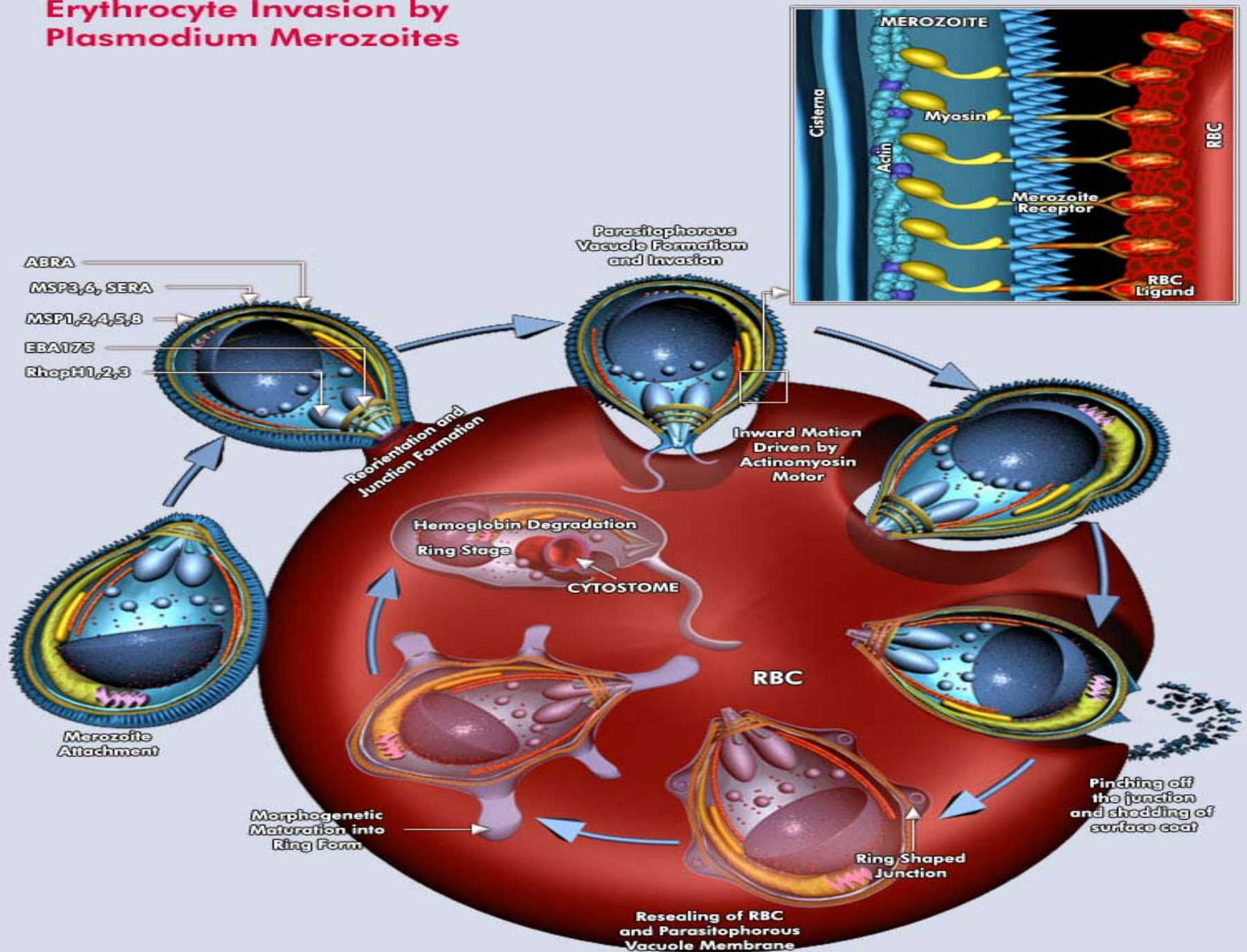
Dewanatil

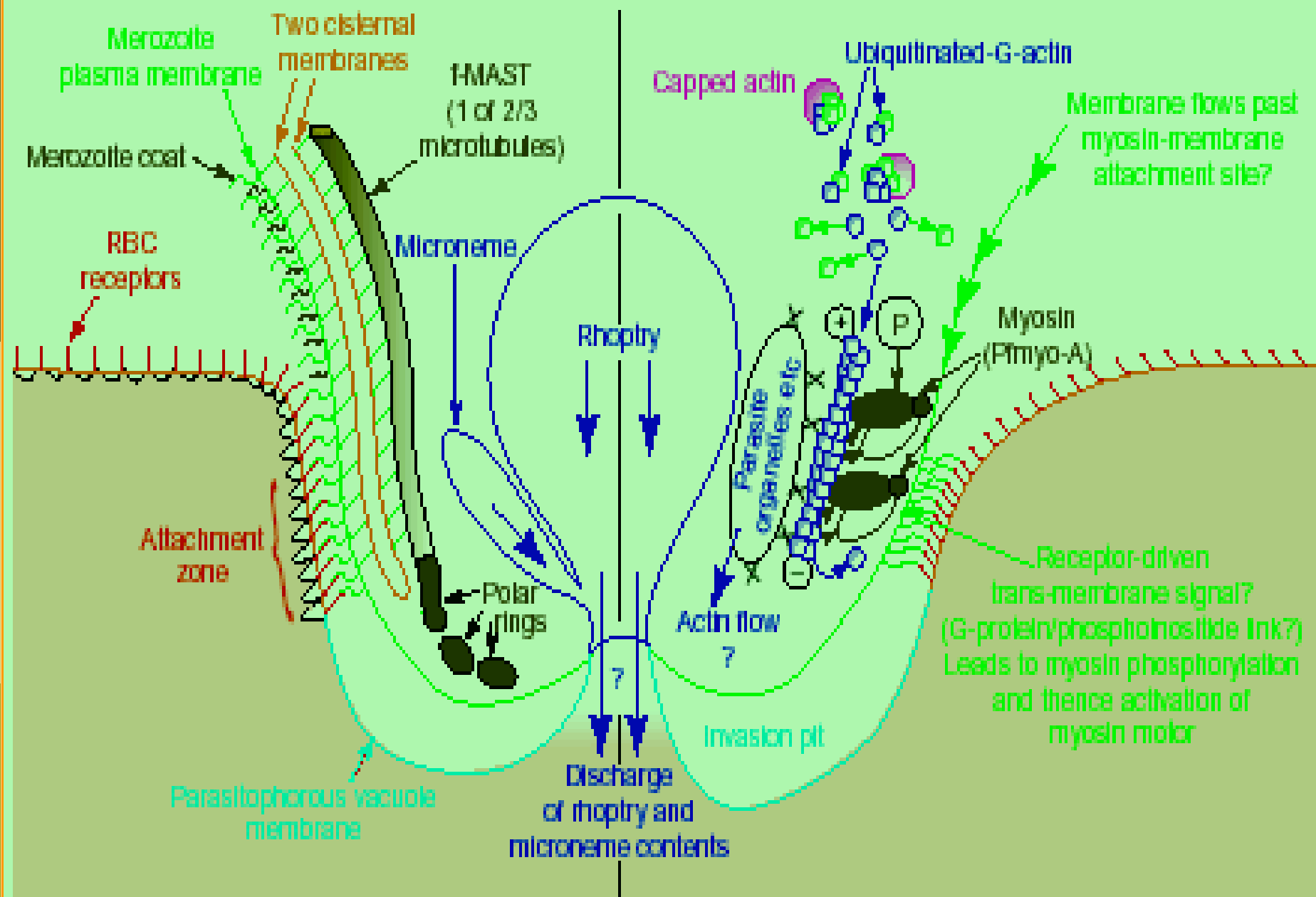
The Life Cycle of Malaria





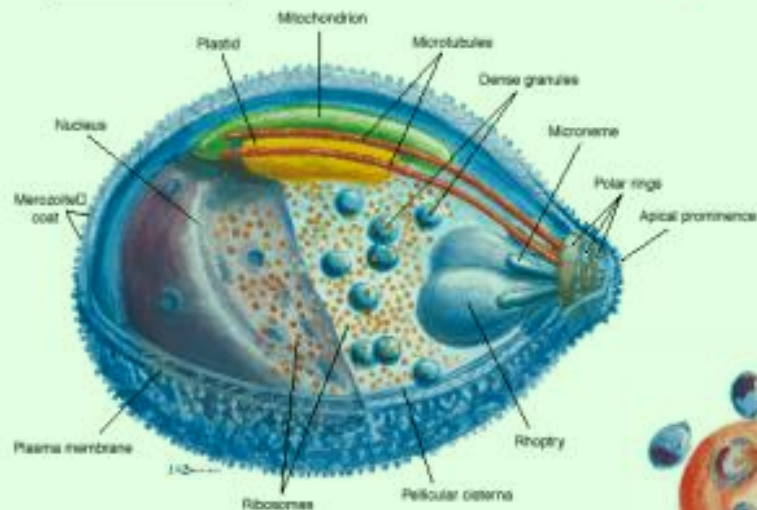
Erythrocyte Invasion by Plasmodium Merozoites



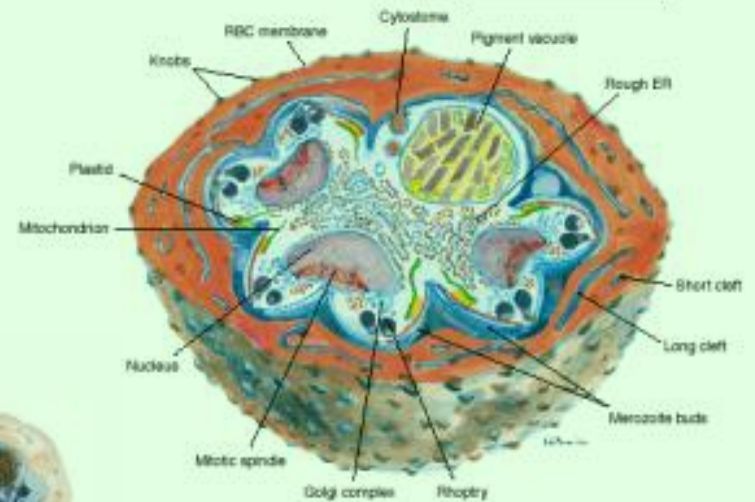


Whole developmental cycle of erythrocytic phase

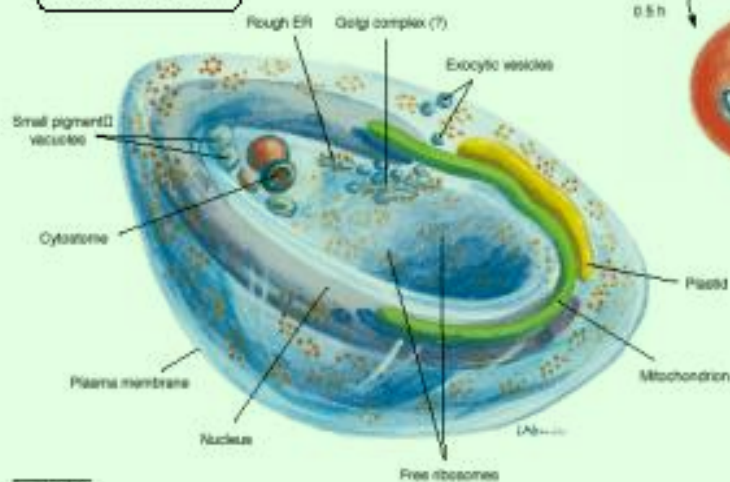
Merozoite



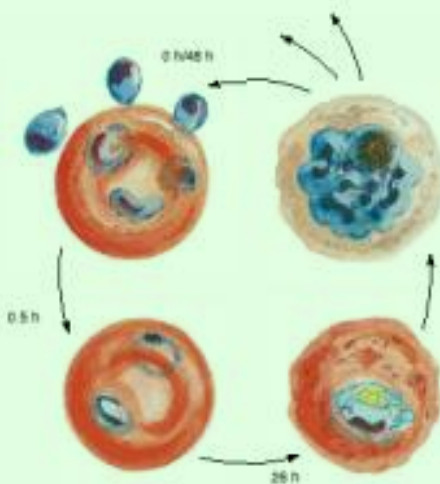
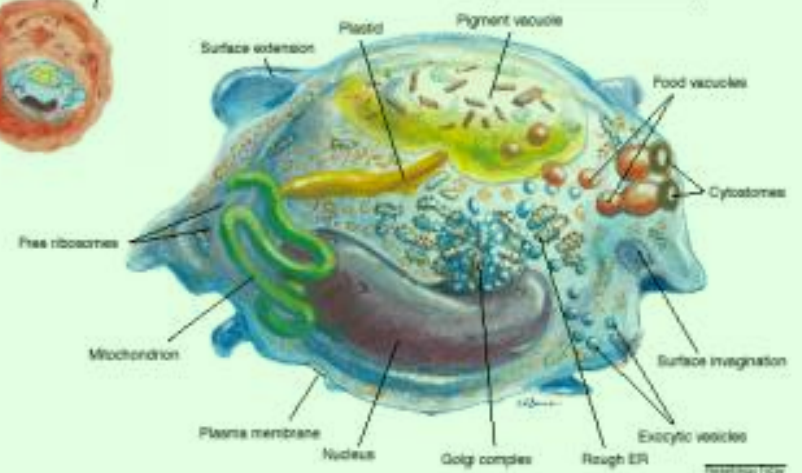
Schizont

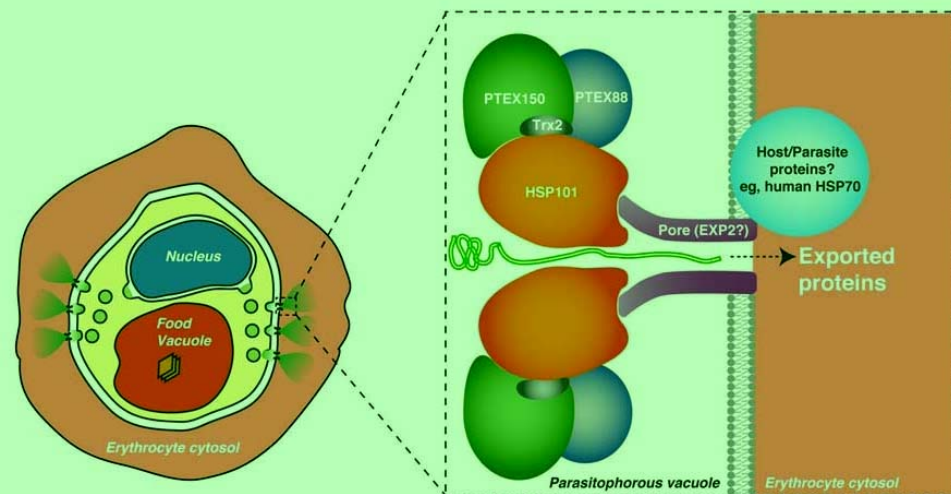
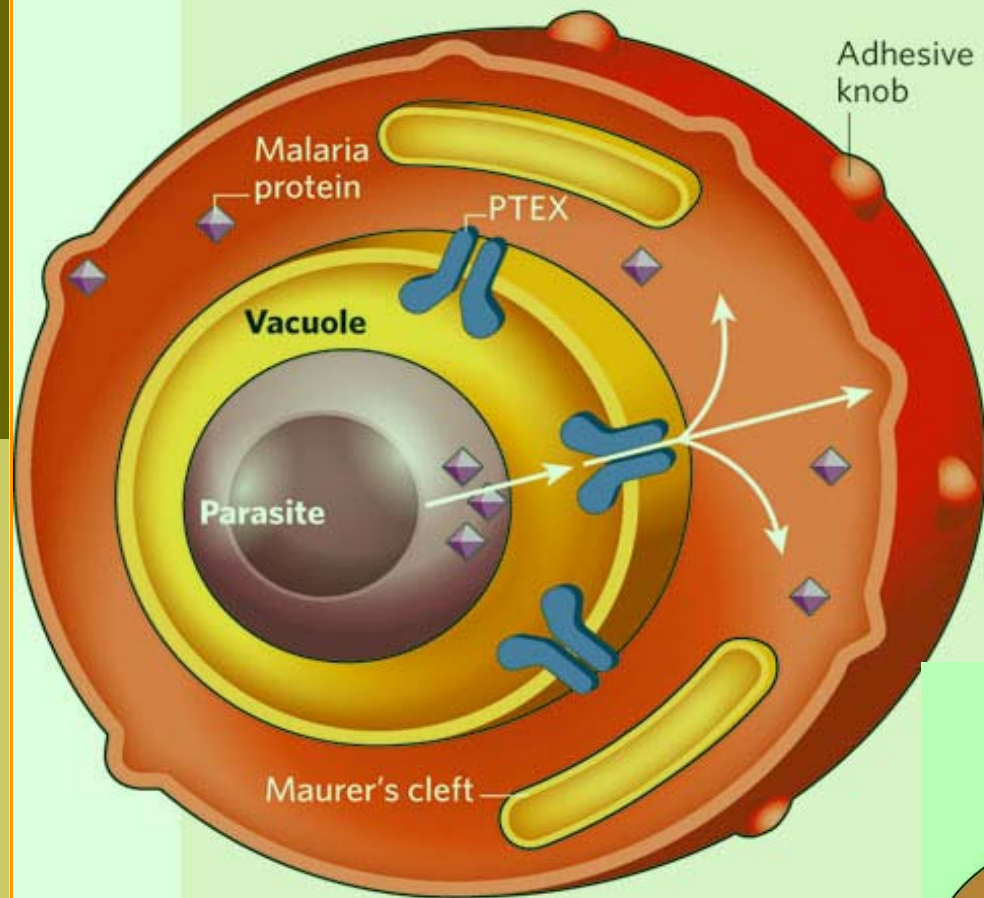


Ring stage



Trophozoite





Plasmodium falciparum parasitizes red blood cells (RBCs) and resides in a specialized vacuole formed during host-cell invasion. A new study³ suggests that the parasite installs a protein complex (PTEX) in the vacuole membrane that enables it to export hundreds of parasite proteins into the RBC cytoplasm. Maurer's clefts and knobs are structures found only in infected RBCs, and their formation and function probably depend on the activity of the exported parasite proteins.

Malaria-carrying female *Anopheles* mosquito tend to bite only between dusk and dawn.

(Image courtesy of James Gathany and the Centers for Disease Control and Prevention)



Plasmodium falciparum-Caused Malaria

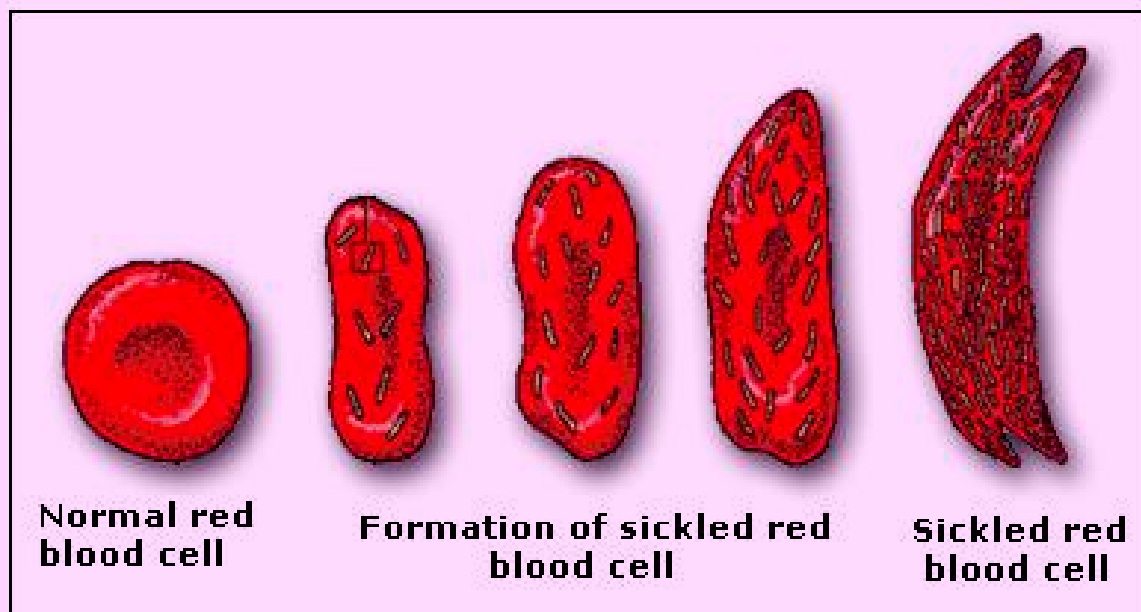
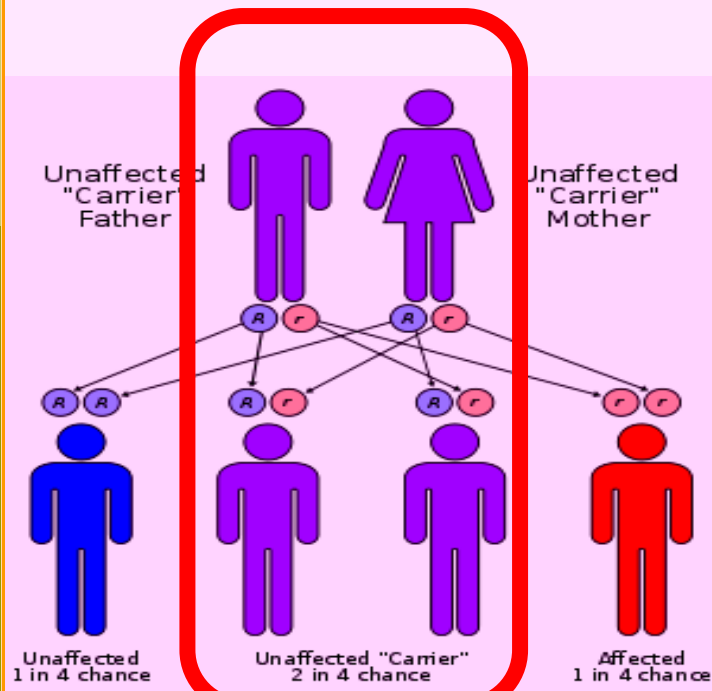
Sickle Cell Allele



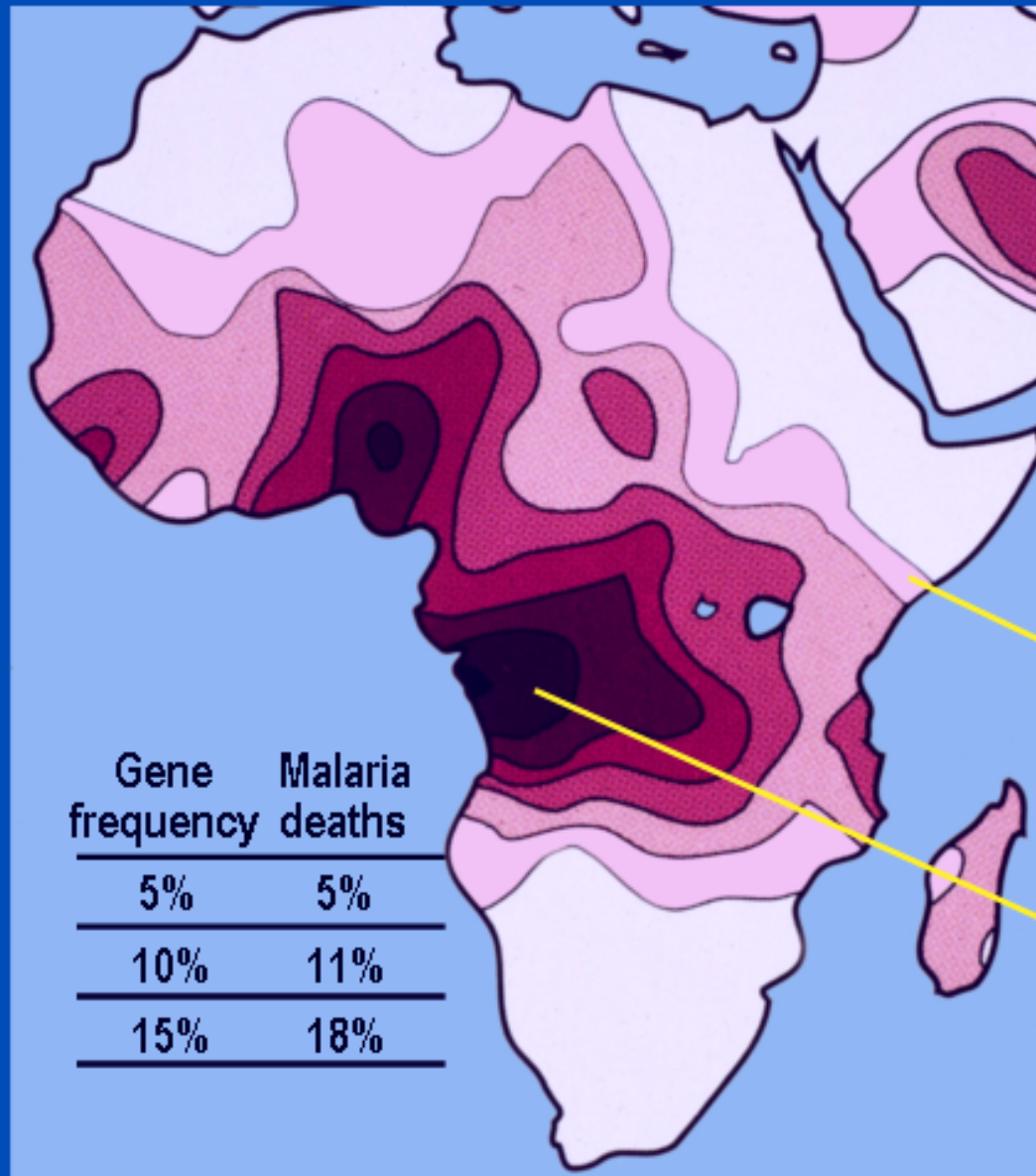
1-10%

10-20%

Gene Frequency



Malaria and Hemoglobin S in Africa



Present Malaria Estimates

500 million cases/yr

1-2 million deaths/yr

3 %

14 %

Sickle Cell Trait and Malaria

- People with sickle cell disease can get malaria just like anyone else. However, people with sickle cell *trait* are less likely to get malaria. The trait doesn't completely protect a person from infection, but it makes death from malaria less likely.

