Some Occupational Diseases in Culture Fisheries Management and Practices Part One: Malaria and River Blindness (Onchocerciasis)

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Abstract: Malaria and Onchocerciasis are some occupational diseases in culture fisheries management and practices discussed to enlighten fish culturist the health implications of the profession. The pond environment forms the breeding grounds the female anopheles mosquito and silmulium fly the vectors of malaria and onchocerciasis, respectively. Malaria is a borne infectious disease of humans and other animals caused by eukaryotic protists of the genus Plasmodium. The disease results from the multiplication of Plasmodium parasites within red blood cells, causing symptoms that typically include fever and headache, in severe cases progressing to coma or death. It is widespread in tropical and subtropical regions, including much of Sub-Saharan Africa, Asia and the Americas. Five species of Plasmodium can infect and be transmitted by humans. Severe disease is largely caused by Plasmodium falciparum; while the disease caused by Plasmodium vivax, Plasmodium ovale and Plasmodium malariae is generally a milder disease that is rarely fatal. Plasmodium knowlesi is a zoonosis that causes malaria in macaques but can also infect humans. Onchocerciasis is the world's second-leading infectious cause of blindness. It is not the nematode, but its endosymbiont, Wolbachia pipientis, that causes the severe inflammatory response that leaves many blind. The parasite is transmitted to humans through the bite of a black fly of the genus Simulium. The larval nematodes spread throughout the body. When the worms die, their Wolbachia symbionts are released, triggering a host immune system response that can cause severe itching and can destroy optical tissue in the eye. The life of the parasite (O. volvulus) can be traced through the black fly and the human hosts. The study reviews the signs and symptoms, causes, life cycle, pathogenesis, genetic resistance, diagnosis, hepatopathy, prevention, medications, vector control, indoor residual, mosquito nets and bedclothes spraying, Immunization, Other methods, treatment, epidemiology, history, prevention, discovery of the parasite, discovery of mosquito transmission, liver stage, in vitro culture, history of treatment, society and culture, counterfeit drugs, war, eradication efforts and research of Malaria and Onchocerciasis.

Keywords: Culture fisheries, malaria, management and practice, occupational diseases, onchocerciasis,

INTRODUCTION

Sustainable culture fisheries management and practices is also associated with its occupational sickness and diseases. The pond environment forms the breeding grounds the female anopheles mosquito and silmulium fly the vectors of malaria and onchocerciasis, respectively. The malaria parasite's secondary hosts are humans and other vertebrates (Beare et al., 2006). Female mosquitoes of the Anopheles genus is the primary, i.e., definitive hosts and act as transmission vectors. Young mosquitoes first ingest the malaria parasite by feeding on an infected human carrier and the infected Anopheles mosquitoes carry Plasmodium sporozoites in their salivary glands (Adak et al., 1998). A mosquito becomes infected when it takes a blood meal from an infected human. Once ingested, the parasite gametocytes taken up in the blood will further differentiate into male or female gametes and then fuse in the mosquito's gut (Adams et al., 2002; Holding and Snow, 2001). This produces an ookinete that penetrates the gut lining and produces an oocyst in the gut wall. When the oocyst ruptures, it releases sporozoites that migrate through the mosquito's body to the salivary glands, where they are then ready to infect a new human host (Bledsoe, 2005). This type of transmission is occasionally referred to as anterior station transfer. The sporozoites are injected into the skin, alongside saliva, when the mosquito takes a subsequent blood meal (Boivin, 2002).

Only female mosquitoes feed on blood while male mosquitoes feed on plant nectar, thus males 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. Onchocerciasis or river blindness or Robles' disease, is a parasitic disease caused by infection by *Onchocerca volvulus*, a nematode (roundworm) (Hoerauf, 2008).

Onchocerciasis is the world's second-leading infectious cause of blindness (Rea *et al.*, 2010). It is not the nematode, but its endosymbiont, *Wolbachia pipientis*, that causes the severe inflammatory response that leaves many blind (Baldo *et al.*, 2010). The parasite is transmitted to humans through the bite of a black fly of the genus *Simulium*. The larval nematodes spread throughout the body (Osei-Atweneboana *et al.*, 2007). When the worms die, their Wolbachia symbionts are released, triggering a host immune system response that can cause severe itching and can destroy optical tissue in the eye (Harder, 2002). The life of the parasite (*O. volvulus*) can be traced through the black fly and the human hosts in the following steps: A *Simulium* female black fly takes a blood meal on an infected human host and ingests microfilaria. The microfilaria enter the gut and thoracic flight muscles of the black fly, progressing into the first larval stage (J1.). The larvae mature into the second larval stage (J2.) and move to the proboscis and into the saliva in its third larval stage (J3.). Maturation takes about 7 days (Marcucci *et al.*, 2004). The black fly takes another blood meal, passing the larvae into the next human host's blood. The larvae migrate to the subcutaneous tissue and undergo two more molts. They form nodules as they mature into adult worms over 6 to 12 months. After maturing, adult male worms mate with female worms in the subcutaneous tissue to produce between 700 and 1,500 microfilaria per day (Osei-Atweneboana *et al.*, 2007). The microfilaria migrates to the skin during the day and the black flies only feed in the day, so the parasite is in a prime position for the female fly to ingest it (James *et al.*, 2006). Black flies take blood meals to ingest this microfilaria to restart the cycle (Köhler *et al.*, 1997).

Although the larval forms of these insects form the zooplankton population facilitating the pond productivity and the adult insects enhancing plant pollination. The negative effects are enormous and cannot be overlooked in culture fisheries management and practices in Nigeria. The study discuss the signs and symptoms, causes, life cycle, pathogenesis, genetic resistance, diagnosis, hepatopathy, prevention, medications, vector control, immunization, other methods, treatment, epidemiology, liver stage, in vitro culture, history of treatment, society and culture, counterfeit drugs, war, eradication efforts and research of malaria and river blindness.

Malaria is a mosquito-mosquito bites by distribution of mosquito nets and insect repellents, or by mosquito-control measures such as spraying borne infectious disease of humans and other animals caused by eukaryotic protists of the genus Plasmodium. The disease results from the multiplication of Plasmodium parasites within red blood cells, causing symptoms that typically include fever and headache, in severe cases progressing to coma or death. It is widespread in tropical and subtropical regions, including much of Sub-Saharan Africa, Asia and the Americas. Five species of Plasmodium can infect and be transmitted by humans. Severe disease is largely caused by *Plasmodium falciparum* (Plate 1) while the disease caused by *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae* is generally a milder disease that is rarely fatal. Plasmodium knowlesi is a zoonosis that causes malaria in macaques but can also infect humans. Malarià transmission can be reduced by preventing insecticides and draining standing water (where mosquitoes breed). Despite a clear need, no vaccine offering a high level of protection currently exists. Efforts to develop one are ongoing. A number of medications are also available to prevent malaria in travelers to malaria-endemic countries (prophylaxis).

A variety of antimalarial medications are available. Severe malaria is treated with intravenous or intramuscular quinine or, since the mid-2000s, the artemisinin derivative artesunate, which is superior to quinine in both children and adults. Resistance has developed to several antimalarial drugs, most notably chloroquine. There were an estimated 225 million cases...
of malaria worldwide in 2009. An estimated 655,000 people died from malaria in 2010, a 5% decrease from the 781,000 who died in 2009 according to the World Health Organization's 2011 World Malaria Report, accounting for 2.23% of deaths worldwide. Ninety percent of malaria-related deaths occur in sub-Saharan Africa, with ~60% of deaths being young children under the age of five. *Plasmodium falciparum*, the most severe form of malaria, is responsible for the vast majority of deaths associated with the disease. Malaria is commonly associated with poverty and can indeed be a cause of poverty and a major hindrance to economic development (Foth et al., 2003).

**Signs and symptoms:** Symptoms of malaria include fever, shivering, arthralgia (joint pain), vomiting, anemia (caused by hemolysis), jaundice, hemoglobinuria, retinal damage and convulsions (Plate 2). The classic symptom of malaria is cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting 4 to 6 h, occurring every 2 days in *P. vivax* and *P. ovale* infections and every 3 days for *P. malariae*. *P. falciparum* can have recurrent fever every 36-48 h or a less pronounced and almost continuous fever. For reasons that are poorly understood, but that may be related to high intracranial pressure, children with malaria frequently exhibit abnormal posturing, a sign indicating severe brain damage. Malaria has been found to cause cognitive impairments, especially in children. It causes widespread anemia during a period of rapid brain development and also direct brain damage. This neurologic damage results from cerebral malaria to which children are more vulnerable. Cerebral malaria is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever.

**Cause:** Severe malaria is almost exclusively caused by *Plasmodium falciparum* infection and usually arises 6-14 days after infection. Consequences of severe malaria include coma and death if untreated-young children and pregnant women are especially vulnerable (Carter et al., 2005). Splenomegaly (enlarged spleen), severe headache, cerebral ischemia, hepatomegaly (enlarged liver), hypoglycemia and hemoglobinuria with renal failure may occur. Renal failure is a feature of black water fever, where hemoglobin from lysed red blood cells leaks into the urine. Severe malaria can progress extremely rapidly and cause death within hours or days. In the most severe cases of the disease, mortality rates can exceed 20%, even with intensive care and treatment. In endemic areas, treatment is often less satisfactory and the overall mortality rate for all cases of malaria can be as high as one in ten. Over the longer term, developmental impairments have been documented in children who have suffered episodes of severe malaria.

Malaria parasites are members of the genus Plasmodium (phylum Apicomplexa). In humans malaria is caused by *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*. While *P. vivax* is responsible for the largest number of malaria infections worldwide, infections by *P. falciparum* account for about 90% of the deaths from malaria. Parasitic Plasmodium species also infect birds, reptiles, monkeys, chimpanzees and rodents. There have been documented human infections with several simian species of malaria; however, with the exception of *P. knowlesi*, these are mostly of limited public health importance. Malaria parasites contain apicoplasts, an organelle usually found in plants, complete with their own functioning genomes. These apicoplasts are thought to have originated through the endosymbiosis of algae and play a crucial role in various aspects of parasite metabolism e.g., fatty acid bio-synthesis. To date, 466 proteins have been found to be produced by apicoplasts and these are now being looked at as possible targets for novel anti-malarial drugs (Gardner et al., 1998).

**Recurrent malaria:** Malaria recurs after treatment for three reasons. Recrudescence occurs when parasites are not cleared by treatment, whereas reinfection indicates complete clearance with new infection established from a separate infective mosquito bite; both can occur with any malaria parasite species. Relapse is specific to *P. vivax* and *P. ovale* and involves re-emergence of blood-stage parasites from latent parasites (hypnozoites) in the liver. Describing a case of malaria as cured by
Pathogenesis: A mosquito infects a person by taking a blood meal. First, sporozoites (Plate 3) enter the bloodstream and migrate to the liver. They infect liver cells (hepatocytes), where they multiply into merozoites, rupture the liver cells and escape back into the bloodstream. Then, the merozoites infect red blood cells, where they develop into ring forms, trophozoites and schizonts which in turn produce further merozoites. Sexual forms (gametocytes) are also produced, which, if taken up by a mosquito, will infect the insect and continue the life cycle.

Malaria develops via two phases: an exoerythrocytic and an erythrocytic phase. The exoerythrocytic phase involves infection of the hepatic system, or liver, whereas the erythrocytic phase involves infection of the erythrocytes, or red blood cells. 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 minutes of being introduced into the human host, the sporozoites infect hepatocytes, multiplying asexually and symptomatically for a period of 8-30 days. Once 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, thus beginning the erythrocytic stage of the life cycle (Plate 4). The parasite escapes from the liver undetected by wrapping itself in the cell membrane of the infected host liver cell. Within the red blood cells, the parasites multiply further, again asexually, periodically breaking out of their hosts 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 (Mueller et al., 2007).

Some P. vivax and P. ovale sporozoites do not immediately develop into exoerythrocytic-phase merozoites, but instead produce hypnozoites that remain dormant for periods ranging from several months (6-12 months is typical) to as long as 3 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 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. This "stickiness" is the main factor giving rise to hemorrhagic complications of malaria. High endothelial venules (the smallest branches of the circulatory system) can be blocked by the attachment of masses of these infected red blood cells. The blockage of these vessels causes symptoms such as in placental and cerebral malaria (Plate 5). In cerebral malaria the sequestrated red blood cells can breach the blood brain barrier possibly 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 variations of the protein within a single parasite and even more variants within whole parasite populations. The parasite switches between a broad repertoires of PfEMP1 surface proteins, thus staying one step ahead of the pursuing immune system. Some merozoites turn into male and female gametocytes. If a mosquito pierces the skin of an infected person, it potentially picks up gametocytes within the blood. Fertilization and sexual recombination of the parasite occurs in the mosquito's gut. (Because sexual reproduction of the parasite defines the definitive host, the mosquito is the definitive host, whereas humans are the intermediate host.) New sporozoites develop and travel to the mosquito's salivary gland, completing the cycle. Pregnant women are especially attractive to the mosquitoes and malaria in pregnant women is an important cause of stillbirths, infant mortality and low birth weight, particularly in *P. falciparum* infection, but also in other species infection, such as *P. vivax*.

**Genetic resistance:** Malaria is thought to have been the greatest selective pressure on the human genome in recent history. This is due to the high levels of mortality and morbidity caused by malaria, especially the *P. falciparum* species. A number of diseases may provide some resistance to it including sickle cell disease, thalassaemias, glucose-6-phosphate dehydrogenase, Duffy antigens and possibly others. The impact of sickle cell anemia on malaria immunity is of particular interest. Sickle cell anemia causes a defect to the hemoglobin molecule in the blood. Instead of retaining the biconcave shape of a normal red blood cell, the modified hemoglobin S molecule causes the cell to sickle or distort into a curved shape. Due to the sickle shape, the molecule is not as effective in taking or releasing oxygen and therefore, malaria parasites are unable to complete their life cycle in the cell.

Individuals who are homozygous for sickle cell anemia seldom survive this defect, while those who are heterozygous experience immunity to the disease. Although the potential risk of death for those with the homozygous condition seems to be unfavorable to population survival, the trait is preserved because of the benefits provided by the heterozygous form Escalante and Ayala (1994).

**Malarial hepatopathy:** Hepatic dysfunction as a result of malaria is rare and is usually a result of a coexisting liver condition such as viral hepatitis and chronic liver disease. To be clear, the term "malarial hepatitis" is sometimes used to describe liver compromise in severe malaria; however, actual inflammation of the liver parenchyma is rarely seen. While traditionally considered a rare occurrence, malarial hepatopathy has seen an increase in malaria endemic areas, particularly in South East Asia and India. Liver compromise in malaria patients correlates with a greater likelihood of complications and mortality.

**Diagnosis:** The mainstay of malaria diagnosis has been the microscopic examination of blood, utilizing blood films. Although blood is the sample most frequently used to make a diagnosis, both saliva and urine have been investigated as alternative, less invasive specimens. More recently, modern techniques utilizing antigen tests or polymerase chain reaction have been discovered, though these are not widely implemented in malaria endemic regions. Areas that cannot afford laboratory diagnostic tests often use only a history of subjective fever as the indication to treat for malaria. It is advised to be cautious diagnosing and treating without the presence of a headache, as it is possible that the patient has dengue; not malaria.

**Prevention:** The female *Anopheles albimanus* mosquito (Plate 6) is a vector of malaria and mosquito
control is a very effective way of reducing the incidence of malaria. Methods used in order to prevent the spread of disease, or to protect individuals in areas where malaria is endemic, include prophylactic drugs, mosquito eradication and the prevention of mosquito bites. The continued existence of malaria in an area requires a combination of high human population density, high 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 will sooner or later disappear from that area, as happened in North America, Europe and much of the Middle East. However, unless the parasite is eliminated from the whole world, it could become re-established if conditions revert to a combination that favours the parasite's reproduction.

Many countries are seeing an increasing number of imported malaria cases owing to extensive travel and migration. Many researchers argue that prevention of malaria may be more cost-effective than treatment of the disease in the long run, but the capital costs required are out of reach of many of the world's poorest people. The economist Jeffrey Sachs estimates that malaria can be controlled for US$3 billion in aid per year. A 2008 study that examined international financing of malaria control found large regional variations in the levels of average annual per capita funding ranging from US$0.01 in Myanmar to US$147 in Suriname. The study found 34 countries where the funding was less than US$1 per capita, including 16 countries where annual malaria support was less than US$0.5.

The 16 countries included 710 million people or 50% of the global population exposed to the risks of malaria transmission, including seven of the poorest countries in Africa (Côte d'Ivoire, Republic of the Congo, Chad, Mali, Democratic Republic of the Congo, Somalia and Guinea) and two of the most densely populated stable endemic countries in the world (Indonesia and India). Brazil, Eritrea, India and Vietnam, unlike many other developing nations, have successfully reduced the malaria burden. Common success factors have included conducive country conditions, a targeted technical approach using a package of effective tools, data-driven decision-making, active leadership at all levels of government, involvement of communities, decentralized implementation and control of finances, skilled technical and managerial capacity at national and sub-national levels, hands-on technical and programmatic support from partner agencies and sufficient and flexible financing.

Medications: Several drugs, most of which are also used for treatment of malaria, can be taken preventively. Chloroquine may be used where the parasite is still sensitive. Jacquerioz and Coft (2009). However due to resistance one of three medications: mefloquine (Lariam), doxycycline (available generically) and the combination of atovaquone and proguanil hydrochloride (Malarone) is frequently needed. Doxycycline and the atovaquone and proguanil combination are the best tolerated with mefloquine associated with higher rates of neurological and psychiatric symptoms. The prophylactic effect does not begin immediately upon starting the drugs, so people temporarily visiting malaria-endemic areas usually begin taking the drugs one to two weeks before arriving and must continue taking them for 4 weeks after leaving (with the exception of atovaquone proguanil that only needs be started 2 days prior and continued for 7 days afterwards).

Generally, these drugs are taken daily or weekly, at a lower dose than would be used for treatment of a person who had actually contracted the disease. Use of prophylactic drugs is seldom practical for full-time residents of malaria-endemic areas and their use is usually restricted to short-term visitors and travelers to malarial regions. This is due to the cost of purchasing the drugs, negative side effects from long-term use and because some effective anti-malarial drugs are difficult to obtain outside of wealthy nations. Quinine was used historically, however the development of more effective alternatives such as quinacrine, chloroquine and primaquine in the 20th century reduced its use. Today, quinine is not generally used for prophylaxis. The use of prophylactic drugs where malaria-bearing mosquitoes are present may encourage the development of partial immunity.

Vector control: Efforts to eradicate malaria by eliminating mosquitoes have been successful in some areas. Malaria was once common in the United States and southern Europe, but vector control programs, in conjunction with the monitoring and treatment of infected humans, eliminated it from those regions. In some areas, the draining of wetland breeding grounds and better sanitation were adequate. Malaria was eliminated from most parts of the USA in the early 20th century by such methods and the use of the pesticide DDT and other means eliminated it from the remaining pockets in the South by 1951. In 2002, there were 1,059 cases of malaria reported in the US, including eight deaths, but in only five of those cases was the disease contracted in the United States.

Before DDT, malaria was successfully eradicated or controlled also in several tropical areas by removing or poisoning the breeding grounds of the mosquitoes or
the aquatic habitats of the larva stages, for example by filling or applying oil to places with standing water. These methods have seen little application in Africa for more than half a century. Sterile insect technique is emerging as a potential mosquito control method. Progress towards transgenic, or genetically modified, insects suggest that wild mosquito populations could be made malaria-resistant. Researchers at Imperial College London created the world's first transgenic malaria mosquito, with the first plasmodium-resistant species announced by a team at Case Western Reserve University in Ohio in 2002. Successful replacement of current populations with a new genetically modified population relies upon a drive mechanism, such as transposable elements to allow for non-Mendelian inheritance of the gene of interest. However, this approach contains many difficulties and success is a distant prospect.

Another way of reducing the malaria transmitted to humans from mosquitoes has been developed by the University of Arizona. They have engineered a mosquito to become resistant to malaria. This was reported on the 16 July 2010 in the journal PLoS Pathogens. With the ultimate end being that the release of this GM mosquito into the environment, Gareth Lycett, a malaria researcher from Liverpool School of Tropical Medicine told the BBC that "It is another step on the journey towards potentially assisting malaria control through GM mosquito release."

**Indoor residual spraying:** Indoor Residual Spraying (IRS) is the practice of spraying insecticides on the interior walls of homes in malaria affected areas. After feeding, many mosquito species rest on a nearby surface while digesting the bloodmeal, so if the walls of dwellings have been coated with insecticides, the resting mosquitoes will be killed before they can bite another victim, transferring the malaria parasite. The first pesticide used for IRS was DDT. Although it was initially used exclusively to combat malaria, its use quickly spread to agriculture. In time, pest-control, rather than disease-control, came to dominate DDT use and this large-scale agricultural use led to the evolution of resistant mosquitoes in many regions. The DDT resistance shown by Anopheles mosquitoes can be compared to antibiotic resistance shown by bacteria. The overuse of anti-bacterial soaps and antibiotics led to antibiotic resistance in bacteria, similar to how overspraying of DDT on crops led to DDT resistance in Anopheles mosquitoes. During the 1960s, awareness of the negative consequences of its indiscriminate use increased, ultimately leading to bans on agricultural applications of DDT in many countries in the 1970s.

Since the use of DDT has been limited or banned for agricultural use for some time, DDT may now be more effective as a method of disease-control.

Although DDT has never been banned for use in malaria control and there are several other insecticides suitable for IRS, some advocates have claimed that bans are responsible for tens of millions of deaths in tropical countries where DDT had once been effective in controlling malaria. Furthermore, most of the problems associated with DDT use stem specifically from its industrial-scale application in agriculture, rather than its use in public health. The World Health Organization (WHO) currently advises the use of 12 different insecticides in IRS operations, including DDT as well as alternative insecticides (such as the pyrethroids permethrin and deltamethrin). This public health use of small amounts of DDT is permitted under the Stockholm Convention on Persistent Organic Pollutants (POPs), which prohibits the agricultural use of DDT. However, because of its legacy, many developed countries previously discouraged DDT use even in small quantities (Mendis et al., 2001).

One problem with all forms of Indoor Residual Spraying is insecticide resistance via evolution of mosquitoes. According to a study published on Mosquito Behavior and Vector Control, mosquito species that are affected by IRS are endophilic species (species that tend to rest and live indoors) and due to the irritation caused by spraying, their evolutionary descendants are trending towards becoming exophilic (species that tend to rest and live out of doors), meaning that they are not as affected-if affected at all-by the IRS, rendering it somewhat useless as a defense mechanism.

**Mosquito nets and bedclothes:** Mosquito nets help keep mosquitoes away from people and greatly reduce the infection and transmission of malaria. The nets are not a perfect barrier and they are often treated with an insecticide designed to kill the mosquito before it has time to search for 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. Although ITNs are proven to be very effective against malaria, less than 2% of children in urban areas in Sub-Saharan Africa are protected by ITNs. Since the Anopheles mosquitoes feed at night, the preferred method is to hang a large "bed net" above the center of a bed such that it drapes down and covers the bed completely.

**Immunization:** Immunity (or, more accurately, tolerance) does occur naturally, but only in response to repeated infection with multiple strains of malaria. A completely effective vaccine is not yet available for
malaria, although several vaccines are under development. SPf66 was tested extensively in endemic areas in the 1990s, but clinical trials showed it to be insufficiently effective. Other vaccine candidates, targeting the blood-stage of the parasite's life cycle, have also been insufficient on their own. Several potential vaccines targeting the pre-erythrocytic stage are being developed, with RTS,S showing the most promising results so far.

Other methods: Education in recognizing the symptoms of malaria has reduced the number of cases in some areas of the developing world by as much as 20%. Recognizing the disease in the early stages can also stop the disease from becoming a killer. Education can also inform people to cover over areas of stagnant, still water e.g., Water Tanks which are ideal breeding grounds for the parasite and mosquito, thus cutting down the risk of the transmission between people. This is most put in practice in urban areas where there are large centers of population in a confined space and transmission would be most likely in these areas. The Malaria Control Project is currently using downtime computing power donated by individual volunteers around the world (see Volunteer computing and BOINC) to simulate models of the health effects and transmission dynamics in order to find the best method or combination of methods for malaria control. This modeling is extremely computer intensive due to the simulations of large human populations with a vast range of parameters related to biological and social factors that influence the spread of the disease. It is expected to take a few months using volunteered computing power compared to the 40 years it would have taken with the current resources available to the scientists who developed the program.

An example of the importance of computer modeling in planning malaria eradication programs is shown in the study by Águas and others. They showed that eradication of malaria is crucially dependent on finding and treating the large number of people in endemic areas with asymptomatic malaria, who act as a reservoir for infection. The malaria parasites do not affect animal species and therefore eradication of the disease from the human population would be expected to be effective. Other interventions for the control of malaria include mass drug administrations and intermittent preventive therapy. Furthering attempts to reduce transmission rates, a proposed alternative to mosquito nets is the mosquito laser, or photonic fence, which identifies female mosquitoes and shoots them using a medium-powered laser. The device is currently undergoing commercial development, although instructions for a DIY version of the photonic fence have also been published.

Treatment: When properly treated, a patient with malaria can expect a complete recovery. The treatment of malaria depends on the severity of the disease; whether patients who can take oral drugs have to be admitted depends on the assessment and the experience of the clinician. Uncomplicated malaria is treated with oral drugs (Dondorp and Day, 2007). The most effective strategy for P. falciparum infection recommended by WHO is the use of artemisinin in combination with other antimalarials artemisinin-combination therapy, ACT, in order to avoid the development of drug resistance against artemisinin-based therapies. Severe malaria requires the parenteral administration of antimalarial drugs (Holding and Snow, 2001). Until recently the most used treatment for severe malaria was quinine but artesunate has been shown to be superior to quinine in both children and adults. Treatment of severe malaria also involves supportive measures. Infection with P. vivax, P. ovale or P. malariae is usually treated on an outpatient basis. Treatment of P. vivax requires both treatment of blood stages (with chloroquine or ACT) as well as clearance of liver forms with primaquine (Dondorp et al., 2010).

Epidemiology: Malaria has been a widely-prevalent disease throughout human history—some scientists believe that one in every two people who have ever lived has died of it. It is estimated that malaria causes 250 million cases of fever and approximately one million deaths annually. The vast majority of cases occur in children under 5 years old; pregnant women are also especially vulnerable. Despite efforts to reduce transmission and increase treatment, there has been little change in which areas are at risk of this disease since 1992. Indeed, if the prevalence of malaria stays on its present upwards course, the death rate could double in the next 20 years. Precise statistics are unknown because many cases occur in rural areas where people do not have access to hospitals or the means to afford health care. As a consequence, the majority of cases are undocumented.

Although co-infection with HIV and malaria does cause increased mortality, this is less of a problem than with HIV/tuberculosis co-infection, due to the two diseases usually attacking different age-ranges, with malaria being most common in the young and active tuberculosis most common in the old. Although HIV/malaria co-infection produces less severe symptoms than the interaction between HIV and TB, HIV and malaria do contribute to each other's spread.
This effect comes from malaria increasing viral load and HIV infection increasing a person's susceptibility to malaria infection.

Malaria is presently endemic in a broad band around the equator, in areas of the Americas, many parts of Asia and much of Africa; however, it is in sub-Saharan Africa where 85-90% of malaria fatalities occur. 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 regions because of the significant amounts of rainfall and consistent high temperatures; warm, consistent 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 can be predicted with reasonable accuracy by mapping rainfall.

Malaria is more common in rural areas than in cities; this is in contrast to dengue fever where urban areas present the greater risk. For example, several cities in Vietnam, Laos and Cambodia are essentially malaria-free, but the disease is present in many rural regions. By contrast, in Africa malaria is present in both rural and urban areas, though the risk is lower in the larger cities. The global endemic levels of malaria have not been mapped since the 1960s. However, the Wellcome Trust, UK, has funded the Malaria Atlas Project to rectify this, providing a more contemporary and robust means with which to assess current and future malaria disease burden. By 2010 countries with the highest death rate per 100,000 population are Cote d'Ivoire with (86.15), Angola (56.93) and Burkina Faso (50.66) -all in Africa. A map of Plasmodium falciparum endemicity in 2010 has been published.

History: Malaria has infected humans for over 50,000 years and Plasmodium may have been a human pathogen for the entire history of the species. Close relatives of the human malaria parasites remain common in chimpanzees. Some new evidence suggests that the most virulent strain of human malaria may have originated in gorillas. References to the unique periodic fevers of malaria are found throughout recorded history, beginning in 2700 BC in China. Malaria may have contributed to the decline of the Roman Empire and was so pervasive in Rome that it was known as the "Roman fever". A number of regions in ancient Rome were considered at-risk for the disease because of the favorable conditions present for malaria vectors. This included areas such as: southern Italy, the island of Sardinia, the Pontine Marshes, the lower regions of coastal Etruria and the city of Rome along the Tiber River. The presence of stagnant water in these places were preferred by mosquitoes for breeding grounds. Irrigated gardens, swamp-like grounds, runoff from agriculture and drainage problems from road construction led to the increase of standing water (Talman et al., 2004).

The term malaria originates from Medieval Italian: mala aria - "bad air"; the disease was formerly called ague or marsh fever due to its association with swamps and marshland. Malaria was once common in most of Europe and North America, where it is no longer endemic, though imported cases do occur. Malaria was the most important health hazard encountered by U.S. troops in the South Pacific during World War II, where about 500,000 men were infected. According to Joseph Patrick Byrne, "Sixty thousand American soldiers died of malaria during the African and South Pacific campaigns."

Prevention: An early effort at malaria prevention occurred in 1896, just before the mosquito malaria link was confirmed in India by a British physician, Ronald Ross. An 1896 Uxbridge malaria outbreak prompted health officer, Dr. Leonard White, to write a report to the Massachusetts State Board of Health, which led to study of mosquito-malaria links and the first efforts for malaria prevention. Massachusetts State pathologist Theobald Smith, asked that White's son collect mosquito specimens for further analysis and that citizens:

- Add screens to windows
- Drain collections of water

Carlos Finlay was also engaged in mosquito related research and mosquito borne disease theory, in the 1880s in Cuba, basing his work on the study of Yellow Fever.

Discovery of the parasite: Scientific studies on malaria made their first significant advance in 1880, when a French army doctor working in the military hospital of Constantine in Algeria named Charles Louis Alphonse Laveran observed parasites for the first time, inside the red blood cells of people suffering from malaria. He, therefore, proposed that malaria is caused by this organism, the first time a protist was identified as causing disease. For this and later discoveries, he was awarded the 1907 Nobel Prize for Physiology or Medicine. The malarial parasite (Plate 7) was called Plasmodium by the Italian scientists Ettore Marchiafava and Angelo Celli (Wellems, 2002).
Plate 7: A continuous *P. falciparum* culture was established in 1976. (http://en.wikipedia.org/wiki/file: falciparium_Gelatine_enrichment..jpg)

**Discovery of mosquito transmission:** A year later, Carlos Finlay, a Cuban doctor treating patients with yellow fever in Havana, provided strong evidence that mosquitoes were transmitting disease to and from humans. This study followed earlier suggestions by Josiah C. Nott and study by Sir Patrick Manson, The Father of Tropical Medicine, on the transmission of filariasis. In April 1894, a Scottish physician Sir Ronald Ross visited Sir Patrick Manson at his house on Queen Anne Street, London. This visit was the start of 4 years of collaboration and fervent research which culminated in 1898 when Ross, who was working in the Presidency General Hospital in Calcutta, proved the complete life-cycle of the malaria parasite in mosquitoes; thus proving that the mosquito was the vector for malaria in humans. He did this by showing that certain mosquito species transmit malaria to birds. He isolated malaria parasites from the salivary glands of mosquitoes that had fed on infected birds. For this work, Ross received the 1902 Nobel Prize in Medicine. After resigning from the Indian Medical Service, Ross worked at the newly established Liverpool School of Tropical Medicine and directed malaria-control efforts in Egypt, Panama, Greece and Mauritius. The findings of Finlay and Ross were later confirmed by a medical board headed by Walter Reed in 1900. Its recommendations were implemented by William C. Gorgas in the health measures undertaken during construction of the Panama Canal. This public-health work saved the lives of thousands of workers and helped develop the methods used in future public-health campaigns against the disease (Fong et al., 1971).

**Liver stage:** Shortt and Garnham discovered the pre-erythrocytic liver stage, first in the primate parasite *P. cynomolgi* and subsequently the human malariais *P. vivax* and *P. falciparum*. Further work confirmed the transformation of sporozoites from mosquitoes into liver forms, essentially completing documentation of the lifecycle (Collins and Barnwell, 2009).

**In vitro culture:** The first successful continuous in vitro malaria culture was established in 1976 by William Trager and James B. Jensen, which facilitated research into the molecular biology of the parasite and the development of new drugs.

**History of treatment:** The first effective treatment for malaria came from the bark of cinchona tree, which contains quinine. This tree grows on the slopes of the Andes, mainly in Peru. The indigenous peoples of Peru made a tincture of cinchona to control malaria. The Jesuits noted the efficacy of the practice and introduced the treatment to Europe during the 1640s, where it was rapidly accepted. It was not until 1820 that the active ingredient, quinine, was extracted from the bark, isolated and named by the French chemists Pierre Joseph Pelletier and Joseph Bienaimé Caventou. In the 20th century, chloroquine replaced quinine as treatment of both uncomplicated and severe falciparum malaria until resistance supervened. Artemisinins, discovered by Chinese scientists in the 1970s, are now recommended treatment for falciparum malaria, administered in combination with other antimalarials as well as in severe disease (Idro et al., 2005).

**Society and culture:** Malaria is not just a disease commonly associated with poverty but also a cause of poverty and a major hindrance to economic development. Tropical regions are affected most; however, malaria’s furthest extent reaches into some temperate zones with extreme seasonal changes. The disease has been associated with major negative economic effects on regions where it is widespread. During the late 19th and early 20th centuries, it was a major factor in the slow economic development of the American southern states. A comparison of average per capita GDP in 1995, adjusted for parity of purchasing power, between countries with malaria and countries without malaria gives a fivefold difference ($1,526 versus $8,268 USD, respectively). In countries where malaria is common, average per capita GDP has risen (between 1965 and 1990) only 0.4% per year, compared to 2.4% per year in other countries (Christopher et al., 2012).

Poverty is both cause and effect, however, since the poor do not have the financial capacities to prevent or treat the disease. In its entirety, the economic impact of malaria has been estimated to cost Africa $12 billion USD every year. The economic impact includes costs of health care, working days lost due to sickness, days lost in education, decreased productivity due to brain
damage from cerebral malaria and loss of investment and tourism. In some countries with a heavy malaria burden, the disease may account for as much as 40% of public health expenditure, 30-50% of inpatient admissions and up to 50% of outpatient visits. The demographic transition in Africa is slow and malaria may provide part of the answer. Total fertility rates were best explained by child mortality, as measured indirectly by infant mortality, in a 2007 study (Sutherland et al., 2010).

A study on the effect of malaria on IQ in a sample of Mexicans found that exposure during the birth year to malaria eradication was associated with increases in IQ. It also increased the probability of employment in a skilled occupation. The author suggests that this may be one explanation for the Flynn effect and that this may be an important explanation for the link between national malaria burden and economic development. A literature review of 44 papers states that cognitive abilities and school performance were shown to be impaired in sub-groups of patients (with either cerebral malaria or uncomplicated malaria) when compared with healthy controls. Studies comparing cognitive functions before and after treatment for acute malarial illness continued to show significantly impaired school performance and cognitive abilities even after recovery. Malaria prophylaxis was shown to improve cognitive function and school performance in clinical trials when compared to placebo groups. April 25 is World Malaria Day (Snow et al., 2005).

Counterfeit drugs: Sophisticated counterfeits have been found in several Asian countries such as Cambodia, China, Indonesia, Laos, Thailand, Vietnam and are an important cause of avoidable death in those countries. WHO said that studies indicate that up to 40% of artesunate based malaria medications are counterfeit, especially in the Greater Mekong region and have established a rapid alert system to enable information about counterfeit drugs to be rapidly reported to the relevant authorities in participating countries. There is no reliable way for doctors or lay people to detect counterfeit drugs without help from a laboratory. Companies are attempting to combat the persistence of counterfeit drugs by using new technology to provide security from source to distribution (Mockenhaupt et al., 2004).

War: Throughout history, the contraction of malaria (via natural outbreaks as well as via infliction of the disease as a biological warfare agent) has played a prominent role in the fortunes of government rulers, nation-states, military personnel and military actions. "Malaria Site: History of Malaria During Wars" addresses the devastating impact of malaria in numerous well-known conflicts, beginning in June 323 B.C. That site's authors note: "Many great warriors succumbed to malaria after returning from the warfront and advance of armies into continents was prevented by malaria. In many conflicts, more troops were killed by malaria than in combat." The Centers for Disease Control ("CDC") traces the history of malaria and its impacts farther back, to 2700 BCE. In 1910, Nobel Prize in Medicine-winner Ronald Ross (himself a malaria survivor), published a book titled The Prevention of Malaria that included the chapter: "The Prevention of Malaria in War." The chapter's author, Colonel C. H. Melville, Professor of Hygiene at Royal Army Medical College in London, addressed the prominent role that malaria has historically played during wars and advised: "A specially selected medical officer should be placed in charge of these operations with executive and disciplinary powers." (Maude et al., 2009)

Significant financial investments have been made to procure existing and create new anti-malarial agents. During World War I and World War II, the supplies of the natural anti-malaria drugs, cinchona bark and quinine, proved to be inadequate to supply military personnel and substantial funding was funnelled into research and development of other drugs and vaccines. American military organizations conducting such research initiatives include the Navy Medical Research Center, Walter Reed Army Institute of Research and the U.S. Army Medical Research Institute of Infectious Diseases of the US Armed Forces. Additionally, initiatives have been founded such as Malaria Control in War Areas (MCWA), established in 1942 and its successor, the Communicable Disease Center (now known as the Centers for Disease Control) established in 1946. According to the CDC, MCWA "was established to control malaria around military training bases in the southern United States and its territories, where malaria was still problematic" and, during these activities, to "train state and local health department officials in malaria control techniques and strategies." The CDC's Malaria Division continued that mission, successfully reducing malaria in the United States, after which the organization expanded its focus to include "prevention, surveillance and technical support both domestically and internationally" (Sturm et al., 2006).

Eradication efforts: Several notable attempts are being made to eliminate the parasite from sections of the world, or to eradicate it worldwide. In 2006, the organization Malaria No More set a public goal of
eliminating malaria from Africa by 2015 and the organization plans to dissolve if that goal is accomplished. Several malaria vaccines are in clinical trials, which are intended to provide protection for children in endemic areas and reduce the speed of transmission of the disease. The Global Fund to Fight AIDS, Tuberculosis and Malaria has distributed more than 160 million insecticide-treated nets intended to stop mosquito-borne transmission of malaria. According to director Inder Singh, the U.S.-based Clinton Foundation has reduced the cost of drugs to treat malaria by 60% and is working to further reduce the spread of the disease. Other efforts, such as the Malaria Atlas Project focus on analyzing climate and weather information required to accurately predict the spread of malaria based on the availability of habitat of malaria-carrying parasites (Cogswell, 1992).

Malaria has been successfully eradicated in certain areas (Kilama and Ntoumi, 2009). The Republic of Mauritius, a tropical island located in the western Indian Ocean (Singh et al., 2004), considered ecological connections to malaria transmission when constructing their current plan for malaria control. In order to prevent mosquitoes from breeding in aquatic areas, DDT is used in moderate amounts. Additionally, larvae eating fish are placed in water sources to remove the malaria vectors before they become a threat to the human population. Obstructions are also removed from these sources in order to maintain water flow and reduce stagnant water. Similarly, marsh or swamp-like environments are drained and filled to diminish mosquito breeding grounds. These actions have produced positive results. The program has cut infection and death rates tremendously and is cost effective, only requiring $1USD per head each year. This success is a clear indication that responses to adverse environmental conditions can decrease rates of disease (Chen et al., 2000).

Research: With the onset of drug resistant Plasmodium parasites, new strategies are required to combat the widespread disease (Trampuz et al., 2003). One such approach lies in the introduction of synthetic pyridoxal-amino acid adducts, which are channelled into the parasite. Thus, trapped upon phosphorylation by plasmodial PdxK (Pyridoxine/pyridoxal Kinase), the proliferation of Plasmodium parasites is effectively hindered by a novel compound, PT3, a cyclic pyridoxyl-tryptophan methyl ester, without harming human cells. Malaria vaccines have been an elusive goal of research. The first promising studies demonstrating the potential for a malaria vaccine were performed in 1967 by immunizing mice with live, radiation-attenuated sporozoites, providing protection to about 60% of the mice upon subsequent injection with normal, viable sporozoites. Since the 1970s, there has been a considerable effort to develop similar vaccination strategies within humans. It was determined that an individual can be protected from a P. falciparum infection if they receive over 1,000 bites from infected yet irradiated mosquitoes (Kain et al., 1998).

ONCHOCERCIASIS

Onchocerciasis also known as river blindness and Robles' disease, is a parasitic disease caused by infection by Onchocerca volvulus, a nematode (roundworm) (Hoerauf, 2008). Onchocerciasis is the world's second-leading infectious cause of blindness. It is not the nematode, but its endosymbiont, Wolbachia pipientis, that causes the severe inflammatory response that leaves many blind. The parasite is transmitted to humans through the bite of a black fly of the genus Simulium. The larval nematodes spread throughout the body. When the worms die, their Wolbachia symbionts are released, triggering a host immune system response that can cause severe itching and can destroy optical tissue in the eye (Harder, 2002).

The vast majority of infections occur in sub-Saharan Africa, although cases have also been reported in Yemen and isolated areas of Central and South America. An estimated 18 million people suffer from onchocerciasis, with approximately 270,000 cases of blindness related to the infection (Marcucci et al., 2004). In 1915, Dr. Rodolfo Robles Valverde's study on patients with river blindness in Guatemala led to the discovery that the disease is caused by filaria of O. volvulus and sheds light on the life cycle and transmission of the parasite. Using case studies of coffee plantation workers in Guatemala, Robles hypothesized the vector of the disease is a day-biting insect and more specifically, two anthropophilic species.
of Simulium flies (Plate 8) found in the endemic areas (Willey et al., 2009). He published his findings on a “new disease” from Guatemala associated with subcutaneous nodules, anterior ocular (eye) lesions, dermatitis and microfilariae in 1917. Treatment may involve the use of the drug ivermectin. For best effect, entire communities are treated at the same time. A single dose may kill first-stage larvae (microfilariae) in infected people and it prevents transmission for many months in the remaining population. Other drugs are also available, including the tetracycline-class antibiotic doxycycline, which kills the Wolbachia and renders the female nematodes sterile. The removal of the palpable nodules is common in Guatemala, Ecuador and Mexico (Murdoch et al., 1993).

Classification: Onchocerciasis may be divided into the following phases or types:
**Erisipela de la costa:** An acute phase, it is characterized by swelling of the face, with erythema and itching. Onchocerciasis causes different kinds of skin changes and these changes vary in different geographic regions. This skin change, erisipela de la costa, of acute onchocerciasis is most commonly seen among victims in Central and South America (James et al., 2006).

**Mal morando:** This cutaneous condition is characterized by inflammation accompanied by hyperpigmentation.

**Sowda:** A cutaneous condition, it is a localized type of onchocerciasis.

Additionally, the various skin changes associated with onchocerciasis may be described as follows:

**Leopard skin:** A term referring to the spotted depigmentation of the skin that may occur with onchocerciasis.

**Elephant skin:** A term used to describe the thickening of human skin that may be associated with onchocerciasis.

**Lizard skin:** A term used to describe the thickened, wrinkled skin changes that may result with onchocerciasis.

**Signs and symptoms:** Adult worms remain in subcutaneous nodules, limiting access to the host’s immune system. Microfilariae, in contrast, are able to induce intense inflammatory responses, especially upon their death. Dying microfilariae have been recently discovered to release Wolbachia surface protein that activates TLR2 and TLR4, triggering innate immune responses and producing the inflammation and its associated morbidity. Wolbachia species have been found to be endosymbionts of *O. volvulus* adults and microfilariae and are thought to be the driving force behind most of *O. volvulus* morbidity. The severity of illness is directly proportional to the number of infected microfilariae and the power of the resultant inflammatory response. Skin involvement typically consists of intense itching, swelling and inflammation. A grading system has been developed to categorize the degree of skin involvement (James et al., 2006):

- **Acute papular onchodermatitis:** Scattered pruritic papules
- **Chronic papular onchodermatitis:** Larger papules, resulting in hyperpigmentation
- **Lichenified onchodermatitis:** Hyperpigmented papules and plaques, with edema, Lymphadenopathy, pruritus and common secondary bacterial infections
- **Skin atrophy:** Loss of elasticity, the skin resembles tissue paper, 'lizard skin' appearance
- **Depigmentation:** 'Leopard skin' appearance, usually on anterior lower leg

Ocular involvement provides the common name associated with onchocerciasis, river blindness and may involve any part of the eye from conjunctiva and cornea to uvea and posterior segment, including the retina and optic nerve. The microfilariae migrate to the surface of the cornea. *Punctate keratitis* occurs in the infected area. This clears up as the inflammation subsides. However, if the infection is chronic, *Sclerosing keratitis* can occur, making the affected area become opaque. Over time, the entire cornea may become opaque, thus leading to blindness. Some evidence suggests the effect on the cornea is caused by an immune response to bacteria present in the worms. As the skin is itchy, it can lead to severe rashes and you can permanently kill off patches of skin (Murdoch et al., 1993). The Mazzotti reaction, first described in 1948, is a symptom complex seen in patients after undergoing treatment of onchocerciasis with the medication Diethylcarbamazine (DEC). Mazzotti reactions can be life-threatening and are characterized by fever, urticaria, swollen and tender lymph nodes, tachycardia, hypotension, arthralgias, oedema and abdominal pain that occur within seven days of treatment of microfilariasis. The phenomenon is so common when DEC is used for the treatment of onchocerciasis that this drug is the basis of a skin patch test used to confirm that diagnosis. The drug patch is placed on the skin and if the patient is infected with the...
microfilaria of *O. volvulus*, localized pruritus and urticaria are seen at the application site.

**Prevention:** Various control programs aim to stop onchocerciasis from being a public health problem. The first was the Onchocerciasis Control Programme (OCP), which was launched in 1974 and at its peak, it covered 30 million people in eleven countries. Through the use of larvicide spraying of fast-flowing rivers to control black fly populations and from 1988 onwards, the use of ivermectin to treat infected people, the OCP eliminated onchocerciasis as a public health problem. The OCP, a joint effort of the World Health Organisation, the World Bank, the United Nations Development Programme and the UN Food and Agriculture Organization, was considered to be a success and came to an end in 2002. Continued monitoring ensures onchocerciasis cannot reinvade the area of the OCP. In 1992, the Onchocerciasis Elimination Programme for the Americas (OEPA), which also relies on ivermectin, was launched. In 1995, the African Programme for Onchocerciasis Control (APOC) began covering another 19 countries, mainly relying upon the use of ivermectin. Its goal is to set up a community-directed supply of ivermectin for those who are infected. In these ways, transmission has declined (Trattler and Gladwin, 2007).

**Treatment:** In Mass Drug Administration (MDA) programmes, the treatment for onchocerciasis is ivermectin (trade name: Mectizan); infected people can be treated with two doses of ivermectin, 6 months apart, repeated every 3 years (Fig. 1). The drug paralyses and kills the microfilariae causing fever, itching and possibly oedema, arthritis and lymphadenopathy. Intense skin itching is eventually relieved and the progression towards blindness is halted. In addition, while the drug does not kill the adult worm, it does prevent them from producing additional offspring. The drug therefore prevents both morbidity and transmission. Ivermectin treatment is particularly effective because it only needs to be taken once or twice a year, needs no refrigeration and has a wide margin of safety, with the result that it has been widely given by minimally trained community health workers (Taylor et al., 2005).

**Antibiotics:** For the treatment of individuals, doxycycline is used to kill the Wolbachia bacteria that live in adult worms. This adjunct therapy has been shown to significantly lower microfilarial loads in the host and may have activity against the adult worms, due to the symbiotic relationship between Wolbachia and the worm. In four separate trials over 10 years with various dosing regimens of doxycycline for individualized treatment, doxycycline was found to be effective in sterilizing the female worms and reducing their numbers over a period of four to six weeks. Research on other antibiotics, such as rifampicin, has shown it to been effective in animal models at reducing Wolbachia both as an alternative and as an adjunct to doxycycline. However, doxycycline treatment requires daily dosing for at least 4 to 6 weeks, making it more difficult to administer in the affected areas (Thylefors et al., 2008).

**Ivermectin:** Ivermectin kills the parasite by interfering with the nervous system and muscle function, in particular, by enhancing inhibitory neurotransmission. The drug binds to and activates Glutamate-gated Chloride channels (GluCls) (Wolstenholme and Rogers, 2005). These channels, present in neurons and myocytes, are not invertebrate-specific, but are protected in vertebrates from the action of ivermectin by the blood-brain barrier. Ivermectin is thought to irreversibly activate these channel receptors in the worm, eventually causing an Inhibitory Postsynaptic Potential (IPSP) (Yates and Wolstenholme, 2004). The chance of a future action potential occurring in synapses between neurons decreases and the nematodes experience flaccid paralysis followed by death. Ivermectin is directly effective against the larval stage microfilariae of *O. volvulus*; they are paralyzed and can be killed by eosinophils and macrophages. It does not kill adult females (macrofilariae), but does cause them to cease releasing microfilariae, perhaps by paralyzing the reproductive tract (Rea et al., 2010).

Since 1988, ivermectin has been provided free of charge for use in humans by Merck through the Mectizan Donation Program (MDP) (Rea et al., 2010). The MDP works together with ministries of health and
nongovernmental development organisations, such as the World Health Organization, to provide free ivermectin to those who need it in endemic areas. A study of 2501 people in Ghana showed the prevalence rate doubled between 2000 and 2005 despite treatment, suggesting the parasite is developing resistance to the drug. A clinical trial of another antiparasitic agent, moxidectin (manufactured by Wyeth), began on July 1, 2009. About 99% of onchocerciasis cases occur in Africa. As of 2008, about 18 million people were infected with this parasite; about 300,000 had been permanently blinded (Osei-Atweneboana et al., 2007). Onchocerciasis is currently endemic in 30 African countries, Yemen and isolated regions of South America (Taylor et al., 2005). Over 85 million people live in endemic areas and half of these reside in Nigeria. Another 120 million people are at risk for contracting the disease. Due to the vector’s breeding habitat, the disease is more severe along the major rivers in the northern and central areas of the continent and severity declines in villages farther from rivers. Travelers who do not stay long in those areas have little risk of developing the disease, as it requires prolonged exposure to the fly bites and parasite introduction (Thylefors et al., 2008). According to a 2002 WHO report, onchocerciasis has not caused a single death, but its global burden is 987,000 Disability Adjusted Life Years (DALYs). The severe pruritis alone accounts for 60% of the DALYs. Infection reduces the host’s immunity and resistance to other diseases, which results in an estimated reduction in life expectancy of 13 years (Osei-Atweneboana et al., 2007).

Research: Animal models for the disease are somewhat limited, as the parasite only lives in primates, but there are close parallels. Litomosoides sigmodontis, which will naturally infect cotton rats, has been found to fully develop in BALB/c mice. Onchocerca ochengi, the closest relative of O. volvulus, lives in intradermal cavities in cattle and is also spread by black flies. Both systems are useful, but not exact, animal models (Köhler et al., 1997).

CONCLUSION

The negative effects are enormous and cannot be overlooked in culture fisheries management and practices in Nigeria. Malaria and Onchocerciasis are some occupational diseases in culture fisheries management and practices. A good understanding of the signs and symptoms, causes, life cycle, pathogenesis, genetic resistance, diagnosis, hepatopathy, prevention, medications, vector control, immunization, other methods, treatment, epidemiology, liver stage, in vitro culture, history of treatment, society and culture, counterfeit drugs, war, eradication efforts and research of malaria and river blindness is necessary to enlighten fish culturist the health implications of the profession.

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