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Oral Poliovirus Vaccine

STATEMENT

By Leroy E. Burney, Surgeon General, Public Health Service, August 24, 1960

During recent months, a number of conferences have been held at which progress in the field of immunization with live poliovirus vaccines was reported. These conferences include the meeting held in Moscow in May, the joint Pan American Health Organization-World Health Organization Conference held in Washington in June, and the 5th International Congress on Poliomyelitis held in Copenhagen in late July. The staff of the Public Health Service and its Advisory Committee on Live Poliovirus Vaccine has given careful consideration to the information available from these meetings—indeed, some members have actively participated in these meetings.

It may be recalled that about a year ago recommendations relating to the manufacture and testing of live poliovirus vaccines were issued to facilitate the entry of interested manufacturers into this complex field. Last week, the committee met with the manufacturers and other interested persons in order to review these recommendations.

Revisions to these earlier recommendations, which will serve as the basis for adoption of regulations for manufacture and testing of the vaccine, have been agreed to by the committee. These include the virus strains to be used, the general processes of manufacture to be followed, tests to be applied during manufacture, and factors relating to the continued safety, purity, and potency of the vaccine.

The Service's Division of Biologics Standards is moving with all speed to complete technical details of the final regulations while the manufacturers proceed with preliminary steps toward meeting these requirements. These details will be available in the near future.

In addition, I have received a general short report from the committee. On the basis of these recommendations, it is considered that live poliovirus vaccine is suitable for use in the United States. It is now possible to visualize the licensing of the establishments for manufacture and sale of these products when manufacturers have individually demonstrated the necessary experience and ability to produce material which conforms with the requirements.

It is not anticipated that the vaccine will be available in any quantity for a number of months, and it is doubtful whether substantial supplies will be available before mid-1961. In any case, I consider it important to note the committee's recommendation for the integrated use of the live poliovirus vaccine with the presently available vaccine and for the rather special requirements concerning use of live poliovirus vaccine in the American population. I shall take up certain of the problems raised by the committee regarding the optimal use of live poliovirus vaccine in the United States with appropriate advisory groups, such as the State and Territorial health officers and representatives of the medical and health professions and of the voluntary health agencies.

COMMITTEE RECOMMENDATIONS

The Public Health Service Committee on Live Poliovirus Vaccine considers that field studies of oral poliovirus vaccines have advanced our knowledge to a stage where recommendations relating to its manufacture can now be written. The committee also has considered the need for careful analysis of the problems associated with adapting such vaccines to immunization programs in this country and made recommendations thereon.

Vaccine Characteristics and Strain Selection

In line with its efforts to further the progress of immunization against poliomyelitis, the committee met on August 19, 1960, with technical representatives of potential manufacturers, with other interested persons, and with the staff of the Division of Biologics Standards, National Institutes of Health, for the purpose of reviewing the proposed requirements for the manufacture and testing of live poliovirus vaccine. The amended requirements which outline the manufacturing and testing objectives will become available shortly from the Division of Biologics Standards and should be helpful in assisting those manufacturers who wish to enter into production. It is hoped that manufacturers can proceed without delay to develop the necessary experience for the mass production of live oral poliovirus vaccine.

The committee feels that three factors when considered together make possible its recommendation regarding strain selection. These factors are: (*a*) neurovirulence in monkeys, (*b*) viremia in man, and (*c*) field experience with all candidate strains. The committee again emphasizes the need for definitive information on the question of viremia in man.

The committee considers that the strains available for preparing live oral poliovirus vaccine the Sabin type 1 and type 2 strains possess the most favorable laboratory and field characteristics and recommends their use. The committee also recommends the use of the Sabin type 3 strain which is satisfactory from the point of view of neurovirulence although it has less than optimum immunogenic capacity and shows a tendency to change its neurovirulence characteristics after passage in man. The committee urges the continued search for a superior type 3 strain. All candidate strains other than those of Sabin which have been studied extensively are of greater neurovirulence for monkeys than the selected reference.

The committee expresses the view that neurovirulence for monkeys is the most important laboratory criterion available. This criterion was used for selecting candidate strains and is still the only measurable laboratory property which can be assumed to be correlated with neurovirulence in man. On the basis of the information available, the committee recommends that the intrathalamic test in monkeys be adopted as the criterion for neurovirulence and that in order to be suitable for vaccine manufacture strains should exhibit little or no evidence of neurovirulence when inoculated in this manner into monkeys. The committee considers that any strain which shows neurovirulence for monkeys by causing paralysis when administered by the intramuscular

route is unsuitable. The committee recommends that the intraspinal test be retained mainly as a measure of the susceptibility of the monkeys used. It recommends that the Sabin type 1 strain be used as a reference in the conduct of these tests.

The committee took cognizance of the great contributions of Dr. Herald Cox and of Dr. Hilary Koprowski, who with their colleagues promulgated the concept of live oral poliomyelitis vaccine and, using their own attenuated strains, provided much of the crucial information which advanced the development of this new vaccine.

The committee concludes that the field data now available indicate that while good levels of immunity can be obtained under certain conditions such levels can only be assured by repeated doses. Schedules of administration will depend upon local conditions since capacity "to take" or "immunogenic effectiveness" of these vaccines is influenced by a number of factors, the most important of which is the prevalence of other enteroviruses in the community being immunized. The committee does not believe that the capacity to immunize of any strain is such that the neurovirulence requirements should be compromised.

Need for Planned Use of Oral Vaccine

In view of the fact that the nationwide programs with killed virus vaccine failed to achieve the hoped-for elimination of all epidemics of paralytic poliomyelitis, the committee emphasizes the need for critical assessment of the place of live poliovirus vaccines in the overall picture of poliomyelitis prevention in the United States. The uncoordinated use of live poliovirus vaccine is unlikely to accomplish more than has been achieved with inactivated poliomyelitis vaccine as presently employed. It appears probable that only a unified national program which utilizes each of the available types of vaccine to its best advantage can accomplish the total prevention of outbreaks.

The committee must also emphasize that when live poliovirus vaccine becomes available generally in this country, its use will be more appropriate on a community than on an individual basis. This will depend upon a number of factors, and special recommendations will be necessary for the guidance of physicians, public health officials, and others who will be engaged in such programs. Attention should be given to such matters as administration to special groups; for example, very young children, pregnant women, susceptible adults, and others, and even more important is the planned continuation of this program as long as necessary to achieve and maintain the required results.

The committee supports the view that the Public Health Service has a function to perform, extending beyond its regulatory responsibilities, to the end that a satisfactory live poliovirus vaccine may not only be made available at an early date, but may be properly integrated into the total pattern of infectious disease prevention in the United States.

Because of the unique nature of live poliovirus vaccine, with its capacity to spread the virus in a limited manner to nonvaccinated persons, the committee cannot make recommendations for manufacture without expressing concern about the manner in which it may be used. The seriousness of this responsibility can be illustrated, for example, by the known potentiality of reversion to virulence of live poliovirus vaccine strains, and the possible importance of this feature in the community if the vaccine is improperly used.

For example, the vaccine has been employed largely in mass administrations where most of the susceptibles were simultaneously given the vaccine, thus permitting little opportunity for serial human transmission; or, it has been administered during a season of the year when wild strains have usually shown limited capacity for spread. This experience should provide the basis for developing usable practices for the United States.—*Respectfully submitted by the Committee on Live Poliovirus Vaccine, Robert Murray, M.D., chairman.*