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YELLOW FEVER VACCINATION, ALONE OR IN ASSOCIATION, USING 17 D VACCINE ADMINISTERED INTRADERMALLY

by

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It was Jenner who first had the idea of applying a vaccine by scarification. Since 1939, yellow fever vaccine prepared on mouse brain has been administered by cutaneous scarification, alone or in association with smallpox vaccine (Peltier et al., 1940). In Brazil, 17 D yellow fever vaccine has been administered intradermally with very good results (Fox et al., 1943).

Needleless injectors have already been used for the administration of 17 D yellow fever vaccine alone or in association with other vaccines (Meyer et al., 1964; Chambon et al., 1967).

Our purpose was to study the effectiveness of yellow fever vaccination using 17 D vaccine administered intradermally with a jet injector (Ped-O-Jet). We also wished to see how far administration in association with BCG vaccination (combined or simultaneous) remained effective. We have set out here the results obtained with a group of children aged from six months to three years attending the family medical centre of the Dakar Garrison.

MATERIALS AND METHODS

VACCINES

1. Yellow Fever

The 17 D yellow fever vaccine (batch 96) used throughout this study was prepared at the Institut Pasteur in Dakar following the methods recommended by the Expert Committee of the World Health Organization. It contained 52 481 mouse LD_{50} per 0.5 ml of vaccine. It was used at a concentration such that, administered alone or in combination with BCG vaccine, it contained 52 481 mouse LD_{50} per volume of 0.1 ml. In all cases, the solvent utilized was glucose solution. Immediately after it had been dispensed into 10 ml ampoules, the vaccine was frozen in a mixture of alcohol and dry ice and kept at -70°C. The ampoules were transported on dry ice and thawed rapidly at the time of utilization. Any ampoule put into the jet injector and not used within an hour was replaced by a new ampoule.

2. BCG

The BCG vaccine utilized (batch 66-59 B) was prepared at the Institut Pasteur in Dakar. It had a titre of 0.625 mg/ml and contained 9×10^6 viable units per ml. It was used at a dilution of 1:2, as recommended for children under two years of age.

JET INJECTOR (Ped-O-Jet)[1]

This apparatus is equipped with a hydraulic appliance which forces a very fine jet through the teguments under high pressure (83 kg/cm^2) through a capillary opening. The jet can be set at 45° to the axis of the piston by means of a special nozzle. The quantity of liquid expelled can be regulated from 0.1 to 1 ml. Owing to the reflux caused by the elasticity of the skin, in order to inject 0.10 ml it is necessary to eject 0.15 ml (Dull, 1968). This ejected volume was measured by weighing on a precision balance. The volume did not vary, throughout the operations, by more than ± 5.3%, which is no greater than in the case of injection by syringe.

The apparatus weighs 4.6 kg, it is robust (500 000 vaccinations without serious incident) and the injector system can easily be sterilized by boiling, in the autoclave or with a 2% iodine solution.

SUBJECTS VACCINATED

A total of 332 children aged from six months to three years and displaying no haemagglutination inhibiting yellow fever antibodies were divided randomly into five groups each corresponding to one mode of vaccination (Table 1). As will be seen from Table 1, out of the 332 children vaccinated, 268 were given serological tests.

The blood specimens taken before vaccination and 35 to 50 days afterwards were obtained by finger tip puncture, the blood being collected in heparinized capillary tubes.[2] As far as possible, two tubes were collected for each child. In the laboratory, the tubes were centrifuged and frozen at -25°C until they were utilized.

TESTING THE EFFECTIVENESS OF THE VACCINATION

1. Yellow fever antibodies

The haemagglutination inhibition (HI) reaction was utilized after the sera had been treated with acetone. The reaction was performed by the microtechnique and the sera were tested against 4 and 8 haemagglutinating units of the FNV (Dakar strain) antigen. The two specimens collected from each child before and after vaccination were both tested at a single sitting.

All sera with a yellow fever antibody titre of 1/10 or over were considered positive.

2. Effectiveness of BCG vaccination

Tuberculin allergy, diameter and quality of vaccination lesions, and degree of lymph node enlargement were checked 12 weeks after vaccination. The results have been reported in a separate communication (Chambon et al., 1970).

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[1] Scientific Equipment MFG Corp., 20 North Avenue, Larchmont, N.Y.

[2] Caraway Micro Blood Collecting Tubes, Clay-Adams, Inc., N.Y. 10010

RESULTS

We shall report here only the results relating to yellow fever.

1. Post-vaccination reactions

None of the children was brought to the medical centre for any complaint connected with the vaccination.

2. Serological findings

The results are set out in tables 2 and 3.

DISCUSSION

The effectiveness of yellow fever vaccination using 17 D vaccine administered intradermally with a jet injector is shown by the percentage of seroconversions obtained in the children vaccinated. It is higher than 80% whatever the mode of vaccination used.

As for the antibody titre, it may perhaps appear low (Table 4). However, it is the titre generally observed with our techniques in Europeans arriving in Dakar after undergoing yellow fever vaccination with 17 D vaccine administered by syringe. Moreover, the subjects concerned were very young children, who generally give weaker responses (Fox et al., 1943).

Association with BCG vaccination, either simultaneous or combined, did not in any way modify the effectiveness of either of the vaccines. The value of associating them in this way for the protection of children under 13 years of age, who are particularly receptive to these two endemic diseases, is evident.

CONCLUSION

17 D yellow fever vaccine can be administered intradermally with a jet injector. It can be associated with BCG without impairing the effectiveness of either of the vaccinations.

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TABLE 1. NUMBER OF INDIVIDUALS TESTED

Mode of vaccination	Number vaccinated	Serological test (HI)	
		Number	Percentage
Yellow fever only	68	53	77.9
Simultaneous yellow fever and BCG	64	52	81.2
Combined yellow fever and BCG	63	50	79.3
BCG only	67	57	85
Control (Placebo)	70	56	80

TABLE 2. RESULTS OF HAEMAGGLUTINATION INHIBITION TEST FOR YELLOW FEVER

Mode of vaccination	Number tested	Positive reactions	
		Number	Percentage
Yellow fever only	53	46	86.79
Simultaneous yellow fever and BCG	52	43	82.69
Combined yellow fever and BCG	50	44	88
BCG only	57	2	3.51
Control (Placebo)	56	1	1.79

TABLE 3. YELLOW FEVER VACCINATION: COMPARISON BY X^2 TEST OF COMBINED VACCINATIONS WITH THE CONTROL GROUP AND THE GROUP RECEIVING YELLOW FEVER VACCINATION ONLY

	Control group 2.65 per cent.*	Yellow fever vaccination only 86.79 per cent.
BCG on one arm and yellow fever on the other (simultaneous vaccination) 82.69 per cent.	X^2 = 113.43 difference very significant	X^2 = 0.034 difference not significant
Mixture of BCG and yellow fever in ampoule (combined vaccination) 88 per cent.	X^2 = 122.81 difference very significant	X^2 = 0.034 difference not significant

TABLE 4. AVERAGE YELLOW FEVER HI ANTIBODY TITRES

Mode of vaccination	Number of individuals	Average (denominator of titre)
Yellow fever only	53	9.06 $\pm$ 1.09
Yellow fever and BCG mixed	50	10.20 $\pm$ 1.43
Yellow fever and BCG separately	52	9.23 $\pm$ 1.41
Placebo	56	0.18 $\pm$ 0.35

* Percentage of children whose HI reaction for yellow fever was less that 1/10 prior to vaccination and became equal to or greater than 10/10 after vaccination.