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Smallpox Vaccination by Intradermal Jet Injection *

2. Cutaneous and Serological Responses to Primary Vaccination in Children

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Primary vaccination by intradermal jet injection, using diluted smallpox vaccine, was compared with multiple-pressure vaccination in 625 Jamaican children. The cutaneous and antibody response patterns were evaluated. The primary take rates among those jet vaccinated were 97 % or more in those receiving vaccines with a titre of $10^{6.3}$ $TCID_{50}$/ml and $10^{7.0}$ $TCID_{50}$/ml, and 96 % in those vaccinated by multiple pressure, using undiluted vaccine. The primary take rates in subjects receiving jet-injected vaccine with titres of $10^{6.0}$ $TCID_{50}$/ml and $10^{5.0}$ $TCID_{50}$/ml were 90 % and 62 %, respectively. Among subjects tested who developed Jennerian vesicles, all but 3 demonstrated seroconversion. In those who failed to develop primary Jennerian vesicles, there was also a failure of neutralizing-antibody development. Vesicle and scar sizes were generally smaller in the jet-vaccinated subjects than in those vaccinated by the multiple-pressure technique. Infants tolerated jet vaccination without difficulty. Vaccinial complications did not occur in any subject. The intradermal jet injection of 0.1 ml of vaccine with a titre $10^{6.3}$ $TCID_{50}$/ml or higher is recommended as a highly effective method for achieving successful primary smallpox vaccination. The method appears best suited for use in mass smallpox-vaccination programmes.

In a previous report (Millar et al., 1969), the feasibility and efficacy of intradermal jet injection for vaccinating a group of adult males against smallpox was described; practically all the subjects were revaccinees. The present report compares cutaneous and serological responses in children given primary smallpox vaccination by the multiple-pressure method and by intradermal jet injection. The results of 3 studies undertaken to evaluate the efficacy of primary vaccination by intradermal jet injection are described and the minimal vaccine concentration required for effective field use is defined. The first study (A) compares the cutaneous and serological responses to multiple-pressure vaccination with those to intradermal jet injection of smallpox vaccines using 2 virus concentrations ($10^{7.0}$ $TCID_{50}$/ml and $10^{6.0}$ $TCID_{50}$/ml). The second study (B), an extension of the first, compares the cutaneous responses to intradermal jet injection of smallpox vaccines using 4 virus concentrations (10^{7} $TCID_{50}$/ml, $10^{6.3}$ $TCID_{50}$/ml, $10^{6.0}$ $TCID_{50}$ ml and $10^{5.0}$ $TCID_{50}$/ml). The third study (C) evaluates intradermal jet injection in vaccinating a limited number of infants against smallpox.

These studies were conducted in 1963 in Kingston, Jamaica, under the auspices, and with the co-operation, of the Ministry of Health of Jamaica. The Virus Laboratory of the Department of Pediatrics, University of Kansas Medical Center, performed the laboratory tests.

MATERIALS AND METHODS

Vaccine

Lyophilized calf lymph smallpox vaccine from a single commercial production lot, meeting standards

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TABLE 1
SUMMARY OF SERIES PROTOCOL

Vaccination method	Group designation in study: A	B	C	Vaccine titre [a]	Dose volume	No. of subjects tested in study: A	B	C	Total
Multiple pressure	A 1			8.5	1 drop	48	—	—	48
Intradermal jet injection									
1	A 2	B 1		7.0	0.1 ml	48	115	—	163
1a		B 2		6.3	0.1 ml	—	112	—	112
2	A 3	B 3	C	6.0	0.1 ml	69	115	11	195
3		B 4		5.0	0.1 ml	—	118	—	118
				Total		165	460	11	636

[a] Expressed as $\log_{10}$ $TCID_{50}$/ml.

set by the Division of Biologics Standards, National Institutes of Health, was used for all vaccinations.[1] The titre was $10^{8.5}$ $TCID_{50}$/ml,[2] as determined in primary rhesus monkey kidney cell culture tubes (Millar et al., 1969).

For multiple-pressure vaccination, the vaccine was reconstituted with the diluent provided commercially containing 50% glycerol and 0.25% phenol in sterile distilled water. Vaccine for jet injection was prepared by reconstituting vaccine from the same lot with 0.85% saline and diluting sequentially. Vaccines with 4 concentrations of virus were used: ID-Jet 1 vaccine, titre $10^{7.0}$ $TCID_{50}$/ml; ID-Jet 1a vaccine, titre $10^{6.3}$ $TCID_{50}$/ml; ID-Jet 2 vaccine, titre $10^{6.0}$ $TCID_{50}$/ml; and ID-Jet 3 vaccine, titre $10^{5.0}$ $TCID_{50}$/ml.

The unreconstituted, lyophilized vaccine was maintained at temperatures below freezing-point during all phases of storage and transport, and showed no change in titre when samples were tested after their return from Jamaica. Vaccine was freshly prepared on each day of vaccination and kept in a vacuum flask on wet ice when not being used. Vaccinations were carried out within 4 hours of the reconstitution of the vaccine.

Study population

All subjects were healthy Jamaica schoolchildren residing in the Kingston–St. Andrews Corporation. Prior to vaccination, all the children were examined for scars of previous successful primary vaccinations and for evidence of any condition contraindicating vaccination. Children with vaccination scars or contraindications to vaccination or both were excluded from the study.

In study A, 165 children, aged 4–10 years, participated; all were students in the first 3 grades at Calabar Primary School. They were further divided into 3 groups: group A1 received undiluted lyophilized smallpox vaccine by the multiple-pressure method; subjects in groups A2 and A3 received an intradermal jet injection of either ID-Jet 1 or ID-Jet 2 vaccines (Millar et al., 1969). A total of 460 children, aged 4–12 years, participated in study B; all were students of the first 3 grades of 4 primary schools. They were divided into 4 groups with an equal proportion from each school represented in each group. Each child received an intradermal jet injection of either ID-Jet 1 (B1), ID-Jet 1a (B2), ID-Jet 2 (B3) or ID-Jet 3 (B4) vaccine. In study C, 11 children less than 2 years of age from the Trenchtown Maternal and Child Health Clinic received an intradermal jet injection of ID-Jet 2 vaccine. The series protocol is summarized in Table 1.

Vaccination methods

A single experienced vaccinator performed all multiple-pressure and intradermal jet injection vaccinations. Subjects were vaccinated on the left arm just posterior to the midline at the level of the deltoid insertion. The site was cleansed with acetone

[1] Kindly provided as Dryvax, Lot 177101, by Wyeth Laboratories, Inc., Marietta, Pa., USA.

[2] Corresponds to approximately $10^{8.0}$ pock-forming units per ml as measured on CAM.

and allowed to dry prior to vaccination; excess vaccine remaining on the skin after inoculation was absorbed with a dry cotton pledget.

Multiple-pressure vaccination conformed with the method described by Leake (1927), consisting of 30 pressures made atraumatically with a sterile single-point needle through a small drop of vaccine placed on the skin. The pressures were confined to a circular area with diameter of less than 1/8 inch (3.5 mm).

Intradermal jet vaccinations were carried out with the automatic hypodermic jet-injection apparatus equipped with the intradermal nozzle manufactured by the Scientific Equipment Manufacturing Corporation of Lodi, N.Y., USA (Millar et al., 1969). Intradermal jet vaccinations were made with the dose adjustment control set at the 0.1-ml calibration.

Clinical evaluation

All children were examined by one of us (R.R.R.) on the 7th and 30th days after vaccination. Except in study C, in which only ID-Jet 2 vaccine was used, the examiner was not aware of the vaccination method, nor the vaccine concentration used, in any individual subject. Measurements were made of erythema, vesicle, and scar sizes, by recording the greatest diameter of each (D_1) and its corresponding right-angle diameter (D_2). Lesion areas were estimated according to the formula $A = \pi (D_1+D_2)^2/4$. Home visits were made to all children absent from school on the 7th post-vaccination day to ensure an evaluation of cutaneous responses and to determine whether their school absence was possibly related to the vaccination. Colour photographs of the vaccination sites were taken at the time of vaccination and on the 7th and 30th days after vaccination.

A successful primary vaccination was defined according to the criteria described by the WHO Expert Committee on Smallpox (1964) as a " typical Jennerian vesicle " present on the 7th day after vaccination. Children who developed a Jennerian vesicle after the 7th day were considered as having " delayed takes ", and considered as vaccination failures when calculating the primary cutaneous success rate.

Serological evaluation

Venous blood was obtained from each child in studies A and C immediately prior to vaccination and on the 30th day after vaccination. Blood was not collected from participants in study B. Specimens were processed and all sera were tested for serum-neutralizing antibody by the plaque-reduction test as previously described (Cutchins, Warren & Jones, 1960; Millar et al., 1969). Antibody testing began at an initial serum dilution of 1 : 4. Seroconversion was said to have occurred in those individuals with no antibody in the prevaccination serum and antibody present at a titre 1 : 8 or greater in the post-vaccination serum.

RESULTS

Study A

Prior to vaccination, 154 of the 165 children tested (93%) did not have demonstrable neutralizing antibody (Table 2). Of the remaining 11 (7%), on careful re-examination, 6 were found to have scars compatible with previously successful primary vaccination. In all, 10 of the 11 developed accelerated cutaneous responses characteristic of revaccination and all showed neutralizing-antibody responses of the anamnestic type. On the basis of this evidence, these 11 seropositive children were excluded from the present analysis, leaving 154 prevaccination seronegative children.

The primary vaccination cutaneous response rate is shown for each group in Table 3. Only 7 of the 154 children failed to respond, 2 in group A1 and 5 in group A3. Development of the primary cutaneous reaction after vaccination was qualitatively similar, irrespective of the vaccination method and vaccine concentration. However, multiple-pressure vaccination generally evoked a larger skin response than did intradermal jet vaccination, as illustrated by the calculated areas of erythema, vesicle and scar formation shown in Table 4. The mean scar area 30 days after vaccination was smaller in the subjects who were jet vaccinated than in those vaccinated by the multiple-pressure technique. Of the scars induced by multiple-pressure vaccination, over 80% had an area greater than 0.3 cm^2; in contrast, less than 30% of the jet-induced scars were greater than 0.3 cm^2 in area (see accompanying figure). Vesicle and scar contours in the jet-vaccinated subjects were more circular than those in subjects vaccinated by multiple pressure, which tended to be irregular in outline.

Only 2 children who received multiple-pressure vaccinations and 5 who received the ID-Jet 2 vaccine did not develop a primary take in 7 days. The 2 children vaccinated by multiple pressure showed no evidence of cutaneous reactions on the 7th, 14th or 30th days after vaccination; neither showed

TABLE 2

STUDY A: CHARACTERISTICS OF SUBJECTS BY GROUP

Group	Vaccination method and vaccine dilution	No. of children tested	Mean age (years)	Age range (years)	Prevaccination neutralizing-antibody status	
					No. negative/ No. tested	Percentage seronegative
A1	Multiple pressure (undiluted)	48	6.2	4–10	44/48	92
A2	ID-Jet 1 [a]	48	6.6	4–10	45/48	94
A3	ID-Jet 2 [b]	69	6.3	4–10	65/69	94
	Total	165	6.3		154/165	93

[a] Intradermal jet injection vaccine 1.
[b] Intradermal jet injection vaccine 2.

TABLE 3

STUDY A: CUTANEOUS REACTIONS IN PRIMARY VACCINEES

Group	Vaccination method and vaccine dilution	Vaccine titre [a]	No. of children tested	Evaluation 7 days after vaccination	
				No. positive [b]/ No. vaccinated	Percentage take
A1	Multiple-pressure (undiluted)	8.5	44	42/44	96
A2	ID-Jet 1 [c]	7.0	45	45/45	100
A3	ID-Jet 2 [d]	6.0	65	60 [e]/65	92
	Totals		154	147/154	96

[a] Expressed as $\log_{10}$ $TCID_{50}$/ml.
[b] Presence of Jennerian vesicle on the 7th day after vaccination.
[c] Intradermal jet injection vaccine 1.
[d] Intradermal jet injection vaccine 2.
[e] Numerator excludes 1 child with delayed take (see text).

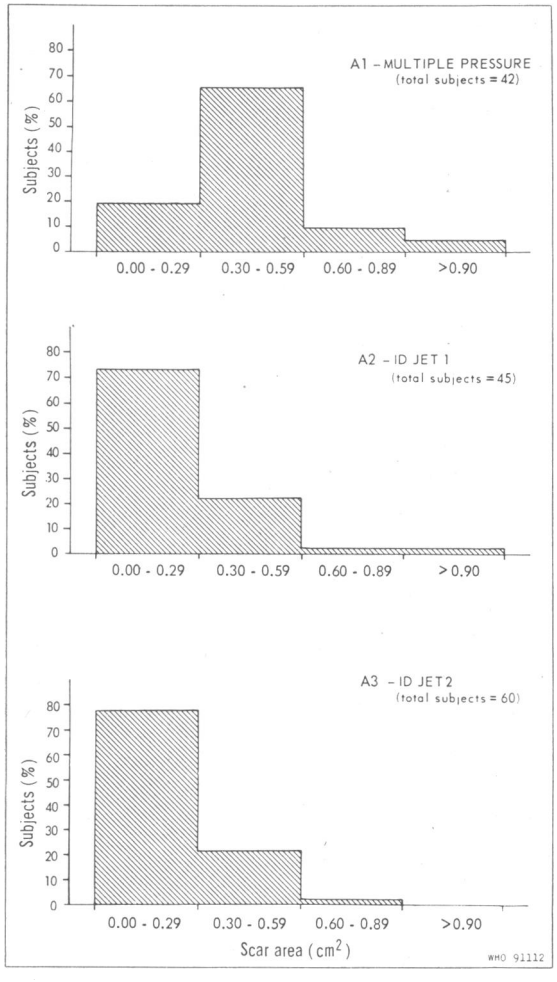
TABLE 4

STUDY A: VACCINATION LESION SIZES IN CHILDREN WITH PRIMARY TAKES

Group	Vaccination method and vaccine dilution	Vaccine titre [a]	No. of children tested	Evaluation after vaccination		
				Day 7		Day 30
				Erythema (cm^2) Mean ± S.D. [b]	Vesicle (cm^2) Mean ± S.D. [b]	Scar (cm^2) Mean ± S.D. [b]
A1	Multiple pressure (undiluted)	8.5	42	2.24 ± 2.09	0.58 ± 0.28	0.47 ± 0.27
A2	ID-Jet 1 [c]	7.0	45	2.99 ± 2.06	0.40 ± 0.20	0.29 ± 0.24
A3	ID-Jet 2 [d]	6.0	60	1.62 ± 0.84	0.23 ± 0.09	0.24 ± 0.13

[a] Expressed as $\log_{10}$ $TCID_{50}$/ml.
[b] Standard deviation.
[c] Intradermal jet injection vaccine 1.
[d] Intradermal jet injection vaccine 2.

AREA OF SCAR 30 DAYS AFTER VACCINATION; PERCENTAGE DISTRIBUTION BY GROUP



serological evidence of response. On repeat vaccination by multiple pressure after 30 days, 1 of these children developed a typical primary reaction while the other reacted only with erythema (measuring 0.16 cm²) by the 7th day.

All 5 children who experienced vaccination failure following intradermal jet injection had some degree of inflammatory response at the site of vaccination on the 7th day. Measurements of erythema ranged from 0.03 cm² to 0.57 cm². In none of the 5 children had a vesicle formed by the 7th day. By the 14th day after vaccination, however, 1 child had developed a small vesicle; his post-vaccination serum showed neutralizing antibody with a titre of 1: 245, similar to that of children with well-developed vesicular responses on the 7th post-vaccination day. The cutaneous response in this subject, therefore, was classified as a delayed take. In the other 4 children, the inflammatory response had faded by the 14th day and none developed vesicles; 3 of the 4 were revaccinated after 30 days, and all developed typical primary takes. Post-vaccination sera were not available for study.

The neutralizing-antibody responses are summarized for each group in Table 5 but the responses for the 7 children who had not developed Jennerian cutaneous responses by the 7th day after vaccination are excluded since they failed to meet the established criterion for successful primary cutaneous response. The child in group A3 with a delayed take who did show seroconversion is among those excluded. The serum-neutralizing antibody geometric mean titre (GMT) of the multiple-pressure group was higher than the GMTs for either of the 2 groups vaccinated by jet injection; in both instances, the difference was less than 2-fold. Of the 147 children who developed Jennerian vesicles, all but 2 demonstrated seroconversion; both received ID-Jet 2 vaccine. The GMTs of the serum-neutralizing antibody were similar in each group.

While no serious reactions or illnesses occurred during the month following vaccination, 19 of the 154 children were absent from school on the 7th day with fevers ranging from 37.2°C to 39.4°C (oral), or malaise. None was absent from school for more than 2 days.

Study B

None of the selected subjects demonstrated scars of primary vaccination. Sera were not studied. Primary take rates among subjects jet inoculated with 4 different dilutions of vaccine are shown in Table 6. Among those receiving vaccines ID-Jet 1 and ID-Jet 1a, 97% in each instance developed primary takes. These rates are comparable to those in persons vaccinated by multiple pressure with undiluted vaccine and with ID-Jet 1 vaccine in study A. Similarly, the primary take rate (90%) among subjects receiving ID-Jet 2 vaccine compares favourably with the primary take rate among those receiving the same vaccine in study A (92%). Among those receiving ID-Jet 3 vaccine, only 62% developed primary takes by the 7th day. (It should be noted that 21 out of 45 subjects recorded as " vaccination failures " on day 7 had erythematous

TABLE 5

STUDY A: NEUTRALIZING-ANTIBODY RESPONSE AFTER CUTANEOUSLY SUCCESSFUL PRIMARY VACCINATION

Group	Vaccination method and vaccine dilution	Vaccine titre [a]	Seroconversion (No. positive/ No. tested)	Post-vaccination neutralizing-antibody titre [b]						Geo-metric mean titre
				<4	4–8	9–16	17–64	65–256	257–⩾1 024 [c]	
A1	Multiple pressure (undiluted)	8.5	42/42	0	0	0	1	24	17 (1)	241
A2	ID-Jet 1 [d]	7.0	45/45	0	0	1	11	15	18	153
A3	ID-Jet 2 [e]	6.0	58/60	1	1	0	4	34	20 (2)	173
				← Non- conversion			Seroconversion →			

[a] Expressed as $\log_{10}$ $TCID_{50}$/ml.

[b] Expressed as reciprocal of serum dilution.

[c] Values in parentheses indicate the number of observations greater than 1 024. These are included in the totals of 17 and 20, respectively. Observations greater than 1 024 were considered as 1 024 in calculating geometric mean titres.

[d] Intradermal jet injection vaccine 1.

[e] Intradermal jet injection vaccine 2.

TABLE 6

STUDY B: CUTANEOUS REACTIONS IN PRIMARY VACCINEES

Group	Vaccine method and vaccine dilution [a]	Vaccine titre [c]	Group mean age (years)	Age range (years)	Evaluation 7 days after vaccination	
					No. positive [c]/ No. vaccinated	Percentage take
B1	ID-Jet 1	7.0	7.2	5-11	112/115	97
B2	ID-Jet 1a	6.3	7.1	5-12	109/112	97
B3	ID-Jet 2	6.0	6.7	4-11	103/115	90
B4	ID-Jet 3	5.0	6.6	5-11	73/118	62

[a] Intradermal jet injection vaccines 1, 1a, 2 and 3.

[b] Expressed as $\log_{10}$ $TCID_{50}$/ml.

[c] Presence of a Jennerian vesicle on the 7th day after vaccination.

papules. While not all were re-examined on the 14th day, several were noted to have developed Jennerian vesicles between days 7 and 14.)

Study C

Altogether, 11 children less than 2 years of age were jet vaccinated with ID-Jet 2 vaccine. (Maternal antibody was not detected in the 6 children aged 5–9 months whose prevaccination sera were tested.) Only 1 child failed to demonstrate a cutaneous primary take (Table 7). All primary vaccination lesions were typical although the average size of a lesion was somewhat smaller than that observed in subjects receiving the vaccine in study A. Only 2 children failed to show seroconversion; 1 without cutaneous response and another with a typical lesion (post-vaccination titre, 1:4). The geometric mean titre of serum-neutralizing antibody was lower among the infants than in subjects receiving ID-Jet 2 vaccine in study A.

Complications

There were no vaccinial complications. Superficial secondary bacterial infection of vaccination lesions occurred in 2 children, both in study A; one child had been vaccinated by multiple pressure and the other by jet injection. Infection apparently was related to excoriation of the vaccinial lesion and responded rapidly to cleansing with soap and water and topically applied bacitracin ointment.

TABLE 7

STUDY C: PRIMARY VACCINATION OF CHILDREN LESS THAN 2 YEARS OF AGE BY ID-JET 2 [a]

No. vaccinated	Age range (years)	Primary cutaneous response (No. positive [b]/ No. vaccinated)	Group average cutaneous response after vaccination			Neutralizing-antibody response	
			Day 7		Day 30		
			Erythema (cm^2) Mean ± S.D. [c]	Vesicle (cm) Mean ± S.D. [c]	Scar (cm^2) Mean ± S.D. [c]	No. positive [b]/ No. tested [d]	GMT [e]
11	5/12 to 1–11/12	10/11	1.36 ± 1.20	0.24 ± 0.15	0.18 ± 0.13	9/10	30

[a] Intradermal jet injection vaccine 2.
[b] Presence of Jennerian vesicle on 7th day after vaccination.
[c] Standard deviation.
[d] Only children with a typical Jennerian cutaneous response are included.
[e] Geometric mean titre expressed as the reciprocal of the serum dilution.

Performance of the jet injector

The jet injector performed satisfactorily throughout the studies. Intradermal wheals comparable to those seen in Mantoux skin testing were produced in all but 1 child. This child was given a second inoculation and primary vaccinial lesions developed at both inoculation sites. Following an injection, a droplet of the vaccine remained on the skin surface in all subjects, indicating that somewhat less than 0.1 ml had penetrated the epidermis. In the children less than 2 years of age, the intradermal wheals were less distinct than in the primary-school children. From inspection and palpation, it appeared the inoculum was generally deposited more deeply than in the older children.

DISCUSSION

The results of our studies indicate that intradermal jet injection of diluted smallpox vaccine is an effective way of performing primary smallpox vaccination. The cutaneous and serological responses evoked compare favourably with those following accepted multiple-pressure vaccination technique. Diluted vaccines, with titres of only $10^{6.3}$ $TCID_{50}$/ml and $10^{7.0}$ $TCID_{50}$/ml, administered by intradermal jet injection in doses of 0.1 ml, produced clearly satisfactory results; vaccine with titre of $10^{6.0}$ $TCID_{50}$/ml produced an acceptably high proportion of cutaneous and serological takes but appears to be the marginal concentration. Intradermal vaccine with a lower concentration of virus gave clearly unsatisfactory results.

These observations on intradermal jet injection primary vaccination do not differ greatly from those published in studies of subcutaneous jet injection primary vaccination, despite differences in injector equipment, nozzle design, depth of vaccine placement, size of inoculum, virus concentration and other methodological considerations. Elisberg, McCown & Smadel (1956) found that 20 out of 21 children developed primary takes when inoculated by subcutaneous jet injection with 0.5 ml of chorioallantoic membrane (CAM) smallpox vaccine containing 10^5 CAM infectious units. While the inoculum was principally deposited subcutaneously, the take was thought to be due to the vaccine virus lodged intradermally as the jet stream traversed the epidermis. Altogether, 11 out of the 14 subjects tested developed serum-neutralizing antibody. Meyer et al. (1964) administered a CAM vaccine containing 1.5×10^6 $TCID_{50}$ in a 0.5-ml dose by using an injector equipped with a modified subcutaneous nozzle which permitted an undefined amount of the dose to be placed intradermally. Of 285 susceptible children, 99% developed typical primary cutaneous vaccinial reactions. Of 237 children tested, 99.6% showed evidence of haemagglutination-inhibiting antibody rises.

The over-all pattern of neutralizing-antibody response we observed agrees with that reported by others studying primary vaccination (Cutchins, Warren & Jones, 1960; Elisberg, McCown & Smadel, 1956; Espmark et al., 1965; McCarthy, Downie & Bradley, 1958). The multiple-pressure group had a higher post-vaccination GMT than either of the 2 groups vaccinated by jet injector, although the difference was less than 2-fold. The

practical significance of these group GMT differences remains conjectural, but could possibly bear a relationship to the persistence of antibody.

Despite the relatively large inoculum of vaccine virus introduced by the intradermal jet technique, the resultant cutaneous lesions and scars are not larger than those seen after primary vaccination by multiple-pressure techniques. In our studies, the scars 30 days after vaccination were significantly smaller than those in subjects vaccinated by the multiple-pressure technique. This finding is by no means unfortunate as there appears to be little virtue in a large scar. Leake & Thomas (1926), studying the relationship between vaccination scar and response to challenge revaccination, concluded that scar size had no practical bearing on individual immunity to vaccinia (and by implication, variola). In young adults from Madras, Downie et al. (1961) found that persons bearing 1 or 2 scars, as opposed to 3 or 4 scars and, hence, having large differences in scar area, had essentially similar neutralizing-antibody levels. That the intradermal jet method does not evoke cutaneous lesions and residual scars larger than those resulting from traditional methods may be an important observation. In some smallpox-endemic areas, where a fear of "horrific" vaccination techniques (resulting in large cutaneous lesions and disfiguring residual scars) contributes to the resistance to vaccination, this attribute of jet injection may hold distinct advantages.

The logistical superiority of jet injection for mass smallpox vaccination has already been described (Millar et al., 1969). The studies reported here confirm that primary smallpox vaccination by intradermal jet injection is as effective as traditional methods, and is significantly more economical of vaccine. As a result of our findings, intradermal jet injection of vaccines with a titre of $10^{6.3}$ $TCID_{50}$/ml, or higher, in doses of 0.1 ml, can be recommended as an acceptable vaccination technique. While vaccines with a titre of $10^{6.0}$ $TCID_{50}$/ml gave acceptable take rates (92%) in jet-vaccinated subjects under the conditions of these experiments, the concentration appears to be marginal; vaccines with titres of $10^{5.0}$ $TCID_{50}$/ml are clearly unacceptable. For field operations in which the vaccine inevitably encounters unfavourable environmental conditions, vaccine with a titre of $10^{6.0}$ $TCID_{50}$/ml cannot be recommended even for primary vaccination; concentrations of $10^{6.3}$ $TCID_{50}$/ml or higher should be used to ensure a satisfactory high rate of primary takes.

This report and our previous one (Millar et al., 1969) confirm the utility of, and set dosage criteria for, intradermal jet injection for primary vaccination and vaccination of previously vaccinated persons with limited residual immunity. Full evaluation of the technique as a field method requires the presentation of data on the dose of virus necessary to ensure adequate immunological challenge in previously vaccinated persons with significant residual immunity.

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RÉSUMÉ

LA VACCINATION ANTIVARIOLIQUE PAR INJECTION INTRADERMIQUE SOUS PRESSION: 2. RÉACTIONS CUTANÉES ET RÉPONSES SÉROLOGIQUES À LA PRIMO-VACCINATION CHEZ DES ENFANTS

Ce deuxième article expose les résultats d'études effectuées à Kingston (Jamaïque) en 1963 et destinées à évaluer l'efficacité de la vaccination antivariolique par injection sous pression chez des enfants non encore vaccinés ainsi qu'à déterminer la concentration minimale de vaccin à utiliser.

Lors de la première étude, portant sur 154 enfants, on a comparé les réactions cutanées et les réponses sérolo-

giques obtenues, d'une part, après vaccination par la technique des pressions multiples à l'aide d'un vaccin non dilué contenant $10^{8,5}$ doses infectantes de culture de tissu ($DICT_{50}$) par millilitre et, d'autre part, par la technique de l'injection sous pression utilisant deux concentrations de vaccin, 10^7 $DICT_{50}$/ml et 10^6 $DICT_{50}$/ml. Les taux de prise ont été respectivement de 96% chez les enfants vaccinés par pressions multiples avec le vaccin non dilué, de 100% (vaccin titrant 10^7 $DICT_{50}$/ml) et de 92% (vaccin titrant 10^5 $DICT_{50}$/ml) chez les enfants vaccinés par l'injecteur sans aiguille. On a noté une très nette corrélation entre les taux de prise et les taux de séroconversion. Aucune complication postvaccinale n'a été observée.

Au cours de la deuxième étude, portant sur 460 enfants, on a comparé les taux de prise obtenus après vaccination par l'injecteur sans aiguille à l'aide de vaccins de concentrations différentes. Ces taux ont été de 97% (vaccin titrant 10^7 $DICT_{50}$/ml), 97% (vaccin titrant $10^{6,3}$ $DICT_{50}$/ml), 90% (vaccin titrant 10^5 $DICT_{50}$/ml) et 62% (vaccin titrant 10^5 $DICT_{50}$/ml).

Enfin, une troisième expérimentation a été menée afin d'étudier les réactions cutanées et les réponses sérologiques chez 11 enfants de moins de 2 ans primo-vaccinés par injection sous pression à l'aide d'un vaccin contenant 10^6 $DICT_{50}$/ml. Dix de ces enfants ont présenté une vésicule jennérienne typique et chez 9 d'entre eux l'examen sérologique a mis en évidence la présence d'anticorps neutralisants. La vaccination a été très bien supportée.

L'injecteur à aiguille a parfaitement fonctionné. La taille des vésicules et des cicatrices vaccinales a été généralement plus petite chez les sujets vaccinés par cette technique qu'en cas de vaccination par pressions multiples. D'après les auteurs, l'injection intradermique sous pression de 0,1 ml d'un vaccin titrant $10^{3,3}$ $DICT_{50}$/ml ou davantage est une méthode efficace de primo-vaccination.

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