Prof. Dr. J. D. Verlinde  
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Dear Dr. Verlinde:

Thank you very much for your most interesting letter of 17 September and all the trouble you have taken to let me know the results that you had obtained.

I was intrigued by some of the data and found it a little difficult to understand others. Perhaps I may take up the various points as they appear in your tables. In the first place, as regards multiplication of the type 1 virus I found it difficult to understand that virus was excreted by only 10 of the 15 individuals, whereas in table 2 it is indicated that antibody developed in all 10 individuals tested. Does this mean that only the 10 individuals who excreted virus are represented in this test, or does it mean that some of those who did not excrete virus nevertheless developed antibody? Somewhat later in your letter you remarked that the low percentage of alimentary infections due to type 2 might be due to a low concentration of excreted virus (less than $10^3$ TCD50 per gram). Does this mean that your test is so set up that you could detect virus in the stools when only approximately $10^3$ TCD50 per gram are excreted? When I inoculate tubes with 0.2 ml of a 10% extract of stools and use 5 tubes for the test a negative result indicates less than 10 TCD50 per gram. The same question seems to apply to the low incidence of excretion of type 2 virus among individuals who developed antibody. In my own studies I have never found any individual who developed antibody when he did not excrete virus. Furthermore, the amount of virus that I detected particularly in children, as shown in the enclosed table, exhibited peak titers of such an order that one would expect to demonstrate virus excretion with regularity particularly during the first 7 to 10 days. I do not use any serum in my tissue cultures and I wonder if something in the procedure that you might be using may render the detection of virus less sensitive.

I assume that the dose of virus that you fed was 0.1 ml of a 1:10 dilution. On page 2 of your letter you stated "I would be inclined to consider the low percentage of type 2 alimentary infections as a result of interference by the preceding and usually long lasting type 3 alimentary infection". In the 5 children that I tested in this manner, as shown in the enclosed table, there was not a single instance in which the type 2 virus failed to multiply when it was fed 3 weeks after type 3. In adults, however, I have occasionally encountered failure of multiplication of type 2 as in the case of [...], as
shown in enclosed chart, but here an examination of the sera suggested
that a very low level of antibody was actually present, possibly as a
result of a preceding infection with type 2 virus. Similarly the one
instance where type 3 multiplied very poorly when it was fed 3 weeks
after type 1 (see in the enclosed chart) there was also
evidence by the pH test of the presence of a small amount of antibody
suggesting a possible previous infection with this virus particularly
since this man possessed neither type 1 nor type 2 antibody.

The data obtained in your 7th family are indeed most intriguing
and are very reminiscent of the results obtained in the case of
and also in the other adult volunteers that I had encountered. On a number
of repeated tests during the past 3 years had no demonstrable
antibody for any of the 3 types of polio and yet when she was fed type 1 virus
simultaneously with all the other members of the family she was the only one
who failed to excrete any virus and also failed to develop antibody. Interest-
ingly enough the type 3 virus which was fed 3 weeks later multiplied exten-
sively in her over a period of at least 24 days and yet her blood, taken 8
weeks after the administration of the type 3 virus, also had no demonstrable
antibody by either the pH test or the cytopathogenic test indicating that she
developed antibody poorly to an established and extensive infection. There-
fore, I consider the possibility that some time in the past she may already
have experienced an infection with type 1 virus which rendered her alimentary
tract resistant without developing any demonstrable antibody by the tests
that are used. That she is capable of developing antibody, however, is
evident from the fact that she developed a fairly good level of type 2 antibody
to the type 2 virus that was fed to her 3 weeks after the type 3. The data
obtained with the -year old boy in family number 7 indicates a similar
situation, namely multiplication of type 3 virus without demonstrable anti-
body development. It will be interesting to see whether in your family number
7 the alimentary tract of the resistant individuals without antibody will continue
to be resistant even when larger doses of virus are fed. I have been waiting
for the summer to pass before feeding a larger dose of type 1 virus to

to determine what her reaction will be. In previous studies on a
volunteer whom I tested for antibody at frequent intervals and found that the
type 3 antibody disappeared between 8 and 12 weeks after feeding of attenu-
ated type 3 virus, it could be shown that his alimentary tract was resistant
to reinfection even when 100 times the previous dose of type 3 virus was
fed, i.e. when $10^6.5$ TCD$_{50}$ were administered. Evidence was thus
established that an individual may have a demonstrable infection for a
period of at least 4 weeks, develop a little antibody and then lose it and nevertheless have a resistance to reinfection of the alimentary tract. Whether this is also the situation in your family number 7 or whether we are dealing here with people in whom polioviruses may have greater difficulty in multiplying is the question at issue.

In the enclosed table you may also be intrigued to notice, as I was, that in general the children developed higher levels of antibody than their parents and that this was not necessarily associated with either a higher level of viral multiplication or longer duration of excretion. This is best brought out by examining the data for type 1 in the case of Mr. [redacted] and his 3 children. However, it does appear that the level of virus multiplication may frequently be somewhat higher among children than among adults.

The large lots of vaccine are now being bottled in 1 ml amounts by the Merck, Sharp and Dohme Company and there is still enough for approximately 2 million doses of each type. The vaccine will be stored in the frozen state in my laboratory and I shall distribute it to various investigators. I would appreciate it very much if you could let me know whether or not you have sent some of the vaccine to England as we had agreed in Geneva. I shall be able to send you more any time that you may need it.

Since my return from Europe my entire time has been occupied with the investigation of a very large epidemic of Echo 9 infection in Milwaukee. Although only about 200 patients were admitted to the hospitals with aseptic meningitis syndrome (90% of which was due to Echo 9) it was possible to show by a study of illnesses occurring in families that were not admitted to hospitals that many thousands of cases of Echo 9 infections were occurring simultaneously in the community. For example, during one week in August a survey was made in Milwaukee and one out of every 40 families was found to have one or more (usually 2 to 5) illnesses, some of them with rash. Stools obtained on 26 such families yielded virus isolates in 24 families (a total of 66 strains from 104 people) and 90% of these viruses were Echo 9. A similar study in families without illness at that time failed to yield Echo 9 virus except in one instance where illness developed subsequently. A rough estimate would suggest that the number of febrile illnesses caused by Echo 9 virus during that one week in Milwaukee was probably close to 10,000 - and the epidemic had been in progress for 8 weeks prior to that time and is still in progress now. Almost all of the strains that we have isolated have proved to be antigenically related but definitely different from the prototype Echo 9 virus.

* A total of 2440 families were visited by 110 public health nurses.
I would be very much interested to know whether the Echo 9 viruses you recovered in Holland in 1956 were antigenically very similar to the prototype virus - that is to say whether the prototype antiserum neutralized your viruses roughly to the same extent as it neutralized the prototype.

When I spoke to you in Geneva you told me that you had isolated Echo 9 virus from the medulla of a fatal case. Since then I think Dr. Melnick told me that you had found that the amount of virus in the medulla was in the range of $10^5$ to $10^6$ per gram. I would very much appreciate it if you could let me know if that was actually so and what the details of this fatal case may be.

Thank you very much for keeping in touch with me and for letting me know the results of your interesting studies.

With best wishes and kindest personal regards,

Sincerely yours,

Albert B. Sabin, M. D.

ABS: meh

Enclosure: Table.