

zoite vaccination of rhesus monkeys against *P. knowlesi*.

Several combinations of muramyl dipeptide derivatives and liposomes were compared as adjuvants for *P. knowlesi* merozoite vaccine in rabbits, by assessment of antibody (by ELISA) and delayed-type hypersensitivity reactions. It was shown that 6-O-Stearoyl substituted MDP was more effective when administered in "soft" (egg yolk lecithin-cholesterol) liposomes than in "hard" liposomes, and that these combinations were more effective than either the compound in saline or norMDP in liposomes. It seems unlikely, however, that such a model system will prove useful for assessing adjuvants to be used in primate malaria vaccination.

#### Antimalarial activity of novel derivatives of primaquine

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Derivatives of Primaquine (PQ), 6-methoxy-8-(4'-amino-1'-methylbutylamino)quinoline, were obtained by peptidic amino acyl (L-leucyl, L-leucyl-L-alanyl) elongation of the aliphatic side-chain via the terminal amino group of PQ.

The acute toxic properties ( $LD_{50}$ ) of the two derivatives (PQ-Leu, PQ-Leu-Ala) were determined after a single i.v. injection to male TB<sub>ESP</sub> mice (18 to 22 g).

The antimalarial, causal prophylactic activities (CPD<sub>50</sub>) of both congeners were then assessed on sporozoite-induced mouse infections of *Plasmodium berghei* (ANKA): the drugs were administered in a single i.v. dose three hours after sporozoite inoculation, and the therapeutic effects examined on the ensuing parasitaemia.

Both toxicity and antimalarial activity of the peptidic derivatives were compared to those of the parent drug.

PQ-Leu and PQ-Leu-Ala were found to be less toxic than PQ ( $LD_{50}$ 's = 27 and 35 mg PQ base equivalent  $\times$  kg<sup>-1</sup>, respectively, *vs.* 22 mg PQ base  $\times$  kg<sup>-1</sup>, for PQ).

This reduction in toxicity permitted the administration of a 100% curative single i.v. dose of PQ-Leu-Ala (20 mg PQ base equivalent  $\times$  kg<sup>-1</sup>), whereas the antimalarial efficiencies *per se* of all three compounds tested were not significantly different (CPD<sub>50</sub> = 11-16 mg PQ base  $\times$  kg<sup>-1</sup>).

#### Amoebic colitis and Crohn's disease—a diagnostic puzzle

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A 43-year-old male patient was admitted to the hospital because of diarrhoea and hepatomegaly. He had been working for 20 years as construction supervisor in the Middle and Far East as well as in the Caribbean area. He had short bouts of watery bowel movements in 1973 and 1974. The diarrhoea recurred in 1977 after travelling through Venezuela

and Mexico. The physical examination revealed only a hepatomegaly. The white blood count was 10,000, the haemoglobin 11.8 g/100 cc, the sedimentation rate 76 mm. A BE disclosed tiny ulcerations in the midtransverse colon. At rectoscopy and colonoscopy ulcers were seen in the rectosigmoid area, at the splenic flexure and from the midtransverse colon to the caecum. Biopsies from different colonic areas were described as unspecific colitis. Diagnosis of Crohn's disease was assumed because of right-sided and segmental colitis according to the criteria of FAWAZ *et al.*, 1976 (*Gastroenterology*, **71**, 372-378). The patient was treated with prednisone and sulfasalazine. As the diarrhoea persisted and shoulder pain developed, the patient was admitted to the hospital. A liver abscess was now clinically suspected and proved by a Tc-scan to be in the right lobe. IFT was suspect, counterimmunoelectrophoresis clearly diagnostic for amoebiasis. *Entamoeba histolytica* trophozoites were finally detected in the stool. The abscess was drained by aspiration. The diarrhoea stopped one day after initiating treatment with metronidazole. Retrospectively the pathologist found amoebae in the biopsy from the transverse colon.

This case demonstrates the importance of travel history and adequate stool examination.

#### Studies on the uptake of sporozoites of *P. yoelii nigeriensis* by perfused rat liver

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Little is known of the uptake of rodent malaria sporozoites and it was decided to investigate the role of the liver in sporozoite uptake using isolated perfused liver. Livers were taken from rats weighing 1 to 200 gm and were flushed with salts solution to remove blood, then subsequently perfused with M199 + 10% serum under normal maintenance conditions (JOHN, D. W. & MILLER, L. L., 1966; *J. Biol. Chem.*, **241**, 4817). After a 30-minute preperfusion period 20 to 50,000 salivary gland sporozoites were added. The percentage of the sporozoites removed from the perfusate was calculated after one and 15 minutes of perfusion. Sporozoite uptake in normal liver was both rapid and efficient, 78.5% of the initial sporozoite load had disappeared within the first passage and 94.47% had been taken up within the 15-min perfusion period. It is therefore quite feasible that liver uptake alone could account for the early disappearance of sporozoites from the circulation (CANNING, E. U. *et al.*, 1972; *J. Protozool.*, **19**, 46).

Sporozoites of avian malarial parasites are taken up by macrophages at the site of inoculation and it is possible that the Kupffer cell plays a similar role in the rodent system. This possibility was investigated by comparing the uptake of sporozoites by livers taken from normal and silica-treated rats. Pretreatment with silica as described by VAN LOVEN *et al.*, 1977; *J. Reticuloendothelial Soc.*, **22**, 000-000) was bound to suppress the phagocytic activity of the liver. Silica-treated livers had a