malaria antigens than aparasitaemic immune individuals might imply that antigen-specific T-cells play a role in the development of sterile immunity in malaria.

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Further trials of a vaccine against American cutaneous leishmaniasis

We have continued studies on a vaccine against American cutaneous leishmaniasis (MAYRINK *et al.*, 1978, 1979, 1985) by carrying out two controlled, double-blind field trials. The trials were conducted at Manaus, State of Amazonas, Brazil, in 1981 and 1983. The participants were 18-year-old healthy males, army conscripts serving in Comando Militar da Amazonia (CMA). The conscripts were randomly assigned to vaccine or placebo groups, and were followed up for 12 months. The vaccine and Montenegro antigen were prepared in the manner previously described, using the same stocks of *Leishmania*. The placebo was phosphate buffer pH 7·4 plus merthiolate 1:10,000.

In the 1981 trial, only 33% of the vaccinated group converted their responses to Montenegro antigen within 35 days. The low conversion rate is attributed to the fact that the experimental vaccine was administered during the period that participants also received yellow fever, typhus and tetanus inoculations. At the end of 12 months, the incidence of leishmaniasis amongst those with changed responses to Montenegro antigen was 67·3% lower than that of the placebo group.

In the 1983 trial, conscripts received yellow fever vaccine 120 days before the experimental leishmaniasis vaccine was administered. Changes in response to Montenegro antigen occurred in 68% of the vaccinated group and the annual incidence of the disease was 85·7% lower than that of the placebo group.

Full details of the two field trials will be published elsewhere.

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Absence of pharmacokinetic interaction between Fansidar® and mefloquine

The ever-growing resistance of plasmodia, particularly *Plasmodium falciparum*, against chloroquine or

other commonly used antimalarials is a big problem today. Newly developed drugs are also likely to induce, with time, resistant forms of the parasite. It has been suggested that this process might be slowed down by the use of combination preparations (PETERS & ROBINSON, 1984; MERKLI *et al.*, 1980).

Fansimef^R, a combination of Fansidar^R (= sulphadoxine + pyrimethamine) and mefloquine, produced remarkable cure rates in the treatment of falciparum malaria resistant to chloroquine (EKUE *et al.*, 1985; TIN *et al.*, 1985; HARINASUTA *et al.*, 1985).

Both pyrimethamine and sulphadoxine show a very long half-life so that their potentiating effects persist for a long time. The addition of mefloquine might lead to kinetic interactions which have not previously been studied.

The pharmacokinetic characteristics of the Fansimef^R combination have been compared to those of Fansidar^R and mefloquine administered alone. Healthy human volunteers received orally and sequentially one dose of Fansidar^R, one dose of Fansimef^R and one dose of mefloquine. Intervals of four weeks and six months were left between the first and second, and between the second and third, applications, respectively. The plasma levels of the components present in each of the three preparations administered were measured and their pharmacokinetic parameters determined using TOPFIT or NONLIN programs based on a two compartment model. The pharmacokinetic parameters t_{max}, C_{max}, $t\frac{1}{2}\beta$, AUC_0^∞, systemic clearance and apparent volume of distribution were practically unchanged for all three components whether Fansidar^R or mefloquine were administered alone or together in the form of Fansimef^R. On average, a slight increase in AUC (13%) was observed for mefloquine. This difference, however, was not significant (t-test : $0{\cdot}5>p>0{\cdot}3$). It is noteworthy that the degree of binding of the single components to human plasma proteins was virtually unmodified by the simultaneous administration of the two other partners, and that multiple dose kinetics of Fansimef^R produced steady-state plasma levels in the range of those predicted from single dose kinetics. The available evidence, therefore, indicates the absence of interaction between the components of the Fansimef^R combination in man.

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Leishmania infantum, causative organism of visceral leishmaniasis at Biskra (Algeria)

Infantile visceral leishmaniasis is known to occur in northern Algeria in a geographical area corresponding to the sub-humid bioclimatic zone (BELAZZOUG *et al.*, 1985). However, the 21 cases diagnosed during the last 10 years at Biskra in southern Algeria corresponding to the arid bioclimatic zone remained until recently an epidemiological mystery. This area is an important focus of zoonotic cutaneous leishmaniasis caused by *Leishmania major* (see BELAZZOUG, 1984). Hence, we were tempted to think that *L. major* might be the causative organism as suggested by SCHNUR *et al.* (1985) for infantile kala-azar at El Agamy in Egypt, an area ecologically similar to Biskra.

We isolated three stocks from children presenting kala-azar, who originated from Biskra and who had never left this area. The isoenzyme identification (two stocks by Prof. J. A. Rioux from Montpellier, and one by Dr. D. A. Evans from London) revealed *L. infantum*.

We conducted a sero-epidemiological enquiry using indirect immunofluorescence and found eight dogs positive out of 102. An isolate from one of these dogs has been isoenzymically identified as *L. infantum*.

It appears, therefore, that visceral leishmaniasis in this area is identical to that of northern Algeria with *L. infantum* as the cause, the dog as reservoir and probably *Phlebotomus perniciosus* or *P. longicuspis*, known to be present in this area (DEDET *et al.*, 1984), as vector. *P. longicuspis*, first considered to be a variety of *P. langeroni* by NITZULESCU (1930), seems to be a more suitable vector as it is well adapted to the climatic conditions of Biskra (PARROT & CLASTRIER, 1956).

Our finding strongly supports KILLICK-KENDRICK's view (1985) that *L. infantum* is the causative organism of kala-azar at El Agamy in Egypt and *P. langeroni* the possible vector.

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