

MALARIA

Facts and figures

- Every year, malaria kills 1-2 million people and infects 300-500 million. 90% of deaths occur in sub-Saharan Africa. The disease is present in over 100 countries, threatening 40% of the world's population.
- Malaria is caused by four species of Plasmodium protozoa (single-cell parasites): *Plasmodium falciparum*, *vivax*, *ovale* and *malariae*. Of the four species, *Plasmodium falciparum* is responsible for most deaths. The parasite transmission by Anopheline mosquitoes is affected by climate and geography, and is often highest during the rainy season.
- Symptoms of malaria include fever, shivering, pain in the joints, headaches, repeated vomiting, convulsions and coma. If left untreated, the disease - particularly that caused by *P. falciparum* - may progress to severe malaria and sometimes death.
- Malaria remains the first cause of death for children under five in Africa - it kills one child every thirty seconds worldwide. The disease also seriously affects children's future: they may suffer neurological after-effects and impaired learning ability.
- Malaria not only cuts lives short but has a huge socio-economic impact: patients are often bedridden and incapable of carrying out normal daily activities. The disease causes considerable loss of income and places a heavy burden on families, health systems and society as a whole.

Diagnosis

Malaria is commonly diagnosed based on clinical symptoms alone - fever, headaches, etc. However, around half the people who present with fever and are treated for malaria in Africa may in fact not be infected with the parasite. Clinical diagnosis without laboratory verification increases drug costs unnecessarily, and it accelerates the emergence of drug resistance. Introducing more effective and more expensive treatment increases the importance of access to reliable biological diagnostics.

State-of-the-art laboratory testing can differentiate between different species and measure parasite load, but this requires specialised equipment and highly trained staff, both not readily available in resource-poor settings. In most cases, laboratories in developing countries are equipped with microscopes and a simple count of parasites in the blood confirms diagnosis. This is an effective means of diagnosis when technicians are well trained and microscopes are well maintained.

The other method is rapid diagnostic testing using a simple "dipstick" test, which is quicker and easier to use, but more expensive and not adapted to all cases. The challenge is to dramatically expand the availability of biological diagnosis. Laboratory capacity needs to be enhanced and rapid tests need to be more widely used, especially where there are no adequate labs.

Treatment and the problem of drug resistance

Chloroquine, developed in 1934, is very cheap (US\$0.10 per treatment), easy to administer and has few side-effects. For a while, it was the ideal anti-malarial, but its effectiveness has decreased dramatically in the last few decades: resistance to chloroquine now reaches

over 90% in many parts of Africa. Resistance to other first-line drugs is also growing rapidly - for example, resistance to sulphadoxine-pyrimethamine (SP or Fansidar®) is already higher than 60% in several regions of Burundi and Uganda.

Antimalarial drugs are often administered on their own (in "monotherapy"), but the World Health Organization now strongly recommends switching protocols to include an artemisinin-based combination therapy (ACT). By hitting different biochemical targets of the parasite, drug combinations are more effective, allow for shorter treatment courses, and protect each individual drug from resistance. It is now widely agreed that the best current treatment solution is ACT. Artemisinin derivatives - which are extracted from a Chinese plant - are fast-acting, highly potent and complementary to other classes of treatment. To date, no resistance to ACT has been reported.

Persuaded by these facts, some African governments are now changing their protocols in favour of ACT: Burundi, Cameroon, Comoros, Cote d'Ivoire, Equatorial Guinea, Gabon, Ghana, Kenya, Mozambique, Senegal, South Africa, Zambia and Zanzibar (Tanzania) have already changed their protocols, and 11 other countries are moving towards ACTs. But the adoption of a protocol does not immediately translate into implementation: as at March 2004, only five African countries were deploying ACTs in the public sector (namely South Africa, Burundi, Zambia, Comoros and Zanzibar, Tanzania).

MSF malaria projects

MSF has been treating patients with malaria in its projects in Africa, Asia and Latin America since 1985. It currently runs malaria projects in nearly 40 countries, treating over one million malaria patients every year. Approximately half of these receive ACT. MSF has also conducted numerous drug resistance studies in collaboration with national health ministries and Epicentre, a Paris-based epidemiological research institute.

For good patient care now and in the future, and to prevent the further spread of the disease, MSF has decided to implement ACT as first-line treatment in all of its malaria programs. MSF has already introduced ACT in its projects in Angola, Afghanistan, Cambodia, Congo Brazzaville, DRC, Ivory Coast, Kenya, Liberia, Myanmar, Pakistan, Sierra Leone, South Sudan, Thailand and Zambia, and plans to implement ACT in all malaria projects by the end of 2004.

What needs to be done

Funding

MSF believes that the only way to prevent the widespread use of sub-optimal, ineffective treatment and effectively address malaria epidemics is to fund the use of ACT. It is expected that 132 million treatments will be needed in 2005. Presently, cost per treatment is US\$1.50-2.40 for adults and US\$0.40-0.90 for children. While this is more than the cost of the old treatments, the increase in cost will be repaid many times over in years to come: using effective treatment saves lives and reduces the enormous socio-economic burden of the disease.

Malaria is one of three priority diseases that the international community has committed to combat through the Global Fund (GF) to Fight AIDS, malaria and tuberculosis. As a result of public pressure, the GF has recently clarified its position regarding malaria treatment and is now clearly in support of ACT: it is requesting that countries apply for the most effective malaria treatments, and a provision has been made for recipients of approved grants of funding for chloroquine or SP to convert to the use of ACTs in case of documented resistance to other drugs. In the first three rounds of funding, the GF committed a total of

US\$ 41 million for a period of 5 years for the purchase of ACTs in African countries, including Zambia and Zanzibar. The amount might increase in round 4, but is still inadequate to finance estimated needs. Also, the GF is still badly under-financed. International donors must increase their contributions and guarantee financing in the long term if countries are to be convinced to switch to more effective but more expensive malaria treatment.

What is required, therefore, is greater political will both from donor and endemic countries, to ensure the accelerated introduction of ACT.

Supply

In many parts of Africa, artemisinin derivatives are already widely available as single drugs in private pharmacies - for those who can afford them. But they must be made available in public health facilities as part of combinations to set the right treatment standard. Blister packs combining artesunate and amodiaquine, SP or mefloquine are available at a price as low as US\$1.50 per adult treatment. In the public and not-for-profit sector only, the fixed dose combination of artemether and lumefantrine (sold as Coartem® by Novartis) is available at US\$2.40 for an adult dose. The price is much higher in the private sector.

Large increases in need will require advance planning/purchases since *Artemisia annua*, the plant from which artemisinin derivatives are extracted, takes over six months to grow. To address the bottleneck of limited artemisinin availability and to avoid acute shortages of ACTs, MSF is urging international donors to support the purchase of artemisinin (raw material) and/or finished products.

Research and development

In the future, ACT fixed dose combinations (two drugs combined into one pill) will improve ease of use. The only currently available fixed dose of ACT is the combination of artesunate and amodiaquine. MSF is supporting the Drugs for Neglected Diseases Initiative (DNDi), a not-for-profit organisation, in developing fixed dose combinations of artesunate/amodiaquine and artesunate/mefloquine, which should be available in 2005-6. Several European and Asian manufacturers are also working on the development of new co-formulations and some of these are promising in terms of price and rapid availability. As existing rapid diagnostic tests still need improvements, development of new rapid tests must also be supported and closer links between end users, clinicians, manufacturers and scientists must be formed.

In the long term, it is also crucial to increase research and development for new vaccines and drugs against malaria. A 1996 report showed that an average of just US\$42 was spent on research for every malaria death, compared to US\$3,270 for every HIV/AIDS-related death.