EPIDEMIOLOGY AND CONTROL OF POLIOMYELITIS

Essay Submitted For
THE CAMERON (LEWIS) UNDERGRADUATE PRIZE
1961
(Proxime accessit.)

by
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The Fifth International Conference on Poliomyelitis was held in Copenhagen, Denmark, from the 26th - 28th July 1960. Over a thousand delegates from 47 countries attended this conference. It might legitimately be asked why poliomyelitis alone among the virus diseases has acquired this honour and importance when some other diseases with greater morbidity and mortality rates have not been deemed worthy of this distinction. The answer lies in the fact that the changes in the pattern of this disease during the last hundred years have caused great anxiety and concern in the minds of epidemiologists and public health authorities all over the world. The relatively uncommon 'infantile paralysis' of the 19th century has become the epidemic poliomyelitis of the 20th century. Contrary to expectations and to the behaviour of most of the other intestinal infections, epidemics of poliomyelitis began to appear after the role of defective sanitation in the spread of enteric infections was recognised. Where the new ideas of sanitation were put into effect with much vigour, poliomyelitis epidemics became more frequent. Thus poliomyelitis presents itself as a threat in epidemic form to all countries which have and aspire to have improved standards of hygiene and living conditions unknown in the early part of the nineteenth century.

Besides this change from an endemic to an epidemic pattern, the disease has evolved in another direction also. Over a hundred years
ago, as the name 'infantile paralysis' suggests, poliomyelitis was mainly a disease of the lowest age group (under 5) in the community. But a shift, showing a significant incidence of the disease in higher age groups, with case-paralysis and case-mortality rates which are very much more pronounced than among the under-five group, has occurred. The inexorable tendency of notification figures to rise in almost every country presents the disease as a menace of world-wide significance.

PAST HISTORY

Acute paralysis in children was not considered a disease entity until the late years of the eighteenth century. The earliest clinical descriptions of the disease came from England in 1795, from Italy in 1813 and from India in 1823. Then it was regarded as due to 'teething', 'foul bowels' or a 'fever', with no observation to suggest its contagious nature. The first account of an epidemic comes from Sir Charles Bell in his description of the disease in St. Helena in 1836. Heine of Cannstadt collected a number of cases of poliomyelitis in 1840 in Germany, but did not regard it as a problem of major importance. But by the latter half of the 19th century, the transition from an endemic to an epidemic disease was beginning to be established in Europe and the United States. Once the epidemicity started, it seemed to be irreversible. Since 1900, epidemics of varying severity have occurred with ever increasing rapidity in areas of the world with the highest standards of living, the best hygiene and modern
sanitation. World War II showed that the disease could be present in epidemic form even in tropical countries where it was once thought that poliomyelitis existed only in the milder infantile paralysis form.

EPIDEMIOLOGY

Dickman in Sweden laid the foundation for the modern concept of the epidemiology of the disease by stating that poliomyelitis was a highly contagious disease spread through human contact by typical, and abortive cases as well as by healthy carriers. In 1908, Landsteiner and Popper discovered the virus and showed its infective nature by causing the disease in monkeys.

THE VIRUS

The poliomyelitis virus is a member of a family of viruses, which multiply predominantly within the cells of the intestinal tract of man, called the Enteroviruses. The poliovirus is the smallest human pathogen so far known and is a spherical particle 27mu in diameter. The most important characteristics of the virus are its narrow host range and its affinity for nervous tissue. The only animals readily susceptible are the primates, though the virus has been adapted to grow in small rodents and in chick embryo. Tissue culture in monkey kidney cells made possible by the brilliant work of Enders et al, has made the detailed study of the virus feasible.

Three immunologically different types of the virus have been
identified by neutralisation tests. Type I is represented by the Brunhilde and Mahoney Strains; type II by the Lansing and M.E.F.1 strains; and type III by the Leon and Saukett strains. Though these types are immunologically distinct in their antigens, a certain amount of overlapping is not infrequent. Type I is the commonest epidemic type and shows the maximum of neurovirulence. Type II is usually associated with endemic infections, while Type III occasionally causes epidemic outbreaks.

The only natural source of the virus is man, and the virus is spread from person to person without any intermediate host. The human reservoir of infection consists of persons who excrete the virus in their faeces and less commonly in their oropharyngeal secretions.

PORTALS OF ENTRY

The earliest theory maintained that the olfactory route was the portal of entry of the virus. This theory was based on the experimental evidence that it was possible to infect rhesus monkeys intranasally. The feature constantly present in disease caused by this route is the involvement of the olfactory bulb. But lesions of the olfactory bulb are rarely observed in human cases and therefore infection by inhalation seems an unlikely route of infection in man.

It has been suggested that the virus might gain access into the body through abrasions in the skin, especially from contaminated water or as a result of injections through unsterilised skin. The cutaneous
route of the infection is a possibility, but must represent a very small proportion of all infections.

The most important and most frequent portal of entry is the mouth. A dose of the virus is ingested and multiplies primarily in the alimentary canal and pharynx. The virus most probably invades the lymphoid tissue associated with the upper respiratory tract, the Peyer's patches of the small intestine and the mesenteric lymph nodes. For the next week or so, the virus continues to multiply in these sites until it spills over into the blood producing a viraemia. At the stage of viraemia, virus particles are found in the pharynx, pharyngeal secretions, intestines and faeces of cases and contacts. Viraemia is accompanied by fever and general toxic symptoms. It is followed by a period of about 48 hours of relative well-being while the virus particles invade the nervous tissue. The disease may be arrested at various stages so that the virus may multiply in the alimentary canal without ever reaching the blood stream, or once in the blood stream may be overcome by the patient's natural defence mechanisms before it can reach nerve cells. However, it is not known whether viraemia is a constant feature of the disease, though it is present in all cases of paralytic attacks. An alternative explanation of the involvement of the nervous tissue is that from the mucous membrane of the alimentary canal, the virus enters the peripheral nerve endings and ascends along the axons to the peripheral ganglia and thence to the central nervous system. Though there is considerable doubt about the ability of the virus to enter intact
nerve endings, there is experimental evidence to show that it can easily do so when the nerve fibre is cut. This seems to be the explanation of the fact that during periods of poliomyelitis epidemics, tonsillectomies have been followed by bulbar paralysis in a significant number of cases. But this close connection between tonsillectomy and bulbar paralysis - some times as early as the second day after operation - may be explained by the possibility of direct drainage of blood and lymph from the area of the pharynx to the brain stem and spinal cord.

PATHOLOGY

Frank disease occurs only when the central nervous system is involved in the disease process. The anterior horn cells of the spinal cord and the brain stem are the most susceptible groups of nerve cells. To a lesser degree, the intermediate dorsal horn and dorsal root ganglia may be affected. The cerebellum, thalamus, hypothalmus, globus pallidum and the cerebral motor cortex may also be invaded. Involvement of the CNS does not necessarily cause paralysis. Even if the virus destroys nerve cells, it is only when certain critical areas are damaged that paralysis results. The neurological aspect of the disease is characterised by acute inflammation of the CNS and the meninges. The virus multiplies in the nerve cells and damages them stage by stage. Lysis of Nissl bodies is the first stage. Acidophilic necrosis of the cell follows. Invasion by scavenger cells (neuronophagia) occurs afterwards. Once this stage is reached the damage is irreversible. A certain degree of nerve cell involvement in the form of mild inflammation may be present in nonparalytic cases - either too small to be detected by present-day
histological techniques, or too little to cause paralysis. Where the
CNS involvement is reversible, only temporary weakness of the involved
muscle groups is seen. Viraemia cannot be demonstrated after the
occurrence of paralysis.

ANTIBODY PRODUCTION

Antibodies to the virus are produced by the body, but only after
the beginning of viraemia. Two types of antibodies are found. Neutralising
antibodies which are type-specific occur from the eighth day of infection
and persist for the rest of life. Complement fixing antibodies which are
not type-specific appear from the 12th day and persist for about 3 - 5
years. Viraemia disappears when the antibody levels have risen to high
titres. The virus has to cross the blood-brain barrier to enter the
central nervous system and it is thought that if the response of antibody
formation is of sufficient speed and magnitude, the virus particles are
neutralised before they have a chance to cross the blood-brain barrier.

IMMUNITY

The immunity provided by infection is type-specific. Therefore it may
seem that immunity to all types is necessary to prevent another paralytic
attack with a different type of virus. But second paralytic attacks are
very rare. It is not yet known whether infection confers life long
immunity or whether 'natural booster' infections keep the antibody titres
high. Antibody levels decrease fairly steadily for two years after an

©. There is some overlap between type I and type II antibodies
infection, but remain constant for long periods thereafter. Investigation of the Eskimos who are not continually exposed to the virus suggests that antibodies may last for over 40 years. Increase in antibodies in later life therefore suggests a reinfection. Present evidence indicates that, though inapparent infection produces long lasting immunity to paralysis, reinfection with homotypic viruses associated with a transitory low level virus excretion may occur in individuals with low levels of antibody.

The level of antibody obtained after an infection is very variable. It is almost consistently high in paralytic cases, though high titres have been observed in inapparent infections. Dosage and virulence of the virus seem to play important parts in this. Small doses repeated on a number of occasions, as well as strains of low virulence seem to cause low levels of antibody. Even in cases of paralytic attack, antibody titres do not continue to rise throughout the whole period of viral excretion, but level off fairly soon and may even begin to decline. It is not yet possible to relate the level of antibodies in blood to the degree of immunity provided to a later infection.

Clinical infection is not necessary for acquiring antibodies under natural conditions. However multiplication of the virus in the alimentary canal as shown by viral excretion seems essential for antibody production. It may be that only the multiplication of the virus within the body provides antigen in sufficiently high doses to stimulate the antibody-forming mechanisms of the host.
There are at least two types of defence against the virus in the body; a central mechanism which involves principally the circulating antibodies and a local immunity which makes multiplication of the virus in the intestinal tract impossible. Only a very small titre of antibody is necessary to prevent neurological complications of the disease. But circulating antibodies have no effect on the multiplication of the virus in the alimentary canal. Even in the presence of high titres of antibody, viral excretion subsequent to alimentary tract infection may take place. However, in places where poliomyelitis is endemic, the virus is incapable of multiplication in the intestines of the majority of the immune adult population.

OUTCOME OF INFECTION

Only a few of those who are infected with the virus develop frank disease. For every frank case of poliomyelitis, there may be about 100 - 1,000 silent or inapparent cases who are infected with the virus and excrete it in different amounts for varying periods without sign or symptom of the disease. The ratio of frank to inapparent attacks is governed by a number of factors. First of all it depends on the neurovirulence of the type of the virus. Type I is much more neurotropic than the other two types. High doses of the virus understandably causes frank disease much more often than small doses. The immunological status of the community is also an important factor. The disease tends to be more severe in patients over 15 years old.

@. Great variation in ratios has been reported by investigators between epidemic and interepidemic periods.
A number of factors reduce the length of the incubation period, enhance the severity of the disease and increase the localisation of the virus in the nervous tissue. These circumstances may precipitate paralytic manifestations of the disease. It is now known that intramuscular injections of diphtheria-pertussis vaccine, especially the alum adsorbed variety are associated with an increased incidence of paralysis in those exposed to the virus. The same holds good for intramuscular injections of heavy metals also, as was shown by the high paralytic rate among those who received organic arsenicals during the outbreak in Tahiti in 1951. Surgical operation in the incubation period, especially tonsillectomy is associated with greater risk of bulbar poliomyelitis. This risk may be present for years after the operation. Muscular activity during the viraemic stage of the disease may cause paralysis of the limbs exerted. Certain endocrine factors, especially those present in pregnancy and lactation increase the susceptibility to paralytic disease. Bacterial and viral infections of the throat or alimentary tract seem to alter the odds in favour of frank disease.

SPREAD OF INFECTION

Infection spreads from one person to another due to the excretion of the virus in faeces and oropharyngeal secretions of all those who are infected, irrespective of whether the disease is frank or inapparent. Pharyngeal carriage lasts for about 3 - 5 weeks: from five to six days before the onset of symptoms to twelve days after it. Faecal carriage which is universal among those infected lasts much longer, varying
from 3 - 12 weeks in most cases. There is no permanent carriage of the virus. Large amounts of virus are present in the excreta of the paralytic cases of poliomyelitis. It has been calculated that 1 gram of faeces may contain as much as a million infective doses. In the early stages of carriage, the disease is highly contagious because the amount of virus in the excreta is highest at this time.

Since there is no intermediate host in the transmission of the virus from one person to another, infection can take place only by direct contact with the infected individual or by indirect contact in the form of environmental contamination. Direct contact with an infected person (frank case, either paralytic or nonparalytic, or healthy carrier) is the commonest form of viral spread, where sanitation is good. Infection may occur through oropharyngeal contamination as a result of intimate contact or in rare cases as a result of droplet spread. Spread through faecal contamination of the hand of an infected person may be a possibility in countries where shaking hands is a common form of greeting. Environmental contamination can be in the form of a direct contamination of the immediate surroundings of an infected person, as in the case of bacillary dysentery. However, more indirect forms of spread through the sewage system, water supply and by mechanical vectors like insects are possible.

The amount of virus present in the sewage system of a community @ Koprowski mentions a case in which intestinal carriage was present for 171 days.
increases when there is infection. Virus particles have been found in the effluent from sewage purification plants where there has been a drop in the efficiency of the different stages of purification. Septic tanks may contaminate streams and rivers, and in turn pollute water which may be used for bathing, washing and irrigation. Vegetables, food articles and milk supply may be contaminated. But since the virus does not multiply in water protozoa, food stuffs or fruits, these materials are but rarely the sources of infection.

Mechanical transmission by flies and cockroaches is not unknown. In areas where genera of faecal feeding flies are present, this is a relatively common form of spread. The virus has been found even in flies from cities with modern sanitation, but the eradication of these insects with DDT spraying has not contributed to a reduction in the incidence of poliomyelitis. This suggests that these insects are neither essential nor play a dominant part in the spread of the disease. Some Japanese scientists have succeeded in artificially infecting mosquitoes and keeping the virus alive for three weeks. Though this may have some importance in view of the incidence of viraemia in human hosts, blood sucking insects do not play any known part in the spread of the virus from one person to another.

Though environmental factors may be relatively insignificant in most of the western countries, they do play a prominent role in producing high and uniform natural immunity by extensive spread of virus in places where poor sanitation, unprotected water supplies
and much faecal contamination are common.

SEASONAL VARIATIONS

In temperate climates, there is a sharp and dramatic seasonal incidence in poliomyelitis infection and epidemics. Late summer and early autumn have the highest incidence of the disease. It has been shown that the amount of virus in the sewage increases during this period and disappears almost completely in the winter months. It has also been established that in such areas of the world, nonimmune persons who acquire antibodies to the virus by inapparent infection do so in the months of summer and early autumn. In the tropical and subtropical regions of the world, the incidence is, however, uniform throughout the year. This raises the question of the survival of the virus in temperate climates between the interepidemic periods and in winter months. Isolated cases of frank disease and subclinical infections may serve as a bridge. A possibility which is of greater epidemiological importance is the suggestion that poliomyelitis is essentially a disease of the tropics and subtropics with a spill over into temperate areas in climatic conditions which are suitable for the spread of the virus. Only advances in identifying strains will help to solve this interesting problem.

PATTERN OF SPREAD

In an epidemic of poliomyelitis, frank cases with their first class contacts - usually members of the family - form the focus of the outbreak. Incidence of infection is very high among house-hold
contacts, though multiple paralysis itself is rare in any family. Extra-household associates of an infected person show a much lower incidence. This means that in countries where the level of sanitation is high, it is possible to localise an outbreak reasonably well, particularly in the interepidemic periods and in the early stage of an epidemic. Infection always spreads in the direction of human movement and the extent of spread depends on the intimacy of contact. An epidemic travels in waves from a central focus, in isolated communities, but outbreaks may suddenly appear in a distant place due to dissemination of the virus by carriers who have travelled into that area. In closed communities, the epidemic travels at a rate of spread which is as high as for measles, which suggests personal contact as the mode of transmission.

ENDEMIC PATTERN

Polio is present in all tropical and subtropical areas as an endemic disease. In such areas sporadic cases are reported throughout the year without any seasonal association. The disease mainly affects children below five years old. Infants below six months are however, very rarely affected. Though the morbidity rate is fairly high, paralytic and case-fatality rates are very low.

The incidence of the disease and paralysis is confined mainly to the lowest age group because almost everyone acquires immunity to all three types of the virus by natural exposure by the age five or six. For example, in Cairo there was 100% immunity by the age of six. All
three types of antibodies are present in the blood of 80% of children at the age of five. Complement fixing antibodies show high titres at the age of six or seven suggesting recent infection. This uniform acquirement of antibodies at such an early age is made possible by the fact that in primitive surroundings people are more often exposed to endemic strains of the virus because of substandard conditions of sanitation and hygiene. Poor and crowded living conditions facilitate the spread of the poliovirus.

The process by which high immunity is acquired with a low paralytic rate is a subject of great interest and considerable debate. It has been suggested that the children in endemic areas are infected during the first six months of their life under 'cover' of placentally transmitted maternal antibodies, or later under 'cover' of antibodies reaching the infant through maternal milk. The milk of lactating mothers contain very high titres of antibodies in tropical and subtropical areas. But the observed fact that weaning occurs before children in such areas begin to acquire active immunity suggests that neither of these two possibilities play a very prominent part. The third and more plausible alternative says that virus strains in endemic areas are less virulent than in epidemic areas. Natural immunisation after sub-clinical infection occurs under conditions of maximum faecal contamination and low virulence, without having to pay a high toll. This hypothesis has been put forward as the explanation of the fact that Malta had an incidence rate of only 2 per 100,000 for forty years before the
epidemic of 1942, but showed a high incidence rate and paralytic ratio during that outbreak, because the virus causing the epidemic was more virulent. Sabin goes as far as to say that, "it is not at all unlikely that future observations will firmly establish that epidemics of poliomyelitis occur when strains of high virulence are disseminated among populations which are insufficiently immunised by infections with strains that are either avirulent or of low virulence". Present evidence does not support this theory because the strains isolated from endemic areas have shown themselves to be virulent. The experience of troops from temperate climates serving in Korea, Philippines, Malaya and India also show that endemic strains are not all avirulent.

In endemic areas, infection with poliovirus invariably occurs at an early age. Since, the manifestations of poliomyelitis, like most other infections, are less severe in the younger age group a high incidence is associated with a very low paralytic rate. The fact that repeated small doses of the virus results in a higher proportion of inapparent infection may explain the paradoxical phenomenon of high incidence and low paralytic manifestations.

However, poor conditions per se provide no guarantee against infection, because virulent strains or previously unknown types of the virus will spread through the community very rapidly causing a very high and severe incidence of poliomyelitis. This is clearly shown in the epidemics of poliomyelitis among the Eskimos in Alaska. On all the three occasions, (type III in 1905; type I in 1915; type II in 1930)
the virus disseminated extensively and in one epidemic the case-paralysis ration was as high as 21%. Even in the tropics, there may be pockets of virgin soil, especially islands where the disease presents itself in epidemic form. The epidemics in St. Helena in 1945 and in Nicobar islands in 1947 illustrate this fact. An epidemic in Palestine showed a high incidence (7.4%) among infants less than six months old, suggesting that they were born of mothers without antibodies against the virus.

In some areas, the disease has reached hyperendemic form. The incidence of poliomyelitis in the Congo during the years 1950 - '52 makes M-J Freyche suggest that the concept of sporadic incidence in tropical countries must be revised, because veritable epidemics are known to occur in many parts of Africa.

EPIDEMIC PATTERN

Towards the end of the last century, the endemic pattern of poliomyelitis was replaced by an epidemic pattern in countries of the world with the highest standards of living, good sanitation and hygiene, namely Western Europe, United States of America, Australia and New Zealand. After the Second World War, epidemics swept through South Africa, France, Italy, Great Britain, Germany and many parts of USA. The important feature of this change in pattern was that there was a shift in the age incidence of the disease. Whereas 90% of all cases were among the lowest age group in the last century, now only a third of the total number of cases was in the under five group. A third belonged to the 5 - 15 age group and a third was among the over 15 (mostly under 40)
age group. Associated with this shift there was an increase in severity of the disease among the older age groups. Two thirds of the 8,000 cases in England and Wales during the epidemic of 1947 were paralytic. A more distressing fact was that among the over 15 age group, the case-fatality rate was as high as 20%. As the years went by, morbidity rates for the disease did not show the slightest sign of any decrease.

The most obvious fact is that somehow, since the introduction of better sanitation, the immunity of the more developed areas of the world to infection by poliomyelitis has decreased considerably. It was a pointer to the fact that large scale interference with the ecology of natural processes may be followed by unexpected and often undesirable side-effects. The chances of obtaining natural immunity by infection were reduced because poliomyelitis is spread in a way that is restricted by hygiene measures associated with the attainment of higher living standards. However the virus is not eliminated from the environment. So in the face of an epidemic, communities in most Western countries had very low immunity. This is reflected in the antibody levels of the population. For example, in Charleston, W. Va, USA, even by the age of 30, only 90% of the population has immunity to all three types of the virus. A significant percentage of newborn infants have no antibody to the virus, since their mothers had never been infected by the virus. This lack of passive protection shows itself in the great frequency of the disease among the 0 - 1 age group in highly developed communities.

© Compare this figure with 100% immunity at the age of six in Cairo.
In endemic areas, infection was mainly transmitted during contacts between children. In most of the developed countries, the social set-up prevents such contacts between children below the school age, except in slum areas where, strikingly enough, there is a tendency towards higher percentage of immunity and the age incidence of the disease is highest among the under-five group. Primary infection is therefore delayed until a later time when contact with infected children occur at school. Therefore there is a shift in incidence of poliomyelitis to the school age group. Since no immunity is acquired merely by the process of growing up, nonimmune adults are prone to infection just as much as children. In fact on epidemiological basis, there is evidence to suggest that the neurones of children are more resistant than those of adults. \(^\text{17}\) The clinical manifestations of the disease are more serious in higher age groups.

The increase in morbidity rates was associated with a decrease in case-fatality rates, during the last 20 - 30 years. This apparent contradiction is explained as a negative correlation which is based on a predominantly psychological factor. A large number of cases of nonpoliomyelitis origin may be included as nonparalytic poliomyelitis during an epidemic. Milder cases which will go unnoticed at other times are reported during outbreaks and tend to increase morbidity rates. On the other hand, treatment of serious forms of the disease has decreased mortality rates to some extent, however small it may be.
CONTROL OF POLIOMYELITIS

In areas where the ratio of frank to silent infection is low and the disease occurs mainly in childhood with an insignificant paralytic rate, free passage of the virus has some justification, since it does confer natural actively acquired immunity on a large majority of the population without cost in life and permanent disability being excessive. But where the disease is present in epidemic form, with no assurance of inapparent infection in those not frankly affected due to limitation of the spread of virus by 'good' sanitation, the virus cannot be allowed free passage. The price that a community has to pay for natural immunisation under such circumstances would be too high. So preventive measures in the form of quarantine of cases and contacts, with passive protection for those exposed to the infection and artificial immunisation for the community at large constitute an integral part of the fight against poliomyelitis - a fight in which good sanitation plays only a small part.

PREVENTION OF PARALYSIS

The first step in the control of the disease lies in the prevention of paralysis in those who may be exposed to the virus. Basically, this involves the avoidance of factors which are known to precipitate paralysis in the infected person. All elective surgery for tonsillectomy should be delayed till the epidemic season is over. Where surgery is imperative, it must be carried out under 'cover' of passive immunisation. Over-exertion of all ill persons should be prevented during an epidemic.

vide supra (page 10)
Intramuscular injections of heavy metal and combined adsorbed vaccines must be used with great care. In severe epidemics it may be necessary to suspend all such injections. Since it is possible that the virus may be present on the skin, measures for adequate sterilisation must be employed to prevent cutaneous entry of the virus into the body. The possibility of contact with frank cases must be reduced to the minimum.

PASSIVE IMMUNISATION

The next line of defence against paralytic manifestations of the disease is the passive immunisation of those who have been exposed to the virus. It is known that the gamma globulin fraction of human plasma contains antibodies to poliomyelitis. This may be obtained from those who have been infected in the past or from convalescent cases. The serum from one person is most likely to contain only one type of antibody, but it is possible to obtain polyvalent serum by pooling sera from a large number of persons and from different areas. This carries with it a certain risk, because pooled sera is often contaminated with the virus of infective hepatitis. This difficulty can be overcome by obtaining a gamma globulin concentrate from pooled sera. Gamma globulin from a large pool will contain antibodies to all three types of the virus, but titration is essential to ensure that sufficiently high titres of each antibody are present. Used prophylactically, gamma globulin in adequate doses causes a slight reduction in the severity of paralysis in the first week and markedly reduces the severity and incidence rate in the following four to five weeks.
The reasons why gamma globulin cannot be used for mass prophylaxis are obvious. It would be necessary to provide passive immunisation to thousands to protect a very few who would develop clinical disease without it. For maximal effectiveness globulin concentrates or human sera have to be given two weeks before exposure to the virus. But present-day epidemic prediction methods are not sufficiently accurate to indicate the time and location of the next outbreak. There is no substitute for human serum and large pools of it are necessary. Moreover standardisation of the globulin fraction is very difficult. It is too expensive a method to be adopted for any large scale use.

Nevertheless, passive immunisation has a prominent place in contact prophylaxis. In the absence of actively acquired natural or artificial immunity the use of gamma globulin is advocated for specially susceptible people. These include house-hold contacts, particularly pregnant women, of diagnosed cases of poliomyelitis; medical staff in hospital wards and those needing surgery, especially tonsillectomy, during the epidemic period. Only very small concentrations of gamma globulin are required to protect against paralytic manifestations of the disease. In a field trial conducted in 1951 - '52, 55,000 children between the ages of 1 - 11 were given 0.14 ml of gamma globulin per pound of body weight, and significant protection was provided by this amount which constituted less than detectable concentrations of antibodies in the blood. The mode of action of gamma globulin is not clearly understood. Horstmann and Bodian have postulated that gamma globulin in blood prevents viraemia
and thus protects against the involvement of the central nervous 18 system.

The use of gamma globulin concentrates from a large pool has a certain theoretical advantage. A broadspectrum antibody fraction resulting from the pooling of sera from many areas may be more effective than a similar or even higher level of antibody resulting from active immunisation with only one strain of each recognised type of the virus. But the different strains are sufficiently closely related for this to be of any practical importance.

Gamma globulins do not have any therapeutic value and hence there is no justification for its use after the onset of paralysis.

ISOLATION AND QUARANTINE

Measures to reduce the spread of infection form the next method of protecting a community which by its low immunity level is in danger of being subject to epidemics of poliomyelitis. Since poliomyelitis is a highly infectious disease, isolation of the patient is essential. In most cases isolation for at least three weeks is necessary; but in major illnesses, a much longer period may be justified. In some cases it will be possible to determine the duration of the isolation period only by the culture of excreta. Cases of doubtful diagnosis also must be isolated till the diagnosis is proved wrong.

Great care is to be exercised in the disposal of the excreta of an infected person. Observance of strict precautions as in diphtheria
and typhoid fever are necessary in dealing with throat discharges and faeces. Sterilisation of all articles used by the patient will reduce spread by contamination of the immediate environment of the infected person. Cross infection must be prevented in hospitals by making sure that medical personnel, especially nurses, who look after cases of poliomyelitis do not attend on other patients. All medical personnel must be immunised before they come into contact with diagnosed or suspected cases of poliomyelitis.

**Terminal disinfection is as important as concurrent disinfection.** Wards used for housing poliomyelitis patients should be disinfected with soap and water. This is particularly necessary since the virus can survive for a considerable time at room temperature. Patients who are in need of surgical treatment as part of their treatment should not be moved to orthopaedic units till the period of isolation is complete. It must be remembered that convalescent patients excrete virus for six to eight weeks and therefore must be kept isolated from other patients. Use of general swimming baths in a hospital must be forbidden to the convalescent patient. Ideally, there should be separate rehabilitation units for poliomyelitis patients.

While it is not possible to trace and isolate all contacts of a diagnosed case of poliomyelitis, family and intimate associates, especially children, must be considered to be infected. Such persons must avoid over exertion for a period of three weeks. Children must be confined during that period. Adults must take maximal hygienic
precautions. They must avoid association with other children and intimate contact with other adults. If a case of poliomyelitis is diagnosed in a day nursery, it is necessary to treat the children as family associates of a case. In residential nurseries or institutions, quarantine for three weeks must be imposed.

MEASURES FOR THE COMMUNITY

In the face of an epidemic, the community as a whole can adopt some measures to limit the spread of infection. Maximum hygiene is imperative under such circumstances. Washing hands with soap and water after defaecation and before eating prevents the dissemination of the virus considerably. Food must be protected from flies and insects which may act as mechanical vectors in the spread of the disease. Over-exertion must be avoided as much as possible, because it may make all the difference between a paralytic and nonparalytic outcome or between paralysis and death where neurological manifestations have begun. During the outbreaks, the public must be specially warned about working off any feeling of malaise. All illnesses, however trivial, must be treated with bed rest and a doctor must always be consulted without resorting to self-medication. Unnecessary travel into other communities must be discouraged.

Notification of all cases of poliomyelitis, both paralytic and nonparalytic, is essential because only then can effective public health measures be introduced to deal with the epidemic. Organisation of medical help to deal with any emergency can best be done through
a central authority which co-ordinates such services. Notification of the disease also facilitates predictions about the extent of the epidemic and the location of the next outbreak. A detailed system of notification also helps studies into the incidence of the disease in its relation to the socioeconomic factors in the life of the community or country.

ACTIVE IMMUNISATION

The only effective form of controlling poliomyelitis lies in either eliminating the virus completely from the environment or in raising the immunity of the community to a level where the presence of the virus can do no harm. Since human beings form the only reservoir of the virus and as there is no intermediate host involved in the transmission of the infection, it is impracticable to eliminate the virus. Good sanitation, one of the usual and most effective methods of preventing dissemination of the causative agent in enteric infections, has only succeeded in doing more harm than good as far as poliomyelitis virus is concerned. Quarantine and isolation of all cases and contacts is impossible because it is difficult to recognise all the trivial infections that the virus causes and because the majority of carriers are healthy persons. So it is obvious that the disease with its tragic and crippling consequences can be controlled only by raising the immunity of the population to a high level.

The object of artificial immunisation is to stimulate body mechanisms to produce an antibody response which will prevent paralytic...
consequences. The ideal poliomyelitis vaccine would be one which is absolutely safe, which would confer complete and lasting immunity and which can be given in a single dose orally. Two types of artificial active immunisation methods are available now. The first is the parenteral administration of inactivated virus vaccine. The second is the oral administration of attenuated live virus vaccine.

INACTIVATED VIRUS VACCINE

The first vaccine of this type was produced by Dr Jonathan Salk in the United States of America. It consisted of strains of the three different types of the virus which had been inactivated by formalin and proved harmless by intracerebral injection into monkeys. In 1953, Salk conducted the first clinical trial on children and proved that formalin-inactivated virus was capable of producing type-specific antibodies without any ill effects. A much larger trial was carried out in 1954. This trial was evaluated in April 1955 by the Francis report which concluded that the Salk vaccine offered a fairly high degree of protection against paralytic poliomyelitis in children of the 6 - 10 age group.

The preparation of this vaccine was based on the result of experiments conducted in monkeys. It was found that strains which caused paralysis in man always caused paralysis in monkeys when injected intracerebrally. But intracerebral inoculation of the virus could be rendered innocuous, if the monkey had received an adequate dose of antibodies passively, or if antibodies had been produced
actively in response to an earlier infection. Thus it was established that antibodies could protect against the paralytic consequences of the disease. Poliomyelitis virus inactivated in formalin or ultraviolet rays was shown to be capable of eliciting an antibody response without causing infection. Antibodies thus induced protected animals when they were later challenged by live virus intracerebrally. These facts form the basis of the inactivated virus vaccine.

The great enthusiasm with which the Salk vaccine was acclaimed received a serious set back in 1955 as a result of the Cutter incident in which 204 cases of poliomyelitis were reported after the use of the vaccine. 79 of these were children who received the vaccine; 105 were family contacts of the vaccinees and 20 were community contacts. Three quarters of these cases developed paralysis and 11 died. The accident was traced to the presence of highly virulent residual virus in a batch of vaccine prepared by one particular firm. It was realised that safety precautions had been inadequate.

New safety standards were laid down in May 1955. The preparation of the vaccine is now controlled in the United States of America by the 'Minimum requirements: Poliomyelitis Vaccine of the National Institute of Health'.

In the vaccine used in America, type I of the virus is represented by the Mahoney strain; type II by M.E.F.1 strain; type III by Saukett strain. A vaccine similar to the Salk vaccine is used in Britain consisting of less virulent strains to provide greater safety. Type I
is represented by an attenuated variation of Brunhilde known as Brun-Enders, type II by a strain of M.E.P.1 adapted to suckling mice and type III by Saukett. Both the American and British vaccines and other similar inactivated vaccines have been used extensively and millions have received them without ill effects. Reports from different parts of Europe, America and Australia suggest decrease in morbidity ranging from 50-85% after the use of the vaccine. Figures from Canada indicate overall effectiveness as high as 96%. In Moscow where almost all children below the age of 14 were inoculated subcutaneously, there was no significant reduction in the incidence of poliomyelitis, between 1955-'59. In fact 80% of cases reported were paralytic. The wide range in the rate of protection afforded by inactivated vaccine has been attributed to variation in vaccine potency and mode of administration. In England and Wales 75% children under the age of 15 and 40% of persons between 15-20 years have been vaccinated. In some areas 90% reduction in paralysis has been observed.

The greatest advantage of the inactivated vaccine lies in the possibility of preparations which are completely free from paralytogenic properties. Every individual who develops poliomyelitis within 30 days of an injection of the vaccine is thoroughly investigated to decide whether the disease was caused by the vaccine. Since the Cutter incident there has not been any case in which the inactivated vaccine has been responsible for poliomyelitis. Neurological sequelae are very remote since the vaccine contains only killed virus and is produced under
very strict precautions and exacting standards of safety.

The use of the inactivated vaccine has some minor risks attached to it. Sensitisation to the constituents of the vaccine is a possibility. Allergic manifestations are inevitable in the use of inactivated vaccines. But they are few and mild in nature. Bacterial and fungal contamination of the culture may cause toxic reactions, but are prevented by ensuring that the vaccine is sterile. Penicillin and streptomycin used for this purpose may cause sensitivity reactions. Though from a theoretical point of view, monkey kidney present in the culture may act antigenically and cause kidney damage, this is a very remote possibility. The animal serum added in the earliest stages of tissue culture growth is too diluted in the final stage of the vaccine to cause any foreign protein sensitisation.

The chief drawback of the killed virus vaccine lies in the need for repeated administration parenterally to ensure a sufficiently high antibody response. In Britain, the public are being offered the fourth dose of the vaccine at the time of writing. Salk vaccine gives only 80-85% protection after 3 doses. The level of immunity is raised to 90-95% after a fourth dose. From the epidemiological point of view, the disadvantage of the vaccine is more serious, and lies in the inability of the vaccine to protect the individual from alimentary tract infection. It is not yet known how long the immunity provided by inactivated vaccine lasts. If killed virus vaccine is used without a systematic effort to maintain immunity to intestinal infection, it
may result in the incidence of the disease shifting to older age
groups if the vaccine induced immunity wanes. Antibody titres decrease
for two years after a booster dose and then remain fairly constant,
according to the data available now. Moreover, the vaccinee can still
act as a carrier of the virus, because antibodies induced by killed
virus antigen do not provide intestinal immunity. Under 'cover' of the
vaccine, he acts as a healthy carrier and may serve to infect more
people than if he had had clinical infection, when quarantine might
have reduced the risk of dissemination.

ATTENUATED LIVE VIRUS VACCINE

The theoretical basis of the attempts to produce an attenuated live
virus vaccine is the assumption that the neurotropic activity of the
virus and its capacity to multiply in the alimentary tract are determined
by distinct genetic complexes. It is also assumed that the primates
occupy an inverse position with regard to susceptibility of the nervous
system and the alimentary tract - the nervous system being more resistant
and the alimentary tract more susceptible in the higher primates. This
provides the possibility of obtaining a live virus which can cause anti-
body production in humans by alimentary canal infection, without causing
any neurological involvement. It is thought that such attenuated virus
will provide a more reliable antigenic stimulus as it multiplies in the
body and that it will give a greater antibody level for a longer time
than can be attained by inactivated virus vaccines. The goal is to produce
a vaccine containing attenuated strains of all the three types which
will provide long lasting immunity after a single oral dose.

Sabin and Koprowsky who are the pioneers in the field of attenuated vaccines have succeeded in producing relatively avirulent strains by the passage of the virus through laboratory animals and tissue cultures. Repeated passage was undertaken to produce avirulent mutants which, while suitable for growth in the unfavourable conditions of tissue culture and mice brain, would have very low neurotropic activity in man. Some avirulent strains were also found to occur naturally in the alimentary tract of human beings.

The first clinical trial with an attenuated virus was carried out by Koprowski in early 1950, when he fed a dose of type II attenuated virus to a six year old boy. He observed that intestinal infection occurred without symptoms and that after 15 days, specific neutralising antibodies were present in the blood. The virus used on this occasion was a Type II TN strain which had been subjected to 8 mouse brain passages.

The criteria of judgement for the use of attenuated vaccine are as follows. It must be incapable of causing serious illness. The virus must be nontransmissible from a vaccinated to a nonvaccinated person. There must be complete stability of the reduced neurovirulence, without reduction in capacity to infect the alimentary canal. The virus must be of sufficient antigenicity and must be present in high concentration to produce an antibody response adequate to meet later infections, after one dose.
The avirulence of the attenuated strain is tested by introducing it in large doses intracerebrally and intraspinally into monkeys. Since the nervous system of the monkey is far more sensitive to the poliovirus than that of man, absence of significant neurological involvement is assumed to show that it will not be neurotropic in man. Absence of viraemia in the human subject may be used as the criterion of safety, since the most well supported theory holds that viraemia is the sine qua non of the involvement of nervous tissue. Therefore, production of antibodies without viraemia along with intestinal carriage indicating alimentary tract infection is the best criterion for the safety and efficiency of the vaccine before extensive field trials are conducted.

A detailed clinical trial conducted with 89 persons who were given attenuated live vaccine containing strains of all three types formed the basis for field trials. None of the 89 persons developed signs or symptoms of illness. 84 of them developed antibodies. There was no detectable viraemia in the 66 cases tested for the presence of virus in the blood. But antibodies were found as early as the 7th day. 14 cases that were checked for antibodies showed presence in high titres upto 41 months. 10 out of a group of 12 did not show intestinal carriage when the virus was fed a second time, but two did. One of them became a carrier even after a third feeding of the virus. It was demonstrated that administration of small doses such as 1 ml produced antibody titres as high as that attained in 5 ml and 10 ml doses.

@ When the results were published in 1955
but did not result in intestinal carriage. Equivocal results were obtained in attempts to produce antibody under cover of gamma globulin.

The factor which caused great concern was the instability of the virus when introduced into the natural host, man. It was argued that the neurotropic activity of the virus depends on a wide spectrum of genes and hence the chances of mutations with greatly increased neurotropic properties emerging as a result of successive passage in the human host are small. Koprowski maintained that six serial passages of attenuated virus in man did not cause increased neurovirulence for 22 man. But some outbreaks of poliomyelitis after the use of the vaccine were reported to be due to the fact that the attenuated variants were less stable than was once hoped for. It was argued that the vaccine strains may revert to greater virulence in the intestinal tract of the inoculees and still more in the intestines of contacts of vaccinees. The fact that production of antibodies after the administration of the vaccine is almost invariably associated with a carrier stage made this possibility a more sinister one.

Recent evidence has however, shown that the problem of spread is not as serious as had been feared. Live attenuated virus vaccine has been used very extensively in USSR, and most of the Eastern European countries as well as in Vietnam and certain parts of the Republic of China. 80% of the spread has been limited to families. It has been established that the tendency to spread decreases progressively with the number of contacts. The virus has not persisted in areas where
mass immunisation programmes were undertaken. No harmful effects have been noticed in the local community. Reports from some Latin American countries are not as favourable as these observations. 12% of the 225 cases reported in Nicaragua had received the attenuated virus.

Most impressive figures have been obtained with the use of live attenuated virus vaccines during the last five years. Antibody conversion rates have varied from 65 - 95%. USSR switched from the use of inactivated vaccine to live vaccine and found it more satisfactory. More than 50 million persons have been given the attenuated vaccine in Russia, and antibodies to all three types were as high as 94 - 98% after three months. Evaluation of USSR trials shows that there were no major illness after administration of the vaccine. Reactions, when present, were mild and consisted of transient fever, nausea, vomiting and intestinal symptoms. It has been suggested that the vaccine can be administered even during epidemics and provide a certain degree of protection.

The greatest advantage of the live attenuated vaccine is the simplicity of administration. In the majority of cases a single oral dose provides high antibody levels. No tolerance develops to the vaccine and in cases where there is no antibody response, an increased second dose may be given. It is possible to induce antibody production in the presence of placentally transmitted passive immunity. Since the vaccine causes intestinal infection, local immunity is also produced.

© Three types of attenuated vaccines are available: they are Sabin, Koprowsky and Lederle vaccines. USSR used Sabin, considered to be the best.
which prevents reinfection with the virus. This is especially true of type I and type II strains, though reinfection with type III strains is common.

The attenuated virus vaccine, apart from the uncertainty which is still present about its stability and safety, has a few other less important disadvantages. When the three different strains are administered together, interference develops on occasion with the result that there is no uniform immunity to all three types. This can be easily overcome by administering the three types, one after another with an interval of about a month between them. In some cases other enteric viruses may cause difficulty in seeding the alimentary tract with poliovirus. Often this interference is more difficult to overcome.

Taking into account these difficulties, Koprowski points out the possibility and advantage of immunising the newborn. Such a procedure ensures proper administration of the vaccine in hospital. Antibodies can develop under cover of placentally acquired maternal antibodies. Enteroviruses do not interfere at this early stage of life, because the intestinal tract of a newborn is free of them. Spread of virus from infants does not occur very often. Nevertheless it has been shown that vaccine administration is most effective not within a few hours after birth, but about three months later.

EVALUATION OF VACCINES

It is clear that neither the inactivated vaccine nor the live attenuated vaccine, conforms completely to the ideal. It seems almost
like the search for the philosopher's stone, when a vaccine which has no risk at all attached to its use, which provides life-long immunity and can be given orally in a single dose is expected. At the same time, no large scale vaccination programme can be undertaken if there is a definite danger of acquiring the disease through the vaccine. Also, there is little point in having a vaccine which must be given every two or three years throughout life. Live attenuated vaccine, especially the Sabin type, has a lot to commend itself. There is economy of production and ease of administration. All the attenuated strains now in use are considered to be safe and so from the epidemiological approach, the live vaccine is superior to the inactive vaccine which provides immunity only to paralysis and not to infection by the virus. Attenuated vaccines provide the possibility of replacing the 'wild' strains in nature by avirulent strains of the virus.

On the other hand, the use of inactivated vaccine can be undertaken in complete confidence about its safety, where as it has been shown that viraemia may occur after the administration of the live vaccine. Such a possibility makes it unwise to use the latter without the protection of the former in older nonimmune adults. In as much as the inactivated vaccine can be freed of all other bacterial, fungal and viral contamination, by suitable methods, pure and standard preparations are more easily available than in the case of live attenuated vaccine where contamination, especially by simian viruses is difficult to avoid.
IMMUNISATION PROGRAMMES

Mass immunisation programmes have been under way since the announcement of the Salk vaccine in 1954. The earliest programmes were conducted in the United States of America, among school children between the ages of 5 - 10. When the production of vaccine was limited, it was offered almost exclusively to the most vulnerable group in the community. The age group showing the highest incidence of paralysis in the immediate past was chosen as the first group to receive protection from poliomyelitis by active immunisation. Priority was also given to pregnant women, those going abroad to endemic areas, medical personnel and laboratory staff. Now that the vaccine production can meet greater demands, vaccination is offered to anyone who desires to benefit from it. Immunisation by inactivated vaccine is extensively undertaken in most countries of Western Europe, Australia, New Zealand, South Africa, United States of America and Canada as well as in the United Kingdom. The schedule of immunisation varies from country to country, but one suggested recently envisages two doses with one month's interval between 7 - 10 months followed by booster doses at 15 - 18 months and 2 - 4 years.

It is not advisable to use the inactivated vaccine in the face of epidemics. The epidemic usually runs its course before immunity is conferred and the fact that vaccination is given by injection may precipitate paralysis. The vaccine may however be used in the peripheral regions of the epidemic area.
The attenuated vaccine also has undergone fairly extensive trials. However, there seems to be a psychological barrier to the use of this type of vaccine. In spite of the glowing reports about its safety and efficiency from the countries of Eastern Europe, Singapore, Mauritius and many other places, there seems to be no great enthusiasm about its use in many of the Western countries. The most opportune time for the use of the attenuated oral vaccine is the season of the year when the incidence of poliomyelitis is at its lowest level. This makes winter months the best time for immunisation. Various schedules with successive use of monovalent vaccines as well as polyvalent preparations have been suggested. One particular schedule proposes a first dose of monovalent type I attenuated vaccine, followed by a bivalent preparation of type II and type III and crowned by a final dose of a trivalent vaccine.

Much heated argument has taken place at international level about which of the two types of vaccines must be used for mass programmes. Whatever the arguments for or against one type of vaccine, the final decision in many countries seems to be taken by economical, sociological and epidemiological factors. The inactivated vaccine is more often used in countries where funds and personnel are available for this more expensive and specialised form of immunisation. Experience in production and administration often decides for one particular type of vaccine. Attenuated vaccine is the immunisation method of choice in countries where the disease is endemic. The danger of increasing virulence on human passage is not a serious problem in such areas because the endemic strains are more virulent than the vaccine strains.
Mass immunisation with vaccines is imperative in the areas of the world where poliomyelitis is present in epidemic form. Even the small risk attached to the use of live attenuated vaccines is relatively insignificant compared with the morbidity and mortality associated with an epidemic in a community which has very low immunity to the disease. In most of the endemic areas, however, there is at present a favourable balance between infection and immunity which is maintained without much cost to the community. So restraint has to be exercised in advising expensive immunisation programmes in such areas. Before mass prophylaxis is advocated in such countries, efforts must be made to conduct statistical surveys which will give information about the type and strains of virus endemically present and the level of immunity. As good sanitation becomes common in these areas, the disease may become epidemic in character and therefore public health authorities must be trained and equipped to maintain the high level of immunity by artificial means.

THE FUTURE

Intensive research work and epidemiological studies have been going on in the field of poliomyelitis during the last three decades. The stage has not yet come when it can be said with confidence that the disease has been conquered. Unlike many other infectious diseases, poliomyelitis is a disease which seems to have triumphed over modern ideas of hygiene and sanitation. As these ideas find acceptance in countries and among peoples where standards of living are low, more epidemics will be reported. Even in the countries of the West, the
disease is still present, sometimes in the very midst of areas where
mass vaccination programmes have been held. It is an indication of
the need for more active research to understand and evaluate the
structure of the poliomyelitis virus, its predilection for the nervous
system and its ability to undergo neurotropic mutations in its natural
host. This must go hand in hand with studies into the epidemiology of
the disease as it is present in endemic areas as well as in countries
which have adopted extensive immunisation programmes. The development
of techniques for the identification and differentiation of strains
belonging to the same type will help to solve problems associated with
geographical and seasonal distribution of the disease. The lack of
absolute correlation between neurovirulence and any of the in vitro
strain markers so far studied, has been responsible for considerable hesi-
tation in the use of the live attenuated vaccine. This has also made
it difficult to follow up satisfactorily cases of paralysis and
nonparalytic disease after the administration of this type of vaccine,
to decide whether viruses identified from such cases are natural
wild strains or those temporarily associated with administration
of the attenuated vaccine. If a stable attenuated strain can be obtained
for each type of the virus, it must be considered that, except in
exceptional circumstances, the live vaccine will ultimately replace
the inactivated virus vaccine.

The International Conferences on Poliomyelitis are an indication
of the co-operation among scientists, epidemiologists and public
health authorities all over the world to study the disease and methods
for preventing it. It may be reasonably hoped that the day is not far off when man's ingenuity, perseverance and co-operation in understanding the world around him will have helped him to conquer one more disease which has caused immeasurable suffering in the past.
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