Competitive Exams: Malaria

Malaria is one of the most common infectious diseases and an enormous public health problem. The disease is caused by a protozoan parasites of the genus Plasmodium, which is usually referred to as malaria parasites.

The term malaria originated from the medieval Italian term, mala aria meaning “bad air” and the disease was formerly called marsh fever due to its association with swamps.

In 1880, a French army doctor working at the military hospital in Algeria named Charles Louis Alphonse Laveran observed malarial parasites for the first time inside the red blood cells of people suffering from malaria. For this and later discoveries, he was awarded the 1907 Nobel Prize for Physiology or Medicine. The protozoan was named Plasmodium by the Italian scientists Ettore Marchiafava and Angelo Celli. A year later, Carlos Finlay, a Cuban doctor treating patients with yellow fever in Havana, first suggested that mosquitoes were transmitting disease to humans. However, it was Sir Ronald Ross working in India who finally proved in 1898 that malaria was transmitted by mosquitoes to birds. He isolated malarial parasites from the salivary glands of mosquitoes that had fed on infected birds. For this work Ross received the 1902 Nobel Prize in Medicine. The findings of Finlay and Ross were confirmed by a medical board headed by Walter Reed in 1900.

Malaria Parasites

Malaria is caused by protozoan parasites of the genus Plasmodium (Phylum Apicomplexa) . In humans malaria is caused by P. Falciparum, P. Malariae, P. Ovale, and P. Vivax, the last one is the most common one responsible for about 80 % of all malaria cases. However, P. Falciparum is the most deadly one, responsible for about 15 % of infections but 90 % of deaths. Parasitic Plasmodium species also infect birds, reptiles, monkeys, chimpanzees and rodents. There have been documented human infections with several simian species of malaria, namely P. Knowlesi, P. Inui, P. Cynomolgi, P. Simiovale, P. Brazilianum, P. Schwetzi and P. Simium.

Life Cycle

The parasite’s primary (definitive) hosts and vectors are female mosquitoes of the Anopheles genus. A mosquito becomes infected when it takes a blood meal from an infected human. Once ingested, the parasite’s gametocytes, taken up along with the

blood differentiate into male or female gametes, which fuse to form zygote in the mosquito gut. The zygote is also called ookinete that penetrates the gut lining and produces an oocyst outside the stomach wall. The diploid zygote first undergoes reduction division and then divides by multiple fission to produce haploid sporozoites inside the oocyst. When the oocyst ruptures, sporozoites are released that migrate through the mosquito's body to reach salivary glands, where they are ready to infect a new human host when the mosquito bites a healthy man. This type of transmission is occasionally referred to as anterior station transfer. Only female mosquitoes feed on blood, thus males do not transmit the disease.

Malaria in humans develops via two phases: An exoerythrocytic (hepatic) and an erythrocytic phase. When an infected mosquito pierces a person's skin to take a blood meal, sporozoites in the mosquito's saliva enter the bloodstream and migrate to the liver. Within 30 minutes of being introduced into the human host, they infect hepatocytes, multiplying asexually to form schizont for a period of 6 15 days. Once in the liver they produce thousands of cryptozoites and secondary metacryptozoites, which, following rupture of their host cells escape into the blood and infect red blood cells, thus beginning the erythrocytic stage of the life cycle. The parasites escape from the liver undetected by wrapping themselves in the cell membrane of the host liver cell. Within red blood cells the parasites multiply further asexually producing schizont that burst to release about two dozens of merozoites that invade fresh red blood cells. Such cycles continue to occur every 48 hours causing chill and fever at the release of merozoites from RBCs.

Some P. Vivax and P. Ovale sporozoites do not immediately develop into exoerythrocytic merozoites but instead produce hypnozoites that remain dormant for periods ranging 6 12 months to as long as three years. After a period of dormancy, they reactivate and produce merozoites. Hypnozoites are responsible for long incubation and late relapses in these two species of malaria.

The parasite is protected from attack by the body's immune system because for most of its life it resides within the liver and blood cells and is hidden from immune surveillance. However, circulating infected blood cells are destroyed in the spleen. To avoid this, P. Falciparum produces adhesive proteins on the surface of the infected blood cells, causing the blood cells to stick to the walls of smaller blood vessels, thereby sequestering the parasite from the passage through the general circulation and spleen. This stickiness of RBCs is the main factor that gives rise to hemorrhagic complications associated with falciparum malaria. The smallest branches of the circulatory system can be blocked by the attachment of masses of these infected red blood cells. In cerebral malaria the sequestrated red blood cells can breach the blood brain barrier, leading to coma.

Although the red blood cell surface adhesive proteins (called PfEMP1 for Plasmodium falciparum erythrocyte membrane protein 1) are exposed to the immune system, they do not serve as good immune targets because of their extreme diversity. There are at

least 60 types of these proteins within a single parasite and perhaps limitless types in general parasite populations. Also, the parasite switches between a broad repertoire of PfEMP1 surface proteins thus staying one step ahead of the pursuing immune system.

Treatment

The first effective treatment for malaria was the bark of cinchona tree, which contains quinine. This tree grows on the slopes of the Andes, mainly in Peru.