

# Malaria vaccine underway

## History of Malaria worldwide

Deadly fevers - probably malaria - have been recorded since the beginning of the written word (6000-5500 B.C.). References can be found in the Vedic writings of 1600 B.C. in India and by Hippocrates some 2500 years ago. Quinine, a toxic plant alkaloid made from the bark of the Cinchona tree in South America, was used to treat malaria more than 200 years ago. Jesuit missionaries in South America learned of anti-malarial properties of the bark of the Cinchona tree and had introduced it to Europe by the 1630s and into India by 1657. In 1927, J. Wagner von Doering was awarded the Nobel Prize in Medicine for his work in treating syphilis with penicillin. Patients infected with a type of bacteria would literally die of a temperature of 40 degrees Celsius. After four cycles of penicillin, the patient was cured. Quinine for malaria therapy was used in the 1940s when it was replaced by antibiotic chemotherapy. The Dutch bought Cinchona seeds from a trader, Charles Smeets, who brought them to Peru. They established Cinchona

plantations in Java (Indonesia) in the mid 1800s and soon had a virtual monopoly on quinine. When the Japanese captured Java during the Second World War, quinine, except for some old stocks became unavailable. The need for a new synthetic antimalarial became a priority at that time. In 1880, the first true sighting of the malaria parasite was made in Algeria by a French Army physician, Charles-Louis-Alphonse Laveran, while viewing blood slides under a microscope. The medical community rejected Laveran's discovery and it was not until 1886 that Italian scientists, the leaders in the field, accepted his discovery at the time. In 1882 the mosquito transmission hypothesis - guilt by association - was first made. The December 18, 1897 issue of the *British Medical Journal* reported that Dr. Ronald Ross discovered malaria cysts in the stomach wall of *Anopheles* mosquitoes that fed on a malaria patient.



Children are always the major victims of malaria (file photo).

By July 1898, malaria transmission through the mosquito was established. At that time, Italian scientist Giovanni Batista Grassi traced the course of the parasite through the

mosquito, and proved that human malarial parasites were transmitted by species of *Anopheles*. Experiments in India in 1932, showed that the

monkey malaria, *Plasmodium knowlesi*, which produced no clinical signs of malaria in Indian rhesus monkeys, was fatal to Malayan irus monkeys

and produced a 24-hour fever cycle in humans that terminated in self cure. Unlike botanical quinine, chloroquine is a synthetically manufactured product that belongs to a class of compounds known as 4-amino quinolines, first developed in 1934 by a German pharmaceutical company.

The first 4-amino quinoline was called Resochin. A slight modification a few years later produced Sontochin. In 1943, the Americans acquired Sontochin when Tunisia was liberated from the Germans. Its composition was again changed slightly and it was renamed Chloroquine.

1950 saw the launch of a pilot project for the control of malaria by spraying with DDT.

WHO initiated strategies for the global eradication of malaria in the mid-1950s.

In the 1960s, chloroquine resistant strains of *Plasmodium falciparum* had arisen; the result of over usage and probably under dosage. At the time, there was no drug to treat chloroquine-resistant malaria except the ancient antimalarial, quinine.

By 1966, it had been shown that 10 species of *Plasmodium*, naturally present in monkeys and apes, were capable of infecting humans. Often an infection in one species that produces no clinical signs of malaria can cause severe illness and death

when transferred, through inoculation, to another. Quinine has now been completely synthesized; a synthetic analogue is called mefloquine.

A 'new' antimalarial drug called Qinghaosu is derived from the sweet wormwood (*Qinghao*) (genus *Artemisia*). It has been used in China for more than two thousand years to treat fevers associated with malaria. The drug has been shown to be effective in the treatment of the most deadly forms of falciparum malaria and has been effective against strains of *Plasmodium falciparum* that are totally resistant to chloroquine.

In 1957, WHO realized that the global eradication of malaria was impossible for a variety of reasons: the focus shifted to control of the deadly disease. In 1972, the Global Eradication of Malaria Programme was formally declared dead.

In 1967, Dr. Manuel E. Patarroyo, a biochemist from Colombia, developed the first synthetic vaccine against the *Plasmodium falciparum* parasite. The vaccine is still being developed and has not been proven to reduce deaths in Africa. In 1992, Dr. Patarroyo donated the vaccine to the World Health Organization.

Desowitz, Robert S. *Malaria Capers (More Tales of Parasites and People, Research and Reality)*. W.W. Norton Company, New York, 1992.

## 100,000 children die of malaria in Uganda

by Jennifer Bakaya

Half a century ago, malaria was unheard of in southwestern Uganda. In Kabale and

temperatures were in the swamps not the same and the land use was different. It is no longer the case. Land is used for agriculture projects; the swamps have been drained with crops like rice, giving the mosquito parasite a friendly environment. The species ambient temperature and water conditions are for malaria.

The situation may have changed in the past but we started to see the effect in the late 1980s," says Dr. Nathan Bakaya of the Ministry of Health.

Recently, people in these areas that originally were exposed to the disease as children, are getting severely ill. In epidemics were seen in 1990, 1991, 1994, 1996, 1998 and a current one which

health officials are trying to stop.

According to Bakaya, people will continue getting attacks of malaria, which could be severe because they are not used to the disease. With more attacks however, they are building immunity, he says.

A paper on general information from the ministry about malaria prevention and control states that typical symptoms of severe or complicated malaria include: change of behaviour, altered consciousness, convulsions, low blood sugar concentration (hypoglycaemia) and high concentration of acid in the blood (acidosis).

There is also acute renal failure, severe anaemia, shock and haemoglobin in the urine and the waste is very dark in colour (haemoglobinuria).

Others are palms, eyes, etc are yellow in colour (jaundice) bleeding tendency, prostration, axillary temperature above 39.5 degrees centigrades (hyperpyrexia) and more than 5% of the red blood cells have parasites (hyperparasitaemia).

Apart from people in very cold areas, pregnant women, children and foreigners who have never been exposed to malaria are susceptible to suffering from complicated malaria.

The ministry estimates that between 70,000 and 100,000 children less than five years in Uganda die of malaria annually. Figures for other children and adults are not yet available.

The good news is that the majority of people in Uganda have suffered from uncomplicated malaria, hence making it endemic in

the country. Uncomplicated malaria is characterised by fever, headache, and backache, joint pains and stages where the patient feels cold at one stage, hot at another and sweats too.

Bakaya says for uncomplicated malaria, it is advised that chloroquine is used as the first line drug in areas where its resistance is still low.

Sulfadoxine/pyrimethamine (fancidar) is given to the patient in case chloroquine does not work. Quinine should come as a reserve drug.

Dr. Frederick Kato, a Senior Medical Officer in the ministry says the World Health Organisation issued guidelines that in areas where malaria parasites are resistant to chloroquine, both chloroquine and fansidar are given as the first line drug.

Kato says that with every

100 people suffering from malaria, 30 of them are resistant to chloroquine.

"It is usually town dwellers than rural people who are more resistant to chloroquine," he adds.

According to Kato, rural people use between Shs 2,000 and Shs 2,500 for treatment of uncomplicated malaria as opposed to urban dwellers who spend between Shs 4,000 to Shs 4,500 on the disease.

Several Ugandans are fearful about anti malaria drugs manufactured from India and Pakistan, believing that they are not effective in treating the fever.

However, Kato says, not all drugs should be labeled ineffective, because it depends on the manufacturer.

He adds that drug manufacturers prefer Asian countries than North America or Europe because of the cheap costs.

"Most drugs that enter the country are first approved by the National Drug Authority. Besides, periodically, samples of drugs are taken off the shelves and tested for its content," he says

But Bakaya says it is quick to see that there could be ineffective drugs because of the poor security at the frontiers.

Boards or no boards Government is determined to fight malaria. Last financial year, it allocated Shs 70m towards the malaria control programme. For 2000/2001 fiscal year, Shs 540m was budgeted for fight.

This is in addition to donors like WHO, UNICEF, DFID, International Development Agency, European Union, USAID who help in the fight. Sometimes the donor channel the funds through the ministry or they can fund independent programmes, says Kato.

Others give the money to Government Organisations and churches.

This may appear to be inadequate.

At a 4th meeting of the Partners for Roll Back Malaria, it was discovered that it is more expensive in Sub-Saharan Africa to use six dollars per capita on treatment instead of \$12 per capita.