PRELIMINARY REPORT ON TRACHOMA VACCINE

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After the isolation and culture of the Jane Furse strain[1] of trachoma virus in South Africa in 1959, the trachoma unit* set about preparing inactivated and live vaccines, the latter according to a method devised by Dr. B. Wolstenholme, under the direction of Dr. J. H. S. Gear at the South African Institute for Medical Research.

This paper reports experiments on sighted human volunteers and a field trial with live vaccine. The results of experiments with baboons and laboratory studies will be published later.

The results add support to the hopes expressed by Bietti,[2] Collier,[3] Grayston,[4] Mitsui,[5] and their collaborators, that a vaccine will prevent, suppress and cure trachoma.

HUMAN VOLUNTEERS

In 1959 the first volunteer developed acute trachoma[6] 3 days after the upper tarsal conjunctiva of his left eye had been rubbed with a 1-in-5 suspension of yolk-sac virus, thus confirming the identity of the isolated virus.

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The second volunteer was inoculated in 1960 with a vaccine prepared from a formalized suspension of virus. He developed weak neutralizing and complement-fixing antibodies. However, when challenged with an inoculum rubbed on the tarsal conjunctiva—a swab dipped in a 1-in-5 suspension of yolk-sac virus—he developed acute trachoma after an incubation period of 3 days, the same as the first volunteer, who was re-infected at the same time (6 months after his first infection had been cured), and the same as a third (control) volunteer.

In 1962 the first volunteer was given 3 injections at monthly intervals of 1 ml. of a suspension of live yolk-sac trachoma virus, of which the EID_{50} was 10^{-3}. Traces of complement-fixing antibodies developed, and his serum protected eggs from infection. After it was established that a 1-in-300 dilution of cultured virus would constantly infect eggs, this dilution was rubbed into the tarsal conjunctiva of the right eye to challenge his immunity. On the 3rd day he developed a transient hyperaemia of the right tarsal conjunctiva, which subsided within a week and did not recur. Virus was isolated from the right eye

on the 22nd day, but neither before nor after. On the 10th day he complained of temporary watering of the other eye and, although there was no hyperaemia, virus was recovered from the left eye on the 10th day, but not on subsequent attempts. This was probably a cross-infection.

Both eyes remained well without treatment for 8 months, and blood samples continued to show traces of complement-fixing antibody.

In May 1963 the right eye was again infected with a 1-in-300 dilution of virus, and the left eye with a 1-in-200 dilution. The upper tarsal conjunctiva of each eye became congested on the 3rd day, but the hyperaemia was fading by the 7th day, and had disappeared by the 13th day. The limbus was not affected.

One may tentatively conclude that the live vaccine enabled the volunteer to suppress an infection with TRIC virus of the Jane Furse strain in its 39th passage, and that the effect has lasted so far for 8 months.

The effect of a 1-in-200 dilution on a control has not been studied.

FIELD TRIAL NEAR JOHANNESBURG

Two kindergarten schools were selected, each having 100 African native children from 2 to 4 years of age in the baby class. Vaccine was given at one school, Entokozweni, and the other, Thabisong, was the control. Only one case reacted adversely to the vaccine (with an urticarial rash after the second injection).

The children were examined every second month from March 1962. Initially about 15% in each school were found with some abnormality of the tarsal conjunctiva. Attendance was erratic, and usually only 70 of the 100 were present, but most of the children were seen on 6 of the 8 visits.

The abnormalities found in the tarsal conjunctiva were follicles and/or hyperaemia, and these were given a value of 1, 2 or 3, according to whether they were mild, moderate, or severe (most were mild). If hyperaemia was fading or in its earliest stage, 1/2 was recorded. A hand slit lamp × 10 was used, and limbal changes were seen in only one case.

The fringe of limbal pigment makes the recognition of pannus difficult, but the general absence of pannus was confirmed by examining 14 of the worst cases in a dark room with a Zeiss biomicroscope.

At first, virus culture was attempted from *all* children, but not one of 62 normal cases yielded trachoma virus. Thereafter, virus culture was attempted as a routine only on cases with hyperaemia or follicles.

On an average visit one saw 70 cases, of whom 10 were abnormal and trachoma virus would grow from 2 or 3, but not always the same 2 or 3, although clinically the cases were unchanged.

After the relatively unchanging pattern of the tarsal conjunctivitis had been established, 81 children at Entokozweni were given 2 ml. of vaccine in 3 subcutaneous doses (usually 0·5, 0·5, 1 ml.) between June and September 1962.

In the 6 months after November there were 4 fresh proved cases at the control school, and none at Entokozweni. Moreover, there was an increased severity of the pre-existing cases at Thabisong, whereas at the vaccinated school there was a lessened severity.

With such numbers, it might have happened by chance that fresh cases occurred at one school but not at the other; but the indications are that the vaccine prevents infection. However, it will require many years to establish whether the vaccine gives full protection, and for how long.

Regarding the clinical improvement, and considering only the cases from whom virus was isolated, the 5 at Entokozweni totalled 7 points before vaccination and three months after vaccination, whereas the 7 at Thabisong changed from $6\frac{1}{2}$ to $12\frac{1}{2}$.

Professor Kerrich kindly submitted the individual figures to standard statistical tests, and found that the difference was significant.

Six months after vaccination 4 of the 5 at Entokozweni were cured, and one had improved; and of the controls 6 remained the same or became worse, and one healed spontaneously. Furthermore, virus was isolated from none of the vaccinated cases in February or April 1963, while it was recovered from 2 of the control group in February, and from 3 in April. These findings support the tentative conclusion drawn from the human volunteer experiment that the vaccine suppresses and cures trachoma.

The results from these schools will be followed up for many years, and each new entrant will be vaccinated at Entokozweni; but the real challenge is in the Northern Transvaal, where trachoma is a blinding scourge, and not the mild disease of the townships.[7]

SUMMARY

1. After vaccination with live trachoma virus a human volunteer suppressed infection with a 1-in-300 dilution of cultured virus, and 8 months later with a 1-in-200 dilution.

2. Six months after the vaccination of 81 African children there was clinical cure in 4 of 5 established cases of trachoma among them and no further virus isolation, compared with 6 of 7 control cases which continued to yield virus and clinically worsened.

3. After vaccination there were 4 fresh cases of trachoma at the control school in six months, and none at the vaccinated school.

4. One case of urticaria was the only complication encountered in 81 children given live vaccine extracted from eggs.

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