
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.***
Estimated deaths from malaria in 2010

Source: WHO World Malaria Report 2012

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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
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
Plasmodium malariae: Ring Stage Parasites
Plasmodium malariae: Trophozoites
Plasmodium malariae: Schizonts
Plasmodium malariae: Gametocytes
### Characteristics of *Plasmodium* Species

<table>
<thead>
<tr>
<th></th>
<th><em>falciparum</em></th>
<th><em>vivax</em></th>
<th><em>ovale</em></th>
<th><em>malariae</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Distribution</strong></td>
<td>Tropics</td>
<td>Tropics, Subtropics</td>
<td>Africa</td>
<td>Subtropics</td>
</tr>
<tr>
<td><strong>Host resistance</strong></td>
<td>Sickle cell</td>
<td>Duffy antigen</td>
<td>Hgb C,D,E receptor neg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hgb C,D,E</td>
<td>Thalassemia</td>
<td>G6PD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thalassemia</td>
<td></td>
<td>Pyridoxine kinase deficiency</td>
<td></td>
</tr>
<tr>
<td><strong>Host RBC’s</strong></td>
<td>All RBC’s</td>
<td>Young RBC’s (reticulocytes)</td>
<td>Old RBC’s</td>
<td></td>
</tr>
<tr>
<td><strong>Incubation</strong></td>
<td>2 weeks</td>
<td>2 weeks</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td></td>
<td>&lt;25% 1 mo</td>
<td>&gt; 25% 6 mo</td>
<td>&gt;25% 6 mo</td>
<td>Chronic</td>
</tr>
<tr>
<td><strong>Avg # merozoite in</strong></td>
<td>40,000</td>
<td>10,000</td>
<td>15,000</td>
<td>2,000</td>
</tr>
<tr>
<td><strong>liver schizont</strong></td>
<td>48 hours</td>
<td>48 hours</td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
<tr>
<td><strong>Severity of attack</strong></td>
<td>++++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

### Notes:
- *falciparum* is primarily found in tropical regions and causes severe symptoms.
- *vivax* is also found in tropical regions but generally causes milder symptoms.
- *ovale* is found in subtropical regions and causes occasional symptoms.
- *malariae* is found in tropical and subtropical regions and causes rare, severe symptoms.
- Host resistance factors vary across species, with some individuals having genetic resistance due to mutations in their hemoglobin or other enzymes.
- Incubation periods vary from 2 weeks to chronic stages.
- The average number of merozoites per RBC can range from 8-24, with *falciparum* having the highest count.
## Characteristics of *Plasmodium* Species

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>1-5%</td>
<td>Rare</td>
<td>Rare</td>
<td>Very rare</td>
</tr>
<tr>
<td><strong>Latent infection</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Chronic persistence</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Large RBC’s</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Schüffner’s dots</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>All forms of life cycle</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>in peripheral bloo</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Gametocyte</strong></td>
<td>Banana shaped</td>
<td>Amoeboid</td>
<td>Amoeboid</td>
<td>Amoeboid</td>
</tr>
</tbody>
</table>
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
<table>
<thead>
<tr>
<th>Agent</th>
<th>Prevent</th>
<th>Treatment</th>
<th>Preg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Quinine</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Artesunate</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Lumefantrine</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Atovaquone/Proguanil</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Primaquine</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>
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