The rise of antimalarial drug resistance

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Artemisinin based combination therapies are the last line of treatment against multiresistant malarial parasites. Malaria is the deadliest and most frequently occurring parasite related disease in the world and it kills around 600 000 people each year. Treatment of malaria has through the years relied heavily on antimalarial drugs but resistance against these drugs has reduced the drugs efficiency. The emergence of antimalarial drug resistance has prompted researchers to develop new drugs and new therapies. One of the most prominent treatments uses artemisinin, derived from sweet wormwood, *and its derivatives alongside another drug. These treatments are called artemisinin based combination therapies and they are the last line of treatment against multiresistant malarial parasites. However, resistance against artemisinin based combination therapies has developed which is very alarming.*

Antimalarial drugs

In the treatment of malaria there are several widely distributed drugs. Of these, chloroquine and sulfadoxine pyrimethamine are the most affordable, easily available and widely used drugs. The role of chloroquine is to inhibit the breakdown and detoxification of hematin, a byproduct in the breakdown of hemoglobin. Sulfadoxine pyrimethamine is a treatment consisting of two separate drugs—both inhibiting enzymes involved in synthesis of folic acid. However, due to the accumulation of parasites resistant to chloroquine and sulfadoxine pyrimethamine new effective therapies had to be evolved. The central treatment strategy, following the rise of resistance, is based around artemisinin and its derivatives. Chinese scientist discovered artemisinin and its antimalarial activity in the 1970s in a research program named Project 523. Artemisinins is used in treatment accompanied by another drug that is mechanistically different. This is advantageous since adaptation has to occur to both drugs. Artemisinin based combination therapies are currently the last effective treatment in a lot of cases since antimalarial drug resistance is so widely spread.

Malaria kills around half a million each year

Malaria is the result of an infection of the malaria parasites. Human infection of the parasites may result in severe complications, including anemia, acute respiratory distress syndrome, abnormal blood clotting, low blood pressure, acute kidney failure, as well as acidification of the blood and tissues. The malaria parasites are a part of the genus *Plasmodium.* There are five different *Plasmodium* species that can infect humans and *P. falciparum* is by far the deadliest. The malaria parasites spread through mosquitoes, belonging to the genus *Anopheles,* carrying the parasites. These complications are the outcome of the parasite invading the red blood cells.

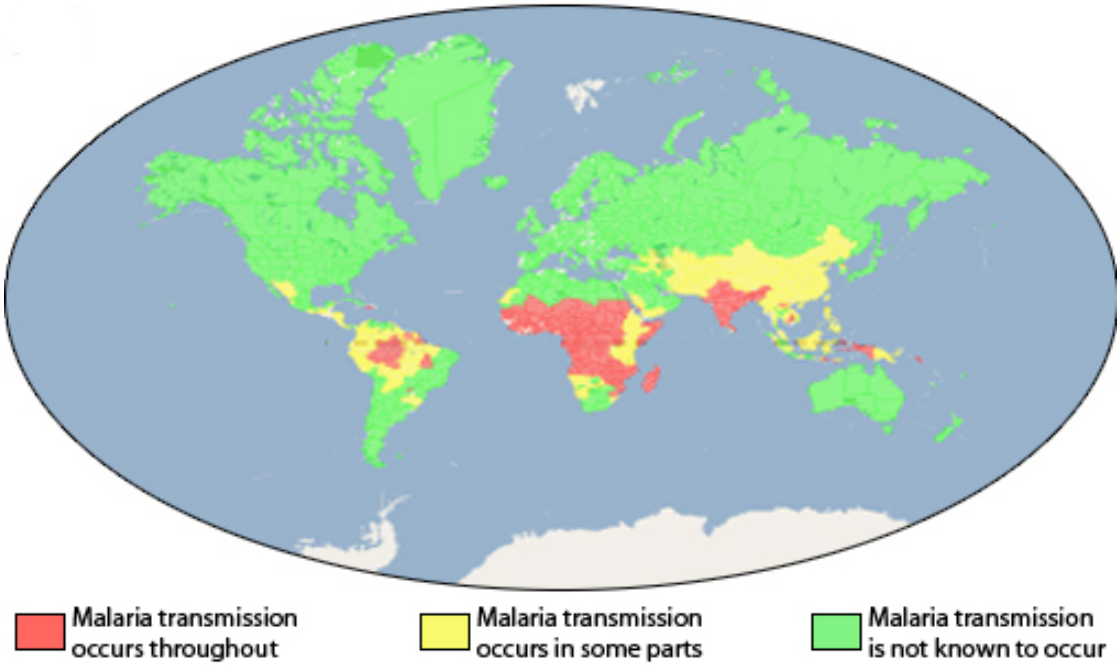

Figure 1. The map shows an approximation of the worldwide distribution of malaria transmission. Showing regions where transmissions occur throughout, where transmissions occur in some part and where transmission is not known to occur. Courtesy of the CDC (under public domain).

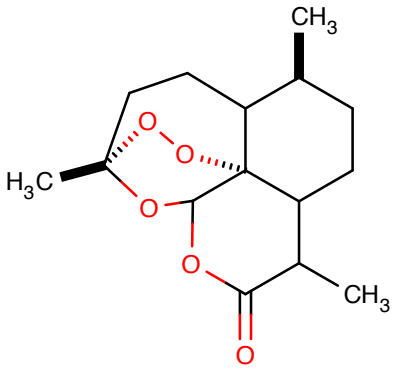

Figure 2. The chemical structure of the antimalarial drug artemisinin, derived from sweet wormwood pictured on the left.

Rise of antimalarial drug resistance

The rise of antimalarial drug resistance is attributed to genetic mutations that happen within the genome of the malaria parasites and the mutations ensure that the parasite can circumvent the often-inhibiting function of the drug. This is recognized in all of the above-described pharmaceuticals and is especially alarming when it comes to ACT resistance since it's the last consistently effective treatment of malaria. The emergence of these multiresistant parasites will deeply impact the international community and an already immense problem can turn into a devastating human catastrophe.

Further reading

Langseth CM. 2015. Uppkomst av läkemedelsresistens vid behandling av malaria – med inriktning på artemisininresistens. Självständigt arbete. Uppsala University (Swedish)