highly impactful to malaria control policy. Imwong and colleagues provide substantial evidence that history is repeating itself with regard to antimalarial drug resistance in the case of ACT resistance.

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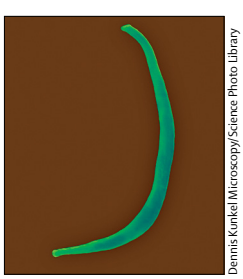
Progress with the PfSPZ Vaccine for malaria

Substantial progress has been made in the control of malaria during the past decade, but it is estimated that in 2015 there were still 429 000 deaths (uncertainty interval 235 000–639 000) from malaria, mainly in children in Africa,[1] and current gains are threatened by the emergence of resistance to artemisinin and insecticides. New tools, including malaria vaccines, are needed. The malaria vaccine RTS,S/AS01 has so far attracted the most attention because it is the first malaria vaccine to obtain positive approval from a regulatory authority[2] after a long period of development and evaluation.[3] However, during this time, substantial progress has been made with the development of several other malaria vaccines, including the *Plasmodium falciparum* sporozoite (PfSPZ) Vaccine.

In an Article in *The Lancet Infectious Diseases*, Mahamadou Sissoko, Sara Healy, and colleagues report the results of one of the first trials to investigate the efficacy of this vaccine in a malaria-endemic country.[4] The development of PfSPZ Vaccine has been based on the observation made in the 1970s that immunisation with irradiated sporozoites, delivered through the bites of more than 1000 infected mosquitoes, provided protection against challenge from a mosquito infected with viable sporozoites.[5] Irradiated sporozoites undergo partial development in liver cells to form a schizont, which induces an immune response, but dies before rupturing into the bloodstream and releasing the blood-stage parasites that cause the symptoms of malaria. Development of a vaccine based on irradiated sporozoites was for many years considered to be impractical because of the need for delivery by mosquito bite and to store the vaccine at a very low temperature. However, the team behind the PfSPZ Vaccine have overcome these challenges by developing novel methods for the production of purified sporozoite and for storing and distributing them with a system based on liquid nitrogen. Many trials of PfSPZ have now been done in non-immune volunteers to define an optimum dose and route of administration. During a recent trial in the USA,[6] seven of ten volunteers who were immunised intravenously five times with $2{\cdot}7\times10^5$ sporozites were protected 6 months after vaccination against challenge with a strain of parasite homologous to that used in making the vaccine. However, only one of ten volunteers challenged with a heterologous strain—the kind of challenge likely to occur in malaria-endemic populations—was protected.[6]

In the study by Sissoko, Healy, and colleagues in healthy adults in Mali,[4] 46 people in the vaccine group were vaccinated intravenously with five doses of $2{\cdot}7\times10^5$ irradiated sporozoites and 47 people in the control group received a saline placebo. The vaccine was safe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and extremely well tolerated, producing minimal local or systemic side-effects, and only one of 502 intravenous injections had to be repeated. Efficacy was 48·3% (95% CI 14·5–68·7) when measured against first infection and 28·8% (8·2–47·2) when measured against all infections during the 5 month follow-up period, which is not as high as that seen in the volunteers in the USA. The geometric mean titre of antibody to the circumsporozoite protein on the surface of the sporozoite, a partial correlate of protection, was substantially lower in the volunteers in Mali than has previously been observed in adults in the USA,[6] suggesting that previous exposure to malaria might have downregulated the immune response to the malaria antigens delivered through the vaccine.[7] Results from immunological studies have provided evidence to support this hypothesis by showing that malaria-exposed individuals have an increased population of atypical memory B cells and a depletion of follicular helper T cells, which are important for the development of immunological memory.[8,9] Use of an increased dose of sporozites and vaccination of children before they are exposed to malaria are potential ways to overcome this challenge for PfSPZ Vaccine that are now being explored.[10]

Although most experience has been obtained with sporozoites attenuated by irradiation, parallel studies have investigated sporozoites attenuated by genetic engineering[11] or by inoculation of viable sporozoites alongside simultaneous chloroquine prophylaxis.[12] These approaches allow more complete development of the liver schizont than occurs with irradiated sporozoites and hence a broader immune response. Genetically modified sporozoite vaccines could be produced with the same manufacturing processes developed for the PfSPZ Vaccine.

The PfSPZ Vaccine is a very promising malaria vaccine candidate that is likely to be deployed first in the military and travellers and perhaps in mass vaccination campaigns targeting elimination. Whether it can become part of the routine expanded programme of immunisation in highly malaria-endemic countries, such as Mali, requires further research.

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MONALISA: a grim picture of listeriosis

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Listeria monocytogenes is a slow-growing food-borne intracellular pathogen that can cause bacteraemia, meningoencephalitis, and maternal–neonatal infections (listeriosis). Risk factors for listerial infection include the extremes of age (neonates and the elderly), alcoholism, malignancy, corticosteroid therapy, immunosuppression, diabetes mellitus, liver or kidney disease, and iron overload.[1]

In *The Lancet Infectious Diseases*, Caroline Charlier and colleagues[2] describe the full range and impact of neurolisteriosis in the largest prospective cohort study to date, the MONALISA study. Over a period of almost 4 years, 818 patients with listeriosis were included in a nationwide surveillance based study in France, including 107 maternal–neonatal infections, 427 patients with bacteraemia, and 252 with neurolisteriosis. The study