In the history of poliomyelitis we have the story of a disease undergoing a series of transitions with a pattern of evolution which has passed through at least three stages: first, the protracted era of old-fashioned "infantile paralysis," then the terrifying stage of epidemic "polio," and finally the present stage, in which paralytic poliomyelitis currently seems to be coming under control through the use of vaccination.

To review the history in more detail one finds that, although infantile paralysis is probably as old as written history, as a clinical entity it does not seem to have attracted the attention of physicians until the late eighteenth century. Subsequently, for more than half a century this affliction was regarded as ubiquitous and a curious aftermath of teething or some short fevers. Not only were there no accounts of large epidemics during the greater part of the nineteenth century, but there was little mention of anything suggesting contagion, nor was the condition regarded as a medical problem of any magnitude. How prevalent poliomyelitis was 100 years ago is unknown, but Jacob Heine of Cannstatt, Germany, was able to collect in 1840 a considerable series of late paralytic cases. Coincidentally, North American surgeons of the 1830's made occasional mention of acute paralysis in infancy, without comment as to rarity. Apparently, this mid-nineteenth century situation with regard to infantile paralysis is reminiscent of that found in certain tropical countries and urban populations today where substandard sanitary conditions exist, where the disease is endemic and limited to infants, and where it is not regarded as a problem of major importance.

The first small outbreaks of what might be called epidemics were noted in the 1830's and 1840's by British and American observers. However, it was not until 1868, when 14 cases were reported in Norway,
and 20 years later, when Cordier described outbreaks in France, and Medin noted others in Sweden (1891), that the medical profession began to take the epidemic character of poliomyelitis seriously. After about 1900 and with ever increasing rapidity, epidemics of this disease appeared in northern Europe, North America and elsewhere. From a comparative curiosity, infantile paralysis emerged as a periodic scourge. It also began to attack young adults as well as infants and school children in ever increasing numbers. Early in the 1900's Wickman in Sweden (whose classic work was done before the discovery of poliovirus) laid the basis for the modern epidemiological concept of this disease, with emphasis on its infectious nature, its spread through human contact, and the importance of mild cases as carriers.

Progress in the control of this disease has come from developments leading to its prevention rather than its cure—and these developments have all stemmed from studies on the causative virus, poliovirus. This virus was discovered in 1908 by Landsteiner and Popper, a discovery which opened up a new vista, although for many years the path was narrow and tortuous and progress was slow, largely because of the difficulties of handling polioviruses, which required monkey inoculation for their demonstration. Landmarks in the subsequent story include the clinical-virologic investigations of Kling and his co-workers in Sweden in 1912; the discovery in 1931 and clarification in 1948 of the three types of the causative virus, poliovirus, and the growth of polioviruses in tissue culture by Enders, Weller and Robbins in 1949. This last discovery enabled the virus to be grown in adequate amounts in a medium which was satisfactory for vaccine production, and the development of this phase of the story was achieved in 1954 by Salk.

POLIOVIRUSES

Few viruses responsible for disease in man have been studied as intensively as have the family of the three known types of polioviruses. It would be amiss to go into a detailed description of these agents here, for there are various sources of information to which the reader can refer. Suffice it to say that experimental infections produced by these polioviruses have a narrow host range in comparison to some of the other so-called neurotropic viruses. Man is the most susceptible animal, primates come next and in some instances rodents and even chick embryos can be infected. The fact that these viruses not only grow well in tissue cultures but that they give rise to cytopathogenic effects in these cultures has enormously enhanced the facility with which these viruses can be handled in the laboratory.

Immunologically the poliovirus family is composed of three serotypes I, II and III, of which Type I is responsible for the great majority of the clinical cases in most parts of the world. Immunity to an infection,
whether it be paralytic or inapparent, which is caused by one type of poliovirus probably protects monkeys from a paralytic reinfection with the same type of poliovirus (homotypic) but does not necessarily protect them from infection with a heterotypic virus. Homotypic, paralytic reinfections are probably rare in man. It is for this reason that any vaccine against poliomyelitis should contain all three types of the virus. Reinfections do occur and fortunately are nearly always inapparent. It is likely that most individuals sustain several such infections in childhood as means of building up natural immunity.

**PATHOGENESIS: PORTALS OF ENTRY AND EXIT**

Evidence that favors the mouth as the usual portal of entry has continued to accumulate. The intranasal portal of entry has much less support. The cutaneous route of infection has never received particular attention but cannot be disregarded. At least with some strains of the virus, cutaneous infection can be readily induced experimentally in various species of monkey. It has also been demonstrated in man.

Although poliovirus may be widespread in the body early in the clinical disease, it has certain sites of predilection, such as the pharynx, intestine and central nervous system (CNS), where it survives for varying periods of time. Only in the CNS does it produce serious lesions. In man, early in the disease or late in the incubation period, the virus has been recovered from the blood stream. The extent to which this viremia indicates the way in which the virus travels on its way from the primary site of implantation to reach the blood-brain barrier and then pass into the CNS, or along nerves whereby it can pass directly into the CNS, has not been settled.

During and after an acute attack of poliomyelitis, the virus can be demonstrated in the oropharynx for from about a week to ten days from onset. In the intestinal tract the virus remains longer (from one to six weeks or even more) and as many as one million infectious doses for the monkey have been detected in a gram of feces. Again it should be emphasized that this acute and convalescent carrier state can often be initiated by an attack so mild as to go unnoticed—the inapparent or alimentary infection. How the virus is maintained in the oropharynx or the intestinal tract during the carrier state is a question as yet unanswered. Possibly it is growing in fairly superficial local cells and being eliminated into the oropharynx or into the lumen of the gut. Epidemiologically speaking, it would seem that these are "dangerous places" for a highly infectious virus to be. Although poliovirus may continue to be excreted from the intestinal tract for as long as 17 weeks from onset, long-term human carriers who excrete virus for years—comparable to persistent carriers in typhoid fever—have not been discovered.
MODES OF SPREAD

Human Contact

It is generally accepted today that poliomyelitis is a highly infectious disease, spread largely by human association or contact. The wavelike peripheral advance of epidemics of poliomyelitis from a central focus is consistent with this theory. However, unlike certain other "contact" or crowd-diseases, such as measles, in which the disease passes from one recognized case to another, the spread of poliomyelitis often occurs through the medium of mild or subclinical cases. More than 90 per cent of them are so slight that their chance of clinical recognition is almost nil. Nevertheless, they can be identified, sometimes by minor symptoms but nearly always by virus isolation and a rise in antibodies. Thus, both clinical cases and people, particularly infants, suffering from inapparent infections represent primary sources from which the virus may spread. The infantile carrier or subclinical case is a particularly dangerous carrier, owing to the unsuspected nature of the illness and the intimate contact between mother and child.

Although any one of these clinical or subclinical forms of poliomyelitis may be responsible for the spread of the disease, there is evidence to suggest that paralytic cases excrete particularly large quantities of virus. "Healthy carriers," on the other hand, are by far the most numerous and uncontrolled. They can act as a huge human reservoir for the spread of the disease and for the maintenance of the virus within a community during interepidemic periods.

As to the type of contact which results in the transfer of infection from one person to another, it is safe to say that poliomyelitis can be acquired by the close association of an infected person with a nonimmune person. It is easy to see how readily dissemination of the virus can occur in the intimate associations between children. Families may form a focus with a high density of infection, and a number of studies indicate that there is a much lower incidence of infection among extrahousehold contacts than among intrahousehold groups.

Environmental Factors in Spread

Important as the "direct-contact" explanation for the spread of poliomyelitis is, it may not be the whole answer. For instance, although seasonal trends occur in a number of diseases spread by human contact, no satisfactory reason has as yet been proposed to explain the dramatic effect of summer weather on poliomyelitis and why epidemics of this disease occur at so much higher a rate in the summer and early autumn than in the winter. The possible explanation is that something happens during summer weather which either introduces poliovirus into a community or enormously facilitates the dissemination of virus throughout a
community, or makes certain people, the nonimmunes, far more susceptible.

In any event it does seem that man can contaminate not only his fellow associates but his immediate environment, and it is possible that an analogy can be drawn in this respect between poliomyelitis and salmonellosis. As an example of contamination of the environment, poliovirus has been found not only in human feces but in urban sewage and in fecal material collected in open privies and in flies, particularly the feces-eating varieties. As to the significance of this, the mere presence of poliovirus in sewage at certain periods of the year does not mean that sewage is the usual avenue of infection. It means, essentially, that here is evidence that the community is “contaminated.” Tubercle bacilli can, for instance, be found with great frequency in any urban sewage; yet one does not regard sewage as the source of tuberculosis through a community. Seldom if ever has there been epidemiologic or laboratory evidence to incriminate the water supply of a community as a source of local poliomyelitis infections. In only a few outbreaks have there been reasons to believe that milk had been contaminated.

A variety of arthropods have been suspected from time to time of spreading poliomyelitis, largely because of the seasonal incidence. Many varieties of insects have been tested for its presence. Such tests have yielded no positive results, except in the case of flies and cockroaches. It is now abundantly clear that various species of flies may carry the virus on their surfaces or within their bodies. It is clear, also, that naturally infected flies can contaminate food with poliovirus. However, there is no reason to regard insects as an essential or a dominant element in the spread of this disease. In some epidemics which have occurred in the Arctic during winter, it would seem definite that flies could have played no part. On the other hand, in certain areas where sanitary conditions are substandard and flies are exceedingly common, such as in cities or villages in Egypt, Latin America or South Africa, it is quite possible that the role which these insects may play as mechanical vectors in spreading the virus of poliomyelitis or even immunizing the population could be appreciable. The word mechanical is used here advisedly, for there is as yet no evidence that poliovirus multiplies within flies.

To summarize, then, what is known about the environment, or so-called extrahuman factors, although no large extrahuman reservoir of virus is recognized, environmental factors do exist in this disease and could enhance its spread. This is primarily manifested by the fact that infection and immunity are so uniformly acquired by infants in areas and communities where poor sanitation and much fecal pollution of the environment exists, and where infant mortality is high, in other words, where infants are not protected from heavy exposure. Sporadic (endemic) poliomyelitis usually thrives in such an environment. Conversely, in areas of good sanitation, where infants are protected from enteric infec-
tion, exposure is more irregular, and infection is usually acquired not in infancy but at a later age. Epidemic poliomyelitis is apt to appear periodically in such communities.

PREVENTION BY VACCINATION

In 1955 the use of the Salk-type formalinized (killed virus) vaccine was officially recommended in the United States and a number of other countries. The reduction of the prevalence of paralytic poliomyelitis in the years 1955–1958 in areas where the vaccine was used has furnished ample proof of its effectiveness in reducing the paralytic form of the disease.

Current techniques for the administration of Salk-type vaccine call for its intramuscular inoculation in three divided doses of 1 ml. each, the second being given one month to six weeks after the first, and the third not earlier than seven to nine months after the second. There is as yet no official ruling as to how often subsequent doses—so-called booster inoculations—might be given in subsequent years after the initial course of three doses. Some have even suggested an annual booster inoculation. This is for the future to decide.

In those countries where clinical poliomyelitis is well recognized as a disease of young adults, it has been recommended that the Salk vaccine be given to all individuals who fall within the age groups of one year to 40 to 45 years, but the age groups which deserve most consideration differ in different places. Contraindications to the use of the Salk vaccine are few. Irritating, allergic and other types of side reactions are uncommon. Young children with eczema represent one group to whom the vaccine should be omitted or given with great caution.

It has generally been recommended that this vaccine be administered during the winter months, i.e., outside the poliomyelitis season. The decision to vaccinate individuals or a whole population during an epidemic of poliomyelitis has both proponents and opponents. The majority of modern opinion supports the view that such a vaccination campaign during an epidemic is indicated, if the chances of heavy exposure to susceptible population groups seem imminent.

In reviewing indications for the use of the Salk-type vaccine one should consider the way that it is supposed to work. One should recall at the onset that it does not prevent infection with poliovirus (i.e., inapparent or alimentary infection) but it does materially reduce the spread of poliovirus within the body of those who become infected. In this fashion it lowers the incidence of paralytic poliomyelitis, but does not eliminate poliovirus from the community. One might compare this vaccine (composed as it is of formalin-inactivated polioviruses) with others whether they be composed of viruses or bacteria. Killed vaccines when injected into the body are expected to stimulate specific antibodies, and coincidentally, immunity against the live agent to which the
vaccinee may become naturally exposed. Such immunity is relative, and may be adequate even when the vaccinee is exposed to large doses of the specific infectious agent. However, in general, postvaccinal immunity of this type eventually declines and booster doses may have to be given repeatedly, i.e., every few years, in order to keep the vaccinee’s immunity in repair. Perhaps this will be the method eventually adopted for poliomyelitis.

However, the situation just described is not completely analogous to what happens with poliomyelitis immunization, for there are fundamental differences which deserve emphasis here. Poliomyelitis is a disease in which a normal unvaccinated individual or child living in the United States usually sustains repeated subclinical or inapparent infections, so-called alimentary infections. These infections may be caused by one or more types of poliovirus, and eventually as a result of such repeated (homotypic or heterotypic) alimentary poliomyelitis infections, natural and fairly solid immunity in the normal unvaccinated child is usually acquired. In a very small percentage of unvaccinated infants, children or young adults, the acquired (or natural) immunity is not achieved in a degree adequate to stave off a serious infection. Thus, in infants at least, one out of a hundred or more cases of such poliovirus infections may become severe enough to give rise to myelitis, which in turn is extensive enough to go on to produce paralysis. The primary aim then of the Salk vaccine against poliomyelitis is to bolster body defenses in an effort to reduce that fraction of 1:100 children who otherwise might become paralyzed, almost as a complication of their alimentary infection. The reduction could be of the order of 1:1000 or 1:10,000. In older children or young adults who have not been vaccinated the ratio of severe infection to mild infection may be at the level of 1:75 more or less. Thus the aim of the Salk vaccine is to keep the vaccinee’s immunity at such a level that when he does become infected his “case” will be mild. Its effect is not that of preventing infection altogether. This latter may or may not be fortunate for reasons to be mentioned presently.

The background for immunization is based on current views on the pathogenesis of paralytic poliomyelitis which, although admittedly incomplete, can be described in terms of a hypothetical anatomical schema. For the virus to enter and penetrate into the body it must traverse various lines of defense. The first line of defense, let us say, is a barrier imposed by the intact mucous membranes of the mouth and/or the intestinal tract. The second line of defense lies perhaps in some lymphoid tissues. There may also be other anatomical areas, as yet poorly visualized, where the virus may be multiplying in early stages of infection. From here, if the virus continues to multiply, it may penetrate a third line of defense and enter the blood stream; there is still a fourth, the so-called blood-brain barrier, and, conceivably a fifth, which represents those factors, poorly defined as they may be, which control the
spread of virus within the central nervous system. Granted it is possible for most of the middle lines of defense to be by-passed now and again by a mechanism which allows the virus to penetrate directly from a mucous surface into a neuron and subsequently along nervous channels directly into the central nervous system, still there is a good deal of information which indicates that viremia represents an important phase in the pathogenesis of paralytic poliomyelitis and, if viremia can be blocked, at a point proximal to the blood stream or by antibody in the blood, this would prevent the mild infection from becoming more extensive.

According to this theory, then, artificial immunity induced by the Salk (killed virus) vaccine tends to be associated with the production of antibodies which may represent the strengthening of the second and third lines of defense. To supplement these defenses of the body are the repeated and naturally acquired postvaccinal, alimentary infections against which Salk vaccine does not protect, and again one might say that this seems fortunate. For it is these repeated alimentary infections by which immunity against severe poliomyelitis may be constantly reinforced.

The discussion does not entirely end here because, if it turns out that natural infection is of value in keeping the vaccinee’s immunity in repair, should this matter of reinfection be left to pure chance or will the live attenuated virus vaccination enter the picture, as an adjunct or conceivably a substitute to the use of the killed vaccine? This refers to the use of attenuated strains of polioviruses found or developed by Koprowski et al.4 and by Sabin8 which have now been used in many field trials of small and large scale in many parts of the world.

Developments with live attenuated poliovirus vaccine are just beginning, and the unanswered questions are many. They concern the safety of the method and the capacity of these strains to produce infection, and, correspondingly, to immunize. They also concern the degree with which attenuated poliovirus will spread from the vaccinees to their immediate associates. Perhaps the most knotty question is whether the attenuated strains will revert on human passage to a more virulent form. To date, in the many trials which have now been reported—and these cover tens of thousands of people, largely children—accidents have not been reported.

Another aspect of the proposed live virus vaccine which will certainly require much further research is the fact that the character of immunity produced may be somewhat different from that resulting from the Salk vaccine, in that by actual topical exposure of the alimentary tract one may produce a kind of “local immunization” whose existence is suspected but whose mechanism is ill-defined. Such local resistance may play some role either in preventing implantation of the virus in the alimentary tract or in limiting its early multiplication there. Hypothetically, this kind of immunity can be visualized as a barrier existing somewhere between the first and second lines of the theoretical defense barriers mentioned earlier in this article. This might be of considerable
Poliomyelitis

virtue. Such local resistance does not always so limit the infection that the production of antibodies is inhibited. On the basis of this theory, the point has been raised many times that there may be some wisdom in combining the two forms of vaccination, first a full course of the attenuated Salk vaccine, to be followed by the live virus vaccine. All this cries out loudly for further investigation.

REFERENCES


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