Malaria life cycle video

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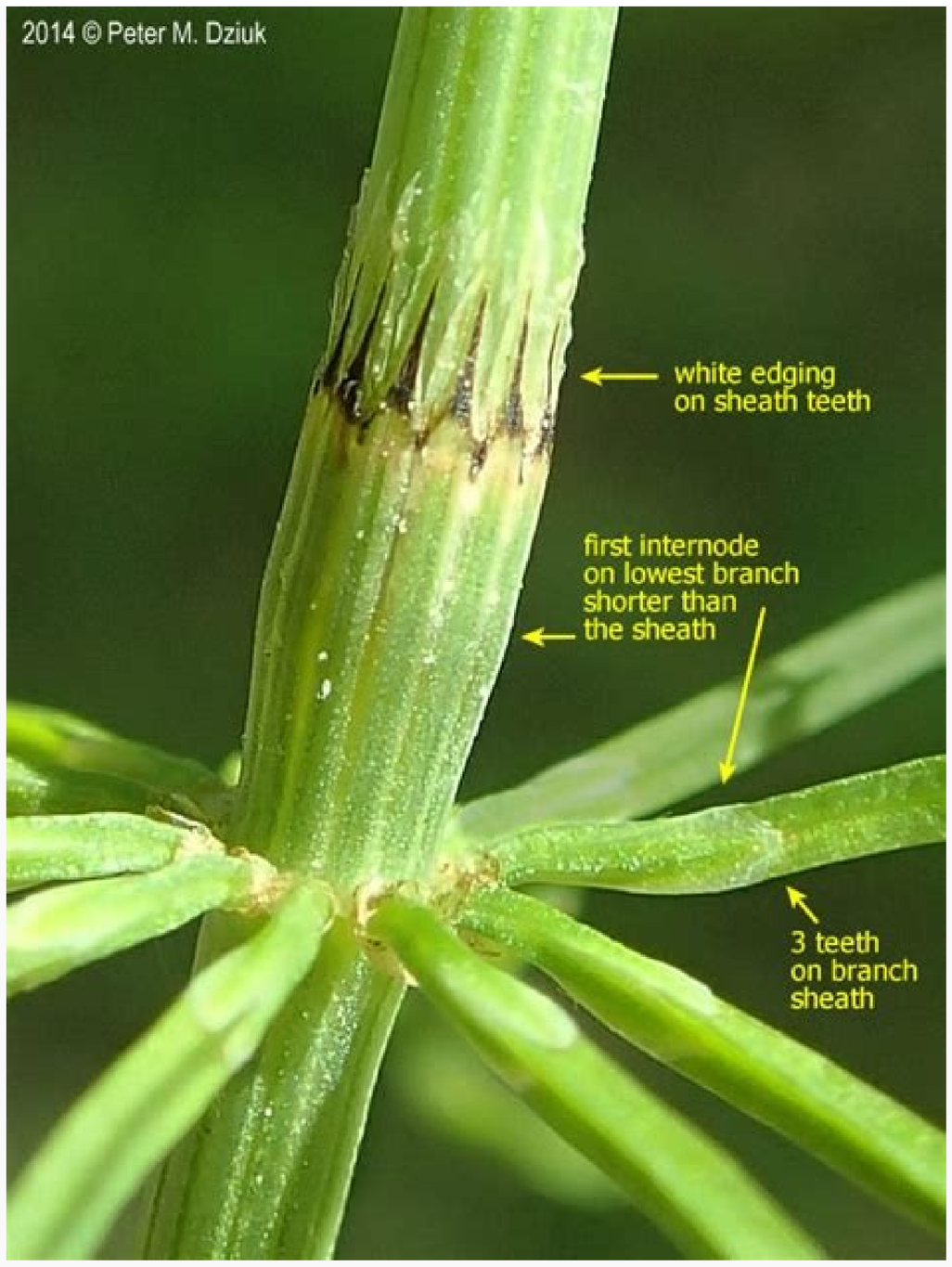
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Life cycle of malaria flowchart. Malaria life cycle days. Malaria life cycle in hindi. Life cycle of malaria vector. Life cycle of malaria in man and mosquito.

Symptoms manifest between eight and 25 days after infection, and are typically flu-like: they include headaches, fever, shivering, joint pain, vomiting, jaundice, retinal damage and convulsions. Paroxysm – feeling suddenly cold and uncontrollable shivering followed by fever and sweating – is extremely common. People with severe malaria – usually caused by P. falciparum – display symptoms such as abnormal posture, inability to turn the eyes in the same direction, seizures, or even falling into a coma. If malaria is not treated quickly, it can progress to severe illness, often leading to multiple organ failure in adults, or even death. Malaria in pregnant women can cause stillbirths, infant mortality, and low birth weight. The best way to fight malaria is to prevent infection in the first place. WHO recommends that all people living in malaria transmission areas practise protection against malaria. Two common methods are: using insecticide-treated mosquito nets and indoor spraying. By forming a physical barrier between mosquitos and humans, nets are a simple and effective means of preventing infection, particularly if people sleep underneath one, as mosquitos emerge to feed at dawn and dusk. More people in Africa are benefiting from insecticide-treated nets. Today, more than half of people at risk from malaria sleep under these nets, whereas in 2010 only 29% of those at risk did so. Fumigating homes on an annual or semi-annual basis can also rapidly reduce malaria transmission. However, this method is not widely used in many sub-Saharan countries. This is because mosquitos are increasingly resistant to earlier, less expensive forms of insecticide, and for some people, the newer, more effective forms are prohibitively expensive. Medicines can also be used for the prevention of malaria, especially for particularly at-risk population groups. These at-risk groups include young children, pregnant women, and travellers from malaria-free parts of the world who might not have built up any residual immunity. WHO recommends that pregnant women in areas of Africa with moderate and high malaria transmission rates take an anti-malarial medicine like sulfadoxine-pyrimethamine. More vulnerable people are receiving this potentially life-saving treatment in Africa each year. Across the 33 African countries which had been carrying out this treatment, an estimated 22% of eligible pregnant women received the recommended three or more doses, compared with 17% in 2015 and 0% in 2010. Malaria can also be prevented by using seasonal malaria chemoprevention. In 2017, a total of 15.7 million children in 12 countries in Africa's Sahel region were protected through seasonal malaria chemoprevention (SMC) programmes. However, about 13.6 million children who could have benefited from this intervention were not covered, mainly due to lack of funding. When malaria infection does occur, it is important that it be quickly diagnosed and treated. This means that a mild case can be stopped from developing into something more dangerous, even fatal, and it can also prevent malaria from spreading further. WHO recommends taking four key steps for the effective diagnosis and treatment of malaria: First, the patient with suspected malaria should have it confirmed either using microscopy or a rapid diagnostic test (RDT); Next, simple infections should be treated with fast-acting artemisinin-based combination therapy (ACT); In areas with low malaria rates, a single dose of primaquine should be added to this treatment to reduce the chance of malaria spreading further; Severe cases of malaria should be treated with injectable artesunate for at least 24 hours. Once the patient can take oral medicines, they should complete a three-day course of artemisinin-based combination therapy. For other uses, see Malaria (disambiguation). Not to be confused with Miliaria. Medical conditionMalariaMalaria parasite connecting to a red blood cellPronunciation/məˈlɛəriə/ SpecialtyInfectious diseaseSymptomsFever, vomiting, headache, yellow skin[1]Complicationsseizures, coma,[1] organ failure, anemia, cerebral malaria[2]Usual onset10–15 days post exposure[3]CausesPlasmodium spread by mosquitoes[1]Diagnostic methodExamination of the blood, antigen detection tests[1]PreventionMosquito nets, insect repellent, mosquito control, medications[1]MedicationAntimalarial medication[3]Frequency241 million (2020)[4]Deaths627,000+ (2020)[4] Malaria is a mosquito-borne infectious disease that affects humans and other animals.[5][6][3] Malaria causes symptoms that typically include fever, tiredness, vomiting, and headaches.[1][7] In severe cases, it can cause jaundice, seizures, coma, or death.[1] Symptoms usually begin ten to fifteen days after being bitten by an infected mosquito.[3] If not properly treated, people may have recurrences of the disease months later.[3] In those who have recently survived an infection, reinfection usually causes milder symptoms.[1] This partial resistance disappears over months to years if the person has no continuing exposure to malaria.[1] Malaria is caused by single-celled microorganisms of the Plasmodium group.[3] It is spread exclusively through bites of infected Anopheles mosquitoes.[3][8] The mosquito bite introduces the parasites from the mosquito's saliva into a person's blood.[3] The parasites travel to the liver where they mature and reproduce.[1] Five species of Plasmodium can infect and be spread by humans.[1] Most deaths are caused by P. falciparum, whereas P. vivax, P. ovale, and P. malariae generally cause a milder form of malaria.[1][3] The species P. knowlesi rarely causes disease in humans.[3] Malaria is typically diagnosed by the microscopic examination of blood using blood films, or with antigen-based rapid diagnostic tests.[1] Methods that use the polymerase chain reaction to detect the parasite's DNA have been developed, but are not widely used in areas where malaria is common due to their cost and complexity.[9] The risk of disease can be reduced by preventing mosquito bites through the use of mosquito nets and insect repellents or with mosquito-control measures such as spraying insecticides and draining standing water.[1] Several medications are available to prevent malaria for travellers in areas where the disease is common.[3] Occasional doses of the combination medication sulfadoxine/pyrimethamine are recommended in infants and after the first trimester of pregnancy in areas with high rates of malaria.[3] As of 2020, there is one vaccine which has been shown to reduce the risk of malaria by about 40% in children in Africa.[10][11] A pre-print study of another vaccine has shown 77% vaccine efficacy, but this study has not yet passed peer review.[needs update][12] Efforts to develop more effective vaccines are ongoing.[11] The recommended treatment for malaria is a combination of antimalarial medications that includes artemisinin.[13][14][1][3] The second medication may be either mefloquine, lumefantrine, or sulfadoxine/pyrimethamine.[15] Quinine, along with doxycycline, may be used if artemisinin is not available.[15] It is recommended that in areas where the disease is common, malaria is confirmed if possible before treatment is started due to concerns of increasing drug resistance.[3] Resistance among the parasites has developed to several antimalarial medications; for example, chloroquine-resistant P. falciparum has spread to most malarial areas, and resistance to artemisinin has become a problem in some parts of Southeast Asia.[3] The disease is widespread in the tropical and subtropical regions that exist in a broad band around the equator.[16][1] This includes much of sub-Saharan Africa, Asia, and Latin America.[3] In 2020 there were 241 million cases of malaria worldwide resulting in an estimated 627,000 deaths. Approximately 95% of the cases and deaths occurred in sub-Saharan Africa. Rates of disease have decreased from 2010 to 2014 but increased from 2015 to 2020.[4] Malaria is commonly associated with poverty and has a significant negative effect on economic development.[17][18] In Africa, it is estimated to result in losses of US$12 billion a year due to increased healthcare costs, lost ability to work, and adverse effects on tourism.[19] Video summary (script) Signs and symptoms Main symptoms of malaria[20] Adults with malaria tend to experience chills and fever – classically in periodic intense bouts lasting around six hours, followed by a period of sweating and fever relief – as well as headache, fatigue, abdominal discomfort, and muscle pain.[21] Children tend to have more general symptoms: fever, cough, vomiting, and diarrhea.[21] Initial manifestations of the disease—common to all malaria species—are similar to flu-like symptoms,[22] and can resemble other conditions such as sepsis, gastroenteritis, and viral diseases.[9] The presentation may include headache, fever, shivering, joint pain, vomiting, hemolytic anemia, jaundice, hemoglobin in the urine, retinal damage, and convulsions.[23] The classic symptom of malaria is paroxysm—a cyclical occurrence of sudden coldness followed by shivering and then fever and sweating, occurring every two days (tertian fever) in P. vivax and P. ovale infections, and every three days (quartan fever) for P. malariae. P. falciparum infection can cause recurrent fever every 36–48 hours, or a less pronounced and almost continuous fever.[24] Symptoms typically begin 10–15 days after the initial mosquito bite, but can occur as late as several months after infection with some P. vivax strains.[21] Travellers taking preventative malaria medications may develop symptoms once they stop taking the drugs.[21] Severe malaria is usually caused by P. falciparum (often referred to as falciparum malaria). Symptoms of falciparum malaria arise 9–30 days after infection.[22] Individuals with cerebral malaria frequently exhibit neurological symptoms, including abnormal posturing, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction), opisthotonus, seizures, or coma.[22] Complications Malaria has several serious complications. Among these is the development of respiratory distress, which occurs in up to 25% of adults and 40% of children with severe P. falciparum malaria. Possible causes include respiratory compensation of metabolic acidosis, noncardiogenic pulmonary oedema, concomitant pneumonia, and severe anaemia. Although rare in young children with severe malaria, acute respiratory distress syndrome occurs in 5–25% of adults and up to 29% of pregnant women.[25] Coinfection of HIV with malaria increases mortality.[26] Kidney failure is a feature of blackwater fever, where haemoglobin from lysed red blood cells leaks into the urine.[22] Infection with P. falciparum may result in cerebral malaria, a form of severe malaria that involves encephalopathy. It is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever.[27] An enlarged spleen, enlarged liver or both of these, severe headache, low blood sugar, and haemoglobin in the urine with kidney failure may occur.[22] Complications may include spontaneous bleeding, coagulopathy, and shock.[28] Malaria in pregnant women is an important cause of stillbirths, infant mortality, miscarriage and low birth weight,[29] particularly in P. falciparum infection, but also with P. vivax.[30] Cause Malaria is caused by infection with parasites in the genus Plasmodium.[31] In humans, malaria is caused by six Plasmodium species: P. falciparum, P. malariae, P. ovale curtisi, P. ovale wallikeri, P. vivax and P. knowlesi.[32] Among those infected, P. falciparum is the most common species identified (~75%) followed by P. vivax (~20%).[9] Although P. falciparum traditionally accounts for the majority of deaths,[33] recent evidence suggests that P. vivax malaria is associated with potentially life-threatening conditions about as often as with a diagnosis of P. falciparum infection.[34] P. vivax proportionally is more common outside Africa.[35] There have been documented human infections with several species of Plasmodium from higher apes; however, except for P. knowlesi—a zoonotic species that causes malaria in macaques[36]—these are mostly of limited public health importance.[37] The life cycle of malaria parasites. Sporozoites are introduced by a mosquito bite. They migrate to the liver, where they multiply into thousands of merozoites. The merozoites infect red blood cells and replicate, infecting more and more red blood cells. Some parasites form gametocytes, which are taken up by a mosquito, continuing the life cycle. Parasites are typically introduced by the bite of an infected Anopheles mosquito. What these inoculated parasites, called "sporozoites", do in the skin and lymphatics, exactly, has yet to be accurately determined.[38] However, a percentage of sporozoites follow the bloodstream to the liver, where they invade hepatocytes.[39] They grow and divide in the liver for 2–10 days, with each infected hepatocyte eventually harboring up to 40,000 parasites.[39] The infected hepatocytes break down, releasing this invasive form of Plasmodium cells, called "merozoites" into the bloodstream. In the blood, the merozoites rapidly invade individual red blood cells, replicating over 24–72 hours to form 16–32 new merozoites.[39] The infected red blood cell lyses, and the new merozoites infect new red blood cells, resulting in a cycle that continuously amplifies the number of parasites in an infected person.[39] However, most of the P. vivax replicating merozoite biomass is now (since 2021) known to be hidden in the spleen and bone marrow (perhaps elsewhere too), thereby supporting the astute, long-standing (since 2011) but previously ignored theory that non-circulating merozoites are the source many P. vivax malarial recurrences (see "Recurrent malaria" section below).[40] Over rounds of this red blood cell infection cycle in the bloodstream and elsewhere, a small portion of parasites do not replicate, but instead develop into early sexual stage parasites called male and female "gametocytes". These gametocytes develop in the bone marrow for 11 days, then return to the blood circulation to await uptake by the bite of another mosquito.[39] Once inside a mosquito, the gametocytes undergo sexual reproduction, and eventually form daughter sporozoites that migrate to the mosquito's salivary glands to be injected into a new host when the mosquito bites.[39] The liver infection causes no symptoms; all symptoms of malaria result from the infection of red blood cells.[32] Symptoms develop once there are more than around 100,000 parasites per milliliter of blood.[32] Many of the symptoms associated with severe malaria are caused by the tendency of P. falciparum to bind to blood vessel walls, resulting in damage to the affected vessels and surrounding tissue. Parasites sequestered in the blood vessels of the lung contribute to respiratory failure. In the brain, they contribute to coma. In the placenta they contribute to low birthweight and preterm labor, and increase the risk of abortion and stillbirth.[32] The destruction of red blood cells during infection often results in anemia, exacerbated by reduced production of new red blood cells during infection.[32] Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar and do not transmit the disease. Females of the mosquito genus Anopheles prefer to feed at night. They usually start searching for a meal at dusk, and continue through the night until they succeed.[41] Malaria parasites can also be transmitted by blood transfusions, although this is rare.[42] Recurrent malaria Symptoms of malaria can recur after varying symptom-free periods. Depending upon the cause, recurrence can be classified as recrudescence, relapse, or reinfection. Recrudescence is when symptoms return after a symptom-free period and the origin is parasites that survived in the blood as a result of inadequate or ineffective treatment.[43] Relapse is when symptoms reappear after the parasites have been eliminated from the blood and the recurrence source is activated parasites which had persisted as dormant hypnozoites in liver cells.[44] Relapse commonly occurs after 8–24 weeks and is often seen in P. vivax and P. ovale infections.[9] However, relapse-like P. vivax recurrences are probably being over-attributed to hypnozoite activation. Some of them might have an extra-vascular or sequestered merozoite origin, making those recurrences recrudescences, not relapses.[45] Newly recognised, non-hypnozoite, possible contributing sources to recurrent peripheral P. vivax parasitemia are erythrocytic forms in the bone marrow and spleen.[46] P. vivax malaria cases in temperate areas often involve overwintering by hypnozoites, with relapses beginning the year after the mosquito bite.[47] Reinfection means that the parasites responsible for the past infection were eliminated from the body but a new parasite(s) was introduced. Reinfection cannot readily be distinguished from relapse and recrudescence, although recurrence of infection within two weeks of treatment for the initial malarial manifestations is typically attributed to treatment failure.[48] But doing this is not necessarily correct.[49] People may develop some immunity when exposed to frequent infections.[50] Pathophysiology Further information: Plasmodium falciparum § Pathogenesis Micrograph of a placenta from a stillbirth due to maternal malaria. H&E stain. Red blood cells are anuclear; blue/black staining in bright red structures (red blood cells) indicate foreign nuclei from the parasites. Electron micrograph of a Plasmodium falciparum-infected red blood cell (center), illustrating adhesion protein "knobs" Malaria infection develops via two phases: one that involves the liver (exoerythrocytic phase), and one that involves red blood cells, or erythrocytes (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 where they infect hepatocytes, multiplying asexually and asymptomatically for a period of 8–30 days.[51] After a potential dormant period in the liver, these organisms differentiate to yield thousands of merozoites, which, following rupture of their host cells, escape into the blood and infect red blood cells to begin the erythrocytic stage of the life cycle.[51] The parasite escapes from the liver undetected by wrapping itself in the cell membrane of the infected host liver cell.[52] Within the red blood cells, the parasites multiply further, again asexually, periodically breaking out of their host cells to invade fresh red blood cells. Several such amplification cycles occur. Thus, classical descriptions of waves of fever arise from simultaneous waves of merozoites escaping and infecting red blood cells.[51] Some P. vivax sporozoites do not immediately develop into exoerythrocytic-phase merozoites, but instead, produce hypnozoites that remain dormant for periods ranging from several months (7–10 months is typical) to several years.[47] After a period of dormancy, they reactivate and produce merozoites. Hypnozoites are responsible for long incubation and late relapses in P. vivax infections,[47] although their existence in P. ovale is uncertain.[53] The parasite is relatively protected from attack by the body's immune system because for most of its human life cycle it resides within the liver and blood cells and is relatively invisible to immune surveillance. However, circulating infected blood cells are destroyed in the spleen. To avoid this fate, the P. falciparum parasite displays adhesive proteins on the surface of the infected blood cells, causing the blood cells to stick to the walls of small blood vessels, thereby sequestering the parasite from passage through the general circulation and the spleen.[54] The blockage of the microvasculature causes symptoms such as those in placental malaria.[55] Sequestered red blood cells can breach the blood–brain barrier and cause cerebral malaria.[56] Genetic resistance Main article: Human genetic resistance to malaria According to a 2005 review, due to the high levels of mortality and morbidity caused by malaria—especially the P. falciparum species—it has placed the greatest selective pressure on the human genome in recent history. Several genetic factors provide some resistance to it including sickle cell trait, thalassaemia traits, glucose-6-phosphate dehydrogenase deficiency, and the absence of Duffy antigens on red blood cells.[57][58][59] The impact of sickle cell trait on malaria immunity illustrates some evolutionary trade-offs that have occurred because of endemic malaria. Sickle cell trait causes a change in the haemoglobin molecule in the blood. Normally, red blood cells have a very flexible, biconcave shape that allows them to move through narrow capillaries; however, when the modified haemoglobin S molecules are exposed to low amounts of oxygen, or crowd together due to dehydration, they can stick together forming strands that cause the cell to distort into a curved sickle shape. In these strands, the molecule is not as effective in taking or releasing oxygen, and the cell is not flexible enough to circulate freely. In the early stages of malaria, the parasite can cause infected red cells to sickle, and so they are removed from circulation sooner. This reduces the frequency with which malaria parasites complete their life cycle in the cell. Individuals who are homozygous (with two copies of the abnormal haemoglobin beta allele) have sickle-cell anaemia, while those who are heterozygous (with one abnormal allele and one normal allele) experience resistance to malaria without severe anaemia. Although the shorter life expectancy for those with the homozygous condition would tend to disfavour the trait's survival, the trait is preserved in malaria-prone regions because of the benefits provided by the heterozygous form.[59][60] Liver dysfunction Liver dysfunction as a result of malaria is uncommon and usually only occurs in those with another liver condition such as viral hepatitis or chronic liver disease. The syndrome is sometimes called malarial hepatitis.[61] While it has been considered a rare occurrence, malarial hepatopathy has seen an increase, particularly in Southeast Asia and India. Liver compromise in people with malaria correlates with a greater likelihood of complications and death.[61] Diagnosis Main article: Diagnosis of malaria The blood film is the gold standard for malaria diagnosis. Ring-forms and gametocytes of Plasmodium falciparum in human blood Due to the non-specific nature of malaria symptoms, diagnosis is typically suspected based on symptoms and travel history, then confirmed with a parasitological test. In areas where malaria is common, the World Health Organization (WHO) recommends clinicians suspect malaria in any person who reports having fevers, or who has a current temperature above 37.5 °C without any other obvious cause.[62] Malaria should similarly be suspected in children with signs of anemia: pale palms or a laboratory test showing hemoglobin levels below 8 grams per deciliter of blood.[62] In areas with little to no malaria, the WHO recommends only testing people with possible exposure to malaria (typically travel to a malaria-endemic area) and unexplained fever.[62] Malaria is usually confirmed by the microscopic examination of blood films or by antigen-based rapid diagnostic tests (RDT). Microscopy – i.e. examining Giemsa-stained blood with a light microscope – is the gold standard for malaria diagnosis.[32] Microscopists typically examine both a "thick film" of blood, allowing them to scan many blood cells in a short time, and a "thin film" of blood, allowing them to clearly see individual parasites and identify the infecting Plasmodium species.[32] Under typical field laboratory conditions, a microscopist can detect parasites when there are at least 100 parasites per microliter of blood, which is around the lower range of symptomatic infection.[62] Microscopic diagnosis is relatively resource intensive, requiring trained personnel, specific equipment, electricity, and a consistent supply of microscopy slides and stains.[62] In places where microscopy is unavailable, malaria is diagnosed with RDTs, rapid antigen tests that detect parasite proteins in a fingerstick blood sample.[62] A variety of RDTs are commercially available, targeting the parasite proteins histidine rich protein 2 (HRP2, detects P. falciparum only), lactate dehydrogenase, or aldolase.[62] The HRP2 test is widely used in Africa, where P. falciparum predominates.[32] However, since HRP2 persists in the blood for up to five weeks after an infection is treated, an HRP2 test sometimes cannot distinguish whether someone currently has malaria or previously had it.[62] Additionally, some P. falciparum parasites in the Amazon region lack the HRP2 gene, complicating detection.[62] RDTs are fast and easily deployed to places without full diagnostic laboratories.[62] However they give considerably less information than microscopy, and sometimes vary in quality from producer to producer and lot to lot.[62] Serological tests to detect antibodies against Plasmodium from the blood have been developed, but are not used for malaria diagnosis due to their relatively poor sensitivity and specificity. Highly sensitive nucleic acid amplification tests have been developed, but are not used clinically due to their relatively high cost, and poor specificity for active infections.[62] Classification Malaria is classified into either "severe" or "uncomplicated" by the World Health Organization (WHO).[9] It is deemed severe when any of the following criteria are present, otherwise it is considered uncomplicated.[63] Decreased consciousness Significant weakness such that the person is unable to walk Inability to feed Two or more convulsions Low blood pressure (less than 70 mmHg in adults and 50 mmHg in children) Breathing problems Circulatory shock Kidney failure or haemoglobin in the urine Bleeding problems, or hemoglobin less than 50 g/L (5 g/dL) Pulmonary oedema Blood glucose less than 2.2 mmol/L (40 mg/dL) Acidosis or lactate levels of greater than 5 mmol/L A parasite level in the blood of greater than 100,000 per microlitre (µL) in low-intensity transmission areas, or 250,000 per µL in high-intensity transmission areas Cerebral malaria is defined as a severe P. falciparum-malaria presenting with neurological symptoms, including coma (with a Glasgow coma scale less than 11, or a Blantyre coma scale less than 3), or with a coma that lasts longer than 30 minutes after a seizure.[64] Prevention An Anopheles stephensi mosquito shortly after obtaining blood from a human (the droplet of blood is expelled as a surplus). This mosquito is a vector of malaria, and mosquito control is an effective way of reducing its incidence. Methods used to prevent malaria include medications, mosquito elimination and the prevention of bites. As of 2020, there is one vaccine for malaria (known as RTS,S) which is licensed for use.[11][10] The presence of malaria in an area requires a combination of high human population density, high anopheles mosquito population density and high rates of transmission from humans to mosquitoes and from mosquitoes to humans. If any of these is lowered sufficiently, the parasite eventually disappears from that area, as happened in North America, Europe, and parts of the Middle East. However, unless the parasite is eliminated from the whole world, it could re-establish if conditions revert to a combination that favors the parasite's reproduction. Furthermore, the cost per person of eliminating anopheles mosquitoes rises with decreasing population density, making it economically unfeasible in some areas.[65] Prevention of malaria may be more cost-effective than treatment of the disease in the long run, but the initial costs required are out of reach of many of the world's poorest people. There is a wide difference in the costs of control (i.e. maintenance of low endemicity) and elimination programs between countries. For example, in China—whose government in 2010 announced a strategy to pursue malaria elimination in the Chinese provinces—the required investment is a small proportion of public expenditure on health. In contrast, a similar programme in Tanzania would cost an estimated one-fifth of the public health budget.[66] In 2021, the World Health Organization confirms that China has eliminated malaria. [67] In areas where malaria is common, children under five years old often have anaemia, which is sometimes due to malaria. Giving children with anaemia in these areas preventive antimalarial medication improves red blood cell levels slightly but does not affect the risk of death or need for hospitalisation.[68] Mosquito control Further information: Mosquito control Man spraying kerosene oil in standing water, Panama Canal Zone, 1912 Vector control refers to methods used to decrease malaria by reducing the levels of transmission by mosquitoes. For individual protection, the most effective insect repellents are based on DEET or picaridin.[69] However, there is insufficient evidence that mosquito repellents can prevent malaria infection.[70] Insecticide-treated nets (ITNs) and indoor residual spraying (IRS) are effective, have been commonly used to prevent malaria, and their use has contributed significantly to the decrease in malaria in the 21st century.[71][72][73] ITNs and IRS may not be sufficient to eliminate the disease, as these interventions depend on how many people use nets, how many gaps in insecticide there are (low coverage areas), if people are not protected when outside of the home, and an increase in mosquitoes that are resistant to insecticides.[71] Modifications to people's houses to prevent mosquito exposure may be an important long term prevention measure.[71] Walls where indoor residual spraying of DDT has been applied. The mosquitoes remain on the wall until they fall down dead on the floor. Insecticide-treated nets A mosquito net in use. Mosquito nets help keep mosquitoes away from people and reduce infection rates and transmission of malaria. Nets are not a perfect barrier and are often treated with an insecticide designed to kill the mosquito before it has time to find a way past the net. Insecticide-treated nets (ITNs) are estimated to be twice as effective as untreated nets and offer greater than 70% protection compared with no net.[74] Between 2000 and 2008, the use of ITNs saved the lives of an estimated 250,000 infants in Sub-Saharan Africa.[75] About 13% of households in Sub-Saharan countries owned ITNs in 2007[76] and 31% of African households were estimated to own at least one ITN in 2008. In 2000, 1.7 million (1.8%) African children living in areas of the world where malaria is common were protected by an ITN. That number increased to 20.3 million (18.5%) African children using ITNs in 2007, leaving 89.6 million children unprotected[77] and to 68% African children using mosquito nets in 2015.[78] Most nets are impregnated with pyrethroids, a class of insecticides with low toxicity. They are most effective when used from dusk to dawn.[79] It is recommended to hang a large "bed net" above the center of a bed and either tuck the edges under the mattress or make sure it is large enough such that it touches the ground.[80] ITNs are beneficial towards pregnancy outcomes in malaria-endemic regions in Africa but more data is needed in Asia and Latin America.[81] In areas of high malaria resistance, piperonyl butoxide (PBO) combined with pyrethroids in mosquito netting is effective in reducing malaria infection rates.[82] Questions remain concerning the durability of PBO on nets as the impact on mosquito mortality was not sustained after twenty washes in experimental trials.[82] Indoor residual spraying Indoor residual spraying is the spraying of insecticides on the walls inside a home. After feeding, many mosquitoes rest on a nearby surface while digesting the bloodmeal, so if the walls of houses have been coated with insecticides, the resting mosquitoes can be killed before they can bite another person and transfer the malaria parasite.[83] As of 2006, the World Health Organization recommends 12 insecticides in IRS operations, including DDT and the pyrethroids cyfluthrin and deltamethrin.[84] This public health use of small amounts of DDT is permitted under the Stockholm Convention, which prohibits its agricultural use.[85] One problem with all forms of IRS is insecticide resistance. Mosquitoes affected by IRS tend to rest and live indoors, and due to the irritation caused by spraying, their descendants tend to rest and live outdoors, meaning that they are less affected by the IRS.[86] Communities using insecticide treated nets, in addition to indoor residual spraying with 'non-pyrethroid-like' insecticides found associated reductions in malaria.[87] Additionally, the use of 'pyrethroid-like' insecticides in addition to indoor residual spraying did not result in a detectable additional benefit in communities using insecticide treated nets.[87] Housing modifications Housing is a risk factor for malaria and modifying the house as a prevention measure may be a sustainable strategy that does not rely on the effectiveness of insecticides such as pyrethroids.[71][88] The physical environment inside and outside the home that may improve the density of mosquitoes are considerations. Examples of potential modifications include how close the home is to mosquito breeding sites, drainage and water supply near the home, availability of mosquito resting sites (vegetation around the home), the proximity to live stock and domestic animals, and physical improvements or modifications to the design of the home to prevent mosquitoes from entering.[71] Other mosquito control methods People have tried a number of other methods to reduce mosquito bites and slow the spread of malaria. Efforts to decrease mosquito larvae by decreasing the availability of open water where they develop, or by adding substances to decrease their development, are effective in some locations.[89] Electronic mosquito repellent devices, which make very high-frequency sounds that are supposed to keep female mosquitoes away, have no supporting evidence of effectiveness.[90] There is a low certainty evidence that fogging may have an effect on malaria transmission.[91] Larviciding by hand delivery of chemical or microbial insecticides into water bodies containing low larval distribution may reduce malarial transmission.[92] There is insufficient evidence to determine whether larvivorous fish can decrease mosquito density and transmission in the area.[93] Medications Main article: Malaria prophylaxis There are a number of medications that can help prevent or interrupt malaria in travellers to places where infection is common. Many of these medications are also used in treatment. In places where Plasmodium is resistant to one or more medications, three medications—mefloquine, doxycycline, or the combination of atovaquone/proguanil (Malarone)—are frequently used for prevention.[94] Doxycycline and the atovaquone/proguanil are better tolerated while mefloquine is taken once a week.[94] Areas of the world with chloroquine-sensitive malaria are uncommon.[95] Antimalarial mass drug administration to an entire population at the same time may reduce the risk of contracting malaria in the population, however the effectiveness of mass drug administration may vary depending on the prevalence of malaria in the area.[96] Other factors such as drug administration plus other protective measures such as mosiquito control, the proportion of people treated in the area, and the risk of reinfection with malaria may play a role in the effectiveness of mass drug treatment approaches.[96] The protective effect does not begin immediately, and people visiting areas where malaria exists usually start taking the drugs one to two weeks before they arrive, and continue taking them for four weeks after leaving (except for atovaquone/proguanil, which only needs to be started two days before and continued for seven days afterward).[97] The use of preventive drugs is often not practical for those who live in areas where malaria exists, and their use is usually given only to pregnant women and short-term visitors. This is due to the cost of the drugs, side effects from long-term use, and the difficulty in obtaining antimalarial drugs outside of wealthy nations.[98] During pregnancy, medication to prevent malaria has been found to improve the weight of the baby at birth and decrease the risk of anaemia in the mother.[99] The use of preventive drugs where malaria-bearing mosquitoes are present may encourage the development of partial resistance.[100] Giving antimalarial drugs to infants through intermittent preventive therapy can reduce the risk of having malaria infection, hospital admission, and anaemia.[101] Mefloquine is more effective than sulfadoxine-pyrimethamine in preventing malaria for HIV-negative pregnant women. Cotrimoxazole is effective in preventing malaria infection and reduce the risk of getting anaemia in HIV-positive women.[102] Giving sulfadoxine-pyrimethamine for three or more doses as intermittent preventive therapy is superior than two doses for HIV-positive women living in malaria-endemic areas.[103] Prompt treatment of confirmed cases with artemisinin-based combination therapies (ACTs) may also reduce transmission.[104] Others Community participation and health education strategies promoting awareness of malaria and the importance of control measures have been successfully used to reduce the incidence of malaria in some areas of the developing world.[105] Recognising the disease in the early stages can prevent it from becoming fatal. Education can also inform people to cover over areas of stagnant, still water, such as water tanks that are ideal breeding grounds for the parasite and mosquito, thus cutting down the risk of the transmission between people. This is generally used in urban areas where there are large centers of population in a confined space and transmission would be most likely in these areas.[106] Intermittent preventive therapy is another intervention that has been used successfully to control malaria in pregnant women and infants,[107] and in preschool children where transmission is seasonal.[108] Treatment An advertisement for quinine as a malaria treatment from 1927. Malaria is treated with antimalarial medications; the ones used depends on the type and severity of the disease.[109] While medications against fever are commonly used, their effects on outcomes are not clear.[110][111] Providing free antimalarial drugs to households may reduce childhood deaths when used appropriately. Programmes which presumptively treat all causes of fever with antimalarial drugs may lead to overuse of antimalarials and undertreat other causes of fever. Nevertheless, the use of malaria rapid-diagnostic kits can help to reduce over-usage of antimalarials.[112][113] Uncomplicated malaria Simple or uncomplicated malaria may be treated with oral medications. Artemisinin drugs are effective and safe in treating uncomplicated malaria.[114] Artemisinin in combination with other antimalarials (known as artemisinin-combination therapy, or ACT) is about 90% effective when used to treat uncomplicated malaria.[75] The most effective treatment for P. falciparum infection is the use of ACT, which decreases resistance to any single drug component.[115][116] Artemether-lumefantrine (six-dose regimen) is more effective than the artemether-lumefantrine (four-dose regimen) or other regimens not containing artemisinin derivatives in treating falciparum malaria.[117][118] Another recommended combination is dihydroartemisinin and piperaquine.[119][120][121] Artemisinin-naphthoquine combination therapy showed promising results in treating falciparum malaria.[122] However, more research is needed to establish its efficacy as a reliable treatment.[123] Artesunate plus mefloquine performs better than mefloquine alone in treating uncomplicated falciparum malaria in low transmission settings.[124] Atovaquone-proguanil is effective against uncomplicated falciparum with a possible failure rate of 5% to 10%; the addition of artesunate may reduce failure rate.[125] Azithromycin monotherapy or combination therapy has not shown effectiveness in treating plasmodium or vivax malaria.[126] Amodiaquine plus sulfadoxine-pyrimethamine may achieve less treatment failures when compared to sulfadoxine-pyrimethamine alone in uncomplicated falciparum malaria.[127] There is insufficient data on chlorproguanil-dapsone in treating uncomplicated falciparum malaria.[128][129] The addition of primaquine with artemisinin-based combination therapy for falciparum malaria reduces its transmission at day 3-4 and day 8 of infection.[130] Sulfadoxine-pyrimethamine plus artesunate is better than sulfadoxine-pyrimethamine plus amodiaquine in controlling treatment failure at day 28. However, the latter is better than the former in reducing gametocytes in blood at day 7.[131] Infection with P. vivax, P. ovale or P. malariae usually does not require hospitalisation. Treatment of P. vivax requires both treatment of blood stages (with chloroquine or artemisinin-based combination therapy) and clearance of liver forms with an 8-aminoquinoline agent such as primaquine or tafenoquine.[132][133] 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).[134][135] There is limited safety data on the antimalarial drugs in pregnancy.[136] Severe and complicated malaria Cases of severe and complicated malaria are almost always caused by infection with P. falciparum. The other species usually cause only febrile disease.[137] Severe and complicated malaria cases are medical emergencies since mortality rates are high (10% to 50%).[138] Recommended treatment for severe malaria is the intravenous use of antimalarial drugs. For severe malaria, parenteral artesunate was superior to quinine in both children and adults.[139][140] In another systematic review, artemisinin derivatives (artemether and arteether) were as efficacious as quinine in the treatment of cerebral malaria in children.[141] 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.[33] Artemisinin derivatives have the same or better efficacy than quinolones in preventing deaths in severe or complicated malaria.[142] Quinine loading dose helps to shorten the duration of fever and increases parasite clearance from the body.[143] There is no difference in effectiveness when using intrarectal quinine compared to intravenous or intramuscular quinine in treating uncomplicated/complicated falciparum malaria.[144] There is insufficient evidence for intramuscular arteether to treat severe malaria.[145] The provision of rectal artesunate before transfer to hospital may reduce the rate of death for children with severe malaria.[146] Cerebral malaria is the form of severe and complicated malaria with the worst neurological symptoms.[147] There is insufficient data on whether osmotic agents such as mannitol or urea are effective in treating cerebral malaria.[148] Routine phenobarbitone in cerebral malaria is associated with fewer convulsions but possibly more deaths.[149] There is no evidence that steroids would bring treatment benefits for cerebral malaria.[150] Managing Cerebral Malaria Cerebral malaria usually makes a patient comatose, if the cause of the coma is in doubt, test for other locally prevalent causes of encephalopathy (bacterial, viral or fungal infection) should be carried out. In areas where there is a high prevalence of malaria infection (e.g. tropical region) treatment can start without testing first.[citation needed] To manage the cerebral malaria when confirmed the following can be done: Patients in coma should be given meticulous nursing care (monitor vital signs, turn patient every 2 hours, avoid lying the patient in a wet bed etc.) A sterile urethral catheter should be inserted to help with urinating To aspirate stomach content, a sterile nasogastric tube should be inserted. In the occasion of convulsions, a slow intravenous injection of benzodiazepine is administered.[151] There is insufficient evidence to show that blood transfusion is useful in either reducing deaths for children with severe anaemia or in improving their haematocrit in one month.[152] There is insufficient evidence that iron chelating agents such as deferoxamine and deferiprone improve outcomes of those with malaria falciparum infection.[153] Resistance Drug resistance poses a growing problem in 21st-century malaria treatment.[154] In the 2000s (decade), malaria with partial resistance to artemisins emerged in Southeast Asia.[155][156] Resistance is now common against all classes of antimalarial drugs apart from artemisinins. Treatment of resistant strains became increasingly dependent on this class of drugs. The cost of artemisinins limits their use in the developing world.[157] Malaria strains found on the Cambodia–Thailand border are resistant to combination therapies that include artemisinins, and may, therefore, be untreatable.[158] Exposure of the parasite population to artemisinin monotherapies in subtherapeutic doses for over 30 years and the availability of substandard artemisinins likely drove the selection of the resistant phenotype.[159] Resistance to artemisinin has been detected in Cambodia, Myanmar, Thailand, and Vietnam,[160] and there has been emerging resistance in Laos.[161][162] Resistance to the combination of artemisinin and piperaquine was first detected in 2013 in Cambodia, and by 2019 had spread across Cambodia and into Laos, Thailand and Vietnam (with up to 80 percent of malaria parasites resistant in some regions).[163] There is insufficient evidence in unit packaged antimalarial drugs in preventing treatment failures of malaria infection. However, if supported by training of healthcare providers and patient information, there is improvement in compliance of those receiving treatment.[164] Prognosis Disability-adjusted life year for malaria per 100,000 inhabitants in 2004 no data

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