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Poliomyelitis Viruses in Tissue Culture

BECAUSE the study of virology, like that of other sciences, is limited to available techniques, the introduction of a new method makes new observations possible and broadens the scope of inquiry. That the introduction of tissue culture methods for the study of poliomyelitis virus by Enders, Weller, and Robins in 1949-50 has accomplished this result was demonstrated in a series of papers presented at the 1952 meetings of the American Association of Immunologists and the Society of American Bacteriologists. Growth of virus is accompanied by cytopathic changes readily observed in test tube cultures of cells. Inhibition of these changes by addition of specific immune serum provides the basis of an *in vitro* method for antigenic classification of poliomyelitis viruses, and quantitative estimation of type-specific antibody, thus making possible the *in vitro* serodiagnosis of poliomyelitis infection. The method has not only supplemented, but for many purposes replaced, the cumbersome and expensive procedures required when studies are carried out in monkeys.

Enders used human tissues, chiefly embryonic, for his work, but the need for this has now been partly offset by the finding that monkey testicular and kidney tissues serve admirably for supporting virus growth. Work with human tissues continues to be of utmost importance, for interaction of virus with tissues of the natural host may be directly studied. When passed through human nonnervous tissue, the Brunhilde strain diminished in pathogenicity for monkey CNS. With passage of the Y-SK and Lansing strains through monkey tissue, both almost lost their capacity to produce paralysis in mice, but retained their virulence for monkeys. The possibility exists that the pathogenic potential may be maintained for the host species in whose tissues the virus is being grown, even though the virulence for other species may be markedly diminished.

Rapid isolation and typing of strains using monkey tissue cultures have already shown that during a single outbreak one antigenic type (Brunhilde) predominated, but that the two other types of poliomyelitis virus were also prevalent. Three other cytopathogenic agents were isolated during the outbreak; two were Coxsackie viruses, and one has not yet been classified. Isolations of similar agents have also been made in human tissue cultures.

Roller tube-grown virus has provided a source of antigen that reacts in the complement fixation test with human sera. Early observations suggest that, following infection with one type of poliomyelitis virus, transient complement fixing antibodies to at least two types appear, whereas the longer-lasting neutralizing antibody response is restricted to the virus type causing the infection. (Similar findings have recently been made in human infections with the poliomyelitis fellow-travelers, the Coxsackie viruses.) Mass surveys of normal populations, for neutralizing antibodies to each of the virus types, are in progress to obtain an objective measure of past infection in different communities, and the new information may perhaps allow us to predict epidemics.

Other fields under active investigation include the preparation of tissue culture vaccines free of foreign and dangerous CNS components, and the screening of a multitude of antibiotics and chemical agents for their effect on the multiplication of viruses in human and monkey cultures.

Even this cursory discussion illustrates how important methodology is to the growth of a science, and virology is no exception to this rule. The observation that poliomyelitis virus may be grown in roller tube cultures of human and monkey tissues has been followed by application of the method to clinical, immunological, and epidemiological investigations of the infection. Further work with this relatively simple system should take us far in our understanding of the reactions that occur when virus and host cell meet.

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SCIENCE, founded in 1880, is published each Friday by the American Association for the Advancement of Science at the Business Press, 10 McGovern Ave., Lancaster, Pa. Entered as second-class matter at the Post Office at Lancaster, Pa., January 13, 1948, under the Act of March 3, 1879. Acceptance for mailing at the special rate postage provided for in the Act of February 28, 1925, embodied in Paragraph (d-2) Section 34.40 P. L. & R. of 1948.

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Annual subscriptions, \$7.50; single copies, \$.25; foreign postage, outside the Pan-American Union, \$1.00; Canadian postage, \$.50. Special rates to members of the AAAS.

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