ROUND TABLE 6 — SUMMARY

CHEMOTHERAPY: DRUG DESIGN AND DRUG RESISTANCE

Chairman: *Raymond Lasserre**
Co-Chairman: *Raul Kessler***

In this session, four topics were developed: molecular biology and basic research, treatment of malaria, problems of resistance, and prophylaxis.

Doctor H. Vial, the first speaker presented a new pharmacological model to select drugs active against *Plasmodium falciparum* malaria. The target of action is based on the blockage of the choline receptor supplying choline for the synthesis of phosphatidylcholine, an essential compound for *P. falciparum* membrane. An antimalarial activity of drugs interfering with this metabolism pathway has been demonstrated and found 20 to 100 fold lower than the toxic dose. These drugs were found active in vitro at a dose of 1 to 10 mMoles. The availability of such inexpensive drugs should be considered as a new approach in therapy of resistant malaria.

Another new model using as a target the aldolase glycolytic enzyme of *P. falciparum* was described by U. Certa. He defined by in vitro mutagenesis the amino acids which are essential for aldolase activity of *P. falciparum*. This basic research as a new target of action against the parasite will be of interest to provide new drugs for malaria treatment.

The second topic of this session was devoted to treatment of malaria. It was developed by R.J. Horton who reported the results of a study using halofantrine suspension for the treat-

ment of 331 children with malaria attack. The treatment of severe cases by arthemeter was found in Brazil more effective than quinine associated with clindamycine or tetracycline and M. Boulos proposed the use of arthemeter as a first line treatment in patients living in countries where quinine sensitivity is decreased. In brasilian amazone country, M. Alacrin observed that in vivo chloroquine resistance reached 47.5 to 85% and mefloquine resistance only 4% of the cases. In vitro resistance was observed in 100% of the cases with chloroquine and in 21.8% with mefloquine. These results emphasized the real therapeutic problems existing in the amazonian areas of Brazil.

The effectiveness of drugs able to reverse resistance was developed by W.K. Milhous in the case of verapamil for chloroquine resistance and penfluridol for reversal activity on halofantrine, mefloquine and artemisinine resistance. Studying emergence of mefloquine resistance in the absence of drug pressure in Africa, P. Brasseur observed a correlation with resistance to quinine but not with resistance to chloroquine.

The last topic of the session was malaria prophylaxis and R. Lasserre, the Chairman of the session, reminded the most reasonable possibilities for the use of drugs in 1991, in respect with the status of malaria resistance. A comparison between efficacy and adverse effects of different drugs used for prophylaxis was presented by R. Steffen in 87,384 non immune travellers visiting East Africa, showing that mefloquine was highly efficacious and tolerated as well as chloroquine.

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