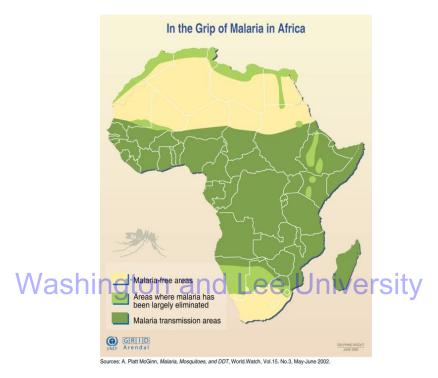
Makhosazana Zandile Dube

Research Seminar

**Professor Beckley** 

April 19, 2009

The Effect of Malaria on Pregnant women and children.



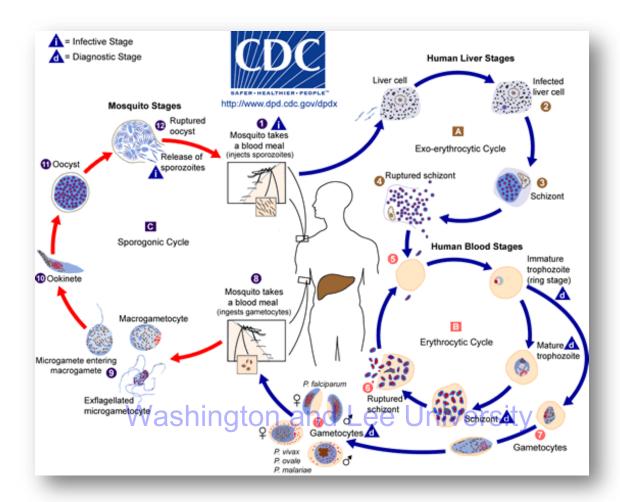
Some say, "where countries prosper least, malaria thrives most," and given the data on the global distribution of malaria, it is true. Malaria thrives most in tropical and hence wet areas, which consist mostly of developing nations. Several factors could be major contributors to the poverty found in these places, and disease is one of them. This paper examines the effect malaria has on African pregnant women and their children. Tanzania and Mozambique which are two bordering countries plagued with malaria will be used as examples to show the reality of this disease. In addition, the role the global community has played and could potentially play in the fight against and possibly eradication of malaria is discussed.

# **Malaria Transmission**

Malaria in humans is transmitted by mosquitoes in the *Anopheles* genus. The mosquitoes themselves are not disease breeding, but they are vectors. This means they get infected with the parasite but it is not harmful to them. However, when they bite a human being, the parasite is transferred from the mosquito to the human body. This is the cause of the potentially fatal human malaria. The disease carried by these mosquitoes is caused by any of four protozoan parasites in the *Plasmodium* genus namely: *P. vivax*, *P. falciparum*, *P. malarie* and *P. ovale*, *which* are distributed around the world. P. *falciparum*, is the most common in Sub Saharan Africa.

The parasite has a life cycle that consists of two parts. The first part is the sporogonic cycle, which takes place in the stomach of the mosquito. There the male and female gametocytes fuse and form zygotes, which mature into sporozoites and are injected into the human being to continue the life cycle of the parasite. The second part takes place after the parasite infects a human being. Inside the human body, the protozoan replicates exponentially in the blood cells. At a certain point, there are so many of them in one red blood cell that the cell ruptures from the pressure and is obviously killed in the process. The now freed protozoan forms both the male and female gametes and can therefore reproduce. It is the killing of the blood cells and infection of more cells that causes different kinds of symptoms in human beings. An illustration of the life cycle is shown below.

<sup>&</sup>lt;sup>1</sup> Baker, R., et al. University of Florida. IFAS Extension. Human Malaria. <a href="http://edis.ifas.ufl.edu/MG103">http://edis.ifas.ufl.edu/MG103</a>.



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The effect of malaria in general is determined by the intensity of malaria transmission in the area the person lives in. Following infection with Plasmodium parasites, the immune system responds in a number of ways as it attempts to kill the parasite. However, if the body does not have antibodies to fight the disease, its functioning slowly deteriorates.

Symptoms of uncomplicated malaria can be rather non-specific and the diagnosis can be missed if health providers are not alert to the possibility of this disease. When malaria is not diagnosed and treated early, it can become severe. Infections with this parasite can be fatal in the absence of prompt recognition of the disease and its complications, and urgent appropriate

<sup>&</sup>lt;sup>2</sup> Center for Disease control and prevention(2009). <a href="http://www.dpd.cdc.gov.dpdx">http://www.dpd.cdc.gov.dpdx</a>.

patient treatment. The situation is complicated by the increasing occurrence of *P. falciparum* parasites that are resistant to chloroquine and other antimalarial drugs. Prompt action is especially important for high-risk groups such as young children and pregnant women.

Pregnant women are more susceptible to malaria because pregnancy reduces their immunity. If they get the disease during pregnancy, it causes severe anemia for the mother,<sup>3</sup> low birth weight and high mortality for their unborn child. *P. falciparum* malaria during pregnancy may also induce spontaneous abortion or premature delivery. In addition, the pregnant woman may die of malaria if the accumulation of the parasites in her blood exceeds a threshold.<sup>4</sup> The plasmodium infects red blood cells that adhere to and accumulate in the placenta. Since the mother and baby do not share blood under normal circumstances, infected red blood cells do not pass from the mother to the fetus, even in cases of heavy infection, in which more than 50% of the red blood cells are parasitized. They accumulate on the maternal side of the placenta, in the vascular spaces between the villi where nutrient and gas exchange occurs. The exact mechanisms by which *P. falciparum* reside in the placenta are not known.<sup>5</sup>

The signs and symptoms associated with malaria can vary substantially depending on the infecting species, the amount of parasites in the blood, and the immune status of the patient. Infections caused by P. *falciparum* (which is mostly common in Africa) can progress to severe, potentially fatal forms. A patient with severe *falciparum* malaria may experience confusion or drowsiness with extreme weakness (prostration). The most frequent symptoms include fever and chills, which can be accompanied by headaches, muscle pain, pain in joints, weakness, vomiting, and diarrhea. Other clinical features include enlargement of the spleen, anemia, abnormal drop in the number of blood cells needed for blood clotting, abnormally low blood

<sup>&</sup>lt;sup>3</sup> This is a condition that develops when your blood lacks enough healthy red blood cells.

<sup>&</sup>lt;sup>4</sup> Gamble C., et al. Insecticide-treated nets for preventing malaria in pregnancy (Review) Cochrane Library 2009, Issue 1.

<sup>&</sup>lt;sup>5</sup> Mats Wahlgren<sup>1</sup> & Dorothe Spillmann. Nature Medicine. Sticky sugars attract malaria to the fetus. 6, 25 - 26 (2000).

sugar levels, pulmonary or kidney dysfunction, and changes in the function of the nervous system.

The table below shows the occurrence of some of the most identified symptoms

Effects	First pregnancy <sup>6</sup>	All pregnancies
High fever	+	+++
Placental infection	+++	+
Puerperal sepsis	++	++
Complicated malaria	+++	+++
Severe anemia	-	++
Cerebral malaria	-	+++
Hypoglycemia	-	++
Pulmonary edema	-	++
Acute renal failure	+	++
Increased maternal mortality	gton and Lee U	niversi <del>ty</del>

(+++ =Very Common, ++ =Common, + =Infrequent, -- =Rare)

The issue of malaria cannot be ignored because each year, more than 30 million women in Africa become pregnant in malaria-endemic areas. There is no data on the exact percentage of infected pregnant women, but small individual studies have suggested that it is high. In a study done at a rural hospital in Mozambique, 77.4% of all pregnant women had symptoms suggestive of malaria (Bardaji et al., 2008). Infection with malaria for pregnant women means sickly children and malaria during pregnancy in malaria-endemic settings may account for:

- 2-15% of maternal anemia
- 5-14% of low birth weight newborns
- 3-5% of newborn deaths

<sup>&</sup>lt;sup>6</sup> First pregnancy.

Areas with malaria have been divided into two groups, namely, stable and unstable areas. Stable areas are those where malaria is endemic while unstable areas have sporadic incidences of the disease. Since people in the stable areas receive frequent infective mosquito bites each month, levels of acquired immunity are high (pregnant women are semi-immune to malaria). On the other hand, people in unstable areas are infrequently exposed to malaria; therefore, they have low levels of acquired immunity. Unfortunately, when the women in these unstable areas do get malaria, their placental parasite levels are low or undetectable. This may cause death because healthcare givers are less likely to make a diagnosis in a timely fashion.

Examples of countries considered unstable areas in Africa are Mozambique and Tanzania. There is therefore an increased risk of infection of mothers and their fetuses in both countries. In Mozambique, the ministry of health is committed to increasing access to health services and increasing the efficiency and quality of those services nationwide, but the weak health infrastructure and shortage of health workers are formidable obstacles.

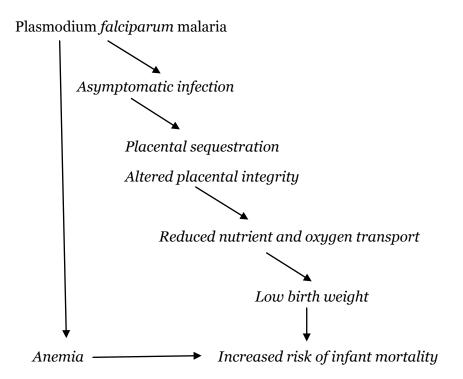
It is crystal clear that somehow these barriers have to be overcome because malaria is a major contributor to Mozambique's high maternal mortality rates. The grim situation is exacerbated by the climate of Mozambique that favors year-round transmission and therefore malaria remains the leading killer of children in Mozambique, although HIV/AIDS is rapidly catching up. In 2006, the World Health Organization (WHO) estimated that malaria kills nearly one in every twenty Mozambican children before they reach the age of five. In Mozambique, this means about 36,000 children die each year (4 every hour) from malaria alone and most of the children who die from malaria do so at home.

Tanzania on the other hand has more than 30 million people (over 96% of Tanzania's population) at risk from malaria and it is the most commonly reported health complaint in the

country. WHO also estimates that there are 16 million cases of malaria each year, contributing to approximately 80,000 deaths annually of children under the age of five.

# **Effect of Malaria on Pregnancy**

In both stable and unstables areas, the plasmodium can cause low birth weight in two different ways. First it can cause anemia in the mother. If the mother has anemia, her red blood cells are not healthy enough to transport oxygen and nutrients to the placenta, which in turn transports them to the baby. The nutrient deficient baby is more vulnerable to all kinds of diseases, including malaria and hence an increased possibility that they will die as an infant, especially if they do not get the proper food and disease treatment right after birth. The second pathway of effect is the pathogen binding directly to the placenta, taking over the blood vessels (placental sequestration), weakening it and therefore compromising its function of supplying the fetus with oxygen and nutrients (altered placental integrity). As a result, a weak baby is born.



Women in areas of unstable malaria transmission, whether or not it is their first pregnancy, are at higher risk of premature delivery (that is, delivery before 37 completed weeks of gestation). They are also at higher risk of spontaneous abortions, stillbirths and congenital malaria. Every once in a while, the parasites move through the placenta from the mother to baby and therefore the baby gets malaria, but this is a *rare* occurrence. The consequences of these adverse effects are an increased risk of infant mortality among all babies born to mothers living in areas of unstable malaria transmission. The table below compares the effects of malarial infection of mother on the Fetus and Newborn in stable and unstable areas.

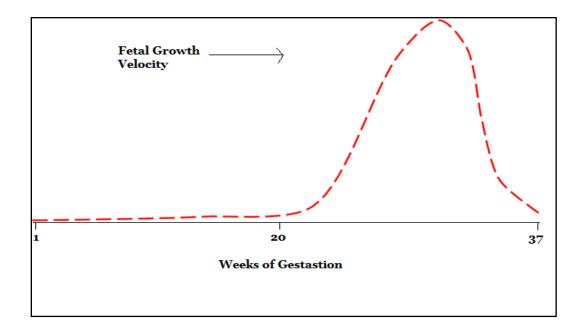
Effects	First pregnancy in Stable malaria areas	All pregnancies in Unstable malaria areas
Low birth weight 1. IUGR	+++	+
2. Prematurity	+	++
Abortion		++
Stillbirth Washington ar	d Lee-Unive	rsity ++
Congenital malaria	-	+
Fetal anemia	?	+
Infant mortality	+	++

(+++=Very Common, ++=Common, +=Infrequent, -- =Rare)

#### **Fetal Growth Velocity**

Fetal growth velocity is relatively slow in the first half of pregnancy but increases rapidly in the second half of pregnancy. Because the presence of any amount of parasites in the placenta interferes with the transfer of nutrients to the fetus, it is important to ensure that the fetus's placenta is free of malaria parasites when fetal growth velocity is fastest.

<sup>&</sup>lt;sup>7</sup> Valecha et al. "Congenital malaria with atypical presentation: A case report from low transmission area in India." Malaria Journal (6). 2007: 43. < http://www.malariajournal.com/content/6/1/43>.



In both stable and unstable areas of transmission, the prevalence of infection and the parasite density in peripheral blood both peak in the first half of the gestation period and then Lee decrease progressively until delivery. Some scientists propose that pregnancy exacerbates malaria through a non-specific, hormone-dependant, depression of the immune system. Two mechanisms have been suggested. The first is that pregnancy is a period of generalized immunesuppression sustained mainly by increased blood levels of cortisol. Cortisol is a hormone produced principally in response to physical or psychological stress and secreted by the adrenal glands. It acts through specific intracellular receptors and affects numerous physiologic systems including immune function, glucose counter regulation, vascular tone, and bone metabolism. Adam et al (2007) show that cortisol levels are higher in pregnant women with malarial infection than in those without and that cell-mediated immune responses to malarial antigens are more markedly suppressed in first pregnancies than subsequent ones. However, this hypothesis does not explain the preferential replication of parasites within the placenta. In addition, serum cortisol levels increase linearly during gestation whereas susceptibility to malaria peaks in the second trimester and then decreases.

The second proposed mechanism for immune-suppression is mainly a local phenomenon at the placental level and sustained by increased local concentrations of estrogen. Estrogen production reduces as a woman has more babies and, possibly, during gestation in infected women, because of decreased production of the hormone by the damaged infected placenta. However, further studies are required to associate placental estrogen concentrations with placental infection and pregnancy outcome.<sup>8</sup>

Even though it is rare for a fetus to contract malaria in utero, they are still at risk of contracting this disease after birth. This is because, if the mother is infected, they are at high risk for low birth weight and weak immune systems, which makes it incredibly easy for them to contract diseases in general. A study of children with cerebral malaria (CM) and generalized convulsions (GC) estimate that each year in Africa, between 9000 and 19 000 children under 5 experience neurological impairments following CM for more than 6 months after discharge from a hospital, but these impairments can be reversible upon extensive treatment. If the impairments are not treated, this may have negative implications for least 250 000 children in Sub-Saharan Africa each year. This problem is likely to be compounded by the fact that the outcome of severe malaria is enmeshed with other health and development factors affecting children in resource-poor countries.

In general, malaria significantly affects the poor who suffer economic, social and educational deprivation.<sup>11</sup> The economically deprived tend to have poor nutrition available to them, and long-term nutritional lack in children is associated with poor performance on cognitive, speech and language assessments. Mild to moderate neuro-developmental dysfunction exerts more negative influence in contexts of environmental turmoil or deprivation,

biovision.org/res/res/files/1578.malaria\_control\_manual\_health.pdf>.

<sup>&</sup>lt;sup>8</sup> Matteelli, S., et al. The placenta and malaria. Clinic of Infectious and Tropical

Diseases, University of Brescia, Piazza Spedali Civili 1, 25125 Brescia, Italy. Apr. 1997

<sup>99</sup> Malaria. Tulane University. <a href="http://www.tulane.edu/~wiser/protozoology/notes/malaria.html">http://www.tulane.edu/~wiser/protozoology/notes/malaria.html</a>.

<sup>&</sup>lt;sup>10</sup> Carter, J., et al. Developmental impairments following severe falciparum malaria in children. Tropical Medicine and International Health.(10).2005: 3-10.

<sup>&</sup>lt;sup>11</sup> Oxfam. Malaria Control Manual.< www.infonet-

suggesting that similar levels of impairment may have more detrimental effects in this context when compared with of resource-rich settings.

#### **Control**

- n. Ante-natal care and health education during pregnancy. This is an intervention where a pregnant woman is examined for any chronic and infectious diseases that may negatively influence the outcome of the pregnancy. Detection of a disease like malaria is followed up with intensive health care throughout the pregnancy. This way the abnormal development of the fetus is detected early and appropriate steps are taken towards alleviating the problem through intermittent preventive treatment. It is difficult to ascertain the extent to which antenatal care is used in general. This is because urban areas provide a lot more care than rural areas and therefore more people can actually get prompt health attention there. Also, there have been sporadic interventions by national and western NGOs in rural areas. Lastly, studies usually concentrate on one place or hospital. As a result there are no generalized findings on how much antenatal care has been used. For antenatal care to be effective, all pregnant women need a minimum of four visits, at specific times and with evidence-based content especially because of the prevalence of HIV and the amplification of complications associated with a combination of malaria and this deadly virus.
- 2. <u>Intermittent preventive treatment (IPT)</u>. This is an approach for effectively preventing and controlling malaria during pregnancy based on an assumption that every pregnant woman in a malaria-endemic area is infected with malaria and therefore recommends that every pregnant woman receive at least two treatment doses of an effective anti-malarial drug. Not many anti-malarial drugs can be utilized by pregnant women, but sulphadoxine-pyrimethamine (s/p) has

<sup>&</sup>lt;sup>12</sup> Brieger, B (2008, Aug) Malaria in Pregnancy & HIV & Integration .

Malaria, HIV - integration into Antenatal Care in Mozambique. <a href="http://www.malariafreefuture.org/blog/?p=508">http://www.malariafreefuture.org/blog/?p=508</a>>.

been found to safely reduce placental malaria in mothers and low-birth-weight in their babies.<sup>13</sup> The statistics on the percentage of women who actually use this mode of therapy proved very difficult to find. However, Fernandez et al (2007) found that the plasmodium is quickly gaining resistance against s/p; therefore, since no other single antimalarial can be used on pregnant women, it may be wise to use s/p in combination with another antimalarial drug.<sup>14</sup>

- 3. <u>Insecticide-treated nets (ITNs).</u> An insecticide-treated net is a mosquito net that repels, disables and/or kills mosquitoes coming into contact with insecticide on the netting material. Compared with a control situation in which there were no mosquito nets, use of ITNs in Africa increased mean birth weight by 0.12lb, reduced low birth weight by 23%, and reduced the amount of parasites in all pregnancies by 23%.<sup>15</sup>
- insecticidal properties were not discovered until 1939. In the second half of World War II, it was used with great effect among both military and civilian populations to control mosquitoes spreading malaria and lice transmitting typhus, resulting in dramatic reductions in the incidence of both diseases. In 1962, *Silent Spring* by American biologist Rachel Carson was published. The book catalogued the environmental impacts of the indiscriminate spraying of DDT in the United States and questioned the logic of releasing large amounts of chemicals into the environment without fully understanding their effects on ecology or human health. The book suggested that DDT and other pesticides may cause cancer and that their agricultural use was a threat to wildlife, particularly birds. 16

This chemical is particularly toxic to fish, aquatic invertebrates and insects (including some that are beneficial). While not immediately toxic to birds, DDT causes long-term

<sup>&</sup>lt;sup>13</sup> Eijk, A. M. et al. Tropical Medicine & International Health. Effectiveness of intermittent preventive treatment with sulphadoxine-pyrimethamine for control of malaria in pregnancy in western Kenya: a hospital-based study van. (9)2004:351-360.

<sup>&</sup>lt;sup>14</sup> Fernandes, N. et al Malaria Journal. Analysis of sulphadoxine/pyrimethamine resistance-conferring mutations of *Plasmodium falciparum* from Mozambique reveals the absence of the dihydrofolate reductase 164L mutant. (6) 2007: 35.

<sup>&</sup>lt;sup>15</sup> Insecticide treated nets. A WHO position statement.

<sup>&</sup>lt;sup>16</sup> < http://en.wikipedia.org/wiki/DDT>.

reproductive problems by causing eggshells to weaken and crack, threatening the survival of many bird species. Because of its chemical nature, once DDT is applied in a field or other environment, it remains in an active form for decades. People throughout the United States still carry DDT and its metabolites in their bodies, 30 years after the pesticide was banned in this country. Most other developed countries have also banned DDT, but it is still used in many developing countries.<sup>17</sup> The World Health Organization, in a sign that widely used methods of fighting malaria have failed to bring the catastrophic disease under control, announced in 2006 that it will encourage the use of DDT, even though the pesticide is banned or tightly restricted in much of the world. For public-health officials in countries losing the fight against the disease, the new guidelines promise difficult choices between fighting malaria and protecting the environment.<sup>18</sup> DDT has been found to be safe and effective for indoor use<sup>19</sup> and hence its use has become more prevalent in malaria endemic countries.

# Difficulty in controlling malarian and Lee University

Malaria control is made difficult by several technical and administrative problems. The first problem is that drug-resistant malaria parasites hinder case management by decreasing the efficacy of anti-malarial drugs and therefore requiring the use of alternate drugs that are often more costly, less safe and less easy to administer. A second problem is the decreased efficacy of interventions that rely on insecticides such as insecticide-treated bed nets and insecticide spraying because of insecticide resistance of malaria. Inadequate health infrastructures in poor countries unable to conduct the recommended interventions are an added barrier to the efficient control of the disease. Lastly, the people most exposed to malaria are often poor and lack

<sup>&</sup>lt;sup>17</sup> The U.S. Ban on DDT. A Continuing Success Story. 2005

 $<sup>&</sup>lt;\! http://www.edf.org/article.cfm? ContentID = 4407 >.$ 

<sup>&</sup>lt;sup>18</sup> McKay, B. WHO Calls for Spraying Controversial DDT to Fight Malaria

The Wall Street Journal. 15 Sept. 2006.

<sup>&</sup>lt;a href="http://yaleglobal.yale.edu/display.article?id=8159">http://yaleglobal.yale.edu/display.article?id=8159</a>.

<sup>&</sup>lt;sup>19</sup>WHO gives indoor use of DDT a clean bill of health for controlling malaria

WHO promotes indoor spraying with insecticides as one of three main interventions to fight malaria

<sup>&</sup>lt;a href="http://www.who.int/mediacentre/news/releases/2006/pr50/en/index.html">http://www.who.int/mediacentre/news/releases/2006/pr50/en/index.html</a>>.

education and often do not know how to prevent or treat malaria. Even when they do know, they often do not have the financial means to purchase the necessary products, such as drugs or bed nets.<sup>20</sup>

#### A Vaccine

Researchers have been trying for more than 70 years to develop a vaccine against the elusive malaria parasite without notable success,<sup>21</sup> but they are still trying. A vaccine is an essential tool in stopping malaria because the current fight against the disease is being waged on a variety of fronts (the distribution of bed nets, the promotion of indoor spraying, and the development of new medicines and insecticides) and a vaccine would close the gap left by these interventions. Also, from small pox to polio to whooping cough, vaccines have offered a cost-effective and successful means of preventing disease and death and even a modestly efficacious malaria vaccine would protect hundreds of thousands of people from disease and death each year.

Washington and Lee University

In recent years, increases in funding and scientific advances have brought malaria vaccines within reach. But more support is needed because it costs about half a billion dollars to move a vaccine from the laboratory to a safe and effective product and current funding is not enough to get a malaria vaccine across the finish line.

The international community is embracing the long-term goal of eradicating malaria. To achieve this goal, the international community needs more donors to provide support, more scientists and vaccine developers to invest their political and intellectual capital, and national, regional, and international policymakers to lay the groundwork for malaria vaccine delivery and use.

<sup>&</sup>lt;sup>20</sup> Center for Disease Control. <a href="http://www.cdc.gov/>">http://www.cdc.gov/>">.

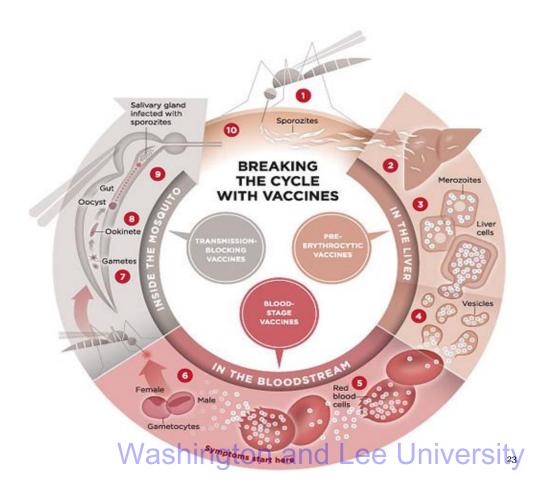
<sup>&</sup>lt;sup>21</sup> The New York Times. The Glaxo-Gates Malaria Vaccine. Close Published: December 13, 2008.

Developing a vaccine against malaria is a huge challenge. Many factors determine whether a vaccine will be safe, effective, and affordable for the people who need it most. If everything goes well with the candidate that is farthest along in the development process, a vaccine could be submitted to relevant international organizations for review as early as 2011. This is much sooner than would have been likely without the renewed global interest and support for malaria vaccines witnessed over the past few years, particularly support from the Bill & Melinda Gates Foundation.<sup>22</sup>

# The RTS,S vaccine

This vaccine has only in recent years moved into widespread testing, thanks to funding from the PATH Malaria Vaccine Initiative supported by the Bill and Melinda Gates Foundation. For vaccinologists, malaria has proved hard to beat. The parasite that causes the disease has a complex life cycle inside mosquitoes and the human body, which helps it evade the immune system. RTS,S, named for the antigen it produces, fuses part of a protein from the parasite to the surface of a hepatitis-B viral particle, stimulating the body's immune response. This hobbles the parasite's ability to infect and develop in the liver, its main repository in humans, which gives partial protection against the disease. The vaccine's largest test so far, in more than 2,000 children in Mozambique starting in 2003, showed it reduced all cases of clinical malaria by 35 percent and the worst cases of the disease by almost 50 percent. There is no guarantee of success. The studies were carried out in areas with relatively low transmission of malaria; no one knows if the vaccine will work as well where malaria is more rampant. And the vaccine must still undergo much larger trials.

<sup>&</sup>lt;sup>22</sup> PATH Malaria vaccine initiative. <www.malariavaccine.org/malvac-vaccine-faqs.php>.



The above information may sound great but realistically speaking, it is not. Malaria is most endemic in poor countries; therefore, the research and development of a malarial vaccine is not a potentially profitable endeavor for pharmaceutical companies. Nevertheless, even if they did develop a good drug, paragraph 2 and 3 of the Trade and Related Intellectual Property Agreement (TRIPS) would make the product subject to a patent. This patent would prevent third parties not having the owner's consent from the acts of: making, using, offering for sale, selling, or importing for these purposes that product; and also from retro-synthesizing the vaccine and forming it another way for the purpose of using, offering for sale or selling the

 $<sup>^{23}\,</sup> The\, Malaria\, Initiative.\, Malaria\, research\, program\, uses\, multifaceted\, approach.\, <\! http://www.malariavaccine.org/>.$ 

product.<sup>24</sup> This poses a huge problem to the developing world in general because if there is only one producer, products are monopolized and prices are artificially kept high and hence many die because of the lack of funds to purchase the medicines. It is clear that for the vaccine to be pushed through and actually make it to pharmacy shelves and hospitals at a price the poor can afford, the current system of running the development and sale of pharmaceutical has to change.

However, this change cannot come from one place if it is to be successful. The entire world has to come together to wage war against this disease.

# Agencies that would have to act

# 1. Nations battling with the problem

Developing countries, although poor, have a responsibility to help themselves as much as economically possible for them. This is a responsibility to take care of their own. Thus far, the goal of malaria control in malaria-endemic countries has been to reduce as much as possible the health impact of malaria on the population, using the resources available, and taking into account other health priorities. Malaria control does not aim to eliminate malaria totally. Complete elimination of the malaria parasite (and thus the disease) would constitute eradication. While eradication is more desirable, given the weak economies, it is not currently a realistic goal for most of the countries where malaria is endemic because most of them are also highly plagued with the notorious HIV virus.

2. Non-governmental Organizations (NGOs) in malaria endemic nations Most African nations have NGOs aimed at targetting different problems. There organizations are usually financed partly by the western world and depending on how they are run, they can either be a good or bad thing for the country. For example, Mozambique provides a valuable case study since it experienced rapid growth of NGO activity over the last decade. Based on key informant interviews, participant-observation, and ethnographic research over a four year

<sup>&</sup>lt;sup>24</sup> World Trade Organization

TRIPS: Agreement on Trade-Related Aspects of Intellectual Property Rights. PART II — Standards concerning the availability, scope and use of Intellectual Property Rights

<sup>&</sup>lt;a href="http://www.wto.org/english/tratop\_e/trips\_e/t\_agm3c\_e.htm#5">http://www.wto.org/english/tratop\_e/trips\_e/t\_agm3c\_e.htm#5</a>.

period, the research findings reported assessed the impact of NGO proliferation on the Mozambique health sector. NGO arrival undermined the National Health System in unanticipated ways by fragmenting services, promoting brain drain, diverting resources, and disrupting coordinated planning processes. Foreign NGOs contributed to greater social inequality by creating sizeable communities of well-paid expatriates and Mozambican cadres with dramatically higher salaries than public sector counterparts. The role of NGOs in the health sector should be re-examined and donors should re-channel aid through the public sector to maximize coordination, planning, service integrity, and national ownership. A more constructive role for NGOs in mobilizing communities and civil society should be debated and redefined.<sup>25</sup>

A great example of NGO work is found in Kenya. The Kenya NGOs Alliance Against Malaria (KeNAAM) brings together over 44 Non-Governmental Organizations (NGOs) working on Malaria and seeks to unite and enhance collaboration through networking in their efforts and programs aimed at preventing, controlling and reducing socio-economic impact burden as a result of malaria. In its endeavors, KeNAAM recognizes the strategic role played by government of Kenya through the Ministry of Health-Division of Malaria Control (MOH-DOMC) in fighting malaria as per the National Malaria Strategy (NMS). Further recognition is given to bilateral, multilateral, private sector and donor communities who aim to Roll Back Malaria in Kenya. Together KeNAAM and the said communities aim at creating and maintaining "effective partnership to have a malaria free Kenya" in line with Millennium Development Goal.<sup>26</sup>

### 3. Developed nations

It is quite a relief to know that Bill and Melinda Gates are not the only highly influential people aware of Africa's struggles. During a visit to Tanzania early last year, President Bush<sup>27</sup>

<sup>&</sup>lt;sup>25</sup> NGOs in Mozambique: The Velvet Glove of Privatization?

James Pfeiffer, PhD, MPH. School of Public Health, Department of Health Services, University of Washington.

<sup>&</sup>lt;sup>26</sup> Stop Malaria now. An Africa-European initiative. Kenya NGO Alliance Against Malaria (KeNAAM). <a href="http://www.stopmalarianow.org/profile-kenaam.html">http://www.stopmalarianow.org/profile-kenaam.html</a>.

<sup>&</sup>lt;sup>27</sup> President and Mrs. Bush traveled to Africa from February 15-21, 2008. Where they visited Benin, Tanzania,

announced that the United States and Tanzania, in partnership with the World Bank and The Global Fund, will distribute 5.2 million free bed nets in Tanzania. The Global Fund is a public-private partnership that has committed millions of dollars to fight AIDS, tuberculosis and malaria in 136 countries.

Handing over to a hospital some insecticide treated mosquito nets manufactured by A to Z textile mill in Arusha, President Bush said the United States was part of an international effort to provide enough mosquito nets to protect every child in Tanzania who is five years or younger. The now former president continued, "the suffering caused by malaria is needless, and every death caused by malaria is unacceptable. It is unacceptable to people here in Africa, who see their families devastated and economies crippled. It is unacceptable to people in the United States, who believe every human life has value, and that the power to save lives comes with the moral obligation to use it."<sup>28</sup>

Malaria eradication efforts have been very successful in Zanzibar where annual malaria deaths have declined significantly from 120,000 to 60,000 and malaria infections among infants have dropped from about 20 per cent to less than 1 per cent. While 500,000 malaria patients were treated in the outpatient clinics in 2004, only 10,000 had been treated in 2007. In 2004, about 40 percent of patients tested positive for malaria in the Isles while in 2007 only 5 per cent tested positive. Tanzania is one of the first three African countries (others are Angola and Uganda) to participate in the initiative to reduce by 50 percent deaths of pregnant women and children under five. Covering 15 countries, the goal of the five year initiative is to reduce the burden of malaria dramatically as a major killer of children in Sub Saharan Africa. The US President's Malaria Initiative, PMI, has pledged USD 1.2 billion to fund this great initiative.<sup>29</sup>

Rwanda, Ghana, and Liberia.

<sup>&</sup>lt;sup>28</sup> Magola C. Tanzania still expecting to eradicate malaria by 2015. IPP media 20 Oct 2008. <a href="http://www.ippmedia.com/cgi-bin/ipp/print.pl?id=124775">http://www.ippmedia.com/cgi-bin/ipp/print.pl?id=124775</a>.

<sup>&</sup>lt;sup>29</sup> Magola C. Tanzania still expecting to eradicate malaria by 2015. IPP media 20 Oct 2008. <a href="http://www.ippmedia.com/cgi-bin/ipp/print.pl?id=124775">http://www.ippmedia.com/cgi-bin/ipp/print.pl?id=124775</a>.

Even though President Bush talked mostly about making sure children do not get malaria, the global fund will also enable about 90 percent of pregnant women to have access to subsidized insecticide treated nets through the National Malaria Control Program. This program plans to subsidize people's purchase of treated nets from all commercial retailers in Tanzania by distributing vouchers throughout the country to pregnant women who attend ante-natal care clinics. Women present these vouchers to commercial retailers, who in turn are reimbursed by a consortium of non-governmental organizations for the cost of the nets. Moreover, free insecticide treatment kits used to sustain the efficacy of insecticide-treated nets are distributed by immunization centers to mothers of children under 18 months of age.

The voucher scheme encourages pregnant women to attend ante-natal clinics to get better prenatal care and the associated health benefits for both mother and child. This innovative scheme not only increases access to insecticide-treated nets, but also stimulates the private-sector production of insecticide-treated nets in Tanzania because all of the nets used in this program are locally produced, procured and distributed.

# 4. Multilateral agencies

Pharmaceuticals are critical to health systems, because, if they are readily available, affordable, of good quality and used appropriately, they can provide a cost-effective solution to many health care problems. The disparity in access to pharmaceuticals between rich and poor becomes more pronounced when a wave of new drugs and biopharmaceuticals of treating formerly untreatable illnesses enters the market. The legal distribution of drugs and medicines is under the Trade and Related Intellectual Property Agreement (TRIPS). This agreement allows pharmaceutical companies to enjoy patent protection for their inventions for 20 years.<sup>30</sup>The TRIPS agreement is good insofar as it can

<sup>30</sup> World Trade Organization. TRIPS: Agreement on Trade-Related Aspects of Intellectual Property Rights Part II — Standards concerning the availability, scope and use of Intellectual Property Rights. <a href="http://www.wto.org/english/tratop\_e/trips\_e/t\_agm3">http://www.wto.org/english/tratop\_e/trips\_e/t\_agm3</a>

possibly prevent free-riding behavior that occurs when intellectual assets are easy to copy. This especially applies to the pharmaceutical sector, as the reverse engineering of patented drugs is not technically demanding. The overuse of knowledge could minimize the economic value of an innovation and limit incentives for others to pursue advances in knowledge. Intellectual property rights thus mitigate the tendency toward free-riding behavior by limiting who has the rights to an intellectual asset. However, this may limit the type of drug therapies available to the poor. Since patents impede progress in technology by precluding other firms from cross learning and building on the original innovation, they reduce the capacity for other firms to exploit the knowledge on a competitive basis, hence allowing pharmaceuticals to sell the product for exorbitant amounts. Cohen and Illingworth (2003) propose the following ways to work with the TRIPS agreement without depriving the developing world of life saving medicines.

First, an international organization, such as the World Bank, could assume an important role in resolving the conflict surrounding the TRIPS Agreement by providing specific loans and grants to developing countries that could enable them to have the financing they need for the purchase of essential medicines that are protected under the patent treaty. Alternatively, the World Bank could provide its client states with loans to purchase drug patents from pharmaceutical firms and license the production of specific drugs to local firms. This solution would enable public financing to reduce the prices of medicines to their marginal costs of production and permit the research and development firms to recoup their sunk costs of research and development by ensuring that they receive payment for their products.

Another possible mechanism that could contribute to abating the conflict surrounding the TRIPS Agreement is for international institutions to forgive the debt of the poorest countries

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<sup>&</sup>lt;sup>31</sup> Maskus, K. The International Regulation of Intellectual Property, paper prepared for the IESG Conference on International Trade and Investment, Nottingham. Sept 1997: 3.

and demand as conditions attached to the forgiveness of debt, that the "surplus" money is spent on priority medicines under patent for those in need. To ensure that the states honor their commitment to purchase patented medicines, the debt relief assigned to drug purchases could be transferred directly to the World Bank.

Third, the World Bank could purchase patents from the research-based pharmaceutical industries and make licensing agreements with generic drug firms, that may or may not, be located in developing states. Using financing provided by donors, the World Bank could then be in a position to provide licenses to generic drug manufactures in developing states to produce the requisite medicines and distribute them widely.<sup>32</sup>

Thomas Pogge (2002) suggests a change in the rules for Global Burden of Diseases (GBD) whereby a patent holder is rewarded out of public funds during the life of the patent in proportion of the impact of the medicine on the GBD.<sup>33</sup> This kind of patent would be incentive for pharmaceutical companies not only to compete on a fair market, but they would eagerly send their medicines to developing countries because that is where most of the GBD hits hardest.

# 5. Private corporations

Large international private corporations could play a major role in the eradication of malaria in two ways. First they could support malaria control and eradication programs financially and/or push for changes in policy. An example of the former is the work done by the Global Business Coalition (GBC). GBC member contributions to the global fight span the full-spectrum of public health interventions, including the distribution of life-saving bed nets, treatment for children and infected pregnant women and the development of new diagnostic tools and medications. Rarely are these efforts made in isolation. Coalition members frequently

<sup>&</sup>lt;sup>32</sup> Cohen, C., and Illingworth, P. Pharmaceutical Patents and International Commitments: The Inherent Tensions and Implications for Public Health.

<sup>&</sup>lt;sup>33</sup> Pogge, T. World Poverty and Human Rights.

engage in leveraged partnerships with governments, multilaterals and on-the-ground NGOs to save more lives.<sup>34</sup>

The Coalition supports member actions against malaria in a number of ways: facilitating member-to-member collaboration and knowledge co-creation; creating practical technical tools to support corporate malaria programs; and engineering structured partnerships that blend each company's resources and competencies for maximal impact. The Coalition serves as the Secretariat for the Corporate Alliance on Malaria in Africa (CAMA), a partnership that provides member companies with increased networking and knowledge-sharing opportunities.

The coalition and CAMA came together in collaboration to draft a management roadmap for malaria action to better guide the coordination and integration of private sector malaria programs. They convened high-level leadership from Chevron Corporation, Halliburton,

Marathon Oil, Pfizer Inc., Sumitomo and Syngenta, along with the President's Malaria initiative to review and fine-tune the draft roadmap. The finished guide will provide direction for private sector collective action on malaria as part of a broader effort to meet the Millennium

Development Goal of reducing malaria deaths by 50 percent by 2010.35

Private pharmaceutical companies can also help by requesting a change in policy, into one that will be developing country friendly. If that kind of change is not feasible because of financial risks, they can simply decide not to exploit the TRIPS agreement for gain at the expense of millions of lives. TRIPS was put in place to protect them from financial harm; therefore, they also have a duty not to harm other people using the exact same policy.

Malaria is preventable and curable and yet it has persisted through several decades. A lot has been done to stop malaria in its tracks but more is still needed. A vaccine is necessary to bridge the gap between different interventions and the world and its organizations have to come

<sup>34</sup> Global Business Coalition. <www.gbcimpact.org>

<sup>&</sup>lt;sup>35</sup> Global Business Coalition. The corporate Alliance on Malaria in Africa. <a href="http://www.gbcimpact.org/about-gbc/cama">http://www.gbcimpact.org/about-gbc/cama</a>.

together for the disease to be eradicated. Many fatal diseases have been totally eliminated before; malaria need not be the exception.

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