A STUDY OF HEAT STABILITY OF STABILIZED YELLOW FEVER VACCINE 17D

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The authors carried out a study of heat stability of stabilized yellow fever vaccine 17D developped by M. MAHAL. The vaccine is prepared on chick embryos from a secondary seed lot and stabilizer is added during the preparation of the bulk.

The tests performed at different temperatures showed a good stability of this vaccine at +4°C and at room temperature (+23°C) during one year. Is also showed that short time exposure at +37°C had no adverse effects. Only at high temperature (+46°C) the decrease of the titre reached about one Log in four days.

During the Upper Volta yellow fever outbreak at the end of the rainy season in 1983 ; 1.500.000 doses of stabilized yellow fever vaccine 17D were sent by the Dakar Pasteur Institute. Samples of vaccine were collected in different places in Upper Volta during the vaccination campaigns. The virus titres of these samples were compared with those of vaccine samples of the same batches stored at -20°C in Pasteur Institute. The results confirm the experimental data on the stability of this vaccine. Some recommandations are given for the use and the storage of this vaccine in tropical areas.

STUDY ON STABILITY OF PURIFIED COBRA VENOM TOXOID

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It is verified that irreversible detoxification of purified Taiwan Cobra *(Naja naja atra)* venom can be obtained by increasing concentration of formalin used for detoxification. A method to fractionate the cobra venom by ethanol precipitation was applied to increase the toxicity of the venom. The F2 fraction precipitated by 70% ethanol increased to 2.3 times as compared with that of the crude venom in mice.

The F2 fractions containing varying amount of venom ranging from 0.25mg to 4mg were tested for detoxification, mixing with varying concentration of formalin ranging from 0.5 to 6 per cent divided into two or four doses at an interval of one week at 37°C. After the detoxification, the toxoids were tested for stability, incubating at 37°C for 20 days. The results indicated that the reversion of the toxicity occurred in proportion to increasing amount of venom in toxoid and the stability of toxoid increased by increasing concentration of formalin. Thus, the F2 toxoid (2mg/ml) was irreversibly detoxified by 5.5 per cent formalin.

Immunogenicity of the toxoid was tested in guinea pigs and rabbits giving three or four shots at an interval of four weeks. The results indicated that the guinea pigs and rabbits showing MLDs of the venom neutralized by 0.2ml of the sera higher than 1.5 MLDs were prevented against the venom of 0.3 or 1.2 mg (one or 4 MLDs) and 2 or 6 mg (2 or 6 MLDs), respectively.

LARVICIDAL AND PUPICIDAL EFFICACY OF THE EXTRACT OF OLIGOCHAETA RAMOSA AGAINST THE MALARIA VECTOR ANOPHELES STEPHENSI LISTON

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The development of resistance in mosquitoes towards several synthetic insecticides and the reported resurgence of malaria in many tropical countries have prompted the research for safer mosquito control agents. In the present study the efficacy of acetone extract of a new indigenous plant Oligochaeta ramosa Wagenitz (Fam: Compositae) against the larvae and pupae of the urban malaria vector Anopheles stephensi Liston has been determined. The extract was prepared in acetone by a soxhlet apparatus. The second, third & fourth instar larvae and the pupae of mosquito A. stephensi taken from the inbred colony were treated by releasing them in extract emulsion prepared in water, using Tween-80 as emulsifier, and mortality counts were taken after 24 hours of treatment. The LC_{50} values of the extract for the second, third and fourth instars come to 215, 400 and 550 ppm, and the LC_{90} values come to 380,600 and 780 ppm, respectively. Such low values indicate that the extract of O. ramosa is a highly effective larvicide as well as pupicide against the malaria vector. The extract causes interference in pupal and adult emergence and usually death ensues during larval-pupal and pupal-adult moults.

The extract, thus, warrants for use against malaria vector. The chemical analysis of the aforesaid extract is being carried out to determine the active components.

IN VITRO DRUG SUSCEPTIBILITY OF P. FALCIPARUM RESISTANT TO FANSIDAR^R AND CHLOROQUINE PROPHYLAXIS

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A 26 year old non-immune man visited Kenya including the coastal areas from 30. June to 13. August 1983. During the stay and until 12. September he took Fansidar^R,1 tablet and chloroquine phosphate, 2 tablets weekly. From 15. October he had repeated attacks of fever. Falciparum malaria with 19 x 10^9 asexual parasites/l was diagnosed on 3. November and mefloquine 1500 mg was given. Asexual parasites were cleared from the blood within 48 h and did not reappear during 28 days of control.

Blood was drawn for drug susceptibility tests before start of treatment. A WHO macro 24 h schizont maturation chloroquine test showed that maturation occurred even at a concentration of 3 x 10^{-6}M, confirming that the isolate was chloroquine-resistant. 48 h merozoite reinvasion tests were performed with 2-fold serial dilutions of pyrimethamine and sulfadoxine at 2 % hematocrit in RPMI medium with AB serum. After 20 days of continuous culture of the isolate (named FCD-40/Kenya), susceptibility to pyrimethamine, sulfadoxine and both drugs in the proportion 1/250 in the same medium was determined by "Desjardins" ^{3}H-hypoxanthine uptake assay. At the same time we tested isolates FCD-9/Tanzania (Fansidar^R R11) and FCD-34/Zambia (Fansidar^R S). The results are summarized below. (Merozoite reinvasion test results in ()).

	IC_{50} (x 10^{-6}M)		
Isolate	Pyrimethamine	Sulfadoxine	Pyrim. 1/Sulfad. 250
FCD-34	0.032	3000	0.048/ 12
FCD-40	15 (20)	2800 (600)	3.2 / 800
FCD- 9	45	3900	10.4 /2600

The results suggest that while inhibitory sulfadoxine concentrations are unrealistically high in RPMI, testing with pyrimethamine alone in this medium may provide an adequate basis for determining levels of Fansidar^R resistance. Furthermore, the fact that the FCD-40 was not more resistant than the FCD-9 suggests that Fansidar^R is not more active against the pre-erythrocytic than against the asexual blood phase.

ABSENCE OF INFLUENCE OF SOME COMMON PATHOLOGICAL CONDITIONS IN SERO-CONVERSION RATES OF AFRICAN CHILDREN FOLLOWED IN AN EXTENDED PROGRAM OF IMMUNIZATION

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Seroconversion rates in measles (Schwartz Strain), yellow fever (17 d), and poliomyelitis (concentrated, killed) were assessed in an African child population (Casamance, Sénégal) after a two-sessions programm of immunization. Some pathological conditions, wide spread among the child population of this area and supposed to alter seroconversion rates, have been looked.

- malnutrition (assessed by anthropometry and laboratory)
- malaria (smear and specific antibodies)
- hepatitis (HBS)
- schistosomiasis, trypanosomiasis, brucellosis and trepanomatosis specific antibodies)

None of those pathological conditions, as we observe usually on the field, affects seroconversion rates.

ARTEFACTITIOUS HEMATOGENIC INVASION OF THE BRAIN BY TRYPANOSOMES IN MICROTUS MONTANUS

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The neurohistological findings in meningo-encephalitis induced by treatment (Schmidt and Bafort, in press) raise the question about the reaction of the brain in hematogenic infestation with trypanosomes. In order to produce such infestations the brains of suckling mice and *Microtus montanus* were punctured with injection needles through the scalp in the early phase of parasitemia after infection with *Trypanosoma b.rhodesiense* EATRO 1989). The trepanation was performed 2 mm lateral of the median line and the brain was pierced till the base of the skull. Histological examination was carried out at different prefixed times up to 4 weeks after puncture.
As a result of the trauma a lesion comparable to a sanguineous puncture channel was found. A few days after the puncture the channel was filled with hematophages. 10 days after the trepanation and stitch of the brain the channel appeared in most animals as a cystic spongiform defect.
In all punctured sucklings trypanosomes were found in the brain in the first hours after puncture in the surroundings of the artificial channel, afterwards at different distances from the latter mainly in the cerebral medulla and the brainstem. Trypanosomes were seen in the contralateral hemisphere too. The dissemination into this one evidently proceeded over the commissural tracts like corpus callosum or commissura rostralis. Clear reactions on behalf of the brain tissue were not observed, neither of the neuroectodermal nor the mesenchymal part.
The findings show that the hematogenic parasitisation of the brain is not able to produce meningo-encephalitis, and confirm in this way the fact that the parasitisation of the CSF, respectively the meningeal connective tissue, is the decisive pathogenic factor of the encephalitis as suggested above.
Considering the absence of clear-cut reactions of the brain tissue the findings further indicate that the parasitisation of the brain might be a symptom of no consequence in meningo-encephalitis too.
The findings do not provide an answer as to the fate of the brain parasitosis and its importance as a possible source of a relapse.

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ABSTRACT AND POSTER VOLUME

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