The Apicomplexans

*Plasmodium* spp.
*Babesia* spp.
*Toxoplasma gondii*
*Isospora belli*
*Cryptosporidium parvum*
*Cyclospora cayetanensis*

All apicomplexans are *obligate intracellular parasites*. This means that they only grow and replicate inside host cells.

Apicomplexans are named for a characteristic group of apical organelles that they use to invade host cells.

Subsets of this diverse group
- coccidia (*Toxoplasma, Cryptosporidium, Cyclospora, Isospora*)
- piroplasms (*Babesia*)
- malarials (*Plasmodium*)
- gregarines (no human parasites)
- haemogregarines (no human parasites)
The Apicomplexa

complex life cycle: both asexual & sexual reproduction
sporozoites infect host
  ➔ **ingested in oocysts**
  (Toxoplasma, Isospora, Cryptosporidium, Cyclospora)
  ➔ **injected by an insect vector**
  (Plasmodium, Babesia)
parasites invade & replicate in host cells ➔ host cells lyse,
releasing parasite to infect new cells ➔ repeated replication
differentiation to **gametes** (1N) ➔ **zygote** (2N) after fertilization
  ➔ **meiosis** to create sporozoites (1N)
in some cases sex is required to make more infectious
organisms (Plasmodium) while in others, it is only one route to
infecting new hosts (Toxoplasma).

The Apicomplexa

classified by:
  • **the apical complex**:
    unique organelles at parasite apex
    used for host cell invasion
    micronemes: secrete proteins for motility & invasion
    rhoptries: secrete proteins to establish a vacuole
    conoid: (some species)
    mechanical aid to invasion
  • **the apicoplast**:
    degenerate chloroplast (plastid)
The Apicoplast

- non-photosynthetic plastid
- plant-like = drug target since we are not biochemically “like” plants
- evolved via secondary endosymbiosis
  Apicomplexan ancestor took up red algae & retained its plastid ancestral genome (>150 kb) \(\rightarrow\) circular 35 kb genome
  new role as plastid (lost ability to photosynthesize)
  encodes \(~30\) proteins, tRNAs & some rRNAs
  ribosomes are present
  nuclearly encoded proteins are imported to plastid
- essential organelle
  inhibited by macrolide antibiotics
  may be involved in lipid metabolism (fatty acid synthesis)
  implicated in heme & amino acid synthesis

Plastids

organelle found in cells of plants, algae & some protozoa
often contain pigments used in photosynthesis (chloroplasts)
site of manufacture & storage of chemical compounds
  photosynthesis (conversion of sunlight into chemical energy)
  starch storage
  fatty acid & terpene synthesis
~50->1,000 copies of a double-stranded, circular DNA genome

thought to have originated from cyanobacteria endosymbiosis
~1500 million years ago
enabled eukaryotes to carry out oxygenic photosynthesis
3 evolutionary lineages differ in pigmentation & ultrastructure
  chloroplasts in green algae & plants
  rhodoplasts in red algae
  cyanelles in the glaucophytes
Complex Plastids

Secondary endosymbiosis creates complex plastids
- Eukaryote engulfs a red or green alga
- Retains the algal plastid →
  - Typically surrounded by >2 membranes
  - May have reduced metabolic capacity

Euglenids & chlorarachniophytes:
- Secondary endosymbiosis of a green alga

Heterokonts, haptophytes & cryptomonads:
- Secondary endosymbiosis of a red alga

Dinoflagellates & apicomplexans: controversial, plastid generally believed to be a secondary endosymbiosis of a red alga

The apicomplexan 'apicoplast'
- No longer capable of photosynthesis
- Is essential to most apicomplexan parasites.
- Promising target for antiparasitic drug development

Some apicomplexans have lost the apicoplast:
*Cryptosporidium parvum* lacks both an apicoplast and full mitochondrion: retains a mitochondrion that lacks a mitochondrial genome (all proteins are encoded by nuclear genes & are imported to this organelle).
Discovery of the Apicoplast

- mysterious organelle surrounded by 4 membranes
- non-mitochondrial circular genome with similar sequences & organization to chloroplast genomes
- lincosamide antibiotics control *Toxoplasma* & *Plasmodium* infections in clinic
- Lincosamides
  - act on prokaryotic-like ribosomes
  - sensitivity based on 50S rRNA sequence
  - Apicomplexan mitochondria are NOT sensitive

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> Discovery of the Apicoplast

- Circular genome is located in the organelle with 4 membranes
  - circular 35 kilobase genome encodes
    - ~30 proteins
    - a full set of tRNAs & some other RNAs
- 35 kb genome rRNA genes are lincosamide-sensitive sequence
- Apicoplast functions are also inhibited by gyrase inhibitors (prevent untwisting of circular genome during replication).
- nuclear-encoded genes with very long signal sequences are imported to this organelle
  - ~500 nuclear-encoded proteins
    - functions include
      - fatty acid synthesis
      - heme synthesis
      - isoprenoid precursor synthesis
Discovery of the Apicoplast

• antibiotics that target global apicoplast functions (transcription & translation) cause a delayed death phenotype
  • parasites die after some time
  • parasites can be treated, the treatment removed but they still die later on
  • *suggests that treatment causes the apicoplast to die & results in death after an essential building block is used up.*

• inhibitors of heme biosynthesis and fatty acid synthesis pathways do not kill parasites

Discovery of the Apicoplast

• In addition to isoprene (rubber), isoprenoid precursors (IPPs) are building blocks for vitamins A & E, & essential precursors for cholesterol synthesis and carbohydrate modification

• Vertebrate IPP synthesis: mevalonate pathway
• Bacteria and apicomplexan parasites: distinct MEP pathway

Cultures of malaria parasites in RBCs in the lab:
• Fosmidomycin inhibits the MEP pathway & kills apicomplexan parasites, like lincosamide antibiotics.
• Adding IPPs to treated cultures rescues them from death
• Rescued parasites lack an apicoplast!
• The only essential pathway in the apicoplast is for IPP biosynthesis: all other pathways are non-essential or redundant with mitochondrial pathways.
The Malarials

*Plasmodium falciparum*
(Welch 1898)

*Plasmodium vivax*
(Grassi & Filetti 1889)

*Plasmodium ovale*
(Stephens 1922)

*Plasmodium malariae*
(Laveran 1881)

~ 300-500 million persons are infected with *Plasmodium*, of whom over 20 million will die during the present decade.

~ 1 million deaths/year of children <5 years of age can be attributed to malaria. *In Africa alone, every hour of the day 120 children aged under 5 years die from malaria. 2 children die per minute = 160 children will die during this lecture.*

40% of the world's population at risk in ~90 countries/territories.

Enormous toll: lives, medical costs & days of lost labor; (*malaria increases poverty*).

Complicated by the spread of parasite drug resistance.
Terms from the documentary- Malaria (Season 1 Episode 2)

Prophylaxis - taking a drug to prevent rather than cure infection
Subsistence farmers: farmers grow only enough food to feed their families. This means there is no extra income for medicine
Paracetamol: acetaminophen
SP: sulfa-pyrimethamine; established antimalarial treatment called fansidar which is less effective due to parasite resistance.
Chloroquine: excellent treatment (low toxicity) for malaria that is no longer useful due to high frequency of parasite resistance.
Artemesinin: active ingredient in traditional Chinese treatment for malaria purified from sweet wormwood plant.
Artesunate: semi-synthetic artemesinin derivative that is water soluble (unlike artemesinin)
Natural product: a drug made by a living organism (ex. penicillin), complicated molecules that are difficult to synthesize in lab.
Zanzibar: a group of islands that is part of Tanzania
Tanzania: East African country; The under-five mortality rate = 118 out of 1,000. Life expectancy = 50 years.

Kill or Cure:
Malaria
Season 1 Episode 2
Malaria kills between one and two million people a year. The two most widely used and affordable drugs now fail in two thirds of all cases because malaria has grown resistant to them. This programme travels to Tanzania to see just how badly new drugs are needed. In Delhi we see how Indian drug companies are getting round the patent laws to produce generic drugs at affordable prices.

http://www.rockhopper.tv/programmes/19/
mosquito-borne infections caused by genus *Plasmodium*
former found throughout much of world (including US)
seasonal outbreaks extend into temperate zones
generally restricted to tropical & subtropical regions
*persistence of mosquito vectors in previously malarious areas could result in reintroduction of these parasites in non-immune populations*

**Malaria History**

• Early writers in China, Syria & India described intermittent fevers, which they attribute to evil spirits
• 5th century B.C. – Hippocrates *classified fever types* as *quotidian* (daily), *tertian* (alternate days) & *quartan* (fever three days apart). He also noticed that those who drank stagnant marsh water had large stiff spleens, a characteristic of the disease.
• Assumed that disease caused by vapors from swamps theories persisted for more than 2000 years
  observation draining of swamps reduced malaria cases
  *(mal aria* means *bad air)*
In 1809, Napoleon flooded Holland to allow malaria to spread (more water = more mosquito vectors). The British Army expedition became so sick between August & October of that year that they were unable to fight the French. >4,000 troops are reported to have died of the disease & another 10,000 could no longer continue with military service. Napoleon said "We must oppose the English with nothing but fever, which will soon devour them all."

• Malaria was endemic in the US until the late 1940's. Most of the transmission occurred in the southeastern states. (This is why the CDC, originally dedicated to malaria control, is in Atlanta, Georgia).
• Eradication by vector elimination: spraying with DDT & draining mosquito breeding grounds.
Malaria in World War II

- World War II → 60,000 US troops died in Africa & the South Pacific from malaria.
- Gen. Douglas MacArthur “This will be a long war if for every division I have facing the enemy I must count on a second division in hospital with malaria & a third division convalescing from this debilitating disease!”
- Dr. Seuss & other artists involved prepared informational brochures for the military.

Plasmodium Life Cycle - Humans

biology of different *Plasmodium* spp. is similar

- **asexual** stages develop in humans
  - first in the **liver** (*liver sporozoites*)
  - then in the circulating **erythrocytes** (*merozoites*)

- **sexual** stages develop in mosquito (gut & salivary glands)

asexual stages in humans:
- infected female *Anopheles* mosquito takes blood meal
- injects salivary fluids containing sporozoites into wound
- sporozoites eventually find liver parenchymal cells
- *route sporozoites follow to liver has not been established*
- sporozoites replicate in liver → merozoites → infect RBCs
- some merozoites differentiate into gametocytes
- gametocytes in RBCs are ingested by mosquito in blood
Plasmodium Life Cycle

gametocytes in RBCs are ingested by mosquito in blood →
Macro- and Micro- gametes form (1N)
  sperm-like microgametes (motile)
  each microgamete can fertilize a macrogamete

→ resulting zygotes (2N) elongate into oozoites (2N)
  penetrate gut wall to lie under basement membrane
  transform into oocyst
  (within 24 hours of ingestion of blood meal)

Oocyst develops into sporozoites (1N)
  >1,000 sporozoites
    mature in 10-14 days
    invade salivary glands

mosquito bites another human host to start a new infection
Microgamete exflagellation -- each flagella is a male gamete.

Portion of an infected mosquito stomach. Note numerous oocysts on outer wall.

**Exoerythrocytic Stage Malaria**

Sporozoites introduced into human by bite of infected mosquito → exocytic schizogony: asexual division inside liver cells → creates merozoites (smaller & specialized to invade RBCs)

Liver stage infection is symptomless, RBC stage causes pathology

Length of exocytic phase & number of progeny is characteristic of species

- *vivax*: matures within 6-8 days  
  sporozoite produces ~10,000 merozoites
- *ovale*: matures within 9 days  
  sporozoite produces ~15,000 merozoites
- *malariae*: matures within 12-16 days  
  sporozoite produces ~2,000 parasites
- *falciparum*: matures within 5-7 days  
  sporozoite produces ~40,000 merozoites

Given these properties, which malaria species is most pathogenic? How about least pathogenic?
Malaria Erythrocytic Phase

Merozoites released from liver schizonts invade RBCs
merozoite-RBC attachment: receptors on parasite & RBC
RBC rapidly deformed →
parasite induces invagination of RBC membrane
forms *moving junction* between parasite & host
intracellular parasite lives in parasitophorous vacuole
membrane bound
vacuole grows as parasite grows & replicates

Transmission EM of a merozoite entering a red cell. Note points of attachment.

Malaria Erythrocytic Phase

Merozoite invades → intracellular parasite growth
RBC hemoglobin is degraded for nutrients
toxic heme is polymerized into pigment called *hemizoin*
forms a ring-like trophozoite (enlarges to fill red cell)
nuclear division → *schizont* (multiple nuclei)
cytokinesis produced individual merozoites
cycle completed with red blood cell rupture & merozoite release
• free merozoites invade other erythrocytes
• asexual cycle is characteristically synchronous & periodic
tertian periodicity: complete invasion to RBC rupture cycle in 48 hours (*falciparum*, *vivax* & *ovale*)
quartan periodicity: 72 hours for completion (*malariae*)

“Troph” = eating → trophozoite is the “eating cell”
“Schizo” = split → schizont is the “dividing cell”
Free Heme is Toxic!

Free heme effects:
Proteins
- oxidation
- covalent cross-linking
- aggregation
Lipid
- intercalation/disruption of bilayers
- cytotoxic lipid free radicals
DNA
- damage through oxidative stress

Free heme is toxic to cells, so parasites (Plasmodium & Schistosoma) convert it to an insoluble crystalline form called hemozoin. In malaria parasites, hemozoin is often called malaria pigment.

Plasmodium RBC Stage Development
The Erythrocytic Cycle

1. Merozoites attach to & invade mature human red blood cells (RBCs)
2. The merozoite develops into a ring stage parasite (24 hours)
3. The ring stage parasite develops into a trophozoite (24–36 hours)
4. Multiple nuclear divisions without cytokinesis produce schizonts (24–36 hours)
5. Each nucleus is encased by a developing merozoite (40 hours)
6. The RBC ruptures, releasing 16–32 daughter merozoites (48 hours)
Plasmodium Erythrocytic Cycle

- The stages of erythrocytic (RBC) development are cell cycle steps.
- Each species has small differences in morphology that allow experts to determine which species is infecting the patient.

<table>
<thead>
<tr>
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<th>ovale</th>
<th>malariae</th>
<th>falciparum</th>
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<td>Schizont</td>
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~48 Hours

trophozoite
late schizont
ring stage
merozoites
**Plasmodium falciparum**

- Aestovoaumnal, malignant tertian (2 day fevers)
- Tropical & subtropical regions
  - primary cause of malaria in sub-Saharan Africa
  - blood smear diagnosis
    - small ring stage parasites
    - infected erythrocytes *not* enlarged
    - multiple infections of a single RBC are common
- **sequestration**: trophozoites in RBCs are retained in capillaries (*heart, brain, spleen, skeletal muscles & placenta*)
  - maturing parasites absent from peripheral circulation

**Sequestration**

- Appearance of more mature asexual stages in circulation indicates increased disease severity

**Plasmodium falciparum**

- Sporozoites injected during second blood meal
- Gametocytes injected during first blood meal
- Macrogametocyte
- Microgametocyte
- "Signet" ring stage in portal blood
- Erythrocytic cycle
- Deep vascular schizogony
- P. falciparum gametocyte
- P. falciparum schizont in RBC
**Plasmodium vivax**

- benign or tertian malaria  
  *vivax* infected RBCs are enlarged  
  blood smear diagnosis  
  **Shuffner’s dots**: RBC membrane is stippled  
  *all stages of the parasite present in peripheral circulation*  
  single infections of RBCs are characteristic

- classic relapsing malaria → **hypnozoites** in liver allow for re-emergent infection (latency)  
  relapses can occur from a few weeks to up to 5 years

- **recrudesces** due to persistent circulating erythrocytic parasites
**Plasmodium ovale**

- Most recently described species of human malaria
- Tropical Africa & discrete areas of Western Pacific (West Africa, Philippines, eastern Indonesia & Papua New Guinea)
- Clinically similar to *vivax* malaria but less severe
- Relapses (similar to *vivax* malaria)

**Diagnostic features:**
- Crenated appearance of infected red cells.
- No more than 12 nuclei in schizont
- Enlarged infected RBCs

**Plasmodium malariae**

- Known as quartan malaria (*3 day fever intervals*)
- Wide but spotty distribution throughout world
- Slow development in mosquito
- Human infection is not as intense as other *Plasmodium* spp.
- Does not relapse
- Recrudescence from chronic erythrocytic infections
- Can persist at a low level in human host for decades

**Diagnostic features:**
- No RBC enlargement
- 8-12 merozoites in schizont

(P. ovale trophozoite - note "crenated" appearance of infected red cells.)

(P. malariae trophozoite.)

(P. malariae schizont (Note that infected and uninfected RBCs are the same size.))
Simian Malarias

*Plasmodium* spp. parasites of chimpanzees & monkeys occasionally infect humans

*reports of human infection with parasites from monkeys becoming common with ability to differentiate morphologically similar human & simian parasites at molecular level*

- disease is relatively mild
  - quotidian fever (24 hour cycle) caused by *P. cynomolgi*
  - vivax-like malaria caused by *P. knowlesi*

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Malarial Relapse & Recrudescence

**Relapse**: reappearance of parasitemia following adequate drug therapy

**Hypnozoites**: latent exoerythrocytic forms that persist in liver

- some sporozoites fail to develop in liver
- can remain latent in liver as long as 5 years
- delayed development → new merozoites → relapse

*to cure it is necessary to destroy merozoites & hypnozoites*

- ovale and vivax develop hypnozoites → treat to kill hypnozoites
- *falciparum* & *malariae* do not develop hypnozoites (can’t relapse)

*Falciparum* & *malariae* do **recrudesce**: continuation of RBC cycle

- *P. falciparum* can recrudesce for 1-2 years
- *P. malariae* can recrudesce for >30 years

*both infections → cure with drugs that eradicate parasites in peripheral circulation (no need to kill hypnozoites)*
Kill or Cure:
Malaria
Season 3 Episode 5

In Mulago hospital in Kampala, Uganda, 30% of all admissions are due to malaria, and it is the highest cause of death amongst patients. The parasite is becoming resistant to the standard treatments, and infecting children of younger ages. More worryingly, however, some mosquitoes are becoming immune to the insecticide commonly used on mosquito nets. Kill or Cure investigates how scientists are also adapting to meet these new threats.

http://www.rockhopper.tv/programmes/55/

Terms from the documentary - malaria (Season 3 Episode 5)

Uganda: in East Africa, one of the world's poorest countries. 1971-9
Idi Amin's dictatorship -- 300,000 deaths & devastated economy.

- Infant mortality = 79 /1,000
- Life expectancy 49-50 years
- 8 physicians/100,000 persons
- GDP = $453./year

Yellow eyes: RBCs destroyed by parasites release hemoglobin, which causes jaundiced appearance in whites of eyes.
Anemia: decreased RBC count, in this case due to malaria.
Quinine injection: effective but toxic treatment for malaria; some parasites are resistant to this drug.
Suppository: drug delivery system that is inserted into the rectum where it dissolves. Artesunate is delivered this way in documentary.
Artemether-Lumefantrine: Coartem combination therapy.
fever, chills & sweating
rupture of infected RBCs release pyrogens (cause fever)
general malaise, myalgia & headache
characteristic periodicity of fever based on synchronous infection
early phases of infection often not synchronous
severe falciparum malaria may be continuously febrile

The length of time between episodes of fever represents the time it takes for merozoites to infect RBCs and to replicate before lysing the erythrocyte.

This is reflected in the quartan versus tertian descriptions for individual Plasmodium species.

Malaria Pathogenesis

Cytoadherence: infected erythrocytes adhere to endothelium – knobs on infected RBC surface attach to capillary endothelium
knobs enhance binding
made of parasite proteins exported to RBC surface
cerebral malaria: cerebral capillaries blocked by infected erythrocytes
Malaria during pregnancy: cytoadherence blocks placental circulation
miscarriage, premature delivery, intrauterine growth retardation, death of the mother.

RBC with knobs that coordinate cytoadherence of this infected cell.
Malaria Clinical Disease

induced malaria: infection with erythrocytic phase merozoites as a result of a needle shared among users or a blood transfusion from an infected donor

congenital malaria: transplacental infection

sequestration of malaria parasites in the placenta is a major cause of death, fetal mortality, fetal wastage & low birth weight

Malaria Pathogenesis

anemia (caused by hemolysis, severe in *falciparum* malaria)

uninfected cells have increased fragility
disseminated intravascular coagulopathy (severe cases)
spleen has major role in host defense against malaria

Spleen pathology:
infected cells accumulate in its capillaries & sinusoids
malarial pigment concentrated in spleen
chronic infection causes persistent splenomegaly
tropical splenomegaly syndrome - “big spleen disease”

- hepatomegaly
- portal hypertension
- leukopenia
- thrombocytopenia

Disseminated intravascular coagulopathy (DIC): pathological blood coagulation inside blood vessels. Disrupts blood flow & can lead to organ damage & death.

Portal hypertension: high blood pressure in the liver blood vessels

Leukopenia: decreased WBCs

Thrombocytopenia: decreased platelets in blood
Malaria Clinical Disease

• symptoms 10-15 days after bite of infected mosquito
• adult-onset malaria
  periodic chills & fever
  frontal headache & myalgia
  fever for several days before periodicity develops
• nonspecific symptoms in young children
  fever
  cough
  vomiting
  diarrhea

Child infected with malaria, probably P. malariae. Note enlarged spleen.

Malaria Clinical Disease

• patients undergoing chemoprophylaxis may not develop symptoms until they stop taking drug
• classical pattern of clinical disease
  attacks of chills & fever (reaching 41°C) lasting 6 hours
  sweating & decreased temperature
  malaise, nausea, anorexia & abdominal pain
  vomiting can develop & may be intense
  mild anemia with elevated reticulocyte count

Reticulocyte: immature red blood cells
Chemoprophylaxis: drug treatment to prevent infection (rather than cure an established infection).
Malaria Clinical Disease

- All forms of untreated malaria tend to become chronic
- Repeated attacks caused by recrudescence or relapse
- Development of immunity → eventual spontaneous cure
  - *falciparum* malaria within 2 years
  - *vivax* & *ovale* malaria within 5 years
- Individuals susceptible to reinfection during & after this time
- Untreated *falciparum* malaria can be fatal

**Relapse**: reappearance of RBC parasitemia following drug therapy from hypnozoites in the liver. **Recrudescence**: reappearance of RBC stage parasites after drug treatment due to insufficient drug treatment.

Genetic Factors & Malaria Resistance

Genetic traits in human populations confer malaria resistance → *These have been selected for in endemic areas.*

- **Glucose-6-phosphate dehydrogenase deficiency**: abnormally low levels of G6PD which supplies energy to RBCs → hemolytic anemia
- **Beta-thalassemia**: reduced expression of β-hemoglobin gene affects many races (Africans, Arabs & Asians)
- **Ovalocytosis**: altered RBC shape increased RBCs filtered by spleen
- **Duffy blood group determinants**: erythrocyte receptor for *vivax* infection
  - Most West Africans do not express the Duffy blood type → not susceptible to infection with *vivax*
Genetic Factors & Malaria Resistance

• sickle cell hemoglobin gene:
  some protection against *falciparum*
  ↓O₂ concentration → RBC shape change → spleen removes
  E6V mutation in β-hemoglobin gene → hemolytic anemia
  balanced polymorphism: (AS heterozygotes have advantage)
    AA homozygotes: normal hemoglobin
    SS homozygotes: resistant, but anemia leads to death
    both AA & SS are disadvantageous
  Africa has high S gene frequency → malaria deaths must exceed 25% to fix S gene

• hemoglobin C mutations: *falciparum* protection
  E6K mutation in β-hemoglobin gene
  causes hemolytic anemia
  found in West Africa

Malaria Treatment

malarial prophylaxis & treatment constantly change
long reliance on chloroquine to treat *falciparum* malaria
  no longer useful → worldwide resistance
  alternative drugs used on a region by region basis
• Fansidar: (PS, pyrimethamine-sulfadoxine combination)
  *resistance in East African countries*
• Malarone: (atovaquone-proguanil)
  *prophylactic for travel where chloroquine resistant* *falciparum*

• infection with chloroquine-resistant *falciparum*
  treatment with quinine sulfate & 2nd agent
  (pyrimethamine-sulfadoxine, tetracycline or clindamycin)
  strains resistant to all of these drugs have been reported
Malaria Treatment & Immunity

Artemisinin derivatives
recommended therapy in areas of high drug resistance
must be used in combination (prevents resistance)
falciparum in central America → can use chloroquine
little resistance to drug in central America
Elsewhere (Asia, Africa) → resistance highly prevalent
all infections are assumed to be chloroquine resistant

acquired immunity to malaria (premunition)
• develops after long exposure
• characterized by low levels of parasitemia
• intermediate to intermittent parasitemia (mild symptoms)
• contrasts with classic immunity which prevents any infection
• No effective vaccines for malaria – experimental vaccines only
  provide short-term immunity.

Malaria Prevention & Control

P. vivax outbreaks in Southern California → new vector A. hermsi
21 outbreaks of P. vivax malaria in US
14 outbreaks in California 1986-89
August 2, 1988: migrant worker infected
lived near Lake Hodges reservoir (25 miles N of San Diego)
diagnosed with P. vivax infection
12 other workers in same area diagnosed later
30 people with P. vivax infections July 24 to September 18, 1988
2 cases: permanent residents with no malaria risk factors
28 cases: agricultural migrant workers near Lake Hodges
  no intravenous drug use or blood transfusions
  chloroquine prophylaxis
traps near lake caught 79 adult female A. hermsi mosquitoes
competent malaria vector
vector-control: application of larvicides & insecticides
Mosquito Vector Control

controlling vectors is most practical method for wide control of malaria

- drainage
- modification of breeding sites
- insecticides: best method for reducing mosquito populations
- rising cost of insecticides
- development of insect resistance
- insecticide impregnated bed nets → significant decrease
  in morbidity (sickness) & mortality (death)

Adult Anopheles
taking a blood meal.

Sporozoites of malaria from infected mosquito stomach.