Malaria
HISTORY
Malaria has been known to mankind for thousands of years.

Increase in temperatures in Africa, rise in humidity creating new water sources and the start of agriculture in the Middle East and North East Africa

favourable climate and area for breeding and transmission of malaria parasites and its carrier, the mosquito.
DISCOVERY OF THE MALARIA PARASITE (1880)
Charles Louis Alphonse Laveran
- French army surgeon stationed in Constantine, Algeria

First to notice parasites in the blood of a patient suffering from Malaria

6th of November 1880

Awarded the Nobel Prize in 1907

(Lambert, 2016)

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1907/laveran.jpg
NAMING OF HUMAN MALARIA PARASITES (1890, 1897)
Giovanni Batista Grassi and Raimondo Filetti

- Italian investigators

First introduced the names *Plasmodium vivax* and *P. malariae* for two of the malaria parasites

An American, William H. Welch, reviewed the subject and, in 1897, he named the malignant tertian malaria parasite *P. falciparum*.
DISCOVERY THAT MOSQUITOES TRANSMIT MALARIA PARASITES (1897-1898)
August 20th, 1897

Ronald Ross
  a British officer in the Indian Medical Service

First to demonstrate that malaria parasites could be transmitted from infected patients to mosquitoes

Awarded the Nobel Prize in 1902

(Lambert, 2016)
TRANSMISSION AND MECHANISM OF ACTION
Female Anopheles Mosquito
- Spotted wings
- 45 degrees
- No buzzing sound

LIFE CYCLE

• http://dx.doi.org/10.1211/pj.2015.20067483
TRANSMISSION

- Blood Transfusions
- Organ Transplants
- Shared needles
- Fetal transmission


http://www.wisegeekhealth.com/what-is-a-homologous-blood-transfusion.htm
SYMPTOMATOLOGY
CAUSE OF SYMPTOMS

- Arise during blood cell infection stage
- Parasite-associated products released:
  - glycophosphatidylinositol (GPI)
  - haemozoin
- Release of inflammatory cytokines
- Lead to symptoms:
  - Fever
  - Chills
  - Aches
  - Vomiting

(Chua et al., 2013) and (CDC, 2015)
STAGES AND SYMPTOMS OF MALARIAL INFECTION

- Initial symptoms begin 7 days after infection
- Three stages of malarial infection
  1. Cold stage
  2. Hot stage
  3. Sweating stage
- Symptoms last 6-10 hours
- Very difficult to diagnose
- If not treated, could worsen and lead to death

http://www.thehealthsite.com/diseases-conditions/malaria/001/

(WHO, 2016)
SEVERE MALARIA INFECTIONS

- Patient experiences serious organ failure or blood abnormalities
- Cerebral malaria → may fall into coma
- Hemolysis → severe anemia
- Hyperparasitemia: >5% of erythrocytes infected
- Acute Respiratory Distress Syndrome: fluid buildup in alveoli

(CDC, 2015)
DEMOGRAPHICS
GEOGRAPHY

- Tropical
- Impoverished areas
- Highest in Africa and South East Asia

CDC (2016)

Retrieved from https://www.cdc.gov/malaria/malaria_worldwide/impact.html
37% decrease in those affected globally
60% decrease in number of deaths
2015
3.2 billion people at risk
214 million people infected
438,000 deaths
3rd leading cause of death in Africa
HIGH RISK

- Children
- Women
- Traveler
- HIV/AIDS Patients


CDC (2016)
TREATMENTS
3 General Classes of Treatment:
1. Pre-exposure Prophylaxis
2. Fast-Acting Antimalarials
3. Slow-acting Antimalarials
PRE-EXPOSURE PROPHYLAXIS
Malarone: Atovaquone + Proguanil Hydrochloride

Administration:
- For travelers going to areas of high transmission (ex. India, African countries)
- Given as a pill, to be taken once a day

Mechanism of Action:
- Atovaquone (fast)
  - Inhibition of mitochondrial electron transport chain in parasite
  - Inhibition of ATP synthesis
  - Parasitic Death

- Proguanil hydrochloride (slow)
  - Inhibition of parasitic dihydrofolate reductase (DHFR)
  - Inhibition of nucleotide synthesis

"Malarone", 2016
FAST-ACTING ANTIMALARIALS: ACT AND CHLOROQUINE

Artemisinin: used in Artemisinin-based Combination Therapy

• Treatment for uncomplicated *P. Falciparum* Malaria

• Discovered by Chinese Scientist, **Tu Youyou**
  (Winner of Nobel Prize in Medicine, 2015)

Chloroquine:

• Treatment for *P. vivax*

NORMAL PARASITIC PATHWAY

Host hemoglobin breakdown by parasite → Heme (toxic) → Hemozoin (polymer, non-toxic)

Tripathi, 2013
FAST-ACTING ANTIMALARIALS: ARTEMSININ

Host hemoglobin breakdown by parasite

R = Artemisinin

Heme (toxic) → Hemozoin (polymer, non-toxic)

Artemisinin Free Radicals

Alkylation of Heme → Porphyrin Degradation → Parasitic Death

Meshnick, 2002; World Health Organization, 2006
FAST-ACTING ANTIMALARIALS: CHLOROQUINE

Host hemoglobin breakdown by parasite

CQ = Chloroquine

CQ → Accumulation of toxic heme → Parasitic Death

Heme (toxic) → Hemozoin (polymer, non-toxic)
SLOW-ACTING ANTIMALARIALS - TETRACYCLINE

- Slow-acting Drug → used in combination with fast-acting drugs

Mechanism: inhibits mitochondrial protein synthesis

Gaillard, 2015
CONCLUSION
FUTURE RESEARCH

- Researchers are contemplating new interventions or updating previously used malaria control interventions.
  - New drugs and vaccines for treatment and prevention
  - New diagnostic tests
  - Innovative insecticide-treated materials
  - Revised systems for delivering and evaluating malaria control

(Hemingway & Bates, 2003)
Development of an effective malaria vaccine faces major challenges.

Targeted against *Plasmodium falciparum*.

Genetic diversity of both the parasite and the human host.

Produce vaccines that target *P. vivax*.

Take into consideration features such as relapses and hypnozoite stages.

(Hemingway & Bates, 2003)
REFERENCES