YELLOW FEVER SCRATCH VACCINE (17D STRAIN)

by

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In the areas of West Africa delineated by the tropical rain forest belt, yellow fever is highly endemic except where it has been controlled by vaccination campaigns. The need for a vaccine that is of low cost, safe, easy to administer, and resistant to tropical conditions is obvious. The vaccine produced at Dakar comes very near to the ideal, but there is in some quarters reluctance to use it owing to fear of encephalitis and of contamination of the vaccine with other viruses. Fear of the former has to some extent been increased by outbreaks of encephalitis with a high mortality rate following use of the vaccine. Even before these outbreaks, however, a vaccine to be administered by scarification was developed incorporating the 17D strain. The cost of this vaccine was less than that of a vaccine given by injection since whole embryo pulp without centrifugation was used in the final product. It is probable that the cost of this vaccine was about one-tenth of that of a vaccine given by injection.

Use of the mouse brain as a source of 17D vaccine was the next step, since 17D virus grows to a very high titre in mouse brain and since mice are readily available in any laboratory working on yellow fever. The 17D vaccine used for scarification will be considered below from its production to a final evaluation of its efficacy.

1. Seed lots

Whether the actual finished vaccine is prepared from chick embryos or mouse brain, the seed lots should be prepared from chick embryos. The reason
for this is to ensure that as far as possible the properties of the strain remain constant, particularly with regard to neurotropism. The neurotropism of the 17D strain may regularly though slowly be enhanced by repeated passages through the brains of white mice, whereas such is not the case with repeated passages through the chick embryo.

2. **Safety tests for seed lots**

These should be the same as those for seed lots of a vaccine given by injection.

3. **Preparation of the vaccine**

(a) **Using chick embryos.** The vaccine may be prepared in exactly the same way as that for a vaccine given by injection, although of course in reconstituting the vaccine much less excipient must be added so that a more concentrated product results. Embryo pulp without centrifugation may also be used in preparing the final vaccine. This results in an increase of the quantity of material available for processing, but the final preparation is less refined than a product subjected to centrifugation, and is more difficult to titrate. These disadvantages are slight, however. If mouse brains are used there are two main fears: that the vaccine may increase its neurotropism, and that extraneous pathogens may be introduced in the vaccine. Although repeated passages of 17D through mouse brain do result in a change in the characteristics of the virus, in one passage the change is very small. The danger of extraneous pathogens is a very real one and will be discussed later.

Mouse brains may be desiccated whole and then ground with celite, which facilitates grinding and dispensing, or they may be titrated in distilled water and the suspension desiccated. The former method has the advantage that the vaccine may be dispensed in ampoules which do not have to stand up to the exigencies of the freeze-drying process and are therefore relatively cheap. The latter method has the advantage that the product is easier to rehydrate and develops less clumping.
Gum arabic may be added to the product before desiccation, and the resulting vaccine has the particular advantage that only sterile water is needed for preparing the vaccine in the field, whereas if gum arabic is not added to the product before desiccation, ampoules of gum arabic solution are required to rehydrate the vaccine. Gum arabic mixed with the vaccine during preparation does, however, add slightly to the difficulty of desiccation. Obviously gum arabic cannot be added to a preparation which is not freeze-dried.

4. Safety tests on the vaccine

Where a vaccine is grown in the tissue of an animal there is always danger of the vaccine being contaminated by viruses and bacteria of the animal. Provided the danger is realized and the animal colonies are well supervised, there should be little risk. Each laboratory should be free to check its animal colonies in the way thought best. Nevertheless some minimum requirements are necessary.

5. Storage and keeping qualities

These should be just as good as, or even better than, those for a vaccine given by injection.

6. Administration

It has been shown that there is little difference in the percentage of persons developing immunity whether they have been vaccinated with a preparation containing gum arabic or not. Nevertheless a vaccine prepared with gum arabic is easier to apply and is less easily wiped off.

There is a strong suggestion that cleaning the skin with ether before applying the vaccine is unsatisfactory. In most cases cleaning with water should be sufficient.

The number of scratches made on the skin has varied from a single linear scratch to cross-hatching. There appears to be little to choose between the different methods, but the more scratches that are made the longer is the time
taken to vaccinate. It has been shown using Dakar vaccine that it makes no appreciable difference whether that vaccine is administered by scarification or by the method of multiple pressure.  

A similar study on 17D virus has not, however, been made.

Yellow fever scratch vaccine combined with vaccinia has been used for many years in the French West African territories, and the production of immunity with the yellow fever strain used in the vaccine has been very good. Using 17D vaccine satisfactory results have been obtained in West Africa, but in East Africa it has been found that a combined vaccine results in an immunity rate which is considerably less than that resulting from the use of 17D vaccine alone. It has been suggested that if yellow fever vaccine and vaccinia are administered simultaneously there is increased risk of subsequent encephalitis. What, if any, is this increased risk is not known, nor is it known whether in the event of encephalitis there is a synergistic or antagonistic action between the two different pathological processes.

7. Results

The results of 17D vaccine administered by scarification have recently been summarized, and they will not be discussed further, other than to consider the meaning of "inconclusives". In the reports of Cannon and Dewhurst the percentage of inconclusives in pre-vaccination surveys compared with the percentage in the post-vaccination results showed a change which was insignificant compared with the change in the percentage of "negatives" and "positives". It is suggested that the easiest interpretation of this fact is that sera which were immune and non-immune, in the neutralization test contributed a similar percentage of themselves towards forming inconclusives. If this was the case, then, when most of the sera were positive as in the post-vaccination studies, most of the inconclusives in the test were derived from what were really immune sera.
Nevertheless, however "inconclusive" may be interpreted, there is little doubt that in its present stage of development vaccination by cutaneous scarification with 17D virus succeeds in producing immunity, as shown by neutralization tests, in a lower percentage of those vaccinated than does vaccination by subcutaneous injection or vaccination with the Dakar Vaccine by cutaneous scarification.

8. Reactions

No serious reactions have been recorded.

9. General considerations

The advantage that the 17D scratch vaccine is derived from a strain of virus that is relatively safe must be balanced against the disadvantage that the vaccine is slightly less efficient than other already established vaccines. The most beneficial way of using the vaccine would in large scale campaigns be for the production of "herd immunity", for which purpose it would seem in many respects highly suitable.
REFERENCES

3. Dick, G. W. A. (1952) Amer. J. Hyg. 55, 140
5. Dick, G. W. A. & Horgan, E. S. (1952) J. Hyg. (Lond.) 50, 376
7. Hahn, R. G. (1951) Amer. J. Hyg. 54, 50
10. Meers, P. D. In press