Malaria

By Anna Zhang

Historical Information: The name malaria is derived from the Italian term for “bad air.” While the parasite was not formally discovered until 1880, early writings describing the symptoms of malaria exist in medical journals in China as early as 2700 BCE. In the early 17th century, Spanish Jesuit missionaries learned of a medicinal bark used for the treatment of fevers. This medicine would later be known as the antimalarial drug, quinine. [10]

In 1880, Charles Louis Alphonse Laveran, a French army surgeon, first noticed the parasites in the blood of a patient infected with malaria in Algeria. In 1886, Camillo Golgi identified at least two forms of the disease, one producing symptoms every other day, and the other producing symptoms every third day. In the 1890’s, the parasites were named – P. vivax, P. malariae, P. falciparum, P. ovale, and P. knowlesi. [10]

In 1897, Ronald Ross became the first to prove that malaria parasites could be transmitted by mosquitoes. [10]

Malaria is common in tropical/sub-tropical regions of the world and is the cause of at least 1 million deaths each year. In the U.S., about 1,200 cases are diagnosed each year, most of whom are immigrants or returning travelers. No documentation of malaria in Texas today was found. [13]

Malaria in endemic in areas within Asia, Africa and Central/South America. It is estimated that 216 million new infections occurred in 2010, of which 655,000 died. [4]

Etiologic agent: There are five malarial protozoan parasites that have been found to cause disease in humans –

- Plasmodium vivax
- P. ovale
- P. malariae
- P. falciparum
- P. knowlesi

Malaria is most commonly caused by the P. vivax and P. falciparum species, with P. falciparum causing the most severe form of malaria. [4]

The protozoan parasites are single celled and fall under the phylum Apicomplexa, some of which posses an organelle called the apicoplast. The organelle is used in penetrating the host cell. Apicomplexas typically do not have flagella, cilia or pseudopods, but are motile through a gliding mechanism. Apicomplexas have complicated life cycles that involve both binary fission and sexual reproduction. The life cycle begins when a sporozoite enters the host cell and divides to form merozoites. This is said to be the infectious portion of the life cycle. [6]

Transmission: Chimpanzees and gorillas are the natural reservoirs for malaria. Transmission of malaria in humans occurs through indirect, vector transmission and natural, living reservoirs. 30 of the 400
different species of *Anopheles* mosquitoes are of significant importance to the transmission of malaria. [1] Transmission begins when a female *Anopheles* bites an infected human and ingests protozoan gametocytes. The parasite incubates in the mosquito for 8-35 days before the infectious sporozoites are formed. The disease is transferred when the mosquito bites a human host and introduces the malarial sporozoites. [4]

**Signs and Symptoms:** Malaria can be classified as uncomplicated or severe (complicated) and symptoms begin when the parasite develops in red blood cells. [3] First signs of illness include fever, headache, chills and vomiting. The onset of symptoms occurs 10-15 days after infection, and varies in severity depending on the infecting species. *P. falciparum*, which causes the most severe form of malaria, can progress and lead to death if not treated within the first 24 hours. Anemia, respiratory distress or cerebral malaria may develop to indicate severe malaria. [1] Classical malaria attacks last 6-10 hours and occurs every second or third day depending on the parasite. The stages of the recurring attacks include the chills, followed by fever and finally sweating. While such cases are rarely observed, the attacks theoretically align with the lifecycle of the parasite, which causes the bursting of infected red blood cells. [7]

**Diagnosis:** A detailed travel history should be taken for a suspected patient with malaria. In addition to testing for malaria, a complete blood count and routine chemistry panel should be performed. This will allow for healthcare professionals to identify signs of severe infection if malaria is confirmed. [8] A Blood smear with observation under a microscope is the recommended procedure to diagnose active malaria. It is recommended that smears be taken in 6-12 hour intervals to confirm the diagnosis. [9] The smear is stained with the Giemsa stain, which give the parasites a distinct appearance. Other methods of detection include the Rapid Diagnostic Test (RDT), polymerase chain reaction (PCR), and serology. Once malaria is confirmed, drug resistance tests must be performed to determine the best course of treatment with antimalarial drugs on specimens collected from the patient. [8]

**Virulence:** Cases of malaria vary from mild to complicated. The virulence factors of malaria are not well known. A study of *P. falciparum* suggests that genetic variation contributes to the varying development of malarial disease. Malarial infection can develop into mild or severe infections, which are pathologically different. As the disease manifests, the patient can develop severe malarial anemia or cerebral malaria, which are distinct from mild malaria. This shows that while the classifications of disease severity are arbitrary, it is driven by the diversity within the infecting protozoan parasites. Some proposed virulence factors include antigenic variation, cytoadherence (adherence of infected cells to epithelial surfaces), resetting (infection of healthy erythrocytes by infected erythrocytes), cytokine production, and their complex lifecycle, which allows the parasite to evade the immune system. [11]

**Prevention and Treatment:** Prophylaxis exists for malaria in the form of various oral medicines. The drugs include atovaquone, chloroquine, doxycycline, and mefloquine. Treatment varies in duration and dosage frequency, allowing travelers to choose a treatment that best fits their habits or needs. [2] Using insecticide and mosquito nets also contribute greatly to the prevention of malaria. [1]

Treatment for those infected with malaria is made difficult by the presence of drug resistance. Drug resistance of the infecting parasite must be determined before designating the final treatment plan. [1] Artemisinin-based combination therapy (ACT), which is a combination of the drug artemisinin and
another partner drug, is the recommended treatment for uncomplicated malaria caused by \textit{P. falciparum}. Chloroquine is recommended for infections caused by \textit{P. vivax}. Severe malaria can be treated with injectable artesunate, followed by a course of ACT. If the infecting parasite is found to be resistant to the recommended treatment, adjustments must be made accordingly. [12]

References:

   \url{http://www.ucmp.berkeley.edu/protista/apicomplexa.html}. December 2, 2015.
   \url{http://www.who.int/malaria/areas/treatment/overview/en/}. December 3, 2015.