13. POLIOMYELITIS AND OTHER ENTEROVIRUS DISEASES

Poliomyelitis is no longer making headlines as it did in the early fifties. In industrial countries the development of effective vaccines has led to the disappearance not only of the fear of infantile paralysis, but also of seriously crippled young adults. The severe paralysis striking various parts of the body, leading to quadriplegia or condemning the victim to live for the rest of his days in an iron lung, are now no more than bad memories.

The situation in Central Africa is less favourable. The circulation of the wild virus, transmitted basically by the faeco-oral route is maintained by rudimentary hygiene and sanitation. The widespread circulation of poliomyelitis virus, the prototype of the enteroviruses, ensures early contact and the possibility of acquiring natural immunity in early childhood; but at what a price! This serious viral infection causes an acute anterior poliomyelitis resulting in flaccid paralysis, particularly of the lower limbs. Tropical poliomyelitis is a childhood disease. On a background of permanent endemicity epidemic outbreaks appear at rather unpredictable intervals. In urban areas, where viral circulation is more intense, improved hygiene may have affected families who did not acquire natural immunity. In the absence of vaccination these families are exposed to infection at a later age, when the risk of developing severe diseases is notoriously high. This is also illustrated by unvaccinated expatriates contracting the disease.

In the absence of virology laboratories, paralysis remains the only evident sign of poliomyelitis. The course of the disease is complex. A flu-like syndrome and meningeal signs make-up the intermediate stage between colonization of the anterior horn cells and paralysis. Isolated cases of paralysis are insufficiently reported.

Epidemiological surveillance focuses on faecal excretion of the virus, even though it is discontinuous, and the excretion of other enteroviruses allows to assess the possibility of interferences. This surveillance must be maintained even during satisfactory vaccination coverage to detect fluctuations in the excretion of virus and particularly the emergence of serotype 1 which is possibly an alarm signal.

In 1983 Burundi, Rwanda and Zaire officially reported 37, 22 and 204 cases, respectively. These data are fragmentary. Surveys conducted in the Congo and the Sudan show that the mean annual incidence ranges from 46 to 25 per 100,000 population. These figures are comparable to the 18 to 20 per 100,000 detected in Kinshasa in 1956. As a result, the actual number of cases should be close to 1,750 in Burundi, 1,975 in Rwanda, and 10,602 in Zaire. Moreover, 75% of these cases may give rise to sequelae. The vaccination rate remains too low to cause a substantial reduction in the number of paralysed victims, 80% of which occur in children less than three years old.

This is a dramatic situation for the health authorities. A large number of children have major irreversible functional disabilities, especially affecting the lower limbs. These physically handicapped children in the absence of satisfactory solutions constitute a major burden to the society. Vaccination is the only means of prevention. WHO's Expanded Programme of Immunization received substantial aid for polio-vaccination from the International Rotary Club, which launched its Polio-Plus *campaign with the objective to celebrate its 100th anniversary – in the year 2005 – with the worldwide polio eradication. The Club hopes to collect through its network of 22,000 local clubs and 1,000,000 members the six billion Belgian francs (or US$ 120 million) required. A magnificient effort.*

HISTORICAL BACKGROUND

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HISTORICAL BACKGROUND

1. Evolution of the poliomyelitis in the world

Poliomyelitis seems to have existed since times gone by, judging by the lesions seen on Egyptian mummies and in ancient engravings. However, the first description dates back to the eighteenth century (Underwood, 1789), while the first epidemic of infantile paralysis was observed by *Sir Charles Bell* on the island of St. Helena in 1836. *Heine* described the sporadic form of infantile spinal paralysis, considered distinct from the epidemic form, in 1840.

In 1855 *Duchenne* studied the histopathology of poliomyelitis, which attacks the anterior horn cells of the spinal cord. *Prevost*, *Charcot*, and *Joffroy* showed that the disease was due to cell lesions in the anterior horn, hence the notion of "anterior poliomyelitis". In 1890 *Medin* confirmed that the endemic of sporadic paralysis was identical to the epidemic form (44 cases in Stockholm in the summer of 1887). Poliomyelitis was thus given the name of Heine-Medin disease. *Ivan Wickman's* remarkable 1913 monograph analysing a major epidemic of 1,031 cases in Sweden also provides proof of the person-to-person transmission.

The responsible virus was discovered by *Landsteiner* and *Popper*, who successfully transmitted poliomyelitis to *Macacus rhesus* in 1908 by intra-cerebral inoculation of an a-bacterial human spinal cord homogenate obtained from a case of infantile paralysis. *Flexner* and *Lewis* (1909) succeeded in transmitting the disease serially. These results were confirmed by *Leiner* and *Wiesner* at Weichselbaum Laboratory in Vienna and by *Landsteiner* and *Levaditi* at the Pasteur Institute in Paris. *Straus* and *Hinton* in New York also succeeded in transmitting infantile paralysis to monkeys in 1920. This strain has since been known as Brunehilde, which is the name of the chimpanzee in which it was isolated; it corresponds to sero-type 1.

In 1939 *Armstrong* adapted a poliovirus strain from a person from Lansing, Michigan, to the cotton rat and mouse. The Lansing strain corresponds to today's sero-type 2 virus.

A third, mouse-adaptable, sero-type 3 strain was named Leon after the patient from whom it was isolated. There is a certain equilibrium amongst these three poliovirus subgroups.

The next major progress came with *Enders*, *Weller*, and *Robbins'* brilliant discovery in 1949, of the multiplication of poliovirus *in vitro* in cell cultures of various human foetal tissues. Numerous investigators found that the virus also replicates in human and monkey kidney cells, human amniotic cells, and various continuous cell lines. This was the starting point for investigations leading to the isolation of the virus from stool specimens, to the definition of the three antigenic types and to epidemiological and immunological studies. Culture techniques allowing the production of large quantities of virus led to the development of a killed virus vaccine by *Salk* in 1953 and to an attenuated live vaccine by *Sabin* in 1958.

2. Epidemics in the Belgian Congo and Ruanda-Urundi

In their epidemiological study of poliomyelitis in Central Africa, *Delville* and *Pattyn* (1958) underlined the literature's silence about poliomyelitis in the Belgian Congo. In their opinion, the only important work on this subject was the research that *J. Rodhain* presented to the First Congress of Tropical Medicine in West Africa (1923). In this contribution Rodhain gave a detailed account of the 1919-1920 epidemic.

Whilst some rare, sporadic cases had been reported earlier in various parts of the Belgian Congo, the 1919-1920 epidemic appears to have been the first epidemic to have invaded this country. It occurred in the Lower Congo region, especially around Leopoldville, from July to December 1919. It appeared among the local inhabitants of the Middle Congo District, where it was called the Kinshasa disease. The disease reached the areas around Bumba, Basoko and Stanleyville (Kisangani) towards the end of January 1920. Rodhain produced a map showing the spread of the epidemic.

This epidemic was characterized by a high proportion of adult cases (16,3%) and a high case-fatality rate (27%). Rodhain isolated the virus in *Cercopithecus*, a remarkable performance at the time, by intraperitoneal injection of a marrow suspension.

Although the first case observed in Leopoldville seemed to originate from Matadi, suggesting an exogenous virus introduction, Rodhain was tempted to postulate that the 1919 epidemic was merely an extension of one of the endemic foci in the Mayumbe (Bas-Congo). This infection allegedly became virulent as a result of favourable host conditions created by the 1919 influenza epidemic. In contrast, according to Rodhain, malaria was not a predisposing condition for infection by the poliomyelitis virus.

After 1919-1920 the disease disappeared from the medical reports until 1933. The table on p. 1572 gives the number of poliomyelitis cases recorded in the Congo from 1934 to 1958 (Annual reports of the Medical Department of the Congo, later to be called Zaire).

Table 1: Number of poliomyelitis cases recorded in the Congo (Zaire), 1934-1958

Year	site	Europeans	Congolese
1934		–	1
1935		2	6
1936	Leopoldville (Kinshasa)	–	49
	Lusambo	–	1
	Costermansville (Bukavu)	–	1
	Elisabethville (Lubumbashi)	1	1
1937		–	14
1938		–	20
1939		1	38
1940		6	3
1941		6	3
1942		3	18
1943		5	22
1944		7	20
1945		2	8
1946		6	32
1947		3	52
1948		5	86
1949		4	77
1950		11	326
1951		14	447
1952		11	592
1953		29	707
1954		40	710
1955		80	1,447
1956		14	571
1957		28	564
1958		27	869

Source: Annual reports (Health Services of the Congo)

These figures refer to a population of some 11,000,000. They show that poliomyelitis had a limited impact until 1945 and except for 1936 no major epidemic occurred for some twenty years after 1920. After the war, however, it gained ground and authentic epidemics struck both the native and the expatriate populations.

Towards the end of 1954 *Delville* and *Pattyn* engaged in immunological research on poliomyelitis and enteroviruses, using HLA cell cultures in the new tissue culture department of the Elisabethville (Lubumbashi) Laboratory.

Vandeputte (1957) isolated a type 2 virus in Leopoldville.

Vandeputte and *Bervoets* (1958) felt that whilst the degree of immunity to polio in the cities was fairly well known and could be considered uniform, there was evidence that such immunity in Upper-Kwango varied greatly from one rural area to another (Barski and Lépine, 1956).

Vandeputte (1960) found cytopathogenic viruses in 36.9% of the 1,200 faecal samples collected from healthy children under the age of two, during a one-year period (from October 1957 through September 1958). These included 104 polio viruses (8.7% prevalence) with the following breakdown by serotype: 25 type 1 (24%), 19 type 2 (18%), and 60 type 3 (58%). These sero-types accounted for 2%, 1.6% and 5% of all the viruses that were detected. The other enteroviruses found in this study included 203 coxsackie viruses (16.9%), of which 132 (65%) were type A and 71 (35%) type B, accounting respectively for 11% and 6% of the total; 72 adenoviruses (6%), especially type 3; 39 echoviruses (3.3%), especially type 6; and 74 unidentified viruses (6.2%).

To protect the population, *Courtois* (1958) started the vaccination of the inhabitants of various endemic foci of the Eastern Province (*Province Orientale*) with attenuated live virus (type 1, Koprowski's Chat strain). This checked the epidemics immediately. He then organized a mass vaccination campaign (215,504 subjects) in the Rusizi Plain, in the Kivu Province, without noting any adverse reactions to the vaccine.

In Ruanda-Urundi poliomyelitis did not take on the same magnitude as it did in the Congo (Zaire). It occurred in this area mostly in the form of sporadic cases, although Delville and Pattyn (1958) felt that some small foci were actually more extensive than was thought. These investigators stressed the fact that the Ruanda-Urundi polio epidemics affected children, whereas the first epidemic that had been studied by Rodhain was characterized by a high proportion of adult cases (16,3%).

MAJOR CHALLENGES

A. POLIOMYELITIS

1. Definition

Poliomyelitis is an infectious viral disease of widely-varying severity. Most of the cases are asymptomatic. It produces an influenza-like syndrome in some subjects, a benign lymphocytic meningitis in others, and in a minority of cases a central nervous system invasion, with elective involvement of the motor neurons, mainly in the anterior horn of the spinal cord, causing flaccid paralysis. This last form of acute poliomyelitis is responsible for the name "infantile paralysis", because it strikes particularly young children.

2. The transmission cycle

2.1. *Infectious agent*

The aetiological agent of poliomyelitis is a neurotropic picornavirus (pico = small, RNA = ribonucleic acid). The RNA genome accounts for 25% of the virus particle's mass. The icosahedral virion is 17 to 28 mμ in diameter. As it does not have a lipid envelope it is resistant to ether. It is inactivated by ultraviolet light and desiccation. It can be stored at low temperatures, but is destroyed if placed in an aqueous suspension at 50 to 55°C for 30 minutes. Milk, cream, ice cream and magnesium chloride have a protective effect. The virus is destroyed by pasteurization, and in the absence of organic matter it is destroyed by 0.1 ppm chlorine. A higher concentration is needed to destroy the virus in the stool.

The virus is easily isolated in human and monkey kidney cell primary cultures, human amniotic cells, and continuous heteroploid cell lines of human origin (such as HLA) at 36° to 37°C. Poliovirus has three antigenic types 1, 2, and 3, corresponding to the three original strains, Brunehilde, Lansing, and Leon.

2.2. *Sources of contamination*

Man is the only known natural host in which the virus causes damage. Monkeys and chimpanzees are receptive to the virus inoculated into the brain or spinal cord, where it produces a paralytic disease. Chimpanzees and cynomolgus monkeys can be infected by the oral route, usually without clinical manifestations. The infected animals become carriers of the virus, harbouring it in their intestines. They will occasionally develop viraemia and very rarely a clinical infection with paralysis.

2.3. *Transmission*

Faeco-oral transmission predominates, although other sources of contamination have been mentioned. Still, the digestive tract remains the portal of entry. The virus is excreted by infected individuals for highly variable lengths of time, sometimes as long as 4 months.

2.4. *Host response*

The host-virus relationship is sometimes perturbing. The older the patient, the greater the severity of the infection (quadriplegic involvement) and the risk of respiratory involvement by reaching the brain stem. There is a correlation between the viral replication rate in the intestine and high antibody levels, such as was clearly proven during the evaluation of live vaccines. Pregnancy increases susceptibility. Tonsillectomy may also be a predisposing factor.

Poliovirus infections produce a serologically-confirmed immunity that can persist for years, probably for life, but only to the causal type. However, some cross-immunity between type 2 and the other types is possible.

When sanitation and hygiene are poor, children have a risk of being contaminated in the first years of life. This infection confers a highly desirable active immunity, however with a risk of a paralytic disease in a small number of these children. The immune mother may transmit passive immunity to her children. The maternal antibodies disappear gradually from the infant's bloodstream during the first six months of its life. If the infant comes in contact with the virus during this period of maternally conferred protection, it may develop lifelong active immunity.

Neutralizing antibodies develop quickly, within a few days after exposure to the virus (often before the onset of clinical signs) and persists apparently for life. This implies that *in vivo* viral replication occurs before the phase of the central nervous system invasion. Once the virus reaches the nervous system it is no longer affected by circulating antibodies. Thus, passive or active immunization is effective only if it precedes the involvement of the nervous system. The passive immunity conferred by the administration of antibodies (convalescent serum or gamma globulins) lasts for only three to five months and affects the viraemic stage only; it does not influence replication of the virus in the nerve cells.

3. Epidemiology

Polioviruses are present worldwide. Cases occur all year round in the tropics, while tending to concentrate in the summer and autumn in the temperate zones. Winter outbreaks are uncommon. Epidemics in the tropics and subtropics used to be so rare that the virus was thought not to be widespread in these regions. The historical overview (p. 1571) showns this was not the case at all. The first major polio epidemic in the Belgian Congo was studied by *Rodhain* in 1919-1920. After the Second World War poliomyelitis spread farther inland each year, giving rise to real epidemics amongst both the natives and the Europeans. In 1955 there were 1,447 reported cases among the Congolese and 80 cases among the white population.

Delville and *Pattyn* studied a polio epidemic in Elisabethville (Lubumbashi) from November 1954 to March 1955. It included 53 natives, all of whom were under 10 years of age, and 24 Europeans, 33% of whom were over 20 years old. Twenty viral strains were isolated in tissue cultures (two from spinal cords and eighteen from stools). Eighteen were identified as belonging to sero-type 1, while the other two remained unidentified. The 1956 Bukavu epidemic struck 109 children aged from three months to six years.

In isolated groups such as the Eskimos, the virus circulates less widely and all age groups are equally sensitive. In densely populated regions with rudimentary hygiene the crowded living conditions promote virus circulation. As a result, children are in contact with the virus from early childhood and all are practically immune by the age of four or five. Poliomyelitis thus remains a predominantly childhood illness in these areas only rarely affecting adults. In contrast, non-immune persons moving to these regions may contract the disease, whatever their age.

Since the beginning of the twentieth century the peak incidence of poliomyelitis has shifted from childhood to older age groups. Before the introduction of vaccines, 25% of the patients in the United States were over fifteen years of age. It is difficult to establish the actual mortality rate since the non-paralytic infections are seldom recognized. In years of high prevalence the specific mortality may seem lower than in years of low prevalence, because non-paralytic cases are more frequently diagnosed during epidemic phases of the disease. The case-fatality rate is 5 to 10% and tends to be higher in the older age groups. In recent epidemics, one third of the cases occurred in patients over fifteen years of age, whilst two thirds of the deaths were in this age group. The disease is more severe in adults than in children. Above the age of sixteen there is a greater frequency of quadriplegia and paralysis of the respiratory muscles. The incidence of polio is twice as high for boys as for girls up to the age of fifteen years. In young adults, however, the incidence is slightly higher in females.

Poliomyelitis is grossly underreported. Between 1974 and 1984 Burundi, with a population of 4.5 million, reported an average of 45 cases a year; Rwanda, with a population of 5.2 million, reported 17 cases; Zaire, with a population of 28.8 million, reported 400 cases. If the rate of paralytic sequelae is 10 to 30 per 100,000 population, these countries should have reported at least 450, 510, and 2,880 cases a year, respectively. *Lebrun* and co-workers (1960) found for 345,000 inhabitants in Leopoldville 18.8 paralytic cases per 100,000 population, or 57 cases per year from 1951 to 1958, whereas the official statistics gave 19 cases per 100,000 population, or 5.8 per year. These figures included both paralytic cases and mortalities.

Generally speaking, three major epidemiological periods can be distinguished. These are the endemic, epidemic, and post-vaccination phases.

a) *Endemic phase*

In some overcrowded developing areas, mainly located in the tropics, paralytic poliomyelitis is a sporadic, endemic disease of early childhood. Virtually all children above four or five years of age are immune. Since almost all women of childbearing age in these countries have antibodies to the three types of poliovirus, they transmit passive immunity to their offspring, so that the first infection in children often occurs under protective maternal antibodies, without presenting any visible clinical symptoms. Consequently paralytic poliomyelitis appears to be relatively rare, explaining why poliomyelitis was long thought to be almost nonexistent. However the reverse is at present the case in the developing world. Poliovirus is extremely widespread, but almost all infections asymptomatic.

b) *Epidemic phase*

During the first half of the twentieth century, in areas where local sanitation and household hygiene had reached acceptable levels, endemic poliomyelitis shifted to a pattern of ever-expanding, increasingly severe epidemics. The improved sanitation and living conditions had reduced the virus circulation and consequently the risk of childhood infection. As a result, initial exposure to the virus occurred later, with a higher risk of paralytic forms. The number of non-immune

subjects rose steadily until a critical mass of receptive individuals was reached, setting the stage for epidemic outbreaks. In developed countries the higher socio-economic classes were the hardest hit. In less advanced countries of the tropics and subtropics, improved hygiene, inducing infant mortality to fall below 75 per thousand, increases the incidence of clinically detectable poliomyelitis.

c) *Post-vaccination phase*

This period began after the widespread introduction of the Salk (killed virus) vaccine (1955) and the Sabin (attenuated live) vaccine (1959). The incidence of poliomyelitis fell dramatically in the countries where mass vaccination campaigns were introduced (most of Europe, the United States, Canada, Australia, New Zealand, a.o.).

Few figures illustrate the value of this policy. In 1955, before the introduction of the Salk vaccine, there were:

17,364 cases of polio reported in the USSR;
27,343 cases in 23 other European countries;
31,582 cases in the USA, Canada, Australia and New Zealand.

The total number of cases reported by these same countries in 1967 was only 1,013. Thereafter the number of cases in the USA, for example, diminished progressively. Eighteen cases were reported in 1969. This was followed by a jump to 31 cases in 1970, but 22 were due to a small epidemic that broke out in a group of non-immunized subjects in Texas. In 1971 seventeen cases were reported, scattered over twelve states. The number of cases increased to 29 in 1972, but only 20 cases were reported from 1973 to 1975.

Polio epidemics flared up in Belgium periodically until 1963. The mean annual number of reported paralytic cases was 479 from 1950 to 1957 (with a peak of 1,038 cases in 1956). The introduction of mass vaccination with a killed virus vaccine (Salk vaccine) for children between the age of six months to fifteen years brought this figure down to 196 cases per year for the period from 1958 to 1963. Mass vaccination of the population between the ages of three months and forty years with an attenuated live vaccine was undertaken in 1963, reaching three million people, and vaccination of all children aged three to eighteen months became compulsory. Poliomyelitis has not reappeared in Belgium since 1964, except for a few imported cases.

Wild poliovirus is seldom isolated in regions where mass immunization campaigns with live vaccine have been carried out routinely so as to reach all young children. The vaccine virus is excreted abundantly by the vaccinated subjects, who consequently infect and vaccinate in turn their non-immune contacts. Thus, almost all of the viruses that are isolated are very closely related to the vaccine strains.

4. **The disease**

Most infections are inapparent with excretion of the virus in the stool, followed by lasting immunity. Clinical symptoms develop in 1% of the infected subjects after an average incubation period of from 7 to 14 days (ranging from 3 to 35 days).

The onset of the disease is marked by an influenza-like syndrome with fever that may be as high as 39° to 40°C, malaise, aches and stiffness, headaches, sore throats, nausea, vomiting, and various digestive disorders. The latter are sometimes interpreted as gastro-intestinal infections. Recovery without sequelae follows in a few days, the individual having acquired specific immunity.

The development of aseptic meningitis, announced by neck stiffness and Kernig's sign, is another possibility. The diagnosis of meningitis must be confirmed by lumbar puncture, the CSF is clear and the diagnosis of aseptic meningitis is made. Moderate pleiocytosis, usually between 10 and 200 leucocytes/mm^3, is the rule, although in rare cases it may exceed 500 leucocytes/mm^3. The polymorphonuclears predominate in the early stage, giving quickly way to lymphocytes. The protein level is elevated – in the order of 40 to 50 mg/100 ml – and persists longer than the pleiocytosis, the glucose concentration is normal. However, as aseptic meningitis can be caused by other viruses as well, the diagnosis must be confirmed by isolation of the virus. Aseptic meningitis caused by poliovirus lasts only from two to ten days and is followed by rapid, complete recovery.

The severest form of the disease is the paralytic type. It may as well appear abruptly or follow the development of a benign symptom complex from the beginning.

The sudden development of flaccid paralysis after an infectious prelude is characteristic of acute anterior poliomyelitis. A large as well as a small number of muscles may be involved. The distribution of paralysis is extremely variable. Mono- and paraplegia of the lower limbs are the commonest forms. The paralysis can also be limited to the muscles of one or both upper limbs, the trunk, or the neck. The paralytic pattern may be irregular, with paralysis of the muscles of one lower limb and the contralateral or homolateral upper limb. It is degenerative and is followed by atrophy of

the muscles. The tendon and skin motor reflexes around the affected muscles disappear. The sphincters are usually intact. Urinary retention may be seen during the febrile period. Sensitivity is unaffected.

In many cases the paralysis may regress, with a slow, gradual return of voluntary movement, depending on the extent of the motor neuron destruction, since the destroyed neurons do not regenerate. Maximum recovery of mobility usually occurs within six months, but improvement after this period cannot be ruled out. The irremediably paralysed muscles will slowly atrophy.

The paralysed limbs are subject to vasomotor disorders, as a result they are usually colder and more cyanotic than the healthy limbs. Trophic disorders may develop, with developmental abnormalities and deformities, usually of the lower limbs.

5. **The diagnosis**

5.1. *Clinical diagnosis*

In the event of an infectious episode accompanied or followed by aseptic meningitis or paralysis, the possibility of poliomyelitis must be considered and the diagnosis confirmed or ruled out.

5.2. *Specific diagnosis*

5.2.1. *Isolation of the virus*

The virus can be isolated from throat swabs during the first few days of illness and over a longer period from rectal swabs or the stool. Isolation on a variety of human or monkey cell cultures is straightforward. The induced cytopathogenic effect can be neutralized by specific antibodies, allowing identification and typing of the infective virus.

The virus can be detected in 80% of cases in the first two weeks of illness. After this period, the viral recovery rate falls. Permanent carriers are not known. Poliovirus is rarely isolated from the CSF, whereas coxsackie and echoviruses, when involved, are more easily isolated from the CSF. In patients deceased at an early stage, the virus can be isolated from the spinal cord, but the chances of success decrease if death occurs four to five days after the onset of paralysis.

Samples for virus isolation must be kept frozen after collection and during transportation to the laboratory.

5.2.2. *Histopathology*

Histological examination of the spinal cord allows post-mortem confirmation of the diagnosis by the lesion of motor neurons in the anterior horn cells.

5.2.3. *Serology*

The serological diagnosis relies on either the titre of neutralizing antibodies or the detection of complement-fixing antibodies. Correct performance of these tests requires one to collect two serum specimens, one taken as early as possible after the onset of the disease, the second two to three weeks later, so as to reveal significant increase in antibody levels. Serum neutralization tests are preferable as they are easy to carry out on cell cultures and also allow typing.

6. **Prevention and control**

Vaccination is the only effective means of preventing and controlling poliomyelitis.

Attempts to develop a vaccine were made very early. Trials by *Römer* and *Flexner* (1910) with infected monkey spinal cord homogenates, modelled after Pasteur's technique for vaccination against rabies, were the first examples. The attenuation of poliovirus strains by adaptation to the rabbit (Blanc and Martin, 1950) lost its attraction even before the technique was adjusted thanks to the success of cell cultures (Enders *et al.*, 1949).

a) *Vaccination with killed vaccine*

The first effective vaccine was introduced by *Salk* in 1953. It was a suspension of the three poliovirus types grown in monkey kidney cells and inactivated by formalin. The vaccine was subjected to wide-scale testing in 1954 and was recognized as being safe and effective. In 1955, shortly after the vaccine received official approval, cases of poliomyelitis appeared in subjects who had been vaccinated with certain lots of vaccine that were found to contain live virus. More care in preparing and checking the vaccine closed this chapter of accidental transmission.

The large-scale use of the Salk vaccine is thought to have reduced the number of cases of paralytic poliomyelitis by 80 to 90%. This vaccine is administered by injection in two doses one month apart, followed by a booster six or seven months later. Childhood vaccination begins at the age of two months; the recommended practice is to vaccinate in three doses at one-month interval, also followed by a booster. This vaccine can be combined with the DPT vaccine.

Unless booster shots are given regularly, vaccination with killed virus does not prevent replication of wild virus in the intestine and thus a carrier stage. As a result, the risk of epidemics is not completely eliminated and outbreaks have been recorded in vaccinated populations, with as many as 20% of the cases of

polio occurring in vaccinated subjects. Still, the number and the extent of epidemics fell sharply after the introduction of this vaccine.

b) *Vaccination with live vaccine*

Koprowski and co-workers (1952) were the first to vaccinate children with an attenuated type 2 poliovirus with reduced CNS virulence in monkeys after passages in cotton-rats and mice. This vaccine produced an inapparent infection with an antibody response comparable with that of a natural inapparent infection. However this highly immunogenic vaccine was also highly unstable and had to be withdrawn from use.

Sabin subsequently obtained attenuated virus strains by rapid passages in tissue culture and selection by the plaque technique developed by *Dulbecco* and *Vogt*. This technique led to the development of a live vaccine containing all three antigenic types. Used on a large scale from 1958 onwards, this vaccine proved to be effective, inducing a rapid antibody production. In addition to this humoral immunity, the vaccine also produced a local immunity in the intestine, manifested by local resistance to wild virus multiplication. It showed no signs of reversion to virulence.

After administration of this live vaccine, the virus localizes in the pharynx and the intestinal tract, where it multiplies, excretion starting after 24 to 48 hours. The viral replication in the intestine of the receptive subject is considerable, but, as in infections with wild virus, individual variations are observed. The circulation of wild pathogenic strains is quickly eliminated. The virus continues to be excreted for three to six weeks and sometimes intermittently, for several months. Neutralizing and complement-fixing antibodies appear seven to ten days after vaccination.

The viruses excreted by vaccinated individuals can contaminate unvaccinated contacts and in this way vaccinate receptive subjects. This has been shown to occur 30 to 40 days after vaccination in day care centres. It was feared that this passage of the virus in man could lead to mutations and increased virulence, with the risk of a resurgence of paralytic cases. However, the results of millions of vaccinations carried out in various parts of the world have shown that this risk is more theoretical than real. The innocuity of the Sabin vaccine is well established. Adverse reactions occur in only three per 100,000 vaccinations and are restricted to low grade fever, transient dyspepsia, and allergic reactions. According to the records, one case of paralysis occurs per one million individuals vaccinated by the Sabin vaccine.

The Sabin vaccine is administered by mouth in the form of a liquid absorbed on a lump of sugar, or as a syrup, or even in tablets. Adding magnesium chloride increases the vaccine's stability during storage: it can be kept one year at 4°C and one month at room temperature.

In the case of primary vaccination the scheme originally recommended was to administer separately the three types of poliovirus at two monthly intervals, in order to avoid interference between types, and then to consolidate the immunity by a trivalent booster. Today a trivalent vaccine is given from the start in two doses two months apart, followed by a booster one year later.

It is advantageous to vaccinate when enterovirus circulation is at its lowest, if such a period exists (as during winter in temperate climates). Optimal protection of the population is achieved by conducting mass immunization campaigns concentrated over a short period of seven to ten days. Repetition of the campaigns is essential. Young children make up the bulk of the receptive subjects and are the main reservoirs for the virus, which may then go on to contaminate adults. In order to set up a barrier against invasion by the wild type virus vaccination must cover at least 80 to 85% of the children between zero and four years of age.

The inactivated vaccine is sometimes administered during the first months of life in conjunction with the DPT vaccine, and followed by two or three doses of live vaccine. Live vaccine should be administered several times over the next few years in order to ensure effective immunity.

Relying on the natural immunity produced by the widespread circulation of wild strains in the tropics, with infection being counterbalanced by the protective effects of maternal antibodies (which are also present in breast milk), is exceedingly risky. The cost in terms of crippled children is very high, as polio accounts for seven to twenty per cent of the physically handicapped in these regions. At most, one might consider the merits of restricting vaccination to receptive children, coming from comfortable urban families. But proponents of such a strategy are deluding themselves, as those who are familiar with the situation in the rural areas know very well.

Courtois (1958) was successful in bringing to a halt the epidemics that swept across the endemic foci of the Eastern Province (*Province Orientale*) in the Belgian Congo in the fifties, by vaccinating the population with an attenuated live virus (type 1, Koprowski's CHAT strain). He then launched a mass vaccination campaign involving 215,504 people on the Rusizi Plain (Kivu Province) without any noticeable adverse effects.

Gammaglobulins can confer brief protection against the paralytic phase, but is effective only if given before infection. It is recommended to give an intramuscular injection of 0.3 ml per kg body weight.

Quarantine measures are not very effective in controlling the spread of the disease, given the high carrier rate that is associated with the epidemic phase. Limiting the movements of relatives and classmates may sometimes be justified, in view of the large proportion of subjects who may be infected.

B. ENTEROVIRUSES OTHER THAN POLIO

1. Introduction

The enteroviruses belong to the Picornaviridae family. They include the polioviruses, coxsackieviruses A and B, and the echoviruses (echo = enteric, cytopathic, human, orphan).

Among enteroviruses polio- and coxsackieviruses do not alone cause diarrhoea. On the other hand, among 31 types of echoviruses that, like the foregoing, can produce febrile exanthematous diseases, types 11, 14, 18, and 19 may cause diarrhoea.

Viral diarrhoea is caused chiefly by members of the rotavirus group. These viruses, discovered in duodenal biopsies performed in Australia in 1973, are related to calf diarrhoea and similar viruses. Norwalk and Norwalk-type viruses, which do not grow on cell cultures, also cause diarrhoea.

Rotavirus diarrhoea is dealt with in the chapter Diarrhoeal diseases p. 616.

2. The infectious agents

The presence of enteroviruses and their infection rates in Zaire were revealed by *Pattyn*, *Delville* and *Vandeputte*. Together with the three types of polio viruses, which are the leading members of the picornaviruses, Coxsackie viruses A and B and Echovirus were proven to occur respectively with the following prevalences in Leopoldville (Kinshasa) and Elisabethville (Lubumbashi): 26 % and 6 to 16 % for coxsackie A, 18 % and 11 to 16 % for coxsackie B, and 8 % for echovirus. These included five of the twenty-five coxsackie A serotypes, namely, 9, 11, 13, 15 and 18; four of the six coxsackie B serotypes (2, 3, 4 and 5) and five of the thirty or so echovirus serotypes (4, 5, 6, 7 and 8). A considerable number of untyped viruses were also isolated, as was the case for 83 of the 132 coxsackie A viruses. The unidentified viruses must have included other types of echoviruses. Attention must be drawn to the aberrant characteristics of some Coxsackie virus strains. For example, some are pathogenic for young adult mice, others are not particularly pathogenic for newborn mice, and still others produce a cytopathogenic effect in tissue cultures.

Belgian virologists working in the fifties called attention to the frequency of mixed picornavirus infections, such as polio and Coxsackie A, polio and Coxsackie B, Coxsackie A and B, Echovirus and Coxsackie viruses, etc. (Pattyn et al. 1957; 1958).

More recently, so-called higher numbered enteroviruses such as enterovirus 70 were isolated during an acute haemorrhagic conjunctivitis epidemic.

Enteroviruses are a special problem. They multiply in the intestine and have been frequently isolated from stools. They occur in successive waves of different types that behave, at least to some extent, like enterotropic viruses. Seven types have been isolated so far; these account for 2 to 14 % of the viruses isolated from faecal material. Types 2 and 6 have also been isolated from water in Elisabethville (Lubumbashi) sewers. Apparently waves of different serotypes followed on one after the other.

3. Epidemiology

Man is the main reservoir for these viruses, which infect a high percentage of very young children, particularly under two years, with a peak occurring around eight months of age. Seventy-five percent of the viruses are isolated in children under five years, and the infection is often prevalent in the families environment.

Unlike cases in temperate climates, there is no clear seasonal pattern of incidence in Central Africa. This is probably due to the lack of noticeable fluctuations in biological conditions.

Enteroviruses often occur simultaneously in the same area, but they are transmitted unevenly because of the great variability of their faecal excretion. Their spread is linked to poor hygiene and faeco-oral transmission with high infection rates. It should be pointed out that adenoviruses are predominant in the dry season.

Generalisations should be avoided, given the discrepancies in the results of studies conducted in

Leopoldville (Kinshasa) and Elisabethville (Lubumbashi). Only investigations on the various biotypes in Zaire, Burundi and Rwanda could give a true picture of the overall situation.

Two small epidemics were seen in Leopoldville (Kinshasa) in 1958. The first one, which occurred in June and July, produced aseptic coxsackie B 1 meningitis. This virus was isolated from five CSF and six faecal specimens from these patients. The second one emerged in August 1958 and was caused by a type 3 adenovirus that had been seen a year earlier by *Defru* and co-workers (1957) in Elisabethville (Lubumbashi).

4. The diseases

Most of the infections are inapparent but can be detected by the presence of specific antibodies that have been acquired through occasional encounter with the viruses. Some of them produce a mild disease which escapes the notice of practitioners who have to deal with an overwhelming number of patients.

The majority of the clinical infections are characterized by an extremely commonplace clinical picture consisting of a flu-like syndrome and febrile diarrhoea. Sometimes there are painful symptoms such as epidemic muscle pains or Bornholm disease, caused by coxsackie B 1, pseudo-measles or rubella-like rashes caused by echovirus 16, oro-pharyngeal symptoms such as herpangina due to Coxsackie virus A 21, neonatal myocarditis caused by coxsackie B, and respiratory symptoms. Aseptic meningitis and other neurological symptoms such as convulsions, problems of consciousness or behaviour, and facial paralysis, as well as a symptom complex evoking infantile paralysis, caused by Coxsackie B viruses may be seen.

5. Diagnosis

Detection of the virus in the stool, blood and CSF is conclusive, particularly if accompanied by a significant rise in serum antibody titres during the course and after recovery of the disease.

Virus isolation from stool is not sufficient for diagnosis, which should be confirmed by a significant increase in the level of the corresponding antibodies.

In the case of meningitis the CSF is aseptic, under pressure, and shows increased cell numbers; protein is elevated only at a late stage and the glucose and chloride levels remain normal.

6. Treatment

The treatment is purely symptomatic.

J. Delville, S. Pattyn and P.G. Janssens

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EXAMENS B

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The author reviews the various observations on poliomyelitis made on both expatriates and natives in the Congo by various investigations of Delville, Pattyn, Lebrun and Van de Putte. He considers the Elisabethville epidemic of 1954-1955, the Bukavu epidemic of 1956 and the Leopoldville epidemic of 1951-1955 and ascertains that three types of poliomyelitis virus were circulating in the Belgian Congo at the time.

COURTOIS G. (1958), Vaccination antipoliomyélitique par virus vivant au Congo belge, – *Ann. Soc. Belg. Méd. Trop.*, 38, pp. 805-816.

Experimental tests of the harmlessness of Koprowski's attenuated live virus vaccine (CHAT strain) in chimpanzees were followed by human vaccination trials in which an oral type 1 polio-vaccine was administered to 215,504 individuals without a single report of an adverse reaction. This vaccine was administered by four centres during a polio epidemic to the entire population. The epidemics were halted immediately and no new cases developed in the vaccinated individuals one week after the start of vaccination.

DELVILLE J.P. & PATTYN S.R. (1958), Epidémiologie de la poliomyélite au Congo belge et au Ruanda-Urundi. Etat actuel de nos connaissances, – *Ann. Soc. Belg. Méd. Trop.*, 38, pp. 283-292.

Summary of the literature on poliomyelitis in the Belgian Congo. The authors describe in detail the virology studies conducted at Elisabethville Medical Laboratory since the end of 1954 up to 1956.

DELVILLE J. & PATTYN S. (1958), Etude épidémiologique et virologique de l'épidémie de poliomyélite d'Elisabethville en 1954-1955, – *Ann. Soc. Belg. Méd. Trop.*, 38, pp. 545-559.

This article is the first virological study of poliomyelitis conducted in the Belgian Congo. Eighteen strains were isolated on tissue cultures. Another eighteen Coxsackie virus strains were isolated on newborn mice, as none of these strains replicated on tissue cultures. The results are discussed from an epidemiological point of view.

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A simple handbook for all those who work with the handicapped victims of poliomyelitis. It dispenses advice and original ideas and is a source of ingenious solutions for urban and even rural centres.

LEBRUN A. (1956), Considérations sur la poliomyélite à Léopoldville, – *Ann. Soc. Belg. Méd. Trop.*, 36, pp. 545-559.

The author studies the extension of poliomyelitis among the local population and the European residents of Leopoldville from 1951 through 1955. He sums up the important facts concerning the epidemiology of the disease and vaccination that were known at the time and applies them to the situation in Leopoldville. The outcome of this analysis prompts him to recommend vaccination for all children under two years of age.

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The author recounts the epidemiological and clinical features of the acute poliomyelitis epidemic that spread upriver from Leopoldville to Stanleyville in 1919-1920.