re rationale for controlling insect vectors in polio epidem.

INTRODUCTION

When I, fresh from obtaining my PhD in biochemistry at Yale University in 1939, began my studies of poliovirus, not much was known about the virus. No one knew how many types existed or even suspected that the poliovirus was the first recognized member of a large group of viruses, which 50 years later was placed in the enterovirus genus.

Basic studies on poliovirus began in 1908 when Landsteiner and associates in Europe transmitted the disease to monkeys, inducing typical histopathological lesions in the animals' spinal cords (47, 48). In 1910, Flexner, of the Rockefeller Institute, surmised that poliovirus was strictly neurotropic because of the way it behaved in experimentally exposed rhesus monkeys (24). He thought that poliovirus entered the human body through the nasal route and proceeded directly to the central nervous system. Some years later, in 1936, Sabin & Olitsky (91) reported that rhesus monkeys succumbing to polio had olfactory lesions only when infected by intranasal instillation of virus, and not when virus had been administered by other routes. Five years later, Sabin & Ward showed that olfactory bulbs from 65 fatal human cases were all negative for virus (92), confirming the rarity with which olfactory lesions had been observed in autopsy studies of human polio cases. In the late 1930s, Howe & Bodian (36) had begun to consider the possibility of an oral-alimentary route of infection. They found chimpanzees to be far more susceptible than other experimental primates to infection by the oral route.

How poliomyelitis is spread was not understood in the 1930s. Cases in epidemics seemed to move out from a focus, but in erratic patterns, for those afflicted usually had no direct contact with an earlier case. At Yale in 1932, Paul & Trask (80) not only found the virus in large quantities in feces, but also recovered virus repeatedly over a period of weeks, from both patients and healthy carriers. The shift to the concept of poliomyelitis as an enteric infection had begun (97).

One of my first research projects on poliovirus was an application of the ultracentrifuge to the preparation from stools of purified materials which could then be inoculated intercerebrally into monkeys (68). The ultracentrifuge has become a well established tool in virus research because this apparatus permits the concentration and purification of viruses due to their size. This method proved highly effective when compared with the then-prevalent method of the intra-abdominal injection of etherized stool suspension in conjunction with the intranasal instillation of the untreated stool suspension.

By means of differential ultracentrifugation, I regularly obtained a purified and concentrated macromolecular fraction (68). This fraction was isolated from 16 stools in which virus was thought to be present and was then inoculated

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intracerebrally into 16 monkeys, of which 15 developed poliomyelitis. With the ultrcentrifugal method, relatively large amounts of stools would be used to prepare the inocula, for the bacteria and toxic materials present are eliminated in the process of concentrating the virus.

Because poliovirus was found in feces, an attractant for flies, we were led to explore the possible transmission of the virus by these insects. Thirty years earlier, Flexner & Clark had not considered transmission by flies because they believed that virus entered the body through the olfactory nerves. With the renewed interest in poliovirus having an enteric habitat, we brought flies back into consideration. We found that virus could be demonstrated either on the surfaces of or within the bodies of flies collected in the field during epidemics (97). Soon thereafter we (104) found virus in food collected from the dinner tables of epidemic victims.

The findings from tests of flies trapped in the field were thought to reflect mechanical transfer of virus by flies. Later work in the 1950s substantiated this hypothesis by breeding flies (*Phormia regina*) in the laboratory, infecting them with poliovirus, and determining how much virus they excreted, and for how long (82). While virus could be detected for weeks, no evidence of multiplication was obtained (59). After the coxsackieviruses and the enteroviruses had been recognized, we found that flies collected in the field were often contaminated with these viruses also (56).

Because of the field work in the 1930s epidemics, still another series of questions was brought into focus: If polio was an enteric infection, could it be isolated from urban sewage? One of my first tasks upon joining the Yale Poliomyelitis Study Unit in 1940 was to devise better methods for testing effluents from one of the large sewage treatment plants of New York City. During periods when paralytic polio was prevalent, I found poliovirus to be present in New York sewage in huge quantities, and I estimated that 6% of the population were carriers of the virus but were asymptomatic (67). Knowing the quantity of virus in sewage, the amount excreted by a carrier each day, and the case rate in the area from which the sewage came, I could establish a ratio of inapparent to apparent (paralytic) infections. I calculated that there were about 100 inapparent or subclinical infections for each paralytic case.

With more scientists entering the field, test systems simpler than use of primates were badly needed. Following isolation of the virus, decades of repeated attempts to grow polioviruses in various kinds of cultures met with little success. Then, in 1936, Sabin & Olitsky reported the successful growth of poliovirus in tissue fragments cultivated in glass vessels (90). However, their study was done with the MV strain of poliovirus, which at the Rockefeller Institute had gone