P.O. Box 131375, Bryanston, 2074

Ground Floor, Block 5
Bryanston Gate, 170 Curzon Road
Bryanston, Johannesburg, South Africa

804 Flatrock, Buiten Street, Cape Town, 8001

www.thistle.co.za
Tel: +27 (011) 463 3260
Fax: +27 (011) 463 3036
Fax to Email: + 27 (0) 86-538-4484
e-mail : service@thistle.co.za

Please read this section first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will not issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT-2014/004**

Each attendee should claim THREE CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

DIFFERENTIAL SLIDES LEGEND

CYCLE 44 SLIDE 3

PLASMODIUM FALCIPARUM

The name malaria, from the Italian *mala aria*, meaning bad air, comes from the linkage suggested by Giovanni Maria Lancisi (1717) of malaria with the poisonous vapours of swamps. This species name comes from the Latin *falx* meaning sickle, and *parere* meaning to give birth. The organism itself was first seen by Laveran on November 6, 1880 at a military hospital in Constantine, Algeria, when he discovered a microgametocyte exflagellating. Patrick Manson (1894) hypothesized that mosquitoes could transmit malaria. This hypothesis was experimentally confirmed independently by Giovanni Battista Grassi and Ronald Ross in 1898. Grassi (1900) proposed an exerythrocytic stage in the life cycle, later confirmed by Short, Garnham, Covell and Shute (1948), who found Plasmodium vivax in the human liver.

While there are no effective vaccines for any of the four species that cause human malaria, drugs have been employed for centuries. In 1640, Huan del Vego first employed the tincture of the cinchona bark for treating malaria: The native Indians of Peru and Ecuador had been using it even earlier for treating fevers. Thompson (1650) introduced this "Jesuits' bark" to England: Its first recorded use there was by Dr John Metford of Northampton in 1656. Morton (1696) presented the first detailed description of the clinical picture of malaria and of its treatment with cinchona. Gize (1816) studied the extraction of crystalline quinine from the cinchona bark and Pelletier and Caventou (1820) in France extracted pure quinine alkaloids, which they named quinine and cinchonine.

Every year 300 to 500 million people suffer from malaria, causing an estimated 1 to 2.7 million deaths. Ninety percent of these deaths occur in sub-Saharan Africa, where a child dies every minute from malaria mostly children younger than five. Malaria mortality rates among children in Africa have been reduced by an estimated 54% since 2000. Malaria is endemic to over 100 nations and territories in Africa, Asia, Latin America, the Middle East, and the South Pacific.

It is caused by a parasite that is transferred by the bite of an infected Anopheles mosquito. Plasmodium falciparum is by far the deadliest of the four human malarial species (Plasmodium falciparum, malariae, ovale, and vivax). P. vivax is the most widespread. P. malariae and P. ovale, although also significant, cause fewer cases and less severe forms of the disease.

Symptoms of malaria include cyclical fever and shivering, pain in the joints, headache, weakness, and repeated vomiting. In severe cases, convulsions and kidney failure can result. Complications of P. falciparum include

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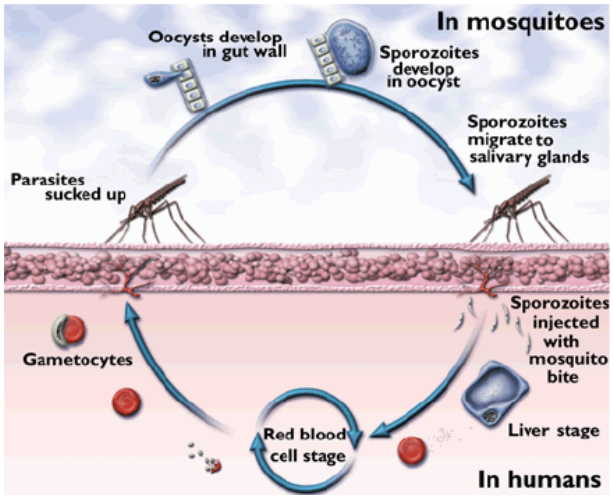
acute anaemia and cerebral malaria. In some patients who seemingly recover, another bout of malaria may occur if the treatment does not completely clear the parasite from the blood and liver.

Life Cycle

All types of malaria have a similar life cycle. Sporozoites, the infectious form of the malaria parasite, are injected into a human host through the saliva of an Anopheles mosquito. These sporozoites enter the liver cells within minutes, take on a new form, and multiply. When the liver cells rupture, blood stage parasites—known as merozoites—are released. Each merozoite invades a red blood cell, and multiplies into more merozoites. The length of this erythrocytic stage of the parasite life cycle depends on the parasite species: irregular cycle for P. falciparum, 48 hours for P. Vivax, and P. Ovale and 72 hours for P. Malariae.

The red blood cell full of merozoites ruptures to release more merozoites. It is this stage of the life cycle that causes disease and, too often, death. Some merozoites change into gametocytes, which do not cause disease but remain in the blood until they are cleared by drugs or the immune system, or taken up by the bite of a mosquito. In the mosquito's stomach a "male" gametocyte fertilizes a "female" to form an egg, or oocyst, which matures into thousands of sporozoites that swim to the mosquito's salivary glands to be injected into another human at the next bite.



In addition to being the deadliest form of malaria, P. falciparum destroys red blood cells, which can cause acute anaemia. Within the 48-hour asexual blood stage cycle, the mature forms change the surface properties of infected red blood cells causing them to stick to blood vessels (a process called cytoadherence). This leads to obstruction of the microcirculation and results in dysfunction of multiple organs, typically the brain in cerebral malaria. A major complication of P. falciparum, cerebral malaria, can lead to coma, transient or permanent neurological effects, and death. Compared to P.vivax, P. falciparum is less widespread, but more likely to result in severe complications and be fatal.

Diagnosis

Among medical professionals, the preferred method to diagnose malaria and determine which species of Plasmodium is causing the infection, is by examination of a blood film under microscope in a laboratory. Each species has distinctive physical characteristics that are apparent under a microscope. In P. falciparum, only early trophozoites (ring-form) and gametocytes are seen in the peripheral blood. It is unusual to see mature trophozoites or schizonts in peripheral blood smears as these are usually sequestered in the tissues. The parasitized erythrocytes are not enlarged, and it is common to see cells with more than one parasite within

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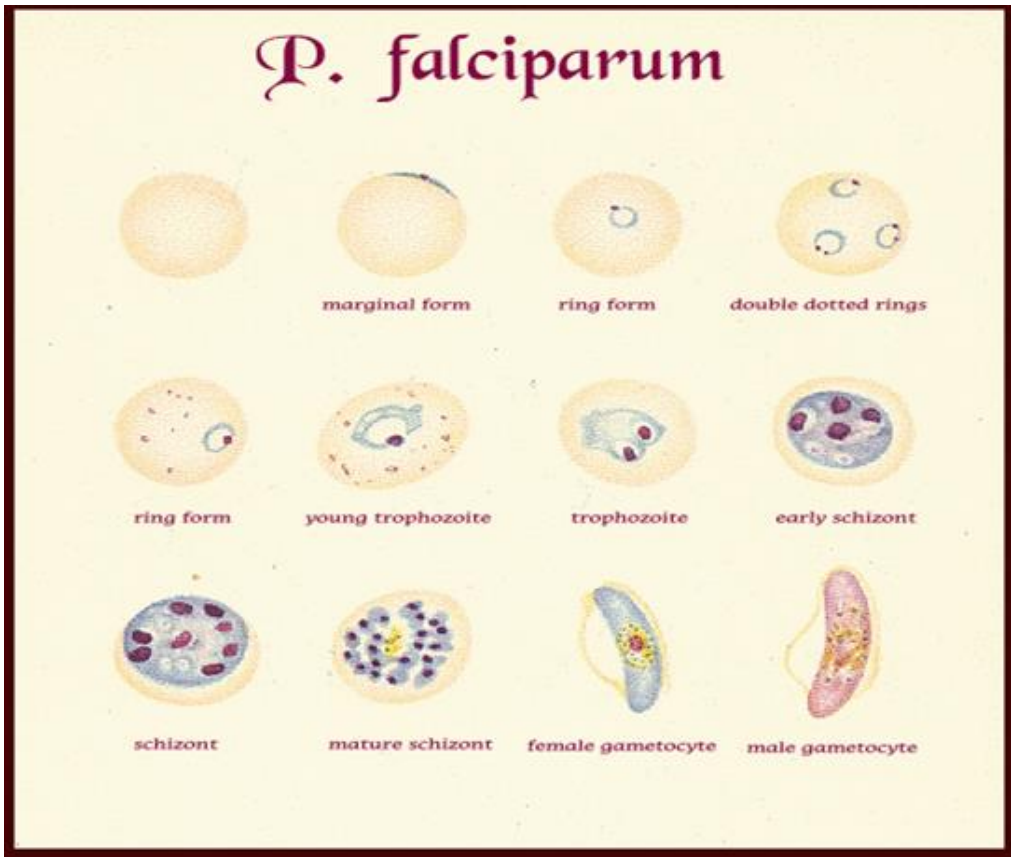
them. On occasion, faint comma-shaped red dots called "Maurer's dots" are seen on the red cell surface. The comma-shaped dots can also appear as pear-shaped blotches.



Treatment Traditional first-line treatments such as chloroquine and Sulphadoxine/Pyrimethamine have lost much of their effectiveness in many countries. This has led to the need for new and more expensive antimalarial drugs, including combination therapies (such as artemisinin combination therapy–ACT) now being introduced by some governments.

Vaccines against malaria

There are currently no licensed vaccines against malaria or any other human parasite. One research vaccine against P. falciparum, known as RTS,S/AS01, is most advanced. This vaccine is currently being evaluated in a large clinical trial in 7 countries in Africa. A WHO recommendation for use will depend on the final results from the large clinical trial. These final results are expected in late 2014, and a recommendation as to whether or not this vaccine should be added to existing malaria control tools is expected in late 2015.

References

1. http://www.malariavaccine.org/files/FS_Pfalciparum-Sept-2004_FINAL.pdf
2. http://en.wikipedia.org/wiki/plasmodium falciparum

Questions

1. Discuss the life cycle of P. falciparum.
2. Discuss the physical characteristics of P. falciparum?
3. Why is P. falciparum worse than other types of malaria?
