IMMUNITY REACTION FOLLOWING VACCINATION AGAINST SMALLPOX AND POST-VACCINAL ENCEPHALITIS

The Permanent Committee of the Office international d'Hygiène publique at its October 1946 session decided to pass to the Interim Commission of the World Health Organization a number of urgent questions which figured on its agenda. Among these questions were “the immunity reaction after vaccination against smallpox” and “post-vaccinal encephalitis”.

These two subjects are of first importance: the former because of the question of the meaning to be attached to the terms laid down in the International Sanitary Convention of 21 June 1926, as modified by that of 1944, for registration of the result of Jennerian vaccinations and revaccinations in the International Certificate of smallpox vaccination; the latter, because of the frequency and the gravity, especially in certain countries and at certain ages, of post-vaccinal encephalitis.

These questions were examined by the Committee on Epidemiology and Quarantine of the Interim Commission of the World Health Organization during its third and fourth sessions, and were dealt with in a number of papers. Although the subjects are still being studied, it seems useful to publish in the Bulletin of the WHO the following documents relating to them.

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1 See Procès-verbaux de la session d'octobre 1946 du Comité permanent de l'Office international d'Hygiène publique, p. 81.

2 Since the fourth session, the new designation of this Committee is "Committee on Technical Questions".
NOTE ON THE "IMMUNITY REACTION"
FOLLOWING VACCINATION AGAINST SMALLPOX

By G. Stuart, M.D., Secretariat, Interim Commission.

In the paper on this subject presented by Dr. Stock 1 to the Permanent Committee of the Office international d'Hygiène publique, at its October 1946 session, the conclusion was reached that "it proved impossible to develop completely objective criteria of the immune reaction". This conclusion was based on the fact that, from observations made on 1,364 UNRRA personnel vaccinated each with one drop of heated and one of active lymph and examined on the third and eighth days thereafter, very considerable difficulty was experienced in deciding what constituted an immune reaction; indeed without the help of the control insertion of killed lymph it would have been virtually impossible.

In the above series of tests carried out at the Weilcome Research Institution, London, it was found that in susceptible persons the killed lymph produced a marked local reaction which is quite unrelated to the level of protection as shown by the subsequent development of accelerated reactions or primary vaccinias.

To the whole subject of "immune or immediate reaction" the following further observations are germane:

"Immune or immediate reaction" is by many regarded as evidence of a high degree of immunity to smallpox and reaches its maximum within 72 hours.

But of 19 proved cases of smallpox vaccinated by Illingsworth and Oliver 2 one to fourteen days after the appearance of the rash, 16 showed the "immune reaction" in 48 hours, in comparison with control uninoculated scratches.

Again the term "immune reaction" is not accepted by Marsden 3 4, who regards it as a misnomer; in his view it indicates only sensitization to lymph and not immunity—although it is often given by immune subjects. In Marsden's words: "Those who

References:
2 Illingsworth and Oliver (1944) Lancet, 2, 681.
show it should be vaccinated again and again; otherwise some of them will die of smallpox as soon as they are exposed to it."

Further in regard to sensitivity and immunity to vaccine virus, CRAIGIE\(^1\) states: "Elementary bodies of vaccinia washed and killed by formalin elicit an 'early reaction' in individuals previously vaccinated, but no skin reaction in those not previously vaccinated. This reaction is a specific response to the virus antigen in those sensitized by previous vaccination. Sensitivity and immunity to vaccine virus are not necessarily related except in so far as they have a common origin in previous vaccination."

Should later consensus prove to be that "immune reaction" is no guarantee of immunity to smallpox, then obviously there could be no justification for the retention of the term on International Certificates of Vaccination such as are recommended by the International Sanitary Conventions of 1944. And in this connexion also the demand of the present International Certificate that a statement of "no reaction" will not be accepted seems—as already pointed out in the paper read by Dr. Strock—difficult to justify in view of the fact that there are individuals who fail to "take", even on repeated inoculation, and are yet immune.

\[\text{Reference:}\]
\(^1\) CRAIGIE (1933) \textit{Canad. publ. Hth. J.} 24, 72.
SIGNIFICANCE OF THE "IMMUNITY REACTION"
FOLLOWING VACCINATION AGAINST SMALLPOX

Note presented by Dr. Melville Mackenzie,
Representative from the United Kingdom on the Interim Commission.

The entire absence of any local reaction at inspection on the third day and later on the occasion of a first attempt at revaccination should not be recorded as "insusceptible to revaccination" or as "complete immunity". It should be regarded as an indication for at least one further attempt with a fresh lymph and a check on the method of lymph storage. A similar result having been obtained on a second occasion it would be reasonable to record "no local reaction to revaccination (repeated)".

A local reaction reaching maximum size on the second or third day and accompanied by elevation and itchiness of the site but without a vesicle is commonly recorded as "reaction of immunity", but this is unwarranted because the lymph used may have been so weakened by time, temperature or other causes, that it was unable to go on to produce the more marked (vaccinoid or vaccinal) reaction which would have been caused in the same person by a lymph of full strength; it is also possible that such a reaction may have been due to the sensitivity of the individual to protein or other substances in the lymph and that it was not a response to the virus of vaccinia. It is preferable therefore to record this type of reaction merely as "maximum local reaction (non-vesicular) on 2nd/3rd day ", and if there be any doubt concerning the potency of the lymph used to make one further attempt at revaccination with a fresh lymph.

When the local reaction reaches a maximum size between three and seven days after insertion and there is some degree of vesicle formation, it is justifiable to record the result as an "accelerated " or "vaccinoid " reaction (vesicular) and to assume that the subject initially retained only a partial degree of the immunity to smallpox conferred by previous vaccination.

When the local reaction reaches a maximum size after the seventh day and there is marked vesicle formation the result may be recorded as "typical (primary) vaccinia " and it can be assumed that the immunity against smallpox conferred by previous vaccination had become negligible at the time of revaccination.

1 The text expresses not the personal views of Dr. Melville Mackenzie, but those communicated by him on behalf of his Government.
THE VALUE TO BE ATTACHED TO SMALLPOX VACCINATION AND TO THE REACTION OF IMMUNITY

*Note presented by Dr. A. Cavaillon, Representative from France on the Interim Commission.*

It is considered desirable to communicate the opinion given on this subject by Dr. R. Dujarric de la Rivière, Assistant Director of the Pasteur Institute and Professor Henri Bénard, Director of the *Institut supérieur de la Vaccine* of the Académie de Médecine:

"It appears that the expression 'reaction of immunity' cannot be retained either in Article 42 (5) of the International Sanitary Convention of 21 June 1926, as modified by that of 1944, or in the International Certificate of Vaccination against Smallpox.

"The absence of reaction at the site of inoculation of vaccinal lymph probably reveals a state of immunity in the great majority of cases, but not necessarily in all. There undoubtedly exist persons insusceptible to the vaccine, in whom no apparent reaction is induced, even after repeated inoculations (the Meynard case, quoted by Kelsch, the Espine and Seaton case, reports by Stock and G. Stuart). But absence of reaction is found also in susceptible subjects; in such cases it may be that inoculation has been insufficient. All vaccinators are agreed that, when giving two inoculations to one subject, with the same vaccine, it sometimes happens that one only of the sites of inoculation is the seat of development of a pustule, the other showing no reaction.

"It is difficult to speak of a 'reaction of immunity' in the case of all local reactions following vaccination, as is customary in respect of some. Such reactions evince hypersensitiveness to the lymph combined with resistance to the specific infection. They are *allergic* reactions, a much more general and accurate expression than that of immunity. The fact that there is no parallelism between the insusceptibility of a subject and the vaccine-neutralizing power of his serum shows that a distinction should be made between the *antigenic* and *immunizing* properties of smallpox vaccine.
"It would therefore be reasonable to use, for the wording of certificates, expressions which correspond to clinical facts, to controllable lesions and not to theoretical interpretations.

"In France, certificates drawn up by the Public Vaccination Service in application of the law of 15 February 1902, and following form 10 of the Annex to the Ministry’s Circular of 25 January 1907, record either ‘successful’ or ‘unsuccessful’ vaccination. In successful cases, the appearance of one of the following lesions, corresponding to Kelsch’s classification, is noted: papules, papular-vesicles, normal pustules. ‘Unsuccessful’ corresponds to absence of reaction.

"The certificate of smallpox revaccination issued by the Institut supérieur de la Vaccine also gives the description of the lesions observed.

"The certificate drawn up in accordance with the Circular of 25 January 1907 is based on the suggestion of the Académie de Médecine which considers as ‘successful’ any eruption appearing at the sites of inoculation and which includes any one of the three lesions enumerated. ‘Successful’ includes: the reaction of the primary type (primary vaccination) and revaccination lesions evincing vaccinal allergy: immediate and accelerated reaction.

"It is thus desirable to reconsider this classification into ‘successful’ and ‘unsuccessful’, but to request the vaccinating doctor to specify, in successful cases, the number and nature of the elements observed (papules, papular-vesicles, pustules) and to consider as ‘unsuccessful’ the absence of any reaction apart from the traumatic reaction.

"Article 42 (5) of the 1926 Convention, as modified by that of 1944, might be modified as follows:

"The third paragraph of number (5). ‘For the purpose of this Article “sufficiently protected by recent vaccination” shall be taken as meaning evidence of a successful vaccination or revaccination not more than two years or less than 14 days previously. The results of the vaccination or revaccination shall be indicated by the words “successful” or “unsuccessful”.’

"The word ‘successful’ corresponds to any reaction which has appeared at the site of inoculation; primary type (pustular
reaction; papulo-vesicular or papulo-pustular accelerated reaction (vaccinoid); precocious maculo-papular reaction ('immune'). 'Unsuccessful'—i.e., the absence of any reaction other than traumatic—shall be taken as indicating that there is no sure guarantee of protection.

"In doubtful cases, an unsuccessful revaccination shall be considered as valueless and revaccination should be repeated. There have been undoubted cases of smallpox in persons who had been unsuccessfully revaccinated.

"The international certificate should also give not only the date of inoculation but also that of inspection. The terms 'reaction of immunity' and 'a certificate of 'no reaction' will not be accepted' should be suppressed. In recording the results, the words 'successful' or 'unsuccessful' shall be employed on the strict understanding that the number and nature of the eruptive elements (papules, papular-vesicles, pustules) are recorded.

"Finally, one could perhaps discuss the feasibility of:

"(1) carrying out, simultaneously, inoculations with active and with heated lymph, as is done with diphtheria toxoid for the Schick reaction. But the considerable difficulties of carrying out this technique in practice should be reckoned with;

"(2) indicating, in unsuccessful cases, that vaccination had been carried out twice or several times, at certain intervals."