

Drug resistance: malaria

Antimalarial drug resistance – the ability of the malaria parasite to survive drugs – is a major public health problem which is threatening to undermine gains in malaria control

>> The problem

Significant progress has been made in recent years in the fight against malaria. Since 2000, mortality from malaria has decreased by over 25 percent globally. Scale-up of effective malaria interventions, including the use of artemisinin-based combination therapies – the most effective drug for treating the disease – have been instrumental to this success. However, growing resistance to artemisinins by the malaria parasite has been emerging in Southeast Asia and is threatening to reverse the gains that have been made to date.

Antimalarial drug resistance first became a global problem in the 1960s when certain malaria parasites developed resistance to chloroquine, the then widely-used antimalarial drug.

This has since evolved with the emergence of malaria parasites that are resistant to artemisinins which is one of the major threats to sustained malaria control and elimination today. These medicines are the basis for artemisinin-based combination therapies (ACTs), the most potent weapon in treating falciparum malaria.

The current tools used remain remarkably effective in the majority of settings; however, resistance to artemisinins has been detected in four countries of Southeast Asia. In addition, antimalarial drug resistance is contributing to the spread of malaria to new areas and the re-emergence of malaria in areas where the disease had been eradicated. Drug resistance has also played a significant role in the occurrence and severity of epidemics in some parts of the world.

Currently, antimalarial drug resistance has not yet led to a failure of malaria control programmes; however, urgent and intensified efforts are required to prevent a future public health disaster.

>> Key issues

Antimalarial drug resistance

There are five malaria species that affect humans and parasite resistance has been documented in three of these: *P. falciparum*, *P. vivax* and *P. malariae*. As a result of this resistance, the clearance of parasites from the human's blood is either delayed or incomplete. This problem is exacerbated by cross resistance. This is where resistance to one drug causes resistance to other similar drugs, resulting in several previously highly effective antimalarials being removed from the market.

Containment of artemisinin resistance

Resistance to anti-malarial drugs first emerged in the Greater Mekong subregion in the 1960s. The spread of resistant parasites from this region to India and Africa triggered a dramatic increase in malaria-related illness and death – particularly among children.

Today the treatment for malaria is ACTs – the most effective anti-malarial we have had to date. However, in 2008, *P. falciparum* resistance to artemisinin was first confirmed on the Cambodia-Thailand border and is now present in four countries of the Greater Mekong subregion: Cambodia, Myanmar, Thailand and Viet Nam.

National efforts to contain resistance have had some impact, but urgent action is needed to fully eliminate resistant strains of the parasite and to ensure that ACTs remain effective. WHO currently estimates that about US\$300-350 million of additional funding would be required from 2013-2015 to fully scale up malaria control and containment activities across affected countries in the Greater Mekong subregion.

As artemisinin resistance is prevalent in border areas and migration is known to be a contributing factor in

the spread of resistance, there is also a need to increase cross-border coordination between national projects and programmes.

Despite this resistance, ACTs continue to cure patients provided that the partner drug is still effective and WHO recommends them for the treatment of uncomplicated malaria caused by *P. falciparum*. ACTs have been integral to the recent successes in global malaria control, and there is broad consensus that protecting the effectiveness of them is an urgent priority.

Mobilising resources

Although major efforts are under way to develop new classes of antimalarials, there are no replacement products on the immediate horizon. Efforts to contain artemisinin resistance in the areas where drug resistance has been most prominent have been effective where implemented, but programmes now need to be strengthened and expanded. This requires a rapid scale-up of core malaria prevention and control measures, considerable investments in monitoring drug efficacy, and an expansion of access to diagnostics and quality-assured, locally appropriate antimalarials.

Drug efficacy monitoring

Routine monitoring must be continued to ensure that the recommended first line ACTs are effective and that timely changes in treatment policies can be made. It is also critical for detecting the emergence of artemisinin resistance.

>> International response

Global plan for artemisinin resistance containment

In January 2011, WHO released the Global Plan for Artemisinin Resistance Containment (GPARC), which puts forward four main goals and recommendations:

- » to stop the spread of resistant parasites
- » to increase monitoring and surveillance to evaluate the artemisinin resistance threat
- » to improve access to diagnostics and rational treatment with ACTs
- » to invest in artemisinin resistance-related research.

The GPARC calls on endemic countries and stakeholders to scale up containment activities in affected countries, and to implement comprehensive plans in other endemic regions to prevent the emergence of resistance.

Emergency response to artemisinin resistance

In April 2013, WHO also launched a new Emergency Response to Artemisinin Resistance, building on the GPARC. The emergency response framework is guiding a major scale-up of strategies to combat artemisinin resistance.

Included in the emergency response framework is a call for the withdrawal of poor-quality antimalarial drugs and oral artemisinin-based monotherapies to reduce their threat to the long-term usefulness of ACTs by fostering the emergence and/or spread of resistance to artemisinin. According to WHO's latest assessment in April 2013, at least 31 companies around the world are still marketing these monotherapies. Globally, 44 countries have withdrawn authorisation for these medicines, but 14 countries continue to allow their use.

Source: World Health Organisation (http://www.who.int/topics/drug_resistance/en/)



Artemisia annua: the critical ingredient in ACTs. Photo: Adam Nadel