



## Symposium 16.2

### Malaria

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The global mortality from malaria has risen in the past 20 years. This is attributed directly to worsening drug resistance in *Plasmodium falciparum*. Control of malaria depends on vector control and effective drugs – there is no vaccine, and there will not be a widely deployed vaccine for at least five years. The widespread and uncontrolled use of inexpensive antimalarial drugs over the past 50 years has provided a tremendous selection pressure on human malaria parasite populations. Resistance has now emerged in *Plasmodium falciparum* to all classes of antimalarial drugs with the exception of the artemisinin derivatives. The progressive decline in chloroquine susceptibility has made this drug partially or completely ineffective in most malaria affected countries. The usual successor to chloroquine is sulfadoxine-pyrimethamine, but high resistance to this antifol combination usually develops within five years of use. *Plasmodium vivax* has also developed resistance to antifols, and more recently in Asia and Oceania, to chloroquine. The emergence of drug resistance can be slowed or prevented altogether by the use of combinations of antimalarial drugs with different modes of action. The Chinese plant derived artemisinin derivatives have emerged as the most effective of all antimalarial drugs. Artemisinin based combination treatments (ACTs) have proved highly effective and well-tolerated in extensive trials and operational use. The world's most drug resistant malaria parasites are found on the northwestern border of Thailand. By 1994 mefloquine resistance had reached 50%. Since then the systematic deployment of artemisinin based combinations has led to a ninefold reduction in the incidence of falciparum malaria and a reversal of drug resistance. In the management of severe malaria most of the world still relies upon quinine. In the past 20 years dosing has been rationalised on the basis of pharmacokinetic and pharmacodynamic studies. The artemisinin derivatives are more rapidly acting, because of their broad stage specificity in the asexual life cycle of *Plasmodium falciparum* and intrinsic activity, and they are safer and easier to use. In the largest ever randomised trial in severe malaria artesunate reduced mortality by 35% compared with quinine. A variety of adjuvant treatments have been evaluated but none has proved beneficial –and several (heparin, dexamethasone, anti-TNF antibody, desferrioxamine, high dose phenobarbitone) proved harmful. On the other hand better understanding of pathophysiological processes has led to considerable improvements in clinical management. In particular the better assessment of severity, the recognition of hypoglycaemia and metabolic acidosis as frequent and dangerous manifestations of severe malaria, the improved management of fluid balance and severe anaemia, and the aggressive early management of acute renal failure in adults have been important developments. In 2006 the World Health Organisation published new treatment guidelines; ACTs should be first-line treatment for falciparum malaria everywhere in the world, and artesunate should become the first-line treatment for severe malaria.