SUMMARY AND REVIEW OF POLIOMYELITIS IMMUNIZATION

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I wish I had the elegance of expression to discuss adequately the excellent foregoing studies on poliomyelitis immunization. Although the basic contents are familiar, the details presented were entirely new, so that I was cold, too, on receiving them. It is difficult to take a position of critic with respect to the material because each writer has so completely built his protective fence by labelling much of his discussion speculation. But then I can feel free to indulge in speculation, too.

Doctor Koprowski has fortunately provided a fine text with his references to Bertrand Russell and Aristotle. It happens that I recall, too, that in one of his *Unpopular Essays*, Russell pointed out that we frequently remember a man for the brilliant sayings ascribed to him and forget many of his absurdities. Despite his other brilliance, Aristotle, according to Russell, belonged to the group that believed that women had fewer teeth than men, whereas all he needed to do was to look in Mrs. Aristotle's mouth and make an observation. This serves only to emphasize that, however deeply we may be impressed by our opinion, the evidence gained by putting the thesis to test is, in the end, the deciding factor.

This may be, however, an appropriate time to consider the concepts involved in the two approaches to immunization against poliomyelitis that are represented in the data contained in the papers presented in this monograph. We grow accustomed to muddied water, just as the cryptobranchs do, but one may try to look at the situation clearly in terms of the immunologic principles involved.

One approach follows the argument that good immunization against virus infection can be attained only by modified infection, and it offers, as support, the statement that the two most effective vaccines are those against smallpox and yellow fever. This is a two-case generalization that deserves some scrutiny. First of all, the pathogenesis of the diseases must be considered. In the case of yellow fever, there is no evidence that inactivated virus will not induce good immunity in man, and, because of the viremic character of the illness, I would wager that it could. Furthermore, proper gamma globulin would probably protect. Measles and hepatitis are outstanding invitations to vaccination with inactive virus by virtue of the extensive evidence that antibodies furnished by gamma globulin are highly protective. The studies of Kempe with gamma globulin in the prevention of small pox again indicate that infection is not a requisite for protection. Similarly, the ready demonstration of protection of experimental animals against poliomyelitis by gamma globulin, as well as the field studies of Hammon and his colleagues in man, again support the concept that antibodies alone can prevent this disease.

The two outlooks are, then, simply this: inactive virus vaccine is apparently a test of the straightforward hypothesis that antibody induced by the adminis-

tration of antigen can provide protection without subjecting the recipient to harmful effects of even the inapparent infection. The other, through the use of modified active virus, seeks to induce antibody formation, but wishes to add some undesignated advantage derived from assumedly harmless infection (I am not certain that any significant infection may not create undesirable tissue reactions). The solidity of immunity after natural infection is quite apparent with certain virus diseases. With others, its impermanence is illustrated by recurrences without added infection. The advantages of infection have been variously ascribed to tissue immunity, persistence of immunogenic virus, and increased or widely dispersed dosage, and the latter seems perhaps the most important.

One is bound to be influenced by his background and experience. Influenced by one of our early studies that demonstrated the capacity of purified pneumonococcus polysaccharide to induce specific immunity in man, I favor an immunologic outlook which would avoid infection and seek the active immunizing principles. This, I think, is the line of future immunologic advance rather than to create an inapparent infection that appears harmless, perhaps only because we are working at such a gross level for detection of injury.

I might point out that our first studies with influenza vaccine were made by injection of active virus, later with inhalation of active virus. The evidence changed our approach because we obtained better results with injection of inactive virus than by intranasal administration of active virus.

Which of these approaches to poliomyelitis will be the more effective is, then, not a decision to be arrived at by authority and debate, but by looking in Mrs. Aristotle's mouth and really making the observations. When the conditions are appropriate, tests should be made. This is the beginning, not the end. Continuing studies on all these lines are highly desirable, and conclusions will be based on the evidence obtained, not upon the weight of opinion.

There are a few comments relating to specific data we have seen. It is apparent that circulating antibodies of significant level do not prevent alimentary infection with poliomyelitis virus. Hence, natural reinforcement is not prevented. Diphtheria is a striking example of the fact, however, that prevention of active disease reduces the reservoir but does not necessarily eliminate the organism. Doctor Sabin's data indicate that intramuscular inoculation of his modified agents requires just about as much active virus to induce antibodies with regularity as is required with inactive virus. If there is no multiplication and the route is not the "presumed" natural one, one wonders what advantage this can have over well-prepared inactive material. Doctor Koprowski, in listing his optimal requirements of active virus for immunization by the alimentary route, stated that it should not be detectable in the feces after feeding. Does this mean it would not multiply, or that it would be concealed or masked in some way? There are those who suggest that modified virus given in this manner might advantageously be distributed and maintained by the usual contaminating methods to support the immunity of a population continuously.

To conclude, I wish to express my thanks for the opportunity of reading these fine reports. I should also repeat that the first efforts are rarely the final ones, but that progress in the field is an unending pursuit.