Back with a vengeance

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A mosquito bite can carry one of the world's deadliest diseases — malaria. It kills two million people every year around the world. It can attack the liver, kidney and brain, and can kill within 48 hours. There are many drugs available to prevent and treat malaria. It was only 100 years ago when doctors discovered that malaria was carried by mosquitoes. Until then, malaria was thought to be an airborne disease, the name deriving from the translation for 'bad air'.

Tracing the history of man versus nature nothing so small and insignificant perplexed scientists so much as a mosquito. Apparently fragile and frail this insect can prove deadly.

Almost two decades ago malaria was eradicated from the US, Europe and some parts of Asia. The next target was Africa and South America. Thanks to DDT, the widespread use of this insecticide ensured a malaria-free environment in these regions at last.

During the second world war, miracle drug 'Chloroquine' was developed to combat this disease. A relatively inexpensive prophylactic drug, it treated many and saved lives.

Then things started to change, but not for the better.

Eradication attempts like the widespread use of DDT have not only proved futile, they have aggravated the problem by creating multi-drug resistant plasmodia strains, a tendency that is threatening the usefulness of current treatments and is urgently calling for new anti-malarial compounds.

According to a World Health Organization report:

* 300-500 million new cases of malaria occur annually
* 280-300 million people harbour the parasite
* 1.5-2.7 million deaths occur each year
* One child dies of malaria after every 30 seconds

The situation has become even more complex over the last few years with the increase in resistance to the drug normally used to combat the parasite that causes the disease.

The increasing resistance of malaria parasites to anti-malarial drugs is a major contributor to the re-emergence of the disease as a major public health problem and its spread in new locations and populations.

Imagine a cheap and easily manufactured drug available to combat a deadly and highly contagious disease; a disease that bursts red blood cells from within and claims millions of lives each year. This drug saved lives and even poor countries could afford it. Now suddenly the drug no longer works.

Malaria is quickly approaching a scenario where the malaria parasites have become increasingly resistant to well-established drugs such as chloroquine and other anti-malarials, with no other drug ready to take over.

Malaria control efforts include attempts to develop an effective vaccine, eradicate mosquito vectors and develop new drugs.

However, the development of a vaccine has proven very difficult and a highly effective vaccine will probably not be available in the near future.

Efforts to control Anopheles mosquitoes have had limited success, although the use of insecticide-impregnated bed nets does appear to reduce malaria-related death rates. In addition, methods to replace natural vector populations with mosquitoes unable to support parasite development are under study and may contribute to malaria control in the long term.

However, the current limitations of vaccine and vector control, as well as the increasing resistance of malaria parasites to existing drugs, highlight the continued need for new anti-malarial agents.

The increasing resistance of malaria parasites to anti-malarial drugs is a major contributor to the re-emergence of the disease as a major public health problem and its spread to new locations. Imagine a cheap and easily manufactured drug available to combat a deadly disease that bursts red blood cells from within and claims millions of lives each year. Now suddenly the drug no longer works

Anti-malarial drugs have been used for centuries. Earlier, natural products, like the bark of the cinchona tree in South America and extracts from the wormwood plant in China, were among the first effective anti-microbial agents to be used. Cinchona bark was used in Europe in the 17th century, and upon its isolation from bark in 1820, quinine became widely used. In the last 50 years, extensive efforts, including screening of thousands of compounds, have led to the development of a number of effective synthetic anti-malarial drugs. The most important of these, chloroquine, has been the mainstay of anti-malarial chemotherapy for the last 50 years. The compound eradicates parasites rapidly, has minimal toxicity, is widely available at low cost throughout the world and needs to be taken only a week for chemoprophylaxis.

However, resistance to chloroquine has been steadily increasing since the drug's initial use in South America and Southeast Asia in the late 1950s. Chloroquine resistance is now widespread in most Plasmodium falciparum endemic areas of the world. Thus the use of chloroquine for presumptive treatment of falciparum malaria or for chemoprophylaxis is usually no longer appropriate. Moreover, resistance to the Chloroquine of Plasmodium vivax, the second most lethal human malaria parasite, is increasing in South Asia.

Relatively few anti-alarial drugs are undergoing clinical testing. Halofantrine, identified in the 1940s, was not developed until the 1980s; its use has been limited by variable oral absorption and cardiac toxicity. The drug is approved in the United States for treatment of Chloroquine-resistant P. falciparum infections, although in most cases quinine (or intravenous quinidine) is preferable.

Key messages

1. With more than 300 million cases every year, malaria remains one of the major public health problems in many developing countries.
2. Children suffer most from malaria. In absolute terms, malaria kills 3,000 children under five years of age every day. This means a death due to malaria occurs every 30 seconds.
3. Chloroquine resistant P. falciparum is present in practically all endemic countries.
4. Drug resistance is expanding geographically and in terms of the number of affected drugs.
5. In recent years, Chloroquine-resistant P. Vivax has been reported.
6. Malaria drug resistance increases morbidity and mortality, especially among children, because of serious anaemia and severe attacks.
7. According to a latest report published in the *Journal of the College of Physicians and Surgeons of Pakistan*, resistance to Chloroquine is reported to an extent of 33 per cent while resistance to Sulphadoxine/Pyrimethamine to an extent of 37 per cent. ■