Human pre-exposure rabies immunization with suckling mouse brain vaccine

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Since the development of non-encephalitogenic rabies vaccines (Koprowski et al., 1952; Peck et al., 1955), several studies have been carried out on human pre-exposure immunization (Anderson et al., 1960; Dieterich et al., 1961; Fox et al., 1957; Schnurrenberger et al., 1961, 1967; Tierkel & Sikes, 1967). In the light of these results, the WHO Expert Committee on Rabies (1966) has recommended this type of prophylaxis for high-risk personnel, such as laboratory personnel working with rabies virus, veterinarians, dog handlers, and field naturalists.

The principal disadvantage of the pre-exposure schedule recommended by the WHO Expert Committee is that it takes at least 3 months to obtain a satisfactory immunological response as determined by antibody titre. There are times when it would be useful to be able to accelerate this response, such as when a new employee is engaged to work in a rabies laboratory or as a dog handler.

Suckling mouse brain vaccine (SMBV) (Fuenzalida & Palacios, 1955) was chosen for this study because it has the highest antigenic titre of vaccines currently in use for human immunoprophylaxis and it is relatively free of the encephalitogenic factor.

A schedule of three doses was chosen because a preliminary study carried out with small groups of volunteers, using 1, 2, 3, or 5 vaccine doses, showed that all the sera from persons who had received 3 or 5 doses had antirabies neutralizing antibodies 21 days after starting immunization, while with those who had received 1 or 2 doses it was necessary to administer an additional dose of vaccine after a further 25 days. The antibody responses after 5 doses were no higher than those obtained with 3 doses (Godoy, 1967).

This paper reports the results obtained with 3 doses of vaccine in 61 persons, as well as some responses produced by a booster dose given to some of these individuals one year or more after the primary immunization.

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Materials and methods

Vaccine. Different lots of SMBV were used during the study: all of them passed the Habel potency test (Habel, 1966).

Volunteers. Sixty-one adults, male and female, working or being trained at the Pan American Zoonoses Center, as well as a small group of persons working for other institutions and interested in receiving preventive rabies immunization, volunteered for this study.

Vaccination schedule. Each volunteer was given three 2-ml doses of 1% SMBV, subcutaneously, on alternate days. A 1-ml booster dose was given 1 year or more after the first dose.

Blood samples and seroneutralization. Initially, 10–20-ml blood samples were obtained from each volunteer before vaccination and, when available, on days 21, 90, 240, and 365 after the first vaccine dose. During the latter part of the study, blood samples were also obtained 10 days after the first vaccine dose. In those individuals given a booster dose of vaccine, a sample was taken shortly before the injection and another sample 8 days after this dose.

The sera obtained were incubated for 30 min at 56°C and kept at −20°C until the SN test was performed. This test was carried out in accordance with the technique described by Atanasiu (1966), against 20–70 LD_{50} of the standard challenge virus strain. Threefold or fivefold series of dilutions were each inoculated into groups of 5 adult mice.

Results

No antibodies were detected in the sera obtained prior to vaccination (Table 1). In general, primary immunization was well tolerated. Of the 61 volunteers who received 3 doses of vaccine, several were dropped from the study after 21 days, either because they left the Center or because they received additional vaccine because of exposure to rabies.

The SN titres of the sera taken at the different intervals are presented in Table 1. It is interesting to note that at 21 days, 58 of the 61 volunteers had positive antibody titres, and that in all except 2 of

Table 1. Serum neutralization antibody titres of sera from 61 volunteers following immunization with 3 doses of suckling mouse brain vaccine administered within 5 days

No. days between first dose of vaccine and blood sampling	No. of persons	Reciprocal of SN antibody titres					% positive
		<2	2–5	6–25	26–125	126–625	
0	61	61	—	—	—	—	0
10	38	11	2	7	18	1	71
21	61	3	—	9	23	26	95
90	35	2	2	4	23	4	94
240	29	6	1	11	8	3	79
365	25	7	2	7	8	1	72

Table 2. The effect of a 1-ml booster dose of suckling mouse brain vaccine on the level of SN antibodies in persons vaccinated previously with 3 doses

Identification	No. of months after first dose	Reciprocal of serum neutralization titre at: [a]			
		21 days after first dose	before booster	8 days after booster	6 months after booster
M.C.P.	8	181	38	698	486
M.I.R.	10	357 [b]	44	>4 374	162
M.C.A.	12	181	31	>4 374	338
A.C.	12	114	19	>625	160
L.L.	12	486	—	45 200	1 000
A.S.	12	342	5	>15 625	125
W.S.	12	213	0	>15 625	160
B.V.	12	206	32	1 400	66
E.P.	12	31	45	6 990	328
M.B.	16	162	0	>15 625	238
H.S.	16	243	18	>3 125	808
R.G.	15	54	0	>1 458	65
J.A.	17	17 [b]	3	210	—
H.R.	17	181	>162	>1 458	>625
A.M.	18	93	18	>3 125	125
F.F.	19	338	25	>15 625	160
C.C.	20	45	2	1 400	1 230
N.B.	21	104	3	1 160	328
A.A.	24	58	10	1 640	—
A.M.	25	93	18	>6 995	—
M.M.	30	250 [b]	280	8 470	3 125
D.M.	30	240	3	6 990	—
J.C.	38	59 [b]	3	1 400	—

[a] = not done; 0 = no antibodies at 1 : 2 dilution.

[b] These persons received 0.25 ml of vaccine, intradermally, 25 days after the first dose.

the 35 volunteers retested at 90 days the positive titres had persisted.

The results of a first booster 1 year or more after the first dose of vaccine are limited to observations made on 23 volunteers (Table 2). The very high antibody titres obtained following these booster doses are particularly striking.

Discussion

The schedules of human prophylactic immunization currently recommended are based on obtaining a secondary immune response by spacing the intervals between inoculations, but this study has shown that three 2-ml doses of SMBV within 5 days produced antibody levels as high as those reported in other studies using other vaccines and a longer immunization schedule.

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Epidemiological survey of rubella immunity in Iran

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Previous epidemiological studies in different parts of the world have demonstrated antibody to rubella in about 50% of children aged 6–8 years and in more than 80% of women of childbearing age. The antibody rates were significantly lower in the island, isolated, and rural populations investigated (Rawls et al., 1967; Dowdle et al., 1970).

This survey was carried out to determine the age incidence of rubella in females and the immune status of the women of childbearing age in urban and rural areas of Iran.

Materials and methods

Sera. A total of 1 559 blood specimens were collected by venepuncture or by finger prick according to the method described by Chin et al. (1966); 731 sera were from school-age girls or from girls aged between 8 months and 15 years attending clinics or health centres in Teheran. From women of childbearing age attending clinics and health centres and from high-school and college girls, 508 sera were obtained in Teheran, a city of about 3 million inhabitants, and 320 sera were collected in rural areas in the north and northwest of Iran. The age of these women ranged from 16 to 45 years. Sera were stored at −20°C prior to examination. Parallel titration of rubella haemagglutination-inhibition antibodies in several paired samples of blood obtained by venepuncture and by finger prick gave similar results with a variation in titre of no more than twofold, the venous samples giving the higher titre.

Haemagglutination-inhibition (HI) test. HI tests were carried out according to the method described

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