# MALARIA AND QUININE

## Historical perspective lends insight to trends

Malaria is thought to have infected humans for over 50,000 years. Although it is not prevalent in some parts of the world, it kills countless millions each year, mostly African children. Because of the interconnectedness of so many systems on our planet, international health experts agree that it is still a global issue that will require a global effort to solve. Malaria also has a global history with an Italian name and a historically popular treatment from Peru.

Malaria is contracted through the bite of an infected female Anopheles mosquito and causes high fevers and chills in the victim. If left untreated it can result in death. However, the word malaria is a misnomer. It has nothing to do with mosquitoes or fever. Instead it is an Italian word that means bad air. It was thought that one developed the symptoms from miasma, or breathing the noxious air from marshes and swamps which were endemic to Rome. For that reason one of malaria's many aliases was Roman Fever.

Ancient Romans believed it was dangerous to be out in the evenings when Roman Fever was thought to be contracted. Coincidentally, this is consistent with current knowledge of the mosquito's feeding time of dusk to dawn. Malaria was also named Intermittent Fever, because epidemics probably came and went with the water levels in the marshes and swamps, stagnant water being ideal breeding ground for mosquito larvae. Along with those tides, scholars such as Angelo Celli feel there was a direct correlation between malarial outbreaks and the political and economic highs and lows of ancient Rome, as he demonstrates in The History of Malaria in the Roman Campagna from Ancient Times.

In early 17th century Europe, the Ague or marsh fever, another malaria alias, was not only killing countless civilians but was making its way up the social ladder through cardinals, kings, and popes. It seems it took that kind of effect for a leader in society to finally take a stance. In 1623 Pope Urban VIII decreed that a cure for malaria be found. Missionaries who were traveling to South America were urged to come back with a treatment. Remarkably, they did.

Fiammetta Rocco describes the events of this time in her book Quinine: Malaria and the Quest for a Cure that Changed the World. Agustino Salumbrino was a Jesuit missionary and apothecary in Lima, Peru. He observed natives using something to treat shivering from the cold air. He speculated it might be effective in treating the shivering from the sweating and chills

***Illustration compliments of the archives at the John W. England Library at the University of the Sciences in Philadelphia. From the book Medical Botany: Affording the Important Articles of the Materia Medica, by Joseph Carson, M.D., Professor of Materia Medica at the Philadelphia College of Pharmacy, 1847.***

of malaria. The substance used was the powdered bark of the Cinchona tree, also known as the fever tree. The bark took on a few clever names such as Indian Fever bark, holy bark, Peruvian bark, Jesuit's bark, and febrifuge bark, a febrifuge being an herbal remedy antipyretic, or substance that reduces fever.

Salumbrino sent the cinchona bark back to Rome. In 1631 it was used to treat the first case of malaria and was determined to be effective. However, its use sometimes stood in the face of the traditions of the

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conservative medical community at the time. Physicians were still trying to hold on to the Greek teachings of Galen, whose theories influenced European medicine for over a thousand years. It would take until 1677 before cinchona was formally recognized and included in the respected London Pharmacopoeia, a technical book for the standardization of preparing medicine. Nevertheless, the treatment spoke for itself and word began to spread. Between the effects of the Jesuit outreach and the already established infrastructure of the shipping trade, the bark would soon become a valuable commodity.

As Saul Jarcho presents in his book, Quinine's Predecessor, by the late 17th and early 18th century cinchona would show up in several other countries such as Spain, France, and England, as one might expect for being so close to Italy. It also made its way to Germany, Belgium, The Netherlands, and Switzerland. It was even traded as far as Russia, China, India, and the Philippines.

As close as it was geographically to some of these locations, cinchona trade seemed to have circumnavigated Africa. The bark may not have found its way to Africa until early attempts at British colonization. Some attribute the success and failure to colonize parts of Africa around the ability of the British to treat their soldiers when outbreaks of malaria would occur.

Quinine, the active ingredient in cinchona, was the drug of choice for the treatment of malaria until World War II. At that time 95% of Cinchona trees were grown on the Indonesian island of Java. The Japanese and their allies were in control of most of it, so a synthetic version called chloroquine was created to supply wartime needs. The synthetic version was shown to be effective, but only for a few decades. Unfortunately there are now chloroquine resistant strains of Plasmodium falciparum, the protozoan parasite that causes the most dangerous form of malaria. Once chloroquine in combination with another drug like proguanil was recommended as combination therapy for resistant strains, but is no longer because of the availability of cheaper and more effective combinations of other drugs. Now, due the resistant strains, the use of the original quinine is experiencing a revival. It is being used again as an ingredient in other drugs and for treating resistant strains. Notably, it is still cheaper to extract quinine from the bark than it is to synthesize it in a lab.

This historic perspective illustrates that we may have come full circle in some ways of addressing this ancient disease. Much like the way Rome's economy was sensitive to malaria outbreaks, so too is the economy and development of parts of Africa. Much like the way a natural cure was effectively used to treat malaria in the past, so too might something natural like quinine or the herb artemisinin be used more in the future.

From a 50,000 year perspective we have been doing extraordinarily well these last couple hundred years - if you compare what was accomplished before the 17th century. However, we can do better. This is the first time in the history of the planet that we have the technology and resources to manage this disease. It is preventable and curable, yet every 30 seconds an infected child dies. The goal of the World Health Organization is to reduce the prevalence by half in 2010, and to make it an insignificant health issue by 2030. Let's hope there is no resistance in getting there.

***By MJoTA staff***

### *Scientific Advancement Time Table*

1820 French chemists Pierre Joseph Pelletier and Joseph Caventou isolate quinine, the active ingredient in the cinchona bark.

1880 French physician Charles Louis Alphonse Laveran identifies parasites in the blood of people infected with malaria. He is awarded a Nobel Prize for his work in 1902 (see pages 29-30).

1881 Cuban physician Carlos Finlay suggests that mosquitoes transmit diseases to humans.

1897 Scottish physician Ronald Ross ties it all together when he discovers the presence of the malaria parasite in the Anopheles mosquito. He is also awarded a Nobel Prize for his work in 1907 (see pages 28-29).