EDITORIAL

THE LONG HAUL

Relying solely on treatment as the mainstay of malarial control is an admission of defeat. Prevention and elimination must be the goal and an effective vaccine is key.

Malaria is back on the agenda. After decades of neglect, the international community is finally showing an increased level of interest in a disease that causes an enormous amount of human suffering. In a typical year, malaria kills at least 1 million people with an estimated 500 million clinical attacks. Indeed, half of the inhabitants of this planet are at risk of acquiring malaria infection. No one knows precisely the scale of the clinical or economic burden of this infectious disease, and obtaining accurate statistics will be a crucial component of any control strategy — an issue addressed by Hay and colleagues on page 84. But whatever the final numbers, the toll of morbidity and mortality is plainly unacceptable.

Tools to control malaria are available but they suffer from a variety of problems including drug and insecticide resistance that limit their overall efficiency and ultimate success in controlling the disease. What is urgently required, especially for the long-term management and potential elimination of the disease, is an effective vaccine. Many successful vaccines have been developed against viruses and bacteria but there are no commercially available vaccines against human parasites, a consequence of their complexity as much as anything else. There are few precedents for a successful vaccine being developed by any method other than *in vitro* culture of the infectious agent, a feat which has, so far, proved impossible for malaria. All commercially available vaccines, with one exception, consist of material from whole viruses or bacteria, or purified components, and the hepatitis B surface-antigen vaccine remains the only publicly available vaccine that was developed using recombinant protein technology. It is therefore disquieting that almost all malaria vaccine candidates are based on individual components that have been developed using recombinant technology. When one also factors in the multi-stage life cycle of the *Plasmodium* parasites, the huge variability of key parasitic proteins and the fact that both the humoral and cellular components of the immune system will be required for protection, the daunting task facing malaria vaccinologists is obvious.

Despite these hurdles, however, there is no doubt that an effective vaccine will have an enormous impact on the toll of malaria and the international community is now rising to the challenge. Last year, some US$85 million dollars was invested in malaria vaccine research, up from US$65 million in 2003, and 41 candidate vaccines are in clinical development. Recently, encouraging results for one candidate vaccine (RTS,S/AS02A) in a Phase IIb trial testing for efficacy in a disease-endemic country were published in *The Lancet*[1]. This vaccine, a recombinant subunit vaccine based on the circumsporozoite protein of *P. falciparum*, has been shown to induce a strong antibody response and stimulate cellular immunity. These latest results involving more than 2,000 Mozambican children revealed an efficacy of nearly 30% in terms of preventing clinical episodes and, perhaps most encouragingly, 57.7% in terms of preventing severe malaria episodes.

The ramifications of this study go further than this encouraging clinical efficacy — these results demonstrate the potential of modern vaccinology to develop novel interventions against complex human parasitic diseases. The study is also an illustration of the power of international partnerships between the public and private sectors and the benefits of including institutions from disease-endemic areas in accelerating the development of an effective vaccine.

Unfortunately, however, 'accelerated' development is a relative phenomenon. At best, the RTS,S/AS02A vaccine might be licensed by 2010. Gearing up to produce enough vaccine for widespread use and effective deployment will take much longer. So, in the intervening period, the expansion of preventive strategies, including insecticide-impregnated bednets and the development of new therapeutic options, must remain a priority. The dedication of many scientists and increased investment has led to a healthy number of vaccine candidates at the beginning of the development process. What must also remain a priority is a concerted effort by all concerned to maintain both the enthusiasm and the investment to see this long process through to completion.

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1. Alonso, P. L. *et al.* Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet* **364**, 1411–1420 (2004).