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LIVE-VIRUS POLIOMYELITIS VACCINE

During the past five years great progress has been made in many countries in the nation-wide use of formalin-inactivated poliovirus of the Salk type as a preventive vaccine against paralytic poliomyelitis. South Africa has not been behindhand in this campaign, and the Poliomyelitis Research Foundation Laboratories of the South African Institute for Medical Research, under the direction of Dr. James Gear, have served the country well in the large-scale manufacture of a vaccine of this type and taken an honourable place as compeers in this field amongst laboratories throughout the world. The protection afforded by these vaccines has proved satisfactory; substantial decreases in the incidence of paralytic poliomyelitis have been noted in countries where large groups of the population have been vaccinated. Nevertheless, it has been generally considered that the vaccines consisting of poliovirus killed with formalin are not so completely effective as the vaccines that are available, for instance, against smallpox and yellow fever—both of them attenuated live viruses—as judged by the proportion of vaccinated subjects who receive complete immunity and by the probable duration of the immunity.

Accordingly, workers in different parts of the world have devoted themselves to research designed to find ways of so attenuating the neurotropic power of poliovirus as to produce a live-virus vaccine that would give as good results as the yellow fever and smallpox vaccines and (like formolized poliovaccine) with as little danger to the vaccinated person and the community. These efforts have met with success, and in different laboratories attenuated polioviruses of all three strains have been elaborated which possess only minimal neurotropism for monkeys and which, given by the mouth, multiply in the alimentary canal of human subjects, leading to the formation of antibodies in the same way as natural infection with poliomyelitis. It has been found that the temporary intestinal infection produced by the live virus results in a local immunity of the intestine which makes it impossible to reinfect with the homologous strain of poliovirus. Since man is the only host of poliovirus this raises the hope that poliovirus (and therefore the disease poliomyelitis may, like smallpox, disappear entirely from a fully vaccinated community. This response is not produced by the Salk vaccine, which does not prevent intestinal infection, but by producing humoral antibodies prevents paralytic complications.

In most countries the large-scale use of live vaccine has been held back by a widely-expressed fear that in the course of *passage* a retrograde mutation might occur in the attenuated virus causing it to regain its neurotropic properties and its power to produce paralytic poliomyelitis. When used as a vaccine the attenuated virus is taken by the mouth and gives rise to a non-paralytogenic infection of the bowel, with excretion of the virus in the stools and possibly from the nose and throat. This excretion, behaving like that of other enteric infections, is known to lead to a spread of the non-paralytogenic virus to contacts. For instance, in a limited trial in Louisiana, USA, it was found that amongst people at a low social and economic level 51 per cent. of household contacts were infected (though amongst people with a higher level of hygiene infection occurred in only 8 per cent.). The fear was that, in consequence of mutation, such infection of contacts might eventually assume the form of virulent poliovirus. It was based on actual observations in which the virus excreted by vaccinated persons was found to be more neurotropic for monkeys than the original vaccine virus. However, it has been found that no further increase in neurotropism takes place as the result of *passage* through a series of human beings, nor have these fears been substantiated in the actual use of live attenuated vaccine.

In 1957 the WHO Expert Committee on Poliomyelitis strongly urged that controlled field trials of live vaccine should be undertaken on a considerable scale under expert supervision but, recognizing that its use was then in the experimental stage, they made no final pronouncement on the relative merits of the two types of poliovaccine or the parts they should respectively play in nation-wide immunization. Such trials were carried out in several countries, first on small groups of people and then on a larger scale, with various attenuated vaccines, particularly the Sabin, the Koprowski and the Lederle vaccines. An account of 20 vaccination campaigns, in 15 countries, has recently been published.

In the USSR, where in 1956 the Sabin attenuated vaccine had been studied in monkeys, it was tested on limited groups of children in 1957 and 1958, and the USSR Ministry of Health then resolved to delay no longer but to embark on a nation-wide campaign with this attenuated virus. By May 1959 it had been given to several million children in various republics of the USSR, and by January 1960 to fifteen million persons. The campaign is still in progress, and it is intended to vaccinate another 60 million people by the end of the year. Large campaigns are also in progress in Poland, with the Koprowski vaccine, and Czechoslovakia, with the Sabin vaccine. It must therefore be recognized that the use of live-virus vaccine has progressed beyond the experimental stage.

The details in this article about the Soviet scheme come largely through Dr. Dorothy Horstmann, Associate Professor of Preventive Medicine and Pediatrics, Yale University, USA, who visited these countries on behalf of the WHO in August - October 1959, spending most of the time in USSR. At first the Sabin attenuated poliovirus strains were given serially (first type 1, then type 3, then type 2), but when it was found, in Lithuania, that it made no difference to the results a simultaneous triple vaccine was used. For each district frozen vaccines sufficient for several days' work is sent to a central town, from which the teams go out every day carrying the vaccine in iced thermos flasks. According to Smorodintsev the vaccine contains 100,000 tissue-culture infective doses ($TCID_{50}$) per 0·1 ml. It is administered with a dropper. The local campaign is pre-

ceded by intensive publicity by radio, television, press and posters. In rural areas the vaccinating teams consist of trained auxiliaries and nurses under medical supervision. It is emphasized that this is a nation-wide vaccination and not a controlled trial. There are no control groups, but before the vaccination began serological surveys were made of different age-groups in the population to determine their immunity status. 'Professor Horstmann concludes that the attenuated live vaccines used appear to have been safe, both to those vaccinated and to the communities in which they live, for at least the six-month period during which surveillance was carried out'. (She reports that this surveillance was efficient.) 'The fall in the number of cases suggested that the vaccine is effective, although the absence of a controlled trial makes it difficult to gauge its effectiveness accurately'.

We have not seen figures reflecting the effect of vaccination in the USSR on the incidence of paralytic poliomyelitis, but favourable results in this respect have been published from other countries, as well as favourable serological data. For instance, amongst 7,000 children in Minnesota vaccinated with successive oral doses of the three types of attenuated vaccines, of those serologically negative before vaccination '91 per cent. responded to the administration of type 1, 72 per cent. to type 2 and 87 per cent. to type 3'. It is believed that the smaller percentage of responses obtained in certain vaccinated groups is the result of prior infection with allied enteroviruses which interfere with the development of immunity to the poliovirus ('interference phenomenon'). The *WHO Chronicle* of April 1960, from which much of the information in this article (and the quoted passages) are drawn, states: 'It remains difficult to assess the results of vaccination campaigns, particularly if a statistically valid verdict on efficacy is required. Such assessments are at present based above all on qualitative comparisons. . . . However imperfect the trials of the live vaccines made so far, nothing has arisen to suggest that it is not harmless, or to throw doubt on its effectiveness once the organism has responded by producing antibodies and excreting viruses'.

As the result of research and community vaccination carried out in the last year or so, it appears that, except for the time factor, the volume of experience with live vaccine is now comparable in magnitude to that with the formol vaccine, and that there is now no reason to wait on further experiments before bringing the live vaccine into use. Representatives of South Africa will be attending the Fifth International Poliomyelitis Congress which will be held in Copenhagen this month. The South African Research Foundation Laboratories have prepared large stocks of live attenuated-poliovirus vaccine (which has recently been used on a large scale with no untoward results in Mauritius and in Kenya in cooperation with the British Colonial Office), and it is understood that , subject to the conclusions of the Congress, the authorities in South Africa are ready to bring it into use in the course of the present year.

World Health Organization (1960): *Live Poliovirus Vaccine* and *Live Poliovirus Vaccination in the USSR, Poland and Czechoslovakia*, WHO Chron., **14**, 137 and 142.
Editorial (1958): S. Afr. Med. J., *Poliomyelitis Vaccines*, 32, 885.

STELLENBOSSE BYDRAES

Soos ons alreeds by vorige geleenthede gedoen het, plaas ons in hierdie uitgawe van die *Tydskrif* sommige van die wetenskaplike bydraes wat gelewer is tydens die Derde Akademiese Jaardag van die Mediese Skool van die Universiteit van Stellenbosch en die Karl Bremer-Hospitaal, Bellville, Kp., op 8 en 9 Oktober 1959. Een van die bydraes wat by daardie geleentheid gelewer is, is alreeds gepubliseer[1] en die res sal omrede van hul meer tegnies-wetenskaplike aard geplaas word in die Junie en September uitgawes van die *Suid-Afrikaanse Tydskrif vir Laboratorium en Kliniekwerk*. Die gebruik om gereeld spesiale ruimte af te staan in die amptelike organe van die Mediese Vereniging van Suid-Afrika vir bydraes van hierdie aard, word dus hiermee voortgesit.

Een van die oogmerke van die organiseerders van dié jaardae is om in en om die hospitaal 'n akademiese atmosfeer te skep waaruit dosente, studente en die praktisyns in die buurt voordeel kan trek. Om hierdie rede moet dit beklemtoon word dat spesialiste sowel as algemene praktisyns by dié geleenthede verwelkom word. Hulle teenwoordigheid en deelname aan die vrae en besprekings wat gewoonlik op die lesings volg, kan 'n addisionele faktor wees om die omvang van die akademiese milieu van die geleentheid te verbreed. Die Vierde Jaardag van die Stellenbosse Mediese Skool sal vanjaar weer gehou word in die Burgersentrum, Bellville, op 8 en 9 September 1960.

Soos professor van Zijl[2] tereg aangetoon het kan die hoogste strewe van 'n moderne mediese skool alleen dan bereik word wanneer die wetenskaplike peil daarin hoog gehou word. Die geneeskundige wetenskap maak sulke snelle vordering dat, om in staat te wees om daarmee tred te hou en om daartoe 'n bydrae te kan lewer, die allergrootste klem op navorsing gelê moet word. Aan die ander, meer gevestigde, mediese skole in ons land het volwaardige navorsingseenhede alreeds ontstaan wat dit vir die onderskeie universiteite moontlik gemaak het om bydraes te lewer waarop ons professie en ons land trots kan wees. Dit is dus verblydend om te weet en te sien dat die jongste lid van ons mediese opleidingsinrigtings van die begin af die noodsaaklikheid van navorsingswerk so hoog beklemtoon.

1. de Villiers, J. P. (1959): S. Afr. T. Geneesk., 33, 1101.
2. van Zijl, F. du T. (1960): *Ibid.*, 34, 425.