Malaria Disease and Transmission

Malaria is the disease caused by parasitic protozoa of the genus *Plasmodium* (1). Symptoms of malaria usually resemble the flu; however, in young children, pregnant women, and immunocompromised patients the disease may lead to eventual death (2). It is the most serious, widespread parasitic disease causing over one million deaths annually. The disease is restricted to tropical and subtropical regions where the insect vectors, *Anopheles* mosquitoes, are present; this encompasses a thick band of countries surrounding the equator. There are four species of *Plasmodium* that infect humans, including *P. falciparum, vivax, ovale*, *and malariae*.

The life cycle includes two hosts, female *Anopheles* mosquitoes and humans (1). A human host is inoculated with *Plasmodium* sporozoites when an infected mosquito takes a human blood meal. The sporozoites of *Plasmodium* travel in the blood stream to the liver where they infect hepatocytes and mature into schizonts. These schizonts rupture after about six days and release 30,000-40,000 daughter cells called merozoites into the blood stream. Erythrocytes are then invaded by single merozoites. In 48 hours the organism undergoes asexual reproduction and produces 8-24 daughter cells. The red blood cells rupture and the new daughter cells invade more red blood cells. The clinical manifestations of Malaria are caused by the blood stage parasites that destroy large numbers of erythrocytes every two days.

The remaining life cycle stages known as the sporogonic cycle occur after *Plasmodium* gametocytes are ingested by an *Anopheles* mosquito. During a 10 – 18 day period ingested macrogametes are penetrated by microgametes to produce zygotes in the stomach of the mosquito. These zygotes penetrate the midgut wall of the mosquito where they develop into oocysts, which rupture to release sporozoites. The sporozoites then travel to the mosquito salivary glands where they can infect a new host.

The *Anopheles* mosquitoes remain asymptomatic when infected with the parasites; they only serve as vectors. The successful completion of the sporogonic cycle is dependent upon if the inoculated mosquito survives long enough for the *Plasmodium* to finish the cycle and if weather conditions are appropriate (hot and humid) for *Plasmodium* development.

State of the Problem

In the early 1950's Malaria was successfully eradicated from the U.S. through the use of DDT, chloroquine, and other anti-malarial medications and insecticides (1, 4). Efforts were made worldwide beginning in 1955 to continue to reduce the malarial burden. In western Europe malaria was declared eradicated in 1975. Due to difficulties with surveillance in developing countries the malaria eradication project was abandoned in 1978.

Malaria is still ever present worldwide with 41% of the global population living in areas where malaria is endemic (1, 2, 4). There are approximately 350 million cases annually, with sub-Saharan Africa being the most heavily impacted. Across all developing countries, malaria is the cause of death for 1 out of every 10 children. Malaria causes a total of over one million deaths annually; 3,000 daily deaths are children's.

Today it is much more challenging to treat and control malaria than it was in the early 20th century. In recent years the evolution of new drug and insecticide resistant strains of *Plasmodium* and *Anopheles* respectively have evolved. Additionally, it has been hypothesized that climate changes due to global warming are beginning to increase disease incidence. Population movements cause non-endemic countries to be at constant risk for introduction of malaria.

Control

Protection from malaria can be attained at the human host level or the *Anopheles* vector level. People living in malaria endemic areas of the world often develop an acquired immunity from continual exposure to the malarial parasite (1). This immunity does not protect them from contracting the *Plasmodium* but does from the severe clinical manifestations of the disease. Some individuals, typically those from endemic regions, do have an innate immunity against *Plasmodium* from genetic blood disorders, such as caring one recessive sickle cell gene for abnormal hemoglobin or lacking Duffy receptors on red blood cells so *Plasmodium* are unable to infect erythrocytes. For individuals without innate or acquired immunity against malaria prophylactic drug therapies are available. These medications do not prevent one from contracting the disease; however, they suppress *Plasmodium* from maturing inside the host and thus minimize symptoms. The distribution of these medications is often difficult in developing nations.

Control at the vector level attempts to prevent initial malaria infections. The most common and currently most effective method involves the use of insecticide treated bed nets (2). However, distribution and retreatment of these nets has proven challenging and costly (1). Insecticide spraying inside of homes is also effective, although over 125 species of *Anopheles* have developed resistance against at least one insecticide. Other effective measures include the destruction of larval breeding sites, the development of genetically altered mosquitoes that actually kill the malaria parasites, and the development of vaccines, but all these solutions require costly resources.

Complete control of malaria is not an unrealistic goal for the future because malaria is a treatable and preventable disease. Implementation of successful, sustainable anti-malaria programs including monitoring and intervention will require a concerted effort by local government authorities in conjunction with international government, NGO, private and public sector resources.

Should the U.S. government be involved in controlling the spread of malaria?

From a humanitarian standpoint the United States government should invest resources in controlling the global spread of malaria; however, even with only America's self serving interests in mind international anti-malarial programs should be supported. Even since the successful U.S. "eradication" in 1951 U.S. citizens remain an at risk population (1). In the U.S. there have been 63 outbreaks of malaria between 1957 and 2003 where locally infected *Anopheles* mosquitoes acted as vectors. These resident mosquitoes (both *A. quadrimaculatus* and *A. freeborni* are common in the United States and capable of acting as vectors for malaria) continue to put Americans at risk for the reintroduction and spread of malaria. In 2002 alone there were 1,337 reported cases of malaria in the States. The vast majority of these cases were acquired outside of the U.S.; although, a small portion of them may have been caused by blood transfusions with *Plasmodium* infected blood, organ transplants, or congenital transmission.

With global warming altering weather patterns, the percentage of American regions with appropriate climates for the survival and reproduction of *Plasmodium* will rise, thus increasing the risk for local malaria outbreaks. Moreover, heightened travel and immigration from malaria endemic regions increases the possibility of malaria reintroduction (or even more frightening, the introduction of drug-resistant strains) into the United States.

Recently much progress has been made towards eliminating the burden of Malaria in the less developed nation of Mexico. After the government implementation of an effective monitoring and intervention program there has been a 97% decrease in malarial cases since 1985. Currently few regions of the country, mostly the southern border territories that are difficult to access, are still at risk for malaria outbreaks. This significant progress towards eradication should encourage a continued commitment to fighting malaria globally.

In 1998, the international Roll Back Malaria Partnership was launched with the ambitious goal of halving the global burden of malaria by 2010 (4). There are 86 participating entities from both malarial endemic and non-endemic nations. The partnership states that, "… a successful fight against malaria will have far-reaching impact on child mortality, maternal health, and poverty, which in turn may increase global stability." For all of the preceding reasons, amongst numerous others, the United States should concern itself with the treatment and prevention of Malaria worldwide.

Comparative Analysis of the Costs and Benefits of a U.S. International Anti-Malaria Program

There are U.S. government supported international anti-malaria programs already in place. In June of 2005 Mr. Bush announced the President's Malaria Initiative (1, 3). The goal of the program is to halve malarial deaths in target sub-Saharan African nations within three years of implementation. US$1.2 billion has been pledged for these efforts over the next five years. Eventually 15 of the most affected African nations will be included in the program with the most at risk populations of young children and pregnant women being targeted. It involves supporting local governments so they can provide insecticide-treated nets, indoor insecticide spraying, combination drug therapies, and education to increase the numbers of individuals who seek care. Additionally, the President's Malaria Initiative is working to improve local infrastructure surrounding intervention, encouraging private sector involvement, and closely monitoring its own program to ensure its success and wise use of resources.

Only implementing this program in 15 countries is hardly enough. The President's Malaria Initiative is expected to effect approximately 175 million people, yet there are well over 300 million cases of malaria annually. The total debt to Africa alone from direct (money spent on medical visits, insecticide treated nets, medications, funerals, ect.) and indirect causes (income and productivity lost) is estimated to be US$12 billion dollars annually – the U.S. government is investing only one-tenth of this annual loss over a period of five years (4). More can be done to protect residents of endemic countries. The cost of potentially life saving anti-malarial drug therapies are incredibly inexpensive, ranging from US$0.13 for chloroquine or US$0.14 for sulfadoxine-pyrimethamine to US$2.68 for a course of quinine (1).

The Roll Back Malaria Partnership estimates that in addition to the current donations and support they receive (of which the President's Malaria Initiative and the U.S. Agency for International Development among other U.S. supported agencies are included) another US$3 billion dollars must be raised annually in order to successfully achieve their goal. US$2 billion is needed in Africa with the remaining US$1 billion required for malaria endemic nations of other continents. It is not the United States' responsibility to supply in full these additional resources. It is feasible for the U.S. government to continue building and strengthening partnerships with both the public and private sector, non-profit and grass-roots organizations (5).

There are social issues inhibiting the success of anti-malaria programs including poverty, civil unrest, war, food shortages, and other complex emergencies that face malaria endemic countries (4). These social problems drastically inhibit adequate treatment and surveillance systems that must be in place to truly combat malaria (1). Education about malaria and its global impact should be presented to those living in developed nations who may be willing to help. One person can save a life in Africa with a US$10 donation.

Impoverished families living in malaria endemic regions may spend up to 25% of their annual income on

prevention and treatment of the disease (4). The reduction of the malarial burden will promote a more stable and productive global market (5). This will set the stage for increased economic development in current malaria endemic nations and for an increased quality of life for their citizens.

Currently the U.S. supports numerous programs committed to fighting public health crises across the globe. Combating infections such as HIV/AIDS and the possible pandemic flu outbreak will have similar positive results to fighting malaria. It is difficult to balance available U.S. resources among all of these quality disease control and prevention programs.

The President's Emergency Plan for AIDS Relief has allotted US$15 billion, for a five year period which began in 2003, to combat the disease in over 120 countries (5). This is a far more extensive endeavor than the President's Malaria Initiative. AIDS affects more individuals worldwide than Malaria, an estimated 40 million are living with HIV. Today over one million American's harbor the AIDS virus, and it is estimated that 40,000 new infections occur annually within the United States. The rate of incidence rises drastically in less developed nations. For these reasons HIV/AIDS programs should be of higher priority and receive more U.S. government funding than anti-malarial programs.

The President's National Strategy for Pandemic Influenza Preparedness and Response was outlined in late 2005 to help plan a course of action for when the United States, and the world, is faced with a pandemic flu outbreak. Such an outbreak is foreseeable in the near future (from the H5N1 avian flu virus) and may have devastating impacts worldwide if proper precautionary measures are not taken. The last three flu pandemics occurred in 1918, 1957, and 1968; they killed 40 million, 2 million and 1 million people respectively. The program's budget of US$7.1 billion is to be used for detection of international outbreaks, national accumulation of vaccines and antiviral medications, and to increase national and local governments' readiness to respond to such an outbreak. Again, the funding for this flu pandemic program is greater than that of the anti-malarial program. The potential devastating effects of a pandemic flu outbreak in the United States are vast, but will they be worse than if malaria is reintroduced?

It is not unrealistic that malaria could one day become endemic in the United States. The main risk for reintroduction of the disease is by frequent travelers to, and immigrants from, South and Central American countries (1). Additional resources should be sent to support the prevention and control of disease in these countries. It is possible for money to be reallocated from the pandemic flu program to support anti-malarial programs outside of sub-Saharan Africa. Both flu and malaria programs in relation to the United States are functionally preventative; however, the anti-malaria program would serve to be more beneficial to current people living in malaria endemic regions. A few hundred million dollars should be reallocated from the President's National Strategy for Pandemic Influenza Preparedness and Response budget to support anti-malaria programs outside of sub-Saharan Africa, focused in the Americas.

References

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