

Poliomyelitis

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Poliomyelitis

Summary

- Poliomyelitis: enteroviral infection with fecal-oral transmission
- There are three related polioviruses, but no immunological cross-protection
- Often asymptomatic infections
- Sometimes flu-like syndrome with muscle pain and fever
- In a minority of patients, an acute asymmetrical flaccid paralysis with sensation intact follows
- Vaccination is very effective as prevention
- Wild-type poliovirus serotype 2 and 3 were last detected in 1999 and 2012 and declared eradicated in 2015 and 2019, respectively
- Vaccination is very effective as prevention
- Emergence of vaccine-derived (reverse mutation) pathogenic viral strains can cause outbreaks in under-vaccinated populations
- Anno 2024, the Global Polio Eradication Programme has not yet achieved the final goal of eradication

General

Poliomyelitis is a disease caused by a picornavirus (family enteroviruses). There are 3 different polioviruses, i.e., serotypes 1, 2 and 3. They do not exhibit immunological cross-reactions. Chimpanzees, Rhesus monkeys and cynomolgus monkeys (syn. *Macaca fascicularis*) can be infected orally and suffer paralysis as a result, but in practice, man is the only reservoir. Chronic latent carriers are very rare, but healthy and immune-compromised long-term virus shedders were identified, excreting poliovirus for more than 20 years. The epidemiological importance of these people is not yet known. The virus does not survive in the wild –ex. sewage and surface water- for more than a few months, and then only under conditions of low temperatures and high humidity.

Historical Note

Poliomyelitis has been known since ancient times. An Egyptian carving from 1580 BC shows typical sequelae of poliomyelitis. At present, it is in the Carlsberg Glyptothek Museum in Copenhagen, Denmark. A 3,500-year-old Egyptian limestone funeral stela represents a man called Roma, giving offerings to the Goddess Astarte. He was a doorkeeper of the Eighteenth or Nineteenth Dynasty.

He is portrayed with a wasted and shortened leg accompanied by an equinus foot deformity. The most likely diagnosis is that these are sequelae from poliomyelitis acquired in childhood. The person appears with a stick which could be used as a crutch. His disability had clearly not prevented his attaining high office, marrying and having at least one child.

In 1916 there was a polio epidemic in the USA with more than 10,000 cases. It was noticeable that most victims with paralysis were found among those groups of the population that observed the greatest possible hygiene precautions. It was referred to as a disease of cleanliness. At that time, the washing of the whole body (rather than just the face and hands) and the installation of bathrooms in the houses of wealthy citizens was greatly on the increase. The improved hygiene ensured the infection did not develop at a very youthful age. The disease follows a more serious course when it occurs at a more advanced age when children are no longer protected by maternal antibodies. Under poor hygiene conditions, children are infected at a very young age, a small proportion of whom will develop paralysis ("infantile paralysis"). In 1952-53 Europe experienced a very severe epidemic. North America also was not spared, with 55,000 cases in 1953.

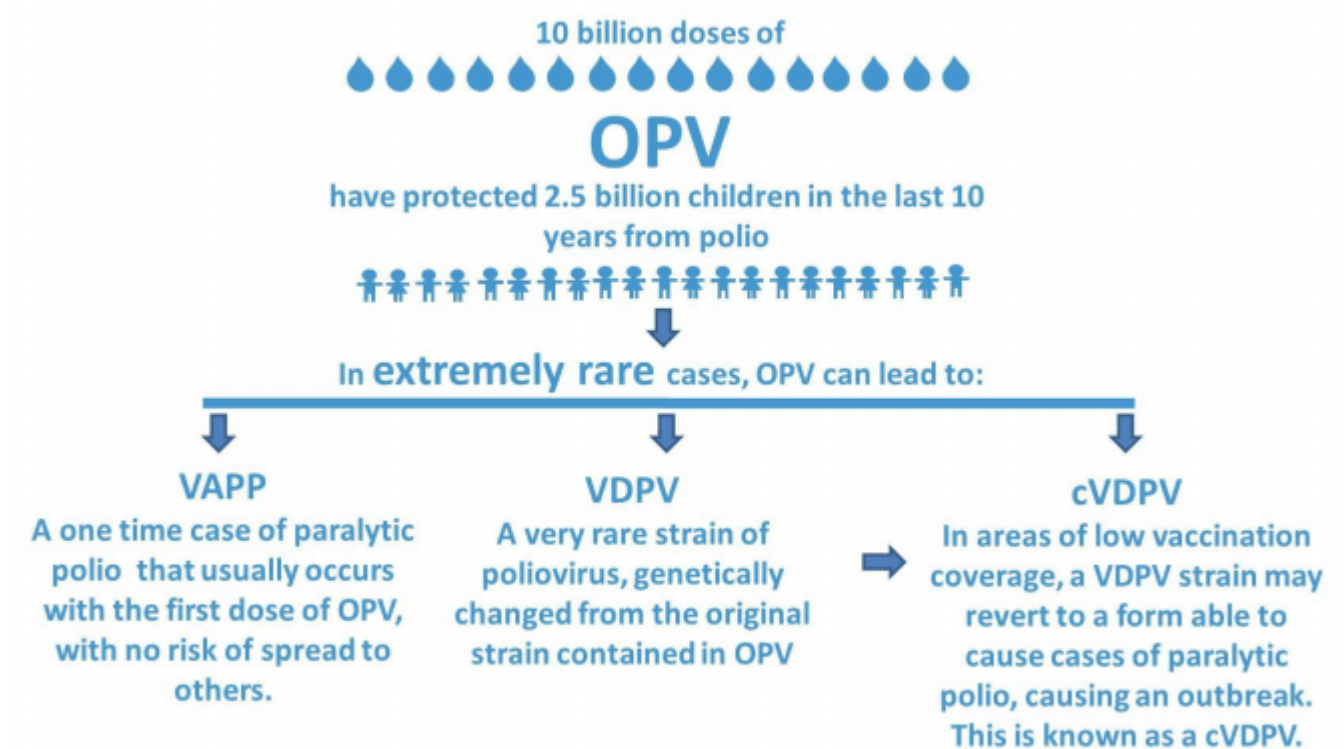
In the early 1950s, Jonas Salk developed the first formalin-inactivated injectable vaccine. This became available in the USA in April 1955. This was followed in 1960 by the oral vaccine developed by the Polish clinician Albert Sabin. Important work was also undertaken by Dr Hilary Koprowski, head of the Wistar Institute in Philadelphia, in relation to an experimental oral poliomyelitis vaccine ("CHAT" vaccine). The incidence of the disease has declined very markedly since the introduction of vaccination. Because the only reservoir is the human being with no persisting infection and because of the efficiency of vaccination, it is an eradicable disease. Though rare persistent carriers exist mostly due to an underlying immune defect. In May 1988, the WHO adopted a resolution to eliminate poliomyelitis ("Global Polio Eradication Initiative"). Since then, huge progress against the disease has been achieved, and until 2016 the number of paralytic cases was reduced by 99.99%, with 42 cases in that year worldwide. As of 2021, the wild-type virus has been found to circulate in Afghanistan and Pakistan only (and one single case in Malawi in 2021).

The hope that it would be possible to achieve the total eradication of poliomyelitis by the turn of the century has not become a reality. As long as a single person remains a carrier of poliovirus, children in all countries are at risk of contracting the disease. The poliovirus can easily be imported into a polio-free country and can spread rapidly amongst unimmunized populations. In 1988, 350,000 cases (1000 children per day) were officially reported in 125 countries. The number is steadily declining. In 1996, the figure was still 4,000 and there were less than 2,000 registered cases in 2002. The last

countries where wild type poliovirus type 2 occurred were Afghanistan in 1997, Nigeria in 1998, and India in 1999. The last known reservoirs of type 2 were in Bihar, Uttar Pradesh and West Bengal. In 2001 the WHO reported that wild-type poliovirus type 2 had been eradicated worldwide. The last poliovirus serotype 3 was seen in 2012 in Nigeria.

In late 2005 however, **vaccine-derived polio virus type 2** reappeared in Nigeria. It was not the wild-type virus that reappeared but a pathogenic reverse mutant from the oral polio vaccine. The emergence of serotype 2 circulating vaccine-derived poliovirus (cVDPV) has complicated the epidemiology of polio. The type 2 component in trivalent OPV accounts for more than 90% of all cVDPV cases. By 2020, 24 cVDPV outbreaks have occurred in 21 countries, resulting in more than 750 cases of paralytic polio. The biggest risk factor for cVDPV emergence is low vaccination coverage. It will take many months for a cVDPV to emerge and cause an outbreak. These cVDPV outbreaks can become endemic and spread further in under-vaccinated communities and even to other countries.

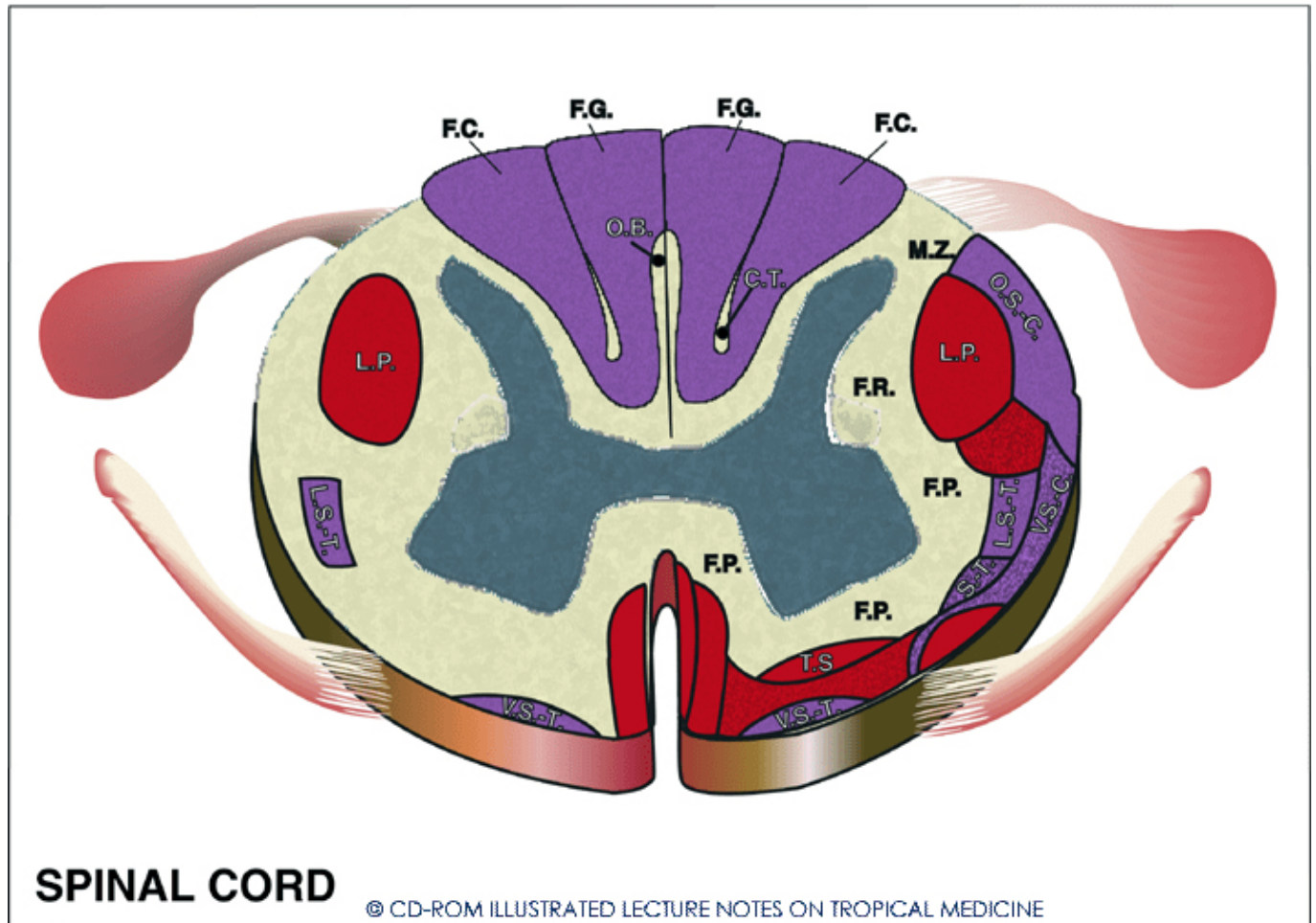
Of note: **cVDPV** (circulating vaccine-derived poliovirus) is not the same as VAPP (vaccine-associated paralytic polio). The latter is caused by a strain of poliovirus that reverts to a neurovirulent variant following OPV administration. This causes a paralysis clinically indistinguishable from poliomyelitis caused by the wild-type poliovirus. VAPP occurs in recently vaccinated patients and sometimes in close contacts of recently vaccinated persons (contact VAPP). The weakened virus in VAPP does not cause outbreaks. It is estimated to occur in 1 out of 2.34 million administered first doses of OPV.



Source: WHO, Polio Global Eradication Initiative

A recent successful event in the polio eradication program was the declaration of a world free of wild-type poliovirus type 3 in October 2019. Since 2012, the only wild-type poliovirus is type 1, and today it is only circulating in Afghanistan and Pakistan. In 2019 176 WPV1 infections were diagnosed in Afghanistan and Pakistan, and 365 cases of cVDPV were diagnosed worldwide of which 40 in Afghanistan and Pakistan and 325 in non-endemic countries, mainly in sub-Saharan Africa. The militant Taliban claim that oral polio vaccination is a Western plot to sterilize Muslim children shows that success can be hampered if the 2019 numbers are compared with 2017: that year only 22 WPV1 cases were reported.

Pathophysiology



Polioviruses can attack motor neurons in the anterior horn of the spinal cord (shown) and in the bulbar area.

Transmission is fecal-oral by ingestion of contaminated food or water, and the incubation period is, on average, 3-6 days. The viruses proliferate in the intestinal mucosa. The virus can still be found in the feces up to a few months after infection. The virus does not cause diarrhea. During the acute phase, it is also found in the throat. After passing into the body from the intestinal tract, the virus becomes localized in various tissues, such as the lymph nodes. On the cell membrane, the virus attaches itself to a specific protein: human poliovirus receptor (CD155). This protein belongs to the immunoglobulin superfamily and occurs in several tissues (brain, spinal cord, kidneys, heart, etc.). However, some cells that express the receptor appear not to suffer any adverse effect, probably because one of the subsequent stages in the intracellular replication of the poliovirus is blocked.

In a small percentage of cases, dissemination occurs to the central nervous system (it is

“neurotropic”), where it can cause non-paralytic aseptic meningitis. In about 1 percent of infections, the virus spreads to the grey matter in the ventral spinal cord (“polios” = grey, “myelon” = marrow), where the motor neurons are found. These are nerve cells that transmit impulses to the muscles. These cells become damaged or destroyed. Damage often occurs at other sites but is usually less pronounced (medulla, cerebellar vermis, midbrain, thalamus, cerebral motor cortex).

Clinical aspects



Poliomyelitis, atrophy of a leg. Such lesions tend to be asymmetric. Copyright ITM

The incubation period is 9 to 12 days (rare extremes 3-35 days). The infection can follow a variety of courses: asymptomatic, flu-like syndrome, aseptic meningitis or paralytic. The most common is an asymptomatic infection (72%). About a quarter of infected cases will develop a short-lasting flu-like syndrome with slight muscle pain: abortive poliomyelitis. In a small minority of cases (1%), non-paralytic aseptic meningitis occurs after this phase of minor signs and symptoms. Fever and muscle weakness can occur initially, sometimes with severe muscle pain. Highly characteristic is the fact that the muscle pain improves on movement. The reason is unclear. Between 1 in 50 and 1 in 500 infections subsequently progress rapidly to paralysis, sometimes within a few hours: "morning paralysis". This is an asymmetrical, flaccid (no tendon reflexes) and often ascending paralysis (exacerbation over a few days). Sensation is not affected. Sometimes the lesions may be localized at a higher level from the onset. Bulbar involvement (10% of the total number of those paralyzed) damages cranial motor nerves such as the glossopharyngeal nerve (9th cranial nerve, palate, swallowing problems), the vagal nerve (10th cranial nerve, including the recurrent laryngeal nerve) and the facial nerve (7th cranial nerve). Occasionally the ocular muscle nerves – the 3rd, 4th and/or 6th cranial nerves – are involved. Hypoxia can occur as a result of involvement of the diaphragm and intercostal muscles. Even though the virus may affect muscles on both body sides, the paralysis is usually asymmetrical. Cerebrospinal fluid contains an increased number of lymphocytes. Recovery can take months, in the course of which marked hypotrophy of the muscles occurs. Mortality during the acute disease can reach 10% due to respiratory paralysis. The sequelae of spinal polio are often permanent if the affected nerve cells are completely destroyed leading to severe disability in a quarter of patients and mild disability in another quarter. In half the patients with spinal polio, cells are not completely destroyed and full recovery will take place with maximum possible improvement occurring within 6 months.

Bulbar versus pseudobulbar paralysis

Bulbar paralysis is caused by injury to the lower motor neurons (motor nuclei of the throat muscles), for example due to poliomyelitis or Guillain-Barré syndrome. Speech is nasal and the tongue is flaccid, atrophic and exhibits fasciculations. The masseter reflex is normal or absent. In pseudobulbar paralysis, there is damage to the higher motor neurons. Speech is monotonous and contains many high tones: spastic dysarthria ("Donald Duck" speech). The tongue is spastic and the masseter reflex increased. There is no atrophy of the tongue.

Dysphasia versus dysarthria

In the case of dysphasia, speech is abnormal in content, usually as a result of a cerebrovascular accident. The disorder may be motor-related in the event of injury to the posterior-interior part of the dominant frontal lobe (Broca aphasia: the patient recognizes an object but cannot say its name) or sensory as a result of damage to the temporal lobe (Wernicke aphasia: the patient does not understand the meaning of words).

In dysarthria, there are difficulties of articulation, but the content of the speech is correct. Injuries to the 9th, 10th and 12th cranial nerves can result in dysarthria, dysphagia and nasal regurgitation.

Post-poliomyelitis syndrome

In some patients, progressive muscle weakness recurs several years after acute paralytic poliomyelitis in the muscle groups involved in the previous episode. Rapid fatigability, swallowing disorders, respiratory difficulties, muscle atrophy, discomfort and pain in muscles and joints can occur. This post-poliomyelitis syndrome affects one in three people who suffered paralytic poliomyelitis forty or fifty years earlier. It is apparently not caused by the reactivation of dormant polioviruses. The exact etiology is unknown. One hypothesis is that the symptoms are due to the natural progressive deterioration of the remaining motor neurons. An as-of-yet unelucidated immunological mechanism might play a role. There is no specific therapy apart from muscle-strengthening exercises. Evidently, further study is necessary to understand this condition better.

Diagnosis

Most victims are children less than 5 years old. The diagnosis is clinical. A predominantly asymmetrical flaccid paralysis of sudden onset with decreased or absent tendon reflexes with normal sensation, normal level of consciousness and preceded by muscle pain is suggestive. Often there is fever and meningeal irritation. Routine laboratory tests show few abnormalities. Lumbar puncture suggests viral meningitis (lymphocytic pleocytosis). In a patient with symptoms suspect for poliomyelitis two stool samples and two oropharyngeal swabs should be obtained at least 24 hours apart in the two weeks after symptom onset. Reverse-transcriptase polymerase chain reaction (RT-PCR) for polio and nonpolio enteroviruses will be performed. Cell cultures will also be done if available. Serological tests with type-specific IgM on serum or on liquor can be performed but, like viral culture, are rarely available. WHO installed worldwide equipped labs for the investigation of acute flaccid paralysis cases (Collaborating Center for Reference and Research on Poliomyelitis). Confirmed cases are usually thoroughly examined with PCR to establish whether it involves a “wild type” virus or

whether it is a reverse mutation of a vaccine strain. For every diagnosed wild-type poliovirus infection, about 2000-3000 asymptomatic carriers exist, underlining the importance of determining the source of the 'outbreak'.

Initial differential diagnosis includes:

1. **Guillain-Barré** syndrome or acute inflammatory demyelinating polyneuropathy is characterized by an ascending symmetrical paralysis with sensory involvement (reduced sensation and paresthesia). A form predominantly affecting the cranial nerves also exists (Miller-Fisher syndrome). Respiration becomes affected in the late stages. Determination of the vital capacity of the lungs is important. In Guillain-Barré syndrome, the cerebrospinal fluid is very typical: large quantities of protein and only a slight increase in cell count. In early stages, the CSF can still be normal. In such cases, repeated lumbar puncture is essential one week later. In the case of poliomyelitis, there is pleocytosis (large numbers of lymphocytes) in the cerebrospinal fluid and a slight elevation of protein. With poliomyelitis there is usually no progression of the paralysis after the 4th day, in contrast to Guillain-Barré.
2. **Tick paralysis:** some ticks secrete a paralytic substance in their saliva. This causes an ascending symmetrical paralysis with paresthesia, often around the mouth. The paralysis gradually increases over 5 to 6 days. Removal of the tick produces a dramatic improvement within a few hours or days. There is no fever or pain.
3. **Paralytic rabies:** previous history of infected bite (sometimes the victim is unaware of the bite: role of bats in South America). Ascending flaccid paralysis with moderate sensory disorders and with a fatal outcome.
4. **Acute transverse myelitis:** transverse lesion with bilateral sensory and motor disorders below a certain level (spinal cord segment) with back pain and flaccid paralysis initially, and subsequently spastic paralysis and major sphincter disorders. The cerebrospinal fluid often exhibits pleocytosis and a raised protein content. Consideration should also be given to trauma, herniated disk, acute schistosomiasis, compression by a spinal abscess or tumour (possibly acute symptoms from bleeding in a tumour), complications of brucellosis and Pott's disease.
5. **Diphtheria:** Caused by toxins secreted by *Corynebacterium diphtheriae*. Aerogenic transmission. Incubation period 2 to 5 days. Mostly throat infection, often with pseudomembranes, dysphagia, airways obstruction, markedly enlarged cervical lymph nodes and leukocytosis. This is followed by heart failure (myocarditis) around the 2nd week and sometimes peripheral paralysis (neuritis) around the 3rd to 6th weeks. The nerve damage often occurs first in the throat, palate and ocular muscles and may subsequently become generalized. Sometimes the infection is localized in the nose or skin, which then tends to follow a less aggressive course. Untreated patients remain infectious for 2 to 3 weeks. Treatment consists of antibiotics [(neo)macrolides or penicillins] and

diphtheria antitoxin.

6. **Buckthorn poisoning.** The clinical picture which follows ingestion of the berries of buckthorn (*Karwinskia humboldtiana* and *K. calderoni*) resembles poliomyelitis and Guillain-Barré syndrome. The neurotoxic effects of this plant are well known in Mexico and Central America (Nicaragua!) and consist of an ascending symmetric flaccid paralysis, often leading to bulbar paralysis and death.
7. **Botulism:** Intoxication by neurotoxins (type A, B or E) secreted by a Gram-positive anaerobic bacterium *Clostridium botulinum*. The toxins (zinc endopeptidases, cf. tetanus) bind presynaptically, interfere with the neurotransmitter vesicles and thus prevent the release of acetylcholine. Botulinum toxins B, D, F and G cleave synaptobrevin. Botulinum toxins A and E cleave SNAP-25 and botulinum toxin C1 cleaves syntaxin (all vesicle-associated proteins). The organism (or heat-resistant spore) can be found in a wound, the colon or in food. The role of food is reflected in the name of the disease: “Botulus” = sausage, after an incident in the 18th century in southern Germany. Bacteria can proliferate in anaerobic conditions and secrete toxins. If this happens and people eat contaminated food, disease will follow. After 12-36 hours a bilateral symmetrical and descending flaccid paralysis occurs with hypotension, dry mouth, ptosis, diplopia with dilated pupils and no light reflex, constipation and often distended abdomen (ileus) and urinary retention. Bulbar paresis with dysarthria and dysphagia may be particularly apparent and result in aspiration pneumonia. Respiratory paralysis can follow. Tendon reflexes are impaired or absent. There is normal sensation, no fever, normal consciousness, normal cerebrospinal fluid. There will be normal base line laboratory test results. Wound botulism causes no intestinal symptoms. A rapid improvement of the symptoms is obtained within a few hours with anti-ABE antitoxin (horse serum; 1 ampoule IV and 1 IM, repeated if no improvement after 2-4 hours), but complete recovery is usually very slow (weeks to months). It is a rare condition and it is difficult to diagnose. Specific EMG patterns can be detected (including a reduction in muscle action potentials at low frequency stimulation and post-tetanic potentiation, i.e. increase in muscle action potentials after high frequency stimulation or maximum voluntary muscle contraction for 30-60 seconds). An EMG as well as specific bacterial cultures and bioassays in mice to detect toxins are in general not available in developing countries. Even in well-equipped medical centres, confirmation of botulism is difficult. Botulinum toxin is used in medicine in a number of different indications, such as for the control of spasms in superficial muscles (e.g. around the eye, blepharospasms), in focal dystonia, in chronic anal fissures, in achalasia and Chagas’ disease and even in axillary hyperhidrosis. In this last case, injections of botulinum toxin A are used. The toxin blocks the release of acetylcholine at the neuromuscular junction but also at the cholinergic autonomic nerve endings (reduced sweat production as a result).
8. **Myasthenia gravis and Lambert-Eaton** myasthenia syndrome (e.g. in bronchial carcinoma) can also cause paralysis of the ocular muscles, ptosis, facial muscle weakness and swallowing difficulties, but the course is slower. If available, an EMG and an edrophonium test (Tensilon®) are

useful.

9. **Viral meningitis.** If the clinical presentation is that of acute viral meningitis, mumps, Coxsackie A7, Enterovirus 71 and echoviruses should be considered in addition to infection with poliovirus. Naturally this can only be established by a sophisticated laboratory.
10. **Enterovirus 71** deserves some additional comment. It was first isolated in a cell culture from a child with encephalitis in California in 1969. It is easily transmissible, which is important for contact persons within a family. The virus can be isolated from stools. There were large epidemics in Eastern Europe in 1975 and 1978 and in Southeast Asia (Malaysia, Singapore, Taiwan) between 1997 and 2000. In most outbreaks hand, foot and mouth disease has been the dominant clinical presentation, although herpangina, interstitial pneumonia, myocarditis, intrauterine infection and neonatal hepatic necrosis occur sporadically. The virus is also neurotropic. In contrast to other enteroviruses, it can invade the ventral brainstem, cerebellum and spinal cord. This results in a spectrum of serious neurological syndromes, ranging from acute flaccid paralysis of one or more extremities, to cranial nerve paresis, tremors, myoclonus and ataxia. Acute pulmonary oedema is thought to result from the destruction of medullary respiratory and vasomotor centres, leading to central sympathetic activation with severe systemic vasoconstriction and pulmonary vascular overload. The nervous damage is due to direct invasion of the neurons by the virus, as well hypoxia. Children who had encephalitis and cardiopulmonary failure have a high risk of poor neurodevelopment and cognitive outcome. Nowadays epidemic paralytic disease is more likely to be caused by EV-71 than by polioviruses.
11. **Acute beriberi** (thiamine deficiency). Develops more slowly with muscle weakness and often also heart failure. Good response to thiamine. See chapter on nutrient deficiencies.

Differential diagnosis of Acute Flaccid paralysis, summary

1. Polio : CSF, lymphocytic meningitis, PCR, viral culture
2. West Nile Fever virus polio-like : CSF, lymphocytic meningitis, serology, PCR, viral culture
3. Enterovirus 71 polio-like : CSF, lymphocytic meningitis, PCR, viral culture
4. Guillain-Barré / Fischer : CSF, protein-cellular dissociation
5. Diphtheria : inflammation throat or nose, LN, cardiomyopathy
6. Botulism : dry mouth, constipation, blurred vision, mydriasis, toxin assay
7. Rabies, paralytic : CSF variable, consciousness variable, agitation, relentless progression till death, IF, PCR
8. Myasthenia crisis, Eaton : Tensilon (edrophonium) or neostigmine test, EMG, anti-acetylcholine-receptor antibodies
9. Beriberi : cardiac, subacute, poor nutrition, vomiting, ethanol, thiaminases
10. Periodic paralysis : recurrent, induced by effort or sugars, K^+ concentrations variable

11. Hypophosphatemia : alcoholism or rapid feeding after starvation, TPN
12. Tick paralysis : specific hard tick present, better after removal
13. Neurotoxic snake : history, ptosis, dysphagia, bite wound
14. Organophosphates : hypersalivation, cramps, diarrhoea, sweat, miosis, wheezing, bradycardia
15. Shellfish poisoning (PSP, NSP) : ingestion shellfish, paresthesia, diarrhoea, ataxia, mydriasis
16. Buckthorn poisoning : ingestion *Karwinskia* berries, New World
17. Curare poisoning (medication) : peracute, only parenteral, New World, consciousness OK
18. Fugu poisoning (TTX = tetrodotoxin) : ingestion fish, Asia; paresthesiae lips, peracute paralysis, consciousness OK
19. TTX, other source : e.g. bite of blue-ringed octopus, see fugu poisoning
20. Thallium poisoning : gastro-intestinal, painful polyneuritis (esp hands and feet), diplopia

Treatment

There is no specific treatment for poliomyelitis. Symptomatic and supportive measures are necessary. Bed rest is compulsory at the beginning of the disease as physical activity may aggravate the nerve damage. Moist heat packs relieve muscle pain. Attention should be paid to the possibility of urinary retention due to bladder paralysis. Physiotherapy should be instituted 3 to 4 days after the regression of the fever and if there is no further progression of the paralysis. Physiotherapy does not prevent the muscular atrophy that occurs as a result of denervation (destruction of the motor neurons). It does, however, maintain the muscles in a good state for the few regenerating neurons. In 1927, Philip Drinker and Louis Agassiz Shaw Jr invented the iron lung at the Harvard School of Public Health. After the widespread use of iron lungs from 1939 onwards and during the largest polio outbreak in the US in the 1950s, the death rate did not show the same strongly correlated increase anymore. This respirator allowed care for patients with paralysis of the respiratory muscles till the paralysis faded on average after one or two weeks. Although improving the survival of many patients, the iron lung also led to dramatic situations where paralyzed people had to remain immobile inside the respirator for the rest of their lives.

Prevention

In the first half of the 20th century, poliomyelitis was a major problem in the West. The development of vaccines had a dramatic effect in a very short space of time. In many countries, it has proved possible to eliminate poliomyelitis by means of a routine vaccination program. Within a generation, the disease has virtually disappeared in the developed countries. In some countries where poliomyelitis still occurs, annual national vaccination days are held in addition to the usual vaccination programs. In 1988, the Global Polio Eradication Initiative was launched and is led by five

organizations: the WHO, the United States Centers for Disease Control and Prevention, the UN Children's Fund, Rotary International and the Bill and Melinda Gates Foundations. Four pillars form the global eradication program:

- Routine infant vaccination
- Supplementary immunization activities in at-risk middle and low-income countries: door-to-door campaigns, eg, a national campaign targeting all <5 years without regard to prior OPV immunization status
- Surveillance for acute flaccid paralysis (AFP)
- Mop-up campaigns: if a poliomyelitis patient or circulation of wild-type virus of cVDPV is found, house-to-house vaccination ("mopping-up" vaccination) is conducted over a large area.

As poliomyelitis is becoming increasingly rare, the importance of good surveillance is increasing. Patients with acute flaccid paralysis form the basis for the detection of "possible poliomyelitis". Acute flaccid paralysis surveillance is the gold standard for surveillance in the polio eradication initiative. Cases of acute flaccid paralysis (AFP) must be officially reported. It may be assumed that every year in a population approximately 1/100,000 persons under 15 years of age will develop an acute flaccid paralysis (non-poliomyelitis). Where possible, a stool specimen should be obtained for virus isolation in a regional Global Polio Laboratory Network laboratory. On top of the AFP investigation, environmental surveillance sampling sewage effluents in high-risk areas complements AFP surveillance. Organisms that are found here (e.g., mutated vaccine strains) can be tested for neurovirulence in transgenic mice that are carriers of the human poliovirus receptor. The rationale for environment surveillance is based on the characteristic poliovirus excretion pattern. Infected individuals excrete poliovirus in feces for periods of up to several weeks, whether or not they are symptomatic. Occasionally very long-term excretors will be encountered. As fewer AFP cases are to be expected, environmental surveillance may become more important to ensure early response, even before clinical cases re-occur.

In 1995, the "Global Commission for the Certification of the Eradication of Poliomyelitis" was established. This commission defined the principles, criteria and the process by which certification is to take place. All countries have to be able to show that they have stopped circulation of wild type virus. Certification, cannot be granted in less than three years from the last report of poliovirus. Each country should set up a national certification commission which should collect the necessary documentation. The national commission is not authorized to declare its own country poliomyelitis-free.

Vaccines

There are two types of vaccine:

Inactivated Polio Vaccine (Salk)

The injectable Salk vaccine (1955) or IPV (Inactivated Polio Vaccine) can be administered IM or SC and has the advantage of being heat-stable, which is important under field conditions. It can also be given to immune-depressed patients. It is more expensive than the Sabin vaccine. These vaccines protect a person against paralytic poliomyelitis but will not combat an asymptomatic infection in the intestinal tract. Vaccinees are still able to pass on the wild-type virus to their environment. With the killed vaccine, no reverse mutations can occur. In most high-resource countries, IPV is integrated in the routine childhood vaccination program.

Oral Polio vaccine (Sabin)

The oral Sabin vaccine (1960, OPV = oral polio vaccine) contains live attenuated viruses. It should be stored in a refrigerator. It is very efficient and cheap. It has the enormous advantage of being able to be administered without a syringe. While IPV only protects the CNS, the OPV also protects the digestive tract, thereby preventing the spread of poliovirus more effectively. If there is an intestinal infection (diarrhea) during the vaccination, the vaccine has less chance of success. The first dose may be given immediately after birth. This is then followed by three doses at intervals of one to two months. A booster at the age of 18 months and at 5 years is indicated. A return to neurovirulence is possible in the case of specific reverse mutations. After vaccination with OPV, the viruses can be excreted for a while and may protect other children as well. As an anecdote, the poliomyelitis virus was isolated from the preflight stools of the Apollo 11 crewmen after the crewmen had been given poliomyelitis boosters.

Vaccination risks and strategic implications

Questions are raised about the putative risks of poliomyelitis vaccination. In the 1950s, there was the so-called “Cutter” incident (named after the Cutter laboratory). Children who received the supposedly inactivated vaccine subsequently developed the disease. This was due to a problem in the filtration process in the preparation of the vaccine. Aggregates that still contained pathogenic viruses were not inactivated by the formalin and were not filtered out. This problem has obviously now long been corrected.

Between 1957 and 1960 the oral “CHAT” vaccine was used, particularly in Central Africa. The developer of this vaccine was accused of having used contaminated chimpanzee kidneys for this vaccine and, therefore of having started the AIDS epidemic. This, however has never been formally confirmed and this hypothesis has been rejected. Strains that were preserved from that time have been studied for the presence of HIV and all found to be negative.

The live viruses in the OPV differ from the pathogenic viruses through a small number of mutations. Occasionally reverse mutations occur, as a result of which a vaccine virus can recover its pathogenicity. Paralysis in receivers of the OPV vaccine can occur in two ways:

- **Vaccine-associated paralytic poliomyelitis (VAPP):** refers to the regeneration of neurovirulence that occurs spontaneously in a recently vaccinated person. This is very rare: for every million doses of OPV, there are between 0.09 and 25 cases of VAPP.
- **Vaccine-derived poliovirus (VDPV):** refers to the regeneration of neurovirulence over a longer period. There are different types of VDPVs:
- **iVDPV:** these are VDPVs that come from people with primary immunodeficiencies
- **cVDPV:** these are VDPVs that have been transmitted between people in the community and cause new outbreaks. They are found in individuals who are not direct contacts of poliomyelitis cases, or they can be detected in environmental samples (e.g., sewage water). In populations with a high polio vaccine coverage, the risk of cVDPVs is very low. In the vaccines against serotypes 1 and 3, there are many genetic mutations that distinguish them from wild-type poliovirus strains. However, in vaccines against serotype 2, there are fewer genetic mutations distinguishing them from the wild-type virus, so the vast majority of cVDPVs come from OPV against serotype 2. cVDPV2 outbreaks occur mostly in communities with low coverage of vaccines for poliovirus serotype 2.

The prospects for eradication are good, but setbacks do occur. In the autumn of 2003, there was a dramatic increase in poliomyelitis cases in Kano, Nigeria. Early November 2003, there were already 217 cases on a global total of 491. Vaccination had been stopped due to false rumors, fear and mistrust between the Muslim population and the government. This created a very dangerous situation, even threatening the accomplishments of the global eradication campaign. Over a year time, the virus spread far and wide to 20 different countries, from countries bordering Nigeria to even Indonesia. As an example, Somalia reported 73 cases in December 2005, after a three year period where not a single case was detected. Later it became clear that a small number of cases in Nigeria were due to the spread of a mutated vaccine strain. The financial price to quell this outbreak was very high, but we have to be prepared to go all the way to eradicate this disease from our planet.

Details on the Polio Eradication and Endgame Strategic Plan can be found at:
<http://polioeradication.org/who-we-are/>

Switch from tOPV to bOPV and the future of OPV

Nearly all vaccine-derived polioviruses in circulation are of type 2. Administration of the trivalent oral polio vaccine (tOPV, containing the three living vaccine strains) led mainly to an immune response against type 2, but the OPV type 2 in tOPV decreased immune responses to type 1 and 3 polioviruses. In April 2016 a new bivalent oral polio vaccine (bOPV) has replaced tOPV in all OPV-using countries, which will decrease cVDPV cases and VAPP cases due to type 2 poliovirus. Along with this, WHO recommended the use of IPV towards serotype 2 instead of the OPV. However, OPV vaccines are much cheaper and easier to administer than IPV vaccines.

Given the WPV1 and WPV3 eradication, the use of all OPV in routine immunizations should be stopped and all countries will rely on IPV alone to prevent poliovirus after OPV withdrawal. As an intermediate step, high-risk countries can give ≥ 1 IPV dose in the routine immunization program on top of the bOPV immunization to maintain immunity levels to type 2 polio. Since 2019, all 126 countries that previously used OPV now use at least one dose of IPV.

Because of an uncertain risk of circulating vaccine-derived poliovirus (cVDPV) reemergence from residual oral poliovirus type 2 circulation and from immunodeficient, long-term VDPV excretors, two inactivated

poliovirus vaccine (IPV) doses at 14 weeks and 9 months of age have been added to the recommended Expanded Program on Immunization (EPI) schedule for oral polio vaccine (OPV)-using countries in addition to routine bivalent OPV (bOPV) doses at 6, 10, and 14 weeks of age. This schedule provides seroconversion rates ≥ 97 percent of all three poliovirus serotypes by nine months of age.

At the same time, stockpiles of monovalent OPV type 2 are maintained to respond to future cVDPV2 outbreaks. Of course, the use of mOPV2 in response to VDPV2 outbreaks increases the risk of seeding new VDPV2 outbreaks. Therefore, since 2020 the novel oral poliovirus (nOPV2) is being rolled out to countries with cVDPV2 cases or outbreaks. nOPV2 is much more genetically stable and less likely to regain neurovirulence. It received a WHO Emergency Use Listing in November 2020 and has since been deployed in 21 countries.

Prevention, comparison of vaccines

Table: Advantages and disadvantages of dead and live attenuated poliomyelitis vaccine

IPV (dead, Salk)	OPV (live, Sabin)
Antibodies in the blood	Antibodies in the intestinal tract and blood
Since there is no immunity in the intestinal tract, wild type virus can still be transmitted faecal-orally	Vaccine virus can spread to the family: beneficial for immunity. Sometimes transmission of virulent mutant.
Possibly dangerous for immune-deficient subjects	Vaccine virus can mutate to neurovirulent type.
Use permitted in immune deficiency	Possibly dangerous for immune deficient subjects
Injection necessary	Oral administration
Booster vaccinations necessary for long-term immunity Higher seroconversion rates than OPV in low-income settings where enteric pathogens/pathology reduces the OPV efficacy	Immunity for life

Future

The GPEI (*Global Polio Eradication Initiative*) implemented the “Polio Eradication and Endgame Strategic Plan” and hopes to finance the last stretch of vaccination campaigns where polio is still endemic today: Afghanistan, Pakistan and Nigeria (Nigeria is declared free from wild-type poliovirus but remains endemic for cVDPV2). If poliomyelitis is successfully eradicated in the early 21st century, no wild-type virus will be present anywhere on the planet (except possibly for a few stocks in protected laboratories). However, OPV strains can revert to the wild-type form. Will the oral poliomyelitis vaccine ultimately have to be destroyed? How long should the injectable, dead vaccine be used and/or kept? Will silent long-term excretors start an epidemic decades after stopping vaccination? Some immunocompromised people excrete wild-type or vaccine-type poliovirus for years (possible for life?). As long as this situation exists, it cannot be stated that the battle against polio has been won.

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