PROBLEMS RESULTING FROM THE USE OF LIVE ATTENUATED POLIOMYELITIS VIRUS TYPE I IN A MASS CAMPAIGN IN A LARGE URBAN AREA

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It was only after the experimental work of Enders, Weller and Robbins,[1] who, in 1949, were successful in artificially cultivating (in various human embryonic tissues) the poliomyelitis virus, that the feasibility of developing a live attenuated virus for the purposes of human immunization became a reality.

The success of Salk and his collaborators[2] in producing a formalin-killed virus of all 3 strains of poliomyelitis, which was antigenically active in monkey and man, are sufficiently recent and have received sufficient world-wide publicity to require no further mention at this stage.

While all virologists are satisfied that the Salk vaccine has played a very important part in preventing the onset of paralytic poliomyelitis in those individuals who have received a full immunization course, they are, nevertheless, disturbed by the fact that the formalized killed virus present in the Salk vaccine, although effective in blocking the invasion by virus of the central nervous system, did nothing to protect the alimentary cells from further invasion by wild strains of the poliomyelitis virus. As a result of the multiplication in these cells of wild poliomyelitis virus, the individual (although rendered reasonably safe from paralytic episodes) nevertheless became a carrier and could be responsible for infecting susceptible individuals.

It was as a result of these deficiencies and the fact that, on general principles, the best hope of developing a really effective prophylactic agent against poliomyelitis was by the development of an attenuated live virus, that Koprowski, Cox, and Sabin continued their experimental work on the development of such a virus.

Sabin appears to have been more successful in the cultivation of a satisfactory avirulent attenuated live virus, as proved on monkey testing, than either Koprowski or Cox. After intensively studied small-scale experiments in man, Sabin's attenuated live virus was accepted by the Russian medical authorities who, over the last 18 months, have successfully immunized over 60 million persons in the USSR against all 3 types of poliomyelitis, without any harmful effect.

These favourable reports by the Russians[3] on the use of the Sabin oral vaccine have, to a very great extent, influenced the Western world in their acceptance of the safety and satisfactory immunizing powers of the vaccine in question.

Our own Poliomyelitis Research Foundation in Johannesburg, under the able directorship of Dr. J. H. Gear, was not slow in realizing the possibilities in this country of the use of live attenuated poliomyelitis virus, and commenced cultivating and reaping the 3 strains of Sabin virus during 1957 (personal communication).

The opportunity to use Type I vaccine occurred in 1959 as a result of the occurrence of epidemic poliomyelitis in the island of Mauritius. Practical and field experience gained in that outbreak, when over 200,000 persons were fed, provided the answer to the safety of the local product.

In October - November 1959 an unusually early, high, seasonal incidence of paralytic poliomyelitis manifested itself in the Cape Western Province — features which in the past had always been associated with the occurrence of epidemic poliomyelitis in the midsummer and early autumn months.

As a result, a meeting of senior medical staff of the Universities, Union Health Department, Cape Town City and Cape Divisional Councils, and the Poliomyelitis Research Foundation, respectively, was convened in Johannesburg with a view to discussing the practicability and feasibility of the release of the live attenuated vaccine in this area of the Union.

As the number of poliomyelitis notifications from Greater Cape Town at this stage (early December) showed evidence of falling, the representatives of the two large local authorities concerned advised against release.

This viewpoint was further influenced by the fact that a marked movement of population in this area (due to the breaking-up of schools and the influx of holiday makers) seemed likely to create insurmountable administrative and practical difficulties in the initiation of a successful campaign; and, even were this to prove successful, the likelihood of a high percentage of successful 'takes' in susceptible persons could not be expected owing to interference in the alimentary tract by other enteroviruses which are all very much more active during this period of the year (summer). In addition, it was felt that the psychological effects on the holiday population of the news of such release in this area was likely to have had far-reaching repercussions on the tourist industry.

Because of technical information supplied to us at this meeting on the results obtained in other countries following the use of live attenuated virus, we in Cape Town were in the very fortunate position of having been able, for some considerable time, to give both conscious and subconscious thought to the planning of such a vaccination campaign. Thus, when the vaccine was eventually released

by the Union Health Department in October 1960, our Department was administratively fully geared and prepared to embark immediately on a short and intensive programme — which is all-important when using this particular type of vaccine.

Full publicity was given in the lay press over a period of several months to the great advantages attaching to the use of this vaccine, while our medical colleagues were kept informed by private circulars and articles in the medical press. The success of this campaign can, in no small measure, be ascribed to the whole-hearted support afforded us by our many colleagues in general practice. To them we are most grateful.

The need for adhering to strict temperature requirements in the storage and handling of the vaccine, so as to maintain potency, made its release through the general practitioner wellnigh impossible, and as a result the Union Health Department decided to make it available to only those large local authorities which had the staff and the necessary facilities for controlling these factors.

Apparatus

Although advice contained in circulars from the Union Health Department, which emanated no doubt from the Poliomyelitis Research Foundation, strongly recommended the use of a semi-automatic filling type of syringe (which delivers to the back of the throat a fixed and given quantity of vaccine), we considered the use of such a piece of apparatus impracticable in so far as our preschool and school-going groups were concerned. As these were the groups which we wished to immunize as fully as possible, it was decided to use an absorbent type of palatable sweet on to which a definite measured amount of vaccine could be dropped. In association with one of the local sweet manufacturers we were successful in obtaining just such a vehicle. The campaign owes its success in no small measure to the use of these sweets for the administration of the virus.

For babies under 1 year, Syrup B.P. was used, and the measured drop of vaccine was added to half a teaspoonful of this syrup.

The maternal and child welfare branch of this local authority has always been charged with the responsibility of carrying out the vaccination and immunization programmes against infectious diseases and, as a result, this branch was considered to be the most suitably organized and capable unit for carrying out the campaign in regard to the use of the oral attenuated poliomyelitis virus.

DILUTION OF VACCINE AND STORAGE

As the Poliomyelitis Foundation had indicated that vaccine would be dispatched to local authorities in 10 ml. vials, each containing 1,000 doses, it was decided that the principal pharmacist at the City Infectious Diseases Hospital should be responsible for collecting the frozen vaccine on its arrival by air or rail, and storing it in his dispensary in a deep-freeze cabinet.

To him, also, was allocated the responsibility of diluting the vaccine and packing it into suitably sized bottles, which were then deposited in wide-necked thermos flasks, containing cube ice, preparatory to its collection by members of the maternal and child welfare branch for distribution to those centres where clinic sessions were due to take place during the day in question.

It became necessary to obtain specially manufactured pipettes which were so constructed as to deliver exactly 0·1 ml. of vaccine in the form of a drop.

In carrying out the dilutions of concentrated vaccine, it is necessary to have available the following:

1. Cold sterile normal saline containing *no bacteriostatic substances*. Such saline should preferably be refrigerated for 24 hours before use.

2. A sealed sterile syringe — 50 ml. capacity.

3. Two sterile needles — one for aspirating the concentrated vaccine (size 19.g × 1½ inches), and one as an air vent (size 24.g × 1 inch).

4. Cold sterile dropper bottles of amber or green glass (capacity, 2 oz.).

In preparing the diluted vaccine, a phial of concentrated vaccine, which is frozen solid, is permitted to thaw out by immersion under the *cold* water tap. The cap is then pierced with the air-vent needle and 5 ml. of the concentrated vaccine drawn up into a 50 ml. syringe containing 45 ml. of sterile cold saline. The contents are expelled into the sterile 2 oz. dropper bottles and gently shaken until well mixed. This dropper bottle will now contain 50 ml. of a 1 : 10 dilution of vaccine, of which a dose will be 0·1 ml. — or 1 drop from the specially manufactured pipette.

As the vaccine contains no preservative, rigid asepsis must be practised throughout the process of dilution.

Unused concentrated vaccine, together with the diluted vaccine, must be immediately replaced in a deep-freeze, and retained there until required for further diluting, or in the case of diluted vaccine, for use.

The bakelite cap of the dropper-bottle containing diluted vaccine should be slightly loosened so as to avoid possible cracking of the glass as the result of the deep-freeze process.

METHODS EMPLOYED AT CLINIC SESSIONS

The groups particularly at risk are preschool children, school-children and young adults, in this order.

In so far as the first and last-named groups were concerned, all-day sessions at child welfare centres or local halls gave good results, mothers attending throughout the day with their families, and many fathers bringing their wives and children after work. Young adults attended first thing in the morning, during the lunch hour, and after 5 p.m. Many businesses and factories sent their entire staff in batches during working hours. Schoolchildren were most expeditiously immunized at school with the help of the principal and teachers, consent from the parents having been obtained in advance.

Record-keeping involves extra work, but is very necessary for any sort of follow-up or assessment of the value of the procedure. Records were kept for preschool children and for schoolchildren, but not for adults since they are better able to give an account of themselves. School record cards were filled in by the school staff or the pupils themselves. The vaccine was administered by nursing staff, under medical supervision. Clerical work was done and general assistance given by V.A.Ds. and other voluntary helpers.

Schools can be dealt with rapidly, provided their cards are filled in and the classes are ready to follow on without delay. In such circumstances 2 workers can complete a school of 400 pupils in half an hour. Thus, where there are a number of large schools in an area, 2,000 - 3,000 pupils can be immunized in a morning. With smaller or more scattered schools more time must be allowed to cover travelling and setting out of equipment.

Preschool sessions, at which adults are also catered for, must be preceded by adequate advertising in the press and by propaganda in child welfare clinics and by health visitors.

In a large hall with 3 nurses and 5 lay helpers, 3,000 - 4,000 persons can be immunized in a one-day session without undue crowding or strain on the staff. In smaller premises, with 1 nurse and 2 lay helpers, up to 1,000 persons can be immunized in a one-day session without difficulty.

The equipment carried (in addition to the flasks containing vaccine bottles packed in ice) should consist of sweets, corresponding to the number of doses of vaccine carried, syrup in convenient bottles, teaspoons (3 doz. for a large session), a sterilizer or other apparatus for boiling the spoons, trays on which to place the sweets, and small bowls in which to place the bottles of vaccine, surrounded by ice while in use.

Syrup and teaspoons are not needed at schools.

Record cards and sheets for counting the total number receiving vaccine according to age groups must be provided for the lay helpers.

Sweets are best arranged on trays in rows of 10 or 20, and *should not be dosed with vaccine in advance of the demand*.

When using a dropper pipette, care must be taken to hold the pipette vertical, ½ inch above the sweet or syrup. Medical supervisors found, time and again, that certain nurses, in spite of a preparatory demonstration, were holding the

vaccine pipette at an angle of 45° and allowing the drop to touch the sweet. This resulted in the vaccine being drawn on to the sweet by osmotic action, unnecessarily increasing the dose given, and thereby adding to the cost.

The vaccine in the bottle must be completely thawed under *a cold tap* before use. During use the bottle should stand in ice, either in a bowl or thermos. At the end of a session, unused vaccine can be returned to deep freeze, but should be used as the first issue the following morning. Partly-used diluted vaccine should not be issued when it is older than 48 hours.

PROBLEMS ENCOUNTERED IN THE VACCINATION CAMPAIGN

Good publicity is essential to the success of any campaign. In our experience insufficient time for clinic and home propaganda, and a poor press at the start of the campaign, resulted in fairly empty clinics at the commencement, followed by almost unmanageable crowds at the end of the campaign.

Estimation of staff requirements was difficult, and transport had to be available to switch assistants from one centre to another as required.

The same difficulty was encountered with regard to the vaccine, since it is not desirable to take more than necessary out of the deep freeze. At the end of each day a survey of the amount of unused vaccine and the probable requirements for the next day had to be made. Transport had to be available to take fresh stocks of vaccine to centres which were running short.

REACTION OF THE PUBLIC TO THE CAMPAIGN

The reaction of the public was very satisfactory, judging by the total figure of 216,910 persons immunized out of a population of 569,990 (197,810 Europeans and 372,180 non-Europeans). The numbers in the various age and racial groups were as follows:

Preschool children	13,257 Eur.	38,204 Non-Eur.
Schoolchildren	35,678 Eur.	62,252 Non-Eur.
Adults	30,589 Eur.	36,930 Non-Eur.
Total	79,524 Eur.	137,386 Non-Eur.

The number of preschool European children fed was not as high as hoped. This might be explained by a certain hesitancy encountered at first among some of the European population of a 'wait-and-see' attitude rather than any antagonism to the vaccine.

A considerable number of European parents refused to sign consent forms for their children to be immunized at school, but later changed their minds and brought them to the general clinic sessions.

CONTRA-INDICATIONS TO THE USE OF THE VACCINE

Vaccine was not given to infants under 4 months of age, on the assumption that maternal antibodies would reduce the likelihood of a successful take.

Vaccination was not encouraged in people over 40, but was made possible for those specifically requesting it.

Pregnancy was not considered a contra-indication, since pregnant women are particularly at risk.

Vaccine was withheld from persons suffering from gastro-intestinal upsets, those with severe colds, or anyone who was out of sorts or running a temperature.

COMPLICATIONS REPORTED

Several reports were received from private practitioners, parents, and school teachers of a variety of conditions attributed to the vaccine, and wherever possible these were followed up.

A child of 18 months was admitted to the City Infectious Diseases Hospital with a history that it had received a dose of vaccine a week previously, and since then had been unable to walk. This child was diagnosed to be suffering from post-varicella encephalitis.

Transient paralysis and muscular pains were the commonest complaints, but not a single case of muscle weakness or absent reflexes in those seen and examined was found. Many persons complained of a sore throat — an entity which was prevalent at the time.

Auto-suggestion undoubtedly played a part in many instances. For example, a young school teacher developed weakness in both legs the evening after being fed the vaccine, followed thereafter by droopiness and weakness of her eyelids.

Dizziness and headaches were reported by a number of adults, and appeared to be more definitely related to the feeding of vaccine than the transient complaints of unconfirmed muscle weakness.

Four cases of allergic skin eruptions were reported and investigated. Two of these had widespread papulo-urticarial lesions, and 2 had a mild urticaria. All were subject to attacks of urticaria and developed these attacks within a few hours of taking the vaccine.

Random Sampling of Preschool and School Population

In order to obtain as fair a picture as possible of the incidence and type of reaction (if any) to the vaccine, random sampling of the preschool and school-going groups was carried out. As record cards for all members of these groups, both White and non-White, were available, it was decided to abstract approximately 250 for each racial group falling into the preschool and school-going groups, i.e. a total of 1,000 cards from the whole batch. Fortunately the cards had not been sorted and, in order to use as far as possible a random sample, a card was abstracted at the beginning of a pack and then at various points, depending on what group was being dealt with, until the requisite number had been obtained. Owing to some slight miscalculation a total of only 931 cards, as listed below, was extracted in this way. The named individuals were then visited with a view to obtaining from the parent or the child itself, or the school teacher, information on any relevant and untoward effect occurring during the period 2 weeks following the ingestion of vaccine.

Preschool children	European	230
	Non-European	215
Schoolchildren	European	234
	Non-European	240
Adults (teaching staff)	European	9
	Non-European	3
Total		931

Of these persons, 30 could not be traced, either because an incorrect address had been given, or because the dwelling was locked when visited or re-visited.

Of the remainder (901), 808 had been perfectly well, and 20 had developed illnesses obviously unrelated to the vaccine, e.g. tonsillitis, pneumonia, epilepsy.

The remaining 72 (8% of sample) had complaints which might have been reactions to the vaccine. Nausea, vomiting and diarrhoea occurred in 32 recipients; 26 of these developed gastro-intestinal symptoms within 3 days of being fed the vaccine, while only 6 developed these symptoms over the rest of the fortnight. Most of these diarrhoeas, grouped in this way, could be presumed to be due to a mild virus infection. There were more schoolchildren in this diarrhoea group than preschool children, which is not the usual picture in summer diarrhoea.

Headache, mild pyrexia, and general malaise were reported in 26 cases. These symptoms were accompanied by dizziness in 6 cases, all occurring within 3 days of taking the vaccine. Only 2 cases of headache were reported as occurring after the third day.

Backache and other muscular pains were reported in 8 cases as having occurred on the second or third day after taking the vaccine.

One case of papular urticaria was discovered in this sample. The child developed the eruption a few hours after taking the vaccine and the rash persisted for 2 days.

CONCLUSIONS

The campaign was successfully conducted for the age groups at risk, and the vaccination has proved to be perfectly safe, in that no cases of paralytic poliomyelitis occurred amongst the 217,000 persons treated.

From the date on which the vaccination campaign was

started, until the end of the first week in January 1961, 7 cases of paralytic poliomyelitis were notified in the Municipal Area of Cape Town and were admitted to the City Infectious Diseases Hospital. Stool typing was carried out in 4 of these cases. In none of them was paralysis due to Type I virus.

Minor upsets, manifesting themselves as nausea, diarrhoea, general malaise, muscular pains and dizziness, occurred in 8% of the random sample of persons immunized. These upsets were very mild and nearly all occurred within the first 3 days after vaccination.

Skin allergy — presumably due to the protein in the medium — was an occasional finding.

SUMMARY

The history of the introduction of the Sabin oral poliomyelitis vaccine is outlined, leading up to its release in South Africa.

Details of the running of the immunization campaign in Cape Town in October - November 1960 are given, including technical details regarding the handling of the vaccine.

Complaints of muscular weaknesses allegedly due to the vaccine, and the findings that these so-called reactions were due to some intercurrent cause or were imaginary, are referred to.

The follow-up history of a random survey of 901 preschool children and schoolchildren, including the teachers, are set out. This reveals the association of a mild gastro-intestinal or general reaction, including headache, in 8% of this sample.

We would take this opportunity of offering our very grateful thanks to the health visitors of the maternal and child welfare branch and to the many voluntary helpers for the manner in which they executed their functions in the successful completion of this mass campaign.

We also wish to record our very sincere thanks to Mr. J. S. Linley and his staff at the City Hospital Dispensary, who were responsible for diluting and packing the vaccine for use at the many centres.

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