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IMMUNITY IN RELATION TO THE NUMBER OF INSERTIONS

by

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The realization that vaccination did not confer lifelong immunity against smallpox led to the practice of multiple insertions toward the end of the nineteenth century. Dixon (1964) quotes Greenwood (1928 - M.G. Rep. of the Committee on Vaccination. Minstr. Hlth, London: HMSO p. 59) who stated: "Other things being equal, the fatality rate increases pari passu with the diminishing in the number of vaccination cicatrices, and the same holds good with regard to the cicatricial area. The correlation is of the order of 0.2 to 0.3. It is thus not high, but "quite significant". . . . "there was a definite but not very high association between fatality rate and area of scars, and also between fatality rate and number of scars, four or less, but little or no distinction between the smaller numbers, but the latter relation is more dependent on the association of area and number than is the former; it does however, still exist, when the area is kept constant, so that for a given area there is rather more probability of death, with only one or two scars than with four".

Statistical evidence of Brownlee is cited, who reported the death rates in a standard population for London cases of 1902-3 to be 117.4 for those with one scar, 90.7 for two scars, 59.5 for three scars, and 56.8 for four scars.

In American studies anti-vaccinal immunity was related to the area of the scars, since multiple insertions were more rarely used. Force (1913), analyzing a small number of cases, reported that 25% of those with scars under 15mm developed vaccinoid or vaccinia reactions, as opposed to 41% of those with scars over 15mm. Of those with pitted or keloid scars, 23% were non immune as opposed to 58% of those with smooth scars. In 1914, Force reported the results on 587 subjects, among whom 75% of those with scars under 15mm were non immune, compared to 58% of those whose scars measured 15 to 20mm, and 51% of those with scars over 20mm in diameter. The interpretation of

this data is difficult because in the same group, 77% of those with scars under 10 years old developed vaccinia or vaccinoid reaction but only 57% of those with scars over 20 years old. Leake and Thomas (1926) related the reaction to vaccination of approximately 890 individuals with their scars and concluded that "the size of the scar of previous vaccination, the character of the scar (whether pitted or smooth) and the amount of scarring (whether marked or faint) have no practical bearing on a person's immunity against vaccinia or variola."

With regard to area of skin involved, Platz (1927) observed that a small area of skin infection failed to produce immunity of the rabbit cornea to challenge with vaccinia, while a larger area of skin involved in the primary infection would produce immunity in the conjunctiva. Cross (1959) reported that immunity to rechallenge is only present on the eighth day after vaccination if a vesicle of more than 1/2 inch in length or diameter is produced; after three weeks there was no difference.

Whether multiple insertions will result in a higher level of immunity as measured by antibody level or duration of immunity is not truly known. Since vaccination consists of infection with a living agent which multiplies until immunity supervenes many feel that the area or number of insertions will have relatively little effect on the level of immunity. Stevenson (1944) felt that variations in immunity were based on personal variations and were not based on potency of the vaccine or area of vaccination. McClean (1955) notes the difference from a killed antigen, and points out that the final concentration of virus bears little relation to the amount originally inserted. Ellisberg et al (1956) noted that the same type lesion developed at the site of successful jet injection of 0.5 ml of vaccine as at the site of faulty skin penetration when only a small wheal formed and the bulk of the dose remained on the surface of the skin. In our studies, we have photographed identical appearing lesions on the two arms in response to vaccines varying in potency by several logs.

Why then the historic data indicating the greater protection from multiple insertions? Peterson (1922) showed that some lots of vaccine were fully effective for primary vaccinations, but were defective on revaccination. Horgan and Haseeb (1944) showed that on revaccination two insertions elicited more vaccinoid reactions than a simple scratch. The quality of vaccines in use a century ago (and in some places now) was such that multiple insertions increased the likelihood that infective virus would contact the appropriate

epithelial cell with subsequent immunity; bacterial contamination was very likely to produce septic infection and scarring. Such "spurious pustules" complicated the early introduction of vaccination.

Folak et al (1963) demonstrated that the morbidity rate was not reduced by a diluted vaccine, there was a suggestion of slight delay. However, the clinical reaction was influenced by the number of primary pocks.

The evidence that multiple insertions increase immunity is not unequivocal. There is evidence that the clinical reaction is more intense; the increase in scarring is self evident. What may be more important in an anti-smallpox campaign is the observation of Bourke and Clarke (1963) that approximately 10% of University students refused smallpox vaccination because of fear of a painful arm or other adverse reactions or scarring; an even higher evasion rate can be expected from less educated populations. With present day high potency and essentially bacterial free vaccines, much of the need for multiple insertions has disappeared and they are unnecessary except when the threat of infection is very high and time for protection short.