Malaria

Introduction

For thousands of years, malaria has remained the world's most pervasive infection, affecting at least 91 different countries and some 300 million people. The disease causes fever, shivering, joint pain, headache, and vomiting. In severe cases, patients can have jaundice, kidney failure, and anemia, and can lapse into a coma.

Malaria is one of the most successful parasites ever known to mankind. It is prevalent in the tropics and countries in sub-Saharan Africa, which account for nearly 90 percent of all malaria cases. The majority of the remaining cases are clustered in India, Brazil, Afghanistan, Sri Lanka, Thailand, Indonesia, Vietnam, Cambodia, and China. Malaria causes 1 to 1.5 million deaths each year, and in Africa, it accounts for 25 percent of all deaths of children under the age of five.

A Brief History of Malaria

Ancient accounts of malaria date back to Vedic writings of 1600 B.C.E. in India and to the fifth century B.C.E. in Greece, when the great Greek physician Hippocrates, often called “the Father of Medicine,” described the characteristics of the disease and related them to seasons and location. The discovery of an association of malaria with stagnant waters led the Romans to develop drainage programs, which were among the first documented preventions against malaria. In seventh-century Italy, the disease was prevalent in foul-smelling swamps near Rome and was named *mal' aria* Italian for “bad air.”

Infectious Knowledge

Some historians believe that malaria epidemics greatly contributed to the fall of the Roman Empire. DNA from the 1,500-year-old bones of a child found in a cemetery near Rome yielded evidence of a malaria epidemic. A large epidemic may explain why one of the greatest military machines in world history was too weak to repel invasions from the Visigoths, Huns, and Vandals. Did moral and urban decay befall Rome, or was it malaria?
Malaria epidemics ravaged Europe and Africa for centuries. Like many diseases, it traveled with tradesmen, settlers, and conquering forces. Over four centuries of the slave trade, millions of Africans died from malaria, which may have come to the New World along with slaves.

Despite malaria's preference for the tropics, the disease has had an impact on the history of the United States, too. Known commonly as “fever and ague,” malaria took its toll on early American settlers. In the book *Little House on the Prairie*, Laura Ingalls Wilder vividly describes its impact. Malaria devastated the 1607 Jamestown colony and regularly ravaged the South and Midwest. The incidence of malaria in the United States peaked in 1875. Yet, in 1914, more than 600,000 new cases were still occurring.

Sir Ronald Ross, born in India in 1857, received the 1902 Nobel Prize in Medicine for his pioneering work on malaria, in which he laid the foundation for successful research on this disease and methods for combating it.

Malaria has been a factor in nearly all United States military campaigns. During the Civil War, armies on both sides sustained more than 1.2 million cases of malaria. It continued to be a problem in World Wars, the Korean War, and the Vietnam War. In the latter, malaria appeared in a newer, more deadly, drug-resistant form.

**EPIDEMIOLOGY**

The WHO estimates that in 2010 there were 219 million cases of malaria resulting in 660,000 deaths. Others have estimated the number of cases at between 350 and 550 million for falciparum malaria and deaths in 2010 at 1.24 million up from 1.0 million deaths in 1990. The majority of cases (65%) occur in children under 15 years old. About 125 million pregnant women are at risk of infection each year; in Sub-Saharan Africa, maternal malaria is associated with up to 200,000 estimated infant deaths yearly. There are about 10,000 malaria cases per year in Western Europe, and 1300–1500 in the United States. About 900 people died from the disease in Europe between 1993 and 2003. Both the global incidence of disease and resulting mortality has declined in recent years. According to the WHO, deaths attributable to malaria in 2010 were
reduced by over a third from a 2000 estimate of 985,000, largely due to the widespread use of insecticide-treated nets and artemisinin-based combination therapies. In 2012, there were 207 million cases of malaria. That year, the disease is estimated to have killed between 473,000 and 789,000 people, many of whom were children in Africa.

Malaria is presently endemic in a broad band around the equator, in areas of the Americas, many parts of Asia, and much of Africa; in Sub-Saharan Africa, 85–90% of malaria fatalities occur. An estimate for 2009 reported that countries with the highest death rate per 100,000 of population were Ivory Coast (86.15), Angola (56.93) and Burkina Faso (50.66).

A 2010 estimate indicated the deadliest countries per population were Burkina Faso, Mozambique and Mali. The Malaria Atlas Project aims to map global endemic levels of malaria, providing a means with which to determine the global spatial limits of the disease and to assess disease burden. This effort led to the publication of a map of *P. falciparum* endemicity in 2010. As of 2010, about 100 countries have endemic malaria. Every year, 125 million international travellers visit these countries, and more than 30,000 contract the disease.

The geographic distribution of malaria within large regions is complex, and malaria-afflicted and malaria-free areas are often found close to each other. Malaria is prevalent in tropical and subtropical regions because of rainfall, consistent high temperatures and high humidity, along with stagnant waters in which mosquito larvae readily mature, providing them with the environment they need for continuous breeding. In drier areas, outbreaks of malaria have been predicted with reasonable accuracy by mapping rainfall.

Malaria is more common in rural areas than in cities. For example, several cities in the Greater Mekong Sub-region of Southeast Asia are essentially malaria-free, but the disease is prevalent in many rural regions, including along international borders and forest fringes. In contrast, malaria in Africa is present in both rural and urban areas, though the risk is lower in the larger cities.
TRANSMISSION

Malaria is transmitted exclusively through the bites of Anopheles mosquitoes. The intensity of transmission depends on factors related to the parasite, the vector, the human host, and the environment.

About 20 different Anopheles species are locally important around the world. All of the important vector species bite at night. Anopheles mosquitoes breed in water and each species has its own breeding preference; for example some prefer shallow collections of fresh water, such as puddles, rice fields, and hoof prints. Transmission is more intense in places where the mosquito lifespan is longer (so that the parasite has time to complete its development inside the mosquito) and where it prefers to bite humans rather than other animals. For example, the long lifespan and strong human-biting habit of the African vector species is the main reason why about 90% of the world's malaria deaths are in Africa.

Transmission also depends on climatic conditions that may affect the number and survival of mosquitoes, such as rainfall patterns, temperature and humidity. In many places, transmission is seasonal, with the peak during and just after the rainy season. Malaria epidemics can occur when climate and other conditions suddenly favour transmission in areas where people have little or no immunity to malaria. They can also occur when people with low immunity move into areas with intense malaria transmission, for instance to find work, or as refugees.

Human immunity is another important factor, especially among adults in areas of moderate or intense transmission conditions. Partial immunity is developed over years of exposure, and while it never provides complete protection, it does reduce the risk that malaria infection will cause severe disease. For this reason, most malaria deaths in Africa occur in young children, whereas in areas with less transmission and low immunity, all age groups are at risk.
PROTOZOA SPECIE TYPES

Malaria is caused by *Plasmodium* parasites. The parasites are spread to people through the bites of infected *Anopheles* mosquitoes, called "malaria vectors", which bite mainly between dusk and dawn.

There are four parasite species that cause malaria in humans:

- *Plasmodium falciparum*
- *Plasmodium vivax*
- *Plasmodium malariae*
- *Plasmodium ovale.*

*Plasmodium falciparum* and *Plasmodium vivax* are the most common. *Plasmodium falciparum* is the most deadly.

In recent years, some human cases of malaria have also occurred with *Plasmodium knowlesi* – a species that causes malaria among monkeys and occurs in certain forested areas of South-East Asia.

PLASMODIUM LIFE CYCLE AND THE PATHOGENESIS OF MALARIA

In the life cycle of *Plasmodium*, a female *Anopheles* mosquito (the definitive host) transmits a motile infective form (called the sporozoite) to a vertebrate host such as a human (the secondary host), thus acting as a transmission vector. A sporozoite travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue schizogony), producing thousands of merozoites. These infect new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that produce 8 to 24 new infective merozoites, at which point the cells burst and the infective cycle begins anew.

Other merozoites develop into immature gametocytes, which are the precursors of male and female gametes. When a fertilised mosquito bites an infected person, gametocytes are taken up with the blood and mature in the mosquito gut. The male and female gametocytes fuse and form
an ookinetea fertilized, motile zygote. Ookinetes develop into new sporozoites that migrate to the insect's salivary glands, ready to infect a new vertebrate host. The sporozoites are injected into the skin, in the saliva, when the mosquito takes a subsequent blood meal.

Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar, and thus do not transmit the disease. The females of the *Anopheles* genus of mosquito prefer to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal. Malaria parasites can also be transmitted by blood transfusions, although this is rare.

**CLINICAL PRESENTATION**

The clinical manifestations of malaria vary with geography, epidemiology, immunity, and age. In areas where malaria is highly endemic, groups at highest risk include young children (6 to 36 months), who can develop severe illness, and pregnant women, who are at risk for anemia and delivering low birth weight newborns. In areas where malaria is transmitted throughout the year, older children and adults develop partial immunity after repeated infections and are at relatively low risk for severe disease.

In patients with suspected malaria, obtaining a history of recent or remote travel to an endemic area is critical. Asking explicitly if they traveled to a tropical area at any time in their life may enhance recall. Maintain a high index of suspicion for malaria in any patient exhibiting any malarial symptoms and having a history of travel to endemic areas. Also determine the patient's immune status, age, and pregnancy status; allergies or other medical conditions that he or she may have; and medications that he or she may be using.

Patients with malaria typically become symptomatic a few weeks after infection, although the host's previous exposure or immunity to malaria affects the symptomatology and incubation period. In addition, each *Plasmodium* species has a typical incubation period. Importantly, virtually all patients with malaria present with headache. Clinical symptoms also include the following:
- Cough
- Fatigue
- Malaise
- Shaking chills
- Arthralgia
- Myalgia

Paroxysm of fever, shaking chills, and sweats (every 48 or 72 h, depending on species)

The classic paroxysm begins with a period of shivering and chills, which lasts for approximately 1-2 hours and is followed by a high fever. Finally, the patient experiences excessive diaphoresis, and the body temperature of the patient drops to normal or below normal.

Many patients, particularly early in infection, do not present the classic paroxysm but may have several small fever spikes a day. Indeed, the periodicity of fever associated with each species (i.e., 48 h for *P. falciparum*, *P. vivax*, and *P. ovale* [or tertian fever] 72 h for *P. malariae* [or quartan fever]) is not apparent during initial infection because of multiple broods emerging in the bloodstream. In addition, the periodicity is often not observed in *P. falciparum* infections. Patients with long-standing, synchronous infections are more likely to present with classic fever patterns. In general, however, the occurrence of periodicity of fever is not a reliable clue to the diagnosis of malaria.

Less common malarial symptoms include the following:

- Anorexia and lethargy
- Nausea and vomiting
- Diarrhea
- Jaundice

Notably, infection with *P. vivax*, particularly in temperate areas of India, may cause symptoms up to 6-12 months after the host leaves the endemic area. In addition, patients infected with *P. vivax* or *P. ovale* may relapse after longer periods, because of the hypnozoite stage in the liver.

*P. malariae* does not have a hypnozoite stage, but patients infected with *P. malariae* may have a prolonged, asymptomatic erythrocytic infection that becomes symptomatic years after leaving the endemic area.
Tertian and quartan fevers are due to the cyclic lysis of red blood cells that occurs as trophozoites complete their cycle in erythrocytes every 2 or 3 days, respectively. *P. malariae* causes quartan fever; *P. vivax* and *P. ovale* cause the benign form of tertian fever, and *P. falciparum* causes the malignant form. The cyclic pattern of fever is very rare.

Travelers to forested areas of Southeast Asia and South America have become infected by *Plasmodium knowlesi*, a dangerous species normally found only in long-tailed and pigtail macaque monkeys (*Macaca fascicularis* and *M. nemestrina*, respectively). This species can cause severe illness and death in humans, but, under the microscope, the parasite looks similar to the more benign *P. malariae* and has sometimes been misdiagnosed.

Because *P. malariae* infection is typically relatively mild, *Plasmodium knowlesi* infection should be suspected in persons residing or traveling in the above geographical areas who are severely ill and have microscopic evidence of *P. malariae* infection. Diagnosis may be confirmed via polymerase chain reaction (PCR) assay test methods.

**DIAGNOSIS**

A patient with fever who had recently traveled to a malaria-endemic country is being evaluated in the emergency room. Malaria must be recognized promptly in order to treat the patient in time and to prevent further spread of infection in the community via local mosquitoes. Malaria should be considered a potential medical emergency and should be treated accordingly. Delay in diagnosis and treatment is a leading cause of death in malaria patients in the United States. Malaria can be suspected based on the patient's travel history, symptoms, and the physical findings at examination. However, for a definitive diagnosis to be made, laboratory tests must demonstrate the malaria parasites or their components.

Diagnosis of malaria can be difficult:

- Where malaria is not endemic any more (such as in the United States), health-care providers may not be familiar with the disease. Clinicians seeing a malaria patient may forget to consider malaria among the potential diagnoses and not order the needed
diagnostic tests. Laboratorians may lack experience with malaria and fail to detect parasites when examining blood smears under the microscope.

- In some malaria-endemic areas, malaria transmission is so intense that a large proportion of the population is infected but not made ill by the parasites. Such carriers have developed just enough immunity to protect them from malarial illness but not from malarial infection. In that situation, finding malaria parasites in an ill person does not necessarily mean that the illness is caused by the parasites.

**Clinical Diagnosis**

Clinical diagnosis is based on the patient's symptoms and on physical findings at examination.

The first symptoms of malaria (most often fever, chills, sweats, headaches, muscle pains, nausea and vomiting) are often not specific and are also found in other diseases (such as the "flu" and common viral infections). Likewise, the physical findings are often not specific (elevated temperature, perspiration, tiredness).

In severe malaria (caused by *Plasmodium falciparum*), clinical findings (confusion, coma, neurologic focal signs, severe anemia, respiratory difficulties) are more striking and may increase the index of suspicion for malaria.

If possible, clinical findings should always be confirmed by a laboratory test for malaria.

In addition to ordering the malaria specific diagnostic tests described below, the health-care provider should conduct an initial workup and request a complete blood count and a routine chemistry panel. In the event that the person does have a positive malaria test, these additional tests will be useful in determining whether the patient has uncomplicated or severe manifestations of the malaria infection. Specifically, these tests can detect severe anemia, hypoglycemia, renal failure, hyperbilirubinemia, and acid-base disturbances.
Microscopic Diagnosis

Malaria parasites can be identified by examining under the microscope a drop of the patient's spread out as a "blood smear" on a microscope slide. Prior to examination, the specimen is stained (most often with the Giemsa stain) to give the parasites a distinctive appearance. This technique remains the gold standard for laboratory confirmation of malaria. However, it depends on the quality of the reagents, of the microscope, and on the experience of the laboratorian.

Antigen Detection

Various test kits are available to detect antigens derived from malaria parasites. Such immunologic ("immunochromatographic") tests most often use a dipstick or cassette format, and provide results in 2-15 minutes. These "Rapid Diagnostic Tests" (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. Malaria RDTs are currently used in some clinical settings and programs. However, before malaria RDTs can be widely adopted, several issues remain to be addressed, including improving their accuracy; lowering their cost; and ensuring their adequate performance under adverse field conditions. The World Health Organization is conducting comparative performance evaluations of many of the RDTs which are commercially available worldwide based on a panel of parasites derived from a global network of collection sites.

Molecular Diagnosis

Parasite nucleic acids are detected using polymerase chain reaction (PCR). Although this technique may be slightly more sensitive than smear microscopy, it is of limited utility for the diagnosis of acutely ill patients in the standard healthcare setting. PCR results are often not available quickly enough to be of value in establishing the diagnosis of malaria infection.

PCR is most useful for confirming the species of malaria parasite after the diagnosis has been established by either smear microscopy or RDT.
Serology

Serology detects antibodies against malaria parasites, using either indirect immunofluorescence (IFA) or enzyme-linked immunosorbent assay (ELISA). Serology does not detect current infection but rather measures past exposure.

Drug Resistance Tests

Drug resistance tests must be performed in specialized laboratories to assess the susceptibility to antimalarial compounds of parasites collected from a specific patient. Two main laboratory methods are available:

In vitro tests: The parasites are grown in culture in the presence of increasing concentrations of drugs; the drug concentration that inhibits parasite growth is used as endpoint.

Molecular characterization: Molecular markers assessed by PCR or gene sequencing also allow the prediction, to some degree, of resistance to some drugs. CDC recommends that all cases of malaria diagnosed in the United States should be evaluated for evidence of drug resistance.

PREVENTION

Vector control is the main way to reduce malaria transmission at the community level. It is the only intervention that can reduce malaria transmission from very high levels to close to zero. For individuals, personal protection against mosquito bites represents the first line of defence for malaria prevention.

Two forms of vector control are effective in a wide range of circumstances:

Insecticide Treated Net (ITN)

Long-lasting insecticidal nets (LLINs) are the preferred form of ITNs for public health distribution programmes. WHO recommends coverage for all at-risk persons; and in most settings. The most cost effective way to achieve this is through provision of free LLINs, so that everyone sleeps under a LLIN every night.
**Indoor spraying with residual insecticides**

Indoor spraying (IRS) with insecticides is a powerful way to rapidly reduce malaria transmission. Its full potential is realized when at least 80% of houses in targeted areas are sprayed. Indoor spraying is effective for 3–6 months, depending on the insecticide used and the type of surface on which it is sprayed. DDT can be effective for 9–12 months in some cases. Longer-lasting forms of existing IRS insecticides, as well as new classes of insecticides for use in IRS programmes, are under development.

Antimalarial medicines can also be used to prevent malaria. For travellers, malaria can be prevented through chemoprophylaxis, which suppresses the blood stage of malaria infections, thereby preventing malaria disease. In addition, WHO recommends intermittent preventive treatment with sulfadoxine-pyrimethamine for pregnant women living in high transmission areas, at each scheduled antenatal visit after the first trimester. Similarly, for infants living in high-transmission areas of Africa, 3 doses of intermittent preventive treatment with sulfadoxine-pyrimethamine is recommended delivered alongside routine vaccinations. In 2012, WHO recommended Seasonal Malaria Chemoprevention as an additional malaria prevention strategy for areas of the Sahel sub-Region of Africa. The strategy involves the administration of monthly courses of amodiaquine plus sulfadoxine-pyrimethamine to all children under 5 years of age during the high transmission season.

**Insecticide resistance**

Much of the success to date in controlling malaria is due to vector control. Vector control is highly dependent on the use of pyrethroids, which are the only class of insecticides currently recommended for ITNs or LLINs. In recent years, mosquito resistance to pyrethroids has emerged in many countries. In some areas, resistance to all 4 classes of insecticides used for public health has been detected. Fortunately, this resistance has only rarely been associated with decreased efficacy, and LLINs and IRS remain highly effective tools in almost all settings.
However, countries in sub-Saharan Africa and India are of significant concern. These countries are characterized by high levels of malaria transmission and widespread reports of insecticide resistance. The development of new, alternative insecticides is a high priority and several promising products are in the pipeline. Development of new insecticides for use on bed nets is a particular priority.

Detection of insecticide resistance should be an essential component of all national malaria control efforts to ensure that the most effective vector control methods are being used. The choice of insecticide for IRS should always be informed by recent, local data on the susceptibility target vectors.

In order to ensure a timely and coordinated global response to the threat of insecticide resistance, WHO has worked with a wide range of stakeholders to develop the "Global Plan for Insecticide Resistance Management in malaria vectors" (GPIRM), which was released in May 2012. The GPIRM puts forward a five-pillar strategy calling on the global malaria community to:

- plan and implement insecticide resistance management strategies in malaria-endemic countries;
- ensure proper and timely entomological and resistance monitoring, and effective data management;
- develop new and innovative vector control tools;
- fill gaps in knowledge on mechanisms of insecticide resistance and the impact of current insecticide resistance management approaches; and
- ensure that enabling mechanisms (advocacy as well as human and financial resources) are in place.

**Surveillance**

Tracking progress is a major challenge in malaria control. In 2012, malaria surveillance systems detected only around 14% of the estimated global number of cases. Stronger malaria surveillance systems are urgently needed to enable a timely and effective malaria response in
endemic regions, to prevent outbreaks and resurgences, to track progress, and to hold governments and the global malaria community accountable.

**Elimination**

Malaria elimination is defined as interrupting local mosquito-borne malaria transmission in a defined geographical area, i.e. zero incidences of locally contracted cases. Malaria eradication is defined as the permanent reduction to zero of the worldwide incidence of malaria infection caused by a specific agent; i.e. applies to a particular malaria parasite species.

On the basis of reported cases for 2013, 55 countries are on track to reduce their malaria case incidence rates by 75%, in line with World Health Assembly targets for 2015. Large-scale use of WHO-recommended strategies, currently available tools, strong national commitments, and coordinated efforts with partners, will enable more countries – particularly those where malaria transmission is low and unstable – to reduce their disease burden and progress towards elimination. In recent years, 4 countries have been certified by the WHO Director-General as having eliminated malaria: United Arab Emirates (2007), Morocco (2010), Turkmenistan (2010), and Armenia (2011).

**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 has been evaluated in a large clinical trial in 7 countries in Africa and has been submitted to the European Medicines Agency under art. 58 for regulatory review. A WHO recommendation for use will depend on the final results from the large clinical trial and a positive regulatory review. The recommendation as to whether or not this vaccine should be added to existing malaria control tools is expected in late 2015.
TREATMENT OF MALARIA

Malaria is treated with antimalarial medications; the ones used depend on the type and severity of the disease. While medications against fever are commonly used, their effects on outcomes are not clear.

Uncomplicated malaria may be treated with oral medications. The most effective treatment for \textit{P. falciparum} infection is the use of artemisinins in combination with other antimalarials (known as artemisinin-combination therapy, or ACT), which decreases resistance to any single drug component. These additional antimalarials include: amodiaquine, lumefantrine, mefloquine or sulfadoxine/pyrimethamine. Another recommended combination is dihydroartemisinin and piperaquine. ACT is about 90% effective when used to treat uncomplicated malaria. To treat malaria during pregnancy, the WHO recommends the use of quinine plus clindamycin early in the pregnancy (1st trimester), and ACT in later stages (2nd and 3rd trimesters). In the 2000s (decade), malaria with partial resistance to artemisins emerged in Southeast Asia.

Infection with \textit{P. vivax}, \textit{P. ovale} or \textit{P. malariae} is usually treated without the need for hospitalization. Treatment of \textit{P. vivax} requires both treatment of blood stages (with chloroquine or ACT) and clearance of liver forms with primaquine.

Recommended treatment for severe malaria is the intravenous use of antimalarial drugs. For severe malaria, artesunate is superior to quinine in both children and adults. Treatment of severe malaria involves supportive measures that are best done in a critical care unit. This includes the management of high fevers and the seizures that may result from it. It also includes monitoring for poor breathing effort, low blood sugar, and low blood potassium.
Resistance

Drug resistance poses a growing problem in 21st-century malaria treatment. Resistance is now common against all classes of antimalarial drugs save the artemisinins. Treatment of resistant strains became increasingly dependent on this class of drugs. The cost of artemisinins limits their use in the developing world. Malaria strains found on the Cambodia–Thailand border are resistant to combination therapies that include artemisinins, and may therefore be untreatable. Exposure of the parasite population to artemisinin monotherapies in sub therapeutic doses for over 30 years and the availability of substandard artemisinins likely drove the selection of the resistant phenotype. Resistance to artemisinin has been detected in Cambodia, Myanmar, Thailand, and Vietnam and there has been emerging resistance in Laos.

COMPLICATIONS OF MALARIA

Malaria is a serious illness which can be fatal if not diagnosed and treated quickly, particularly in pregnant women, babies, young children and the elderly. The Plasmodium falciparum parasite causes the most severe malaria symptoms and most deaths. As complications of severe malaria can occur within hours or days of the first symptoms, it is important to seek urgent medical help as soon as possible.

Anaemia

The destruction of red blood cells by the malaria parasite can cause severe anaemia. Anaemia is a condition where the red blood cells are unable to carry enough oxygen to the body's muscles and organs, leaving you feeling drowsy, weak and faint.

Cerebral malaria

In rare cases, malaria can affect the brain. This is known as cerebral malaria and it can cause your brain to swell, sometimes leading to permanent brain damage. It can also cause seizures (fits) or coma (a state of unconsciousness).
Other complications

Other complications that can arise due to severe malaria include:

- liver failure and jaundice (yellowing of the skin and whites of the eyes)
- shock (a sudden drop in blood pressure)
- pulmonary oedema (a build-up of fluid in the lungs)
- acute respiratory distress syndrome (ARDS)
- abnormally low blood sugar (hypoglycaemia)
- kidney failure
- swelling and rupturing of the spleen
- dehydration

Malaria in pregnancy

The World Health Organization (WHO) recommends that pregnant women should avoid travelling to areas where there is a risk of malaria. If you get malaria while pregnant, you and your baby have an increased risk of developing serious complications, such as:

- Premature birth (birth before 37 weeks of pregnancy)
- Low birthweight
- Restricted growth of the baby in the womb
- Still birth
- Miscarriage
- Death of the mother.

PROGNOSIS

When properly treated, people with malaria can usually expect a complete recovery. However, severe malaria can progress extremely rapidly and cause death within hours or days. In the most severe cases of the disease, fatality rates can reach 20%, even with intensive care and treatment. Over the longer term, developmental impairments have been documented in children who have suffered episodes of severe malaria. Chronic infection without severe disease can occur in an
immune-deficiency syndrome associated with a decreased responsiveness to *Salmonella* bacteria and the Epstein–Barr virus.

During childhood, malaria causes anemia during a period of rapid brain development, and also direct brain damage resulting from cerebral malaria. Some survivors of cerebral malaria have an increased risk of neurological and cognitive deficits, behavioral disorders, and epilepsy.

Malaria prophylaxis was shown to improve cognitive function and school performance in clinical trials when compared to placebo groups.