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Malaria: old challenge, new ideas

About one third of the earth's six billion people live with a serious risk of contracting malaria. Approximately 300–500 million are infected every year. And each day, 3,000 children die of the disease. It isn't a new disease that has taken us by surprise—the ancient Egyptians recognized and described malaria in detail—but it is going to take new ideas to tackle it globally.

Identified as the cause of malaria in 1889, the parasite *Plasmodium falciparum* is transmitted by the *Anopheles* mosquito and, historically, most efforts to limit malaria have focused on vector control. During World War II the military recognized the tremendous threat posed to their overseas troops in malaria-endemic regions and DDT—the first chlorinated organic insecticide—was introduced to great effect in curbing mosquito populations. At about the same time, chloroquine was also introduced, a drug which interferes with the digestion of hemoglobin in the blood stages of the malaria parasite life cycle. This two-pronged attack initially produced spectacular results, but a lack of infrastructure, coordination and funding culminated in sporadic initiatives, in turn leading to the emergence of new strains of the vector and drug resistance. The result? From 1970 to 1997, sub-Saharan Africa has suffered a 40% increase in infection rates.

Compounding this deteriorating situation is the realization that even if used carefully, DDT is not a long-term solution. Although an effective and affordable insecticide, DDT is toxic and its widespread use is dangerous to people and wildlife. So much so that it is now one of a dozen substances that the United Nations proposes to ban worldwide. This proposal (known as the P.O.P. treaty) is being hotly contested by many scientists (370 researchers from 57 countries) and health organizations (WHO included) that argue its use is essential in those areas most at risk of malaria until an alternative to DDT is available (see Commentary *Nature Med.* **6**, 729-731 2000).

In addition to health concerns, malaria causes tremendous economic suffering. A conservative estimate by economist J.D. Sacks suggests that on average, African countries are losing approximately 1% of GDP dealing with malaria. The economic argument is a powerful one and is at least partly responsible for reawakening interest in the disease. As a result, a number of important new initiatives have been started.

The Multilateral Initiative on Malaria (MIM, http://www.who.int/tdr/diseases/malaria/mim.htm) aims to promote malaria research in Africa; The Roll Back Malaria initiative (RBM, http://www.who.int/rbm/) is devoted to improving health systems with the goal of halving the burden of malaria by 2010; and the Medicines for Malaria Venture (MMV,http://www.who.int/tdr/diseases/malaria/mmv.htm) hopes to develop one new antimalarial drug every five years.

A fourth initiative The Malaria Vaccine Initiative (MVI http://www.malariavaccine.org/) was created through a grant by the Gates Foundation.

A malaria vaccine remains the 'holy grail' of the malaria research community and the Gates injection of $50 million has been particularly welcomed by a field in which most of the pharmaceutical companies have few plans to invest because of the poor prospects for economic returns.

A malaria vaccine will not come easily. Immunologists recognize that the complexity of the parasite life cycle is a principal hurdle to the development of a successful vaccine (see Commentary http://www.nature.com/nm/special_focus/malaria). But now they have an exciting new prospect. It is hoped that the well-advanced malaria genome project will provide new information to push forward vaccine strategies. Three groups (The Institute for Genomic Research and the Naval Medical Research Center, The Sanger Center, and Stanford University) sequencing individual chromosomes have agreed to release preliminary annotation in addition to the sequence data and assembled contigs. Almost all of the parasite's estimated 6,000 genes are represented in the sequences obtained so far. The sequencing effort will also enable rapid advances in understanding the biology of the parasite and will help to identify new biochemical pathways suitable as drug targets.

Still, major technological advances will be required before the genome information can be translated into vaccine and drug development. A recent workshop organized by the Harvard Malaria initiative, "From genome to drugs and vaccine development," gathered scientists from developed and malaria-endemic countries, funding agencies and industry to set priorities on how to use the genome information and translate it efficaciously into drug and vaccine development.

But for the next five to ten years until an effective vaccine is developed, vector control will continue to be an immediate obligation. Provision of bed netting and insecticide treatment will require close cooperation between developed and developing endemic countries.

For more information about malaria research see our special web focus sponsored by TDR and MMV http://www.nature.com/nm/special_focus/malaria/