news and views

Vaccination against malaria

ATTEMPTS to find a vaccine against malaria began in the 1930s but gave way to searches for new drugs during the war and anti-mosquito programmes after it. The combined use of anti-malaria drugs and insecticides has been one of the success stories of this century. The number of people infected with malaria has decreased considerably over the past decade in spite of the fact that, because of the increasing world population, more people than ever before now live in malarious areas. But resistance to drugs and insecticides, lack of money and political instability have reduced the future prospects of malaria eradication and thoughts have again turned to the possibility of developing a successful vaccine.

Three different sorts of vaccine are at present being investigated: irradiated sporozoites from the mosquito, extracts from schizonts (developing stages in the blood) and emulsified merozoites (the stages which pass between blood cells). After promising results using irradiated sporozoites in rodents, an experiment with *Plasmodium falciparum* in humans has resulted in one of three volunteers being protected against homologous (Clyde *et al., Am. J. Med. Sci.*, **226**, 169; 1973) and heterologous strains of the same parasite (Clyde *et al., Am. J. Med. Sci.*, **266**, 398; 1974). Earlier this year Simpson, Schenkel and Silverman (*Nature*, **247**, 304; 1974) succeeded in protecting rhesus monkeys against *Plasmodium knowlesi* using non-viable fractions extracted from disintegrated parasites. This and earlier studies, taken together, have shown that eleven out of seventeen vaccinated monkeys survived challenge whereas eight controls did not. Both these kinds of approach obviously have some potential promise but they still need a considerable amount of development.

The most promising vaccination results so far achieved with monkeys are reported in this issue of *Nature* by Mitchell, Butcher and Cohen from Guy's Hospital Medical School. They used *Plasmodium knowlesi* and their vaccine consisted of emulsified cultured merozoites. Six monkeys were immunised in various ways and challenged some time later with the homologous parasite or heterologous variants. Protection against the homologous parasite was absolute in two monkeys and strong in the third. There was also considerable protection against heterologous variants and the parasitaemias never rose above 1.5% whereas control animals died after about a week. Subsequent challenges with other variants resulted in equally encouraging results. The merozoite vaccine was found to be species specific and afforded only minimal protection against challenge with *Plasmodium cynomolgi bastianellii*.

These results show that the merozoite vaccine induces immunity better than that obtained after repeated challenges and cures. This contradicts the belief that vaccination against malaria cannot induce an immunity better than that which can be acquired naturally. The fact that the immunity induced transcends challenge with several variants suggests that the antigenic variation that occurs in malaria is not an insuperable barrier to vaccination, as has already been shown by Clyde and his co-workers. Of particular interest is the fact that the merozoite vaccine is simple to prepare and that 1 ml of parasitised blood cells provides twenty immunising doses. These are early days yet and the next step will have to be the evaluation of the merozoite vaccine in owl monkeys, which are the only suitable primates that can be infected with human malaria. These monkeys are becoming increasingly difficult to obtain as thousands have been used for testing drugs. Very soon malariologists will have to draw up priorities for the use of owl monkeys and the whole drug/vaccine argument will have to be thrashed out afresh.

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Messenger RNA doing without poly(A)

ONE of the tenets of cell biology has been that all messengers in the cytoplasms of eukaryotic cells (with the sole exception of the histone mRNAs) contain a length of poly(A), which fulfils some essential, although as yet unidentified function. When polysomal mRNA is examined for poly(A) content by reaction with poly(U)–sepharose or oligo(dT)–cellulose, most is bound; the fraction that is not retained has generally been thought to result from breakages in mRNA during isolation—since there is only one length of poly(A) in each mRNA, a single breakage would release a molecule altogether lacking poly(A). In two quite different systems, however, it now seems that an appreciable proportion of the cellular mRNA may lack poly(A). Working with HeLa cells, Milcarek, Price and Penman (*Cell*, **3**, 1–10; 1974) find that about 30% of the mRNA lacks poly(A); and using early sea urchin embryos of two species (*Strongylocentrotus purpuratus* and *Lytechinus pictus*), Nemer, Graham and Dubroff (*J. molec. Biol.*, **89**; 1974) report that about 40% of the messages may lack poly(A).

To examine mRNA of HeLa cells, it is necessary both to prevent labelling of ribosomal RNA and also to exclude contaminants derived from the non-messenger RNA population. The second can be achieved by releasing mRNA from polysomes with EDTA and in these experiments the first condition was met by using fluorouridine to suppress labelling of rRNA. The labelled mRNA fraction was then passed through a column of oligo(dT)–cellulose under conditions in which more than 96% of the poly(A)-containing mRNA is retained. This divides the mRNA into a major (70%) fraction containing poly(A) and a minor (30%) fraction apparently lacking it. Both poly(A)$^+$ and poly(A)$^-$ mRNA have the same size distribution. That both classes of mRNA are in use in the HeLa cell as templates for protein synthesis is suggested by the use of puromycin, which releases both from the polysomes.

Only the demonstration that the nucleotide sequences of poly(A)$^+$ and poly(A)$^-$ mRNA fractions are different can provide satisfactory evidence that they represent two genuine cellular species and that the poly(A)$^-$ is not in fact derived from the poly(A)$^+$. The sequences of the poly(A)$^+$ mRNA can be scrutinised by production of a complementary cDNA probe through the reverse transcription mediated by the enzyme of RNA tumour viruses; and in hybridisation