S320

INFECTIOUS DISEASE

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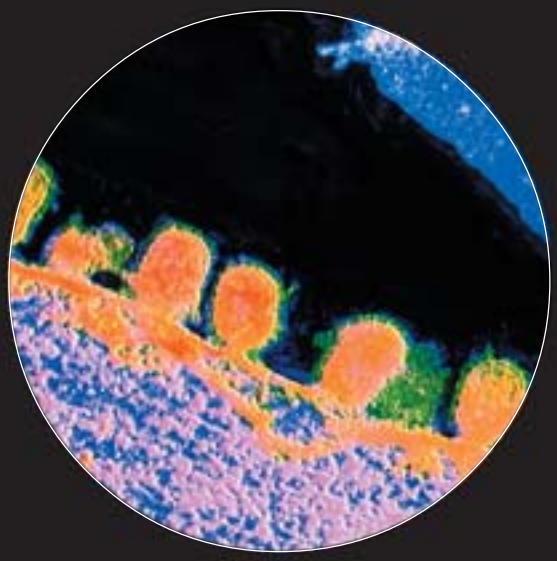
POLIO CASE STUDY

prepared for the Course Team by
David Male and Basiro Davey



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Cover pictures

Top left: Schistosome parasites. Coloured scanning electron micrograph of adult female (upper, thinner) and male (lower, fatter) *Schistosoma mansonii* parasitic worms, cause of the disease bilharzia (schistosomiasis).

Top right: Scanning electron micrograph of *Staphylococcus* sp.

Lower left: Coloured electron transmission micrograph of *Mycobacterium tuberculosis*.

Lower right: False colour transmission electron micrograph of influenza viruses (orange) budding from the surface of an infected cell.

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CONTENTS

FIGURE 1.1 About 1% of people who contract polio develop muscular weakness or flaccid paralysis, usually in the legs, due to the destruction of motor neurons in the spinal cord. Muscular wasting occurs in the paralysed limbs. Children with partial paralysis may be helped to walk by supporting the affected limb with iron braces. Here a doctor examines a boy who was paralysed in a polio epidemic in the USA in the 1920s.

POLIO CASE STUDY

We have chosen polio (poliomyelitis) to illustrate the use of mass vaccination to control an infectious disease that was formerly a major health problem in many parts of the world. By 2001, polio had almost been eradicated by an aggressive global programme of vaccination coordinated by the WHO, but there was a setback in 2002 when it resurged in India and Nigeria. In this case study we use the example of polio to explain why vaccination is an effective strategy against some infectious diseases, but not against others, and to illustrate the biological and social reasons why even a vaccine-preventable disease such as polio may still be difficult to eradicate completely. We suggest that you spend no more than 3 hours on this case study, including time to explore some Internet resources concerning polio, which can be located by following the links under *Course Resources* on the S320 website.

1 The history of polio

Poliomyelitis or **polio** is an acute viral illness, which produces muscular paralysis in about 1% of infected individuals. The disease was described by Landsteiner and Popper in 1909, although the earliest case report of a paralytic disease that may have been polio dates from England in 1789. The polio virus was not identified until the 1930s. It only infects humans, so there is no separate animal reservoir – a feature that hugely increases the prospects for successful control of an infectious disease through vaccination.

In the first half of the 20th century, frequent outbreaks of polio occurred in temperate countries, particularly during the summer months. For example, in the summer of 1916 an epidemic in New York left 27 000 people paralysed and 9000 dead. Epidemics in the Western hemisphere increased in frequency and in severity (Figure 1.1), until they were brought under control by the introduction of polio vaccination in the USA in the 1950s and 60s and, subsequently, in other parts of the developed world. The last case of polio in the USA as a result of person-to-person transmission of the **wild-type** (i.e. naturally occurring) **polio virus** occurred in 1979.

However, attempts to tackle polio in developing countries lagged far behind the progress made in the Western world. Surveys of 'lameness' in Africa and Asia in the 1970s concluded that hundreds of thousands of children were paralysed each year due to polio virus infection, and a concerted effort to introduce vaccination programmes worldwide began. By 1988, the rapid decline of polio in North America and Western Europe encouraged the WHO to adopt the goal of global eradication by 2000 – a target which has subsequently been put back to 2005. Figure 1.2 overleaf shows the geographical distribution of wild-type polio virus in 1988, when an estimated 350 000 cases of polio were occurring worldwide, and the position in December 2002, when most regions of the world had been officially certified as free of polio infection. The Americas (North and South) were the first region to be declared polio-free in 1994, the Western Pacific region and China followed in 2000, and the entire continent of Europe in June 2002 – four years after the last known European case of paralytic polio caused by wild-type virus was detected in Turkey.

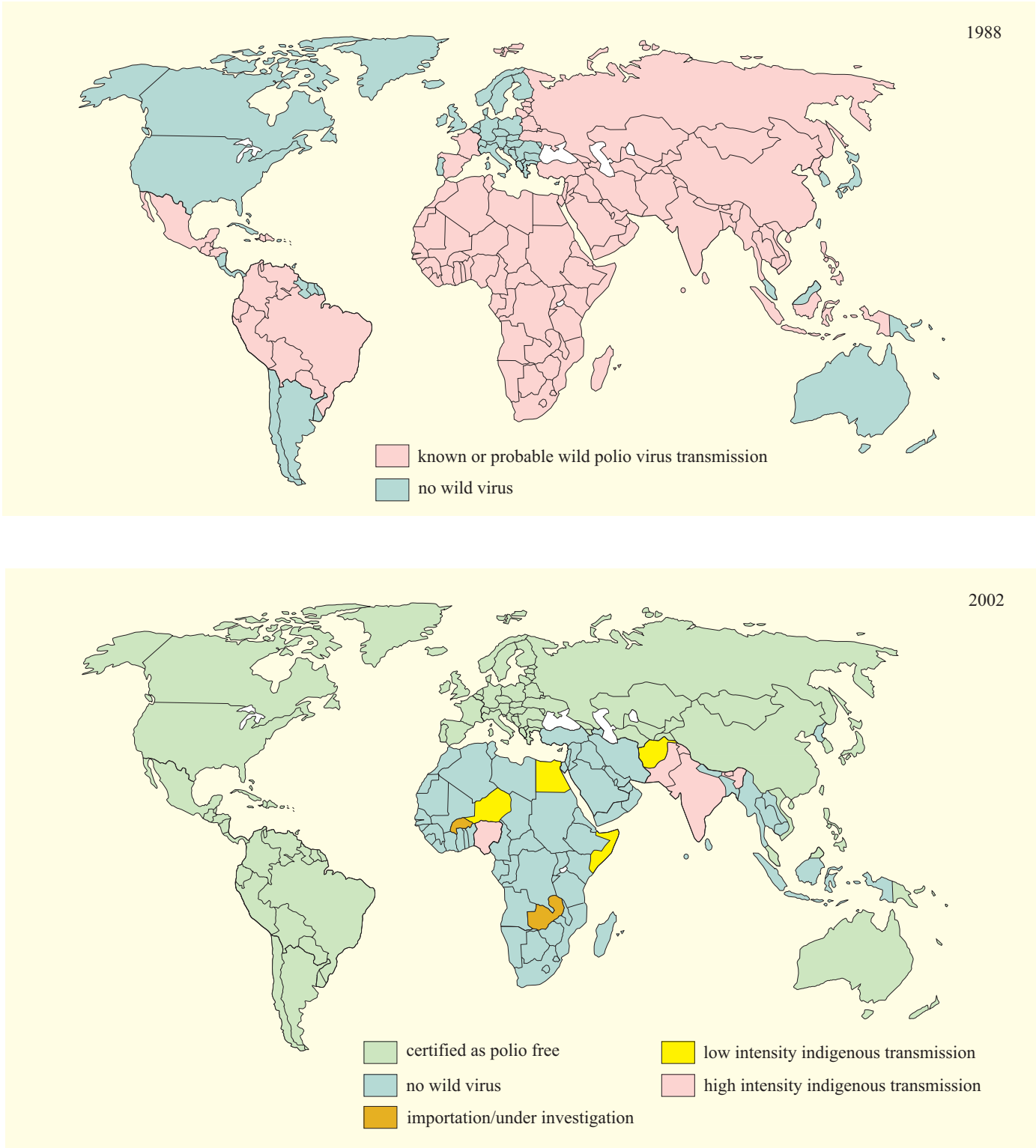


FIGURE 1.2 (a) Regions with known or probable transmission of wild-type polio virus in 1988. (b) Global polio status in December 2002. The designation 'no wild virus' indicates countries reporting no cases of wild-type polio virus transmission in 2002, within a WHO region that has not yet been certified polio free. Isolated cases in countries with no other evidence of wild-type virus are probably imported and shown as 'under investigation'.

The speed of decline in case reports since the global eradication initiative began in 1988, and the slower progress in the regions where it remains endemic, can be traced in Figure 1.3. The presumed endemic countries in 2002 are Afghanistan, Bangladesh, India and Pakistan in South Asia, and the African states of Angola, Democratic Republic of Congo, Egypt, Ethiopia, Niger, Nigeria, Somalia and Sudan. However, Afghanistan, Egypt, Niger and Somalia reported a combined total of only 25 cases of polio in 2002, and several other countries had no reports. The greatest concern is focused on India and Nigeria, where rates rose sharply in 2002; for example, reports of polio in India increased from 268 in 2001 to 1562 cases a year later. We consider the organization of the global eradication campaign in the final section of this case study.

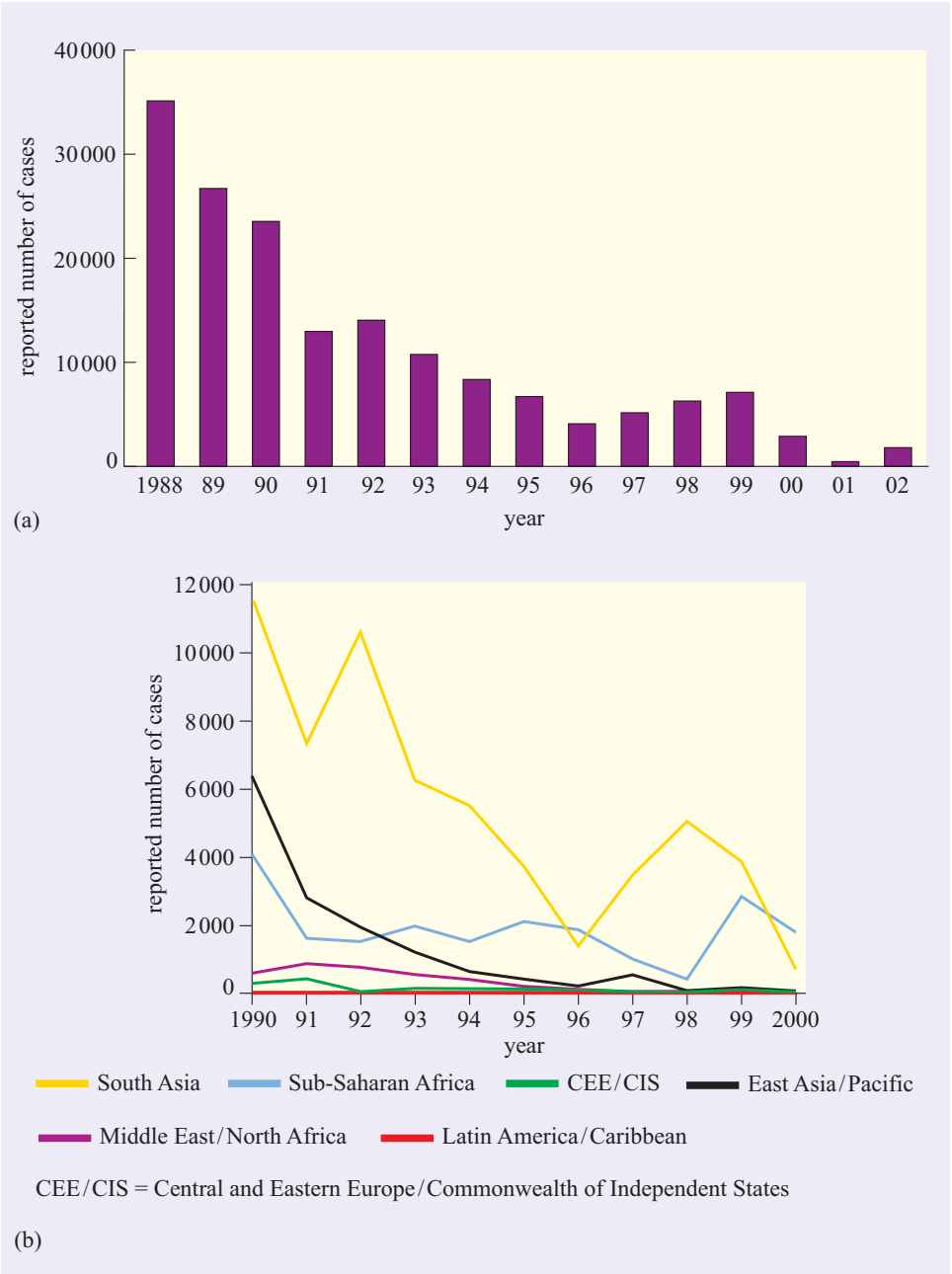


FIGURE 1.3
Decline in the global incidence of polio. (a) Total number of new cases (incidence) reported to the WHO annually, 1988–2002. (b) Reported incidence in most affected WHO regions, 1990–2000. (CEE/CIS refers to countries in Central and Eastern Europe, including independent states such as Armenia, Belarus, Russian Federation, Ukraine and Uzbekistan.)

2 Pathology and immunology

The incubation period for polio virus infection is variable, but is commonly between 1 to 3 weeks. The virus is transmitted primarily from person to person via the faecal–oral route, because large quantities of virions are shed in the faeces of infected individuals. In the early stages of an infection, the virus may also be passed on via the respiratory route, when aerosol droplets of infected saliva are coughed or sneezed into the local atmosphere, but the virus does not remain long in the throat.

The initial sites of infection are the tonsils (the main lymphoid tissues in the pharynx) and the gut-associated lymphoid tissues or GALT, including Peyer's patches (Figure 2.1). Soon after initial replication in these sites, the virus circulates in the blood (viraemia) and distributes to other lymphoid organs, where it undergoes a secondary replication phase. In under 10% of cases, a transitory flu-like illness occurs lasting less than a week, with symptoms of sore throat and fever, and occasionally nausea and vomiting. The secondary viral replication may result in the virus load in the blood reaching a high level, and in 1–2% of individuals it can spread to the central nervous system (CNS) and cause a mild meningitis, with stiffness in the neck, back and limbs, which resolves spontaneously. In less than 1% of cases, the motor neurons in the spinal cord and brain stem become infected and paralysis can result. Motor neurons innervate the skeletal muscles and are central to the initiation and control of movement.

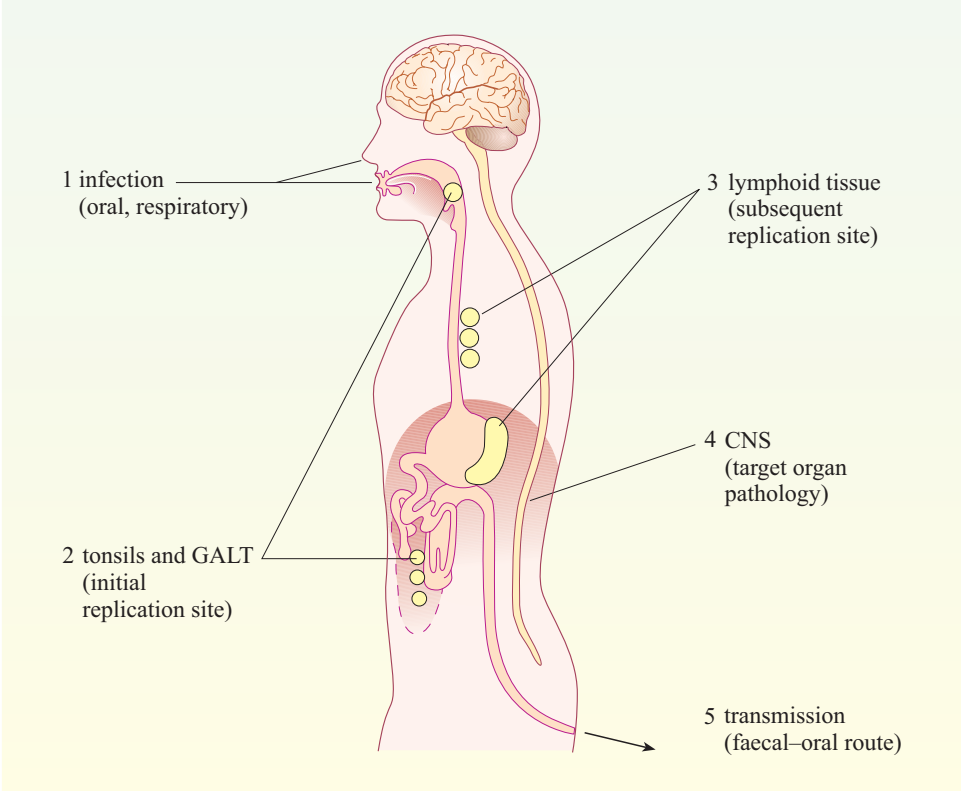


FIGURE 2.1 Polio infection is mainly acquired orally (or less often by the respiratory route), and initially the virus replicates in the tonsils and gut-associated lymphoid tissues (GALT). Later, the virus spreads via the blood (viraemia) to other lymphoid tissues and a second phase of replication may occur. The virus may then spread to the central nervous system (CNS) and infect motor neurons, especially in the brain stem and spinal cord.

- Within a week of initial infection, polio virus is excreted in the faeces and continues to be shed for several weeks. What problems does this pose for the control of polio virus transmission?

- Over 95% of infected individuals remain asymptomatic, and even those who become ill generally develop only mild transitory symptoms, which are easily confused with other viral flu-like illnesses. Thus the majority of infected people remain unaware that they are shedding large amounts of polio virus in their faeces and are infectious to others. Lack of adequate resources for washing and for maintaining food hygiene increases the risk of transmission.

- The typical R_0 for polio virus infection is between 4 and 7. Explain what this means. (If you are unsure, revise Book 6, Section 1.2.)

- Polio virus is highly infectious: 4–7 secondary infections can be expected among the contacts of each case in a totally susceptible population.

The sites of polio virus replication are determined by the tissue distribution of the receptor to which it binds on the surface of human cells. The polio-virus receptor is expressed on monocytes and macrophages in the lymphoid tissues, epithelial cells in the gut and motor neurons in the CNS. The receptor has structural similarities to the immunoglobulins (and has been designated CD155), but the normal physiological function of this molecule has not yet been determined. (The CD system of cell surface markers is described in Book 3, Box 1.1.)

- What immune defences are available to prevent viruses from infecting the gut epithelium or spreading in the blood?

- Antibodies: particularly IgA at epithelial surfaces in the gut and IgG in the blood (Book 3, Section 2.1.1). From 7 days after initial infection, IgG antibodies that bind specifically to polio-virus antigens appear in the blood (Book 3, Figure 2.6).

The infection is controlled by the immune response in the majority of individuals, particularly by the rapid increase in IgG antibodies. But if the virus reaches the CNS it can replicate in motor neurons and has a cytopathic (cell damaging) effect which may kill the nerve cells directly. It is not yet known exactly how the virus causes cell death, but within 1–2 hours of it entering the host cell a rapid decline in the synthesis of the cell's own macromolecules occurs. It appears that the virus is able to shut down the translation of host proteins and divert resources to make new virus particles.

Virus infection in the CNS also provokes a strong local inflammatory response. Infiltrating neutrophils and monocytes can damage infected neurons by the local release of toxic molecules and inflammatory cytokines (Figure 2.2 overleaf). Up to 1% of individuals who have a polio virus infection will develop an **acute flaccid paralysis** (**AFP**), usually of the lower limbs, due to the destruction of motor neurons. This characteristic form of paralysis is so named because it develops so quickly (acute) and the paralysed muscles are relaxed (flaccid) rather than contracted. Polio virus mainly infects children aged under 5 years, but it is more likely to result in paralysis in older children, adolescents and young adults for reasons that remain unclear. No effective drug treatment for polio virus infection has ever been developed.

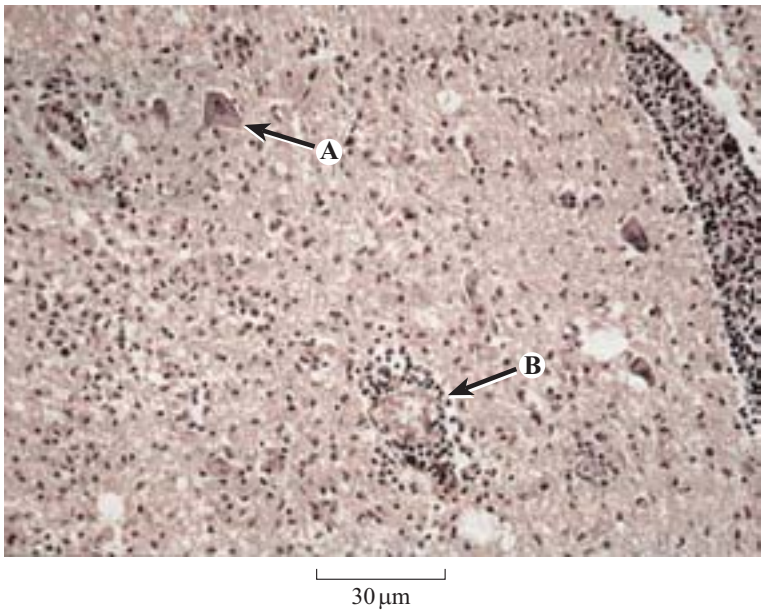


FIGURE 2.2 Polio virus infection in the spinal cord. Compare the distinct outline of an uninfected neuron (A), with the damaged appearance of an infected neuron (B), surrounded by a dense infiltrate of inflammatory cells.

Deaths from polio occur in 5–10% of those with AFP if they cannot be artificially ventilated, because the virus infects motor neurons in the brain stem, leading to paralysis of the muscles required for breathing. In the 1940s and 50s, some patients with respiratory paralysis in the USA and Western Europe were kept alive for several years in an 'iron lung', which mimicked normal respiratory movements by rhythmically increasing and decreasing the atmospheric pressure on the patient's thorax.

Neurons cannot be replaced by cell division, so there is generally some permanent disability in individuals who have developed any degree of paralysis after polio infection. However, there may be partial recovery of function, because motor neurons can develop collateral branches to replace the functions of cells that have been lost. People who have recovered from paralytic polio may develop **post-polio syndrome**, with pain and progressive muscular weakness occurring decades later. They remain free of polio virus and so are not infectious. It is thought that the reduction in neurons during the original infection leaves these individuals with insufficient capacity to compensate for the slow loss of neurons that normally occurs with age.

3 The polio virus

The structure, genome and replication cycle of the polio virus were described in detail in Book 2, Chapter 3, see particularly Figures 3.5, 3.13 and 3.14. The main points are summarized briefly here.

The polio virus, like all Picornaviridae, is an un-enveloped virion with a small positive-sense RNA genome ('pico' means small). Picornaviruses display varying degrees of genetic homology, as shown in Figure 3.1 (a dendrogram is a conventional way of depicting the proportion of nucleotide sequences common to related strains or species). Polio viruses belong to the Picornavirus subgroup known as enteroviruses, which infect the gut. They are most closely related to the coxsackie viruses and to rhinoviruses (the causative agent of the common cold). As with other Picornaviridae, the viral capsid consists of 60 protomers each formed from four proteins generated by the cleavage of a single original protomer. Figure 3.2 shows a computer-generated model of the polio virus capsid, in which its icosahedral symmetry is clearly visible.

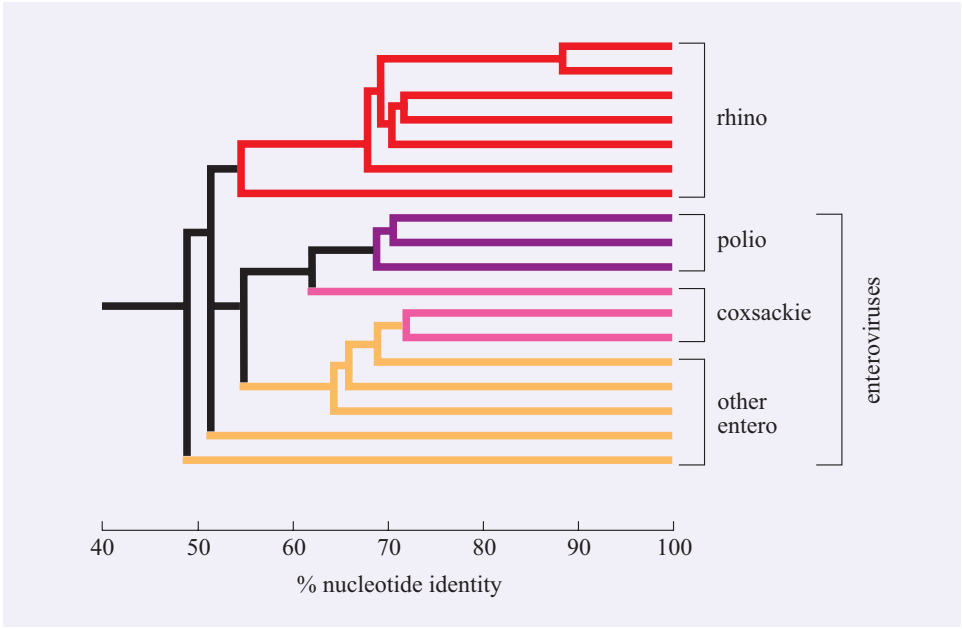


FIGURE 3.1 A dendrogram showing the genetic relationship between different Picornaviruses based on nucleotide homology. There are three serotypes of polio viruses with 60–70% genetic homology. The polio viruses are related to the coxsackie and other enteric viruses and to the rhinoviruses that cause colds.

The polio virus is extremely stable. Its genome is highly resistant to mutation under natural conditions and only three strains of wild-type polio virus are known: the P1, P2 and P3 serotypes, distinguished on the basis of the antibodies that bind to them. Although the three strains show 60–70% genetic homology, there is minimal cross-reactivity between them in terms of the antibodies they elicit. Thus, recovery from infection with one polio strain confers little or no protection against infection with another. The P2 serotype now appears to be extinct in the wild.

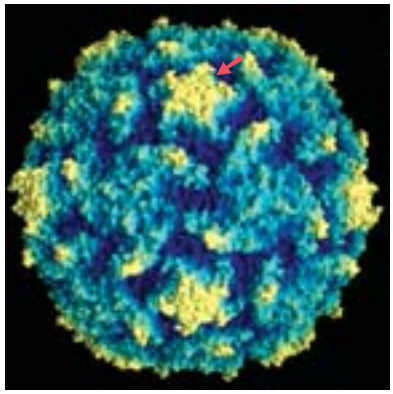


FIGURE 3.2
A computer-generated model of the polio virus capsid. The arrow points to one of the vertices of the icosahedral structure.

4 Diagnosis

A diagnosis of polio is confirmed by testing for the presence of polio virus in swabs from the throat or rectum of a suspected case.

- What laboratory methods are most commonly used to determine the identity of a virus in such a sample? (If you are unsure, you may need to revise parts of Book 4.)

- The concentration of the virus is increased to testable levels by growing it in tissue culture in suitable host cells (Book 4, Section 2.2.1). The identity of the virus is usually determined by serological methods employing specific antibodies that bind to unique antigens in the viral structure, linked to some method of visualizing whether they have bound (Book 4, Section 3). Advanced molecular biological methods are increasingly being used to amplify sections of the viral RNA genome by RT-PCR technology (reverse transcriptase-polymerase chain reaction, Book 4, Section 3.5) to reveal characteristic nucleotide sequences.

Efficient laboratory confirmation of polio virus infection is an essential feature of the WHO's global eradication campaign. Countries whose system of surveillance, case notification and laboratory testing are considered to be inadequate to detect every case are given assistance to improve their methods and technology. A high standard of detection efficiency is required before 'polio-free' certification can be awarded after a minimum of three years with no laboratory-confirmed isolates of wild-type virus.

5 Polio vaccines

The repeated summer epidemics of polio in the USA during the earlier part of the 20th century led to a major research effort to develop a polio vaccine. The first vaccine to progress to clinical trials in 1954 was a chemically-inactivated preparation developed from all three wild-type virus strains by Dr Jonas Salk. The Salk vaccine is given by intramuscular injection and was tested in the USA on a huge sample of 623 972 children aged 7–8 years, who received either the vaccine or a placebo. The results of the trial announced the following year showed that the incidence of polio and its sequelae had been reduced by 80–90% in the vaccinated children compared with the controls. The American government immediately introduced a mass vaccination programme for polio using the **i**ntramuscular **p**olio **v**accine (IPV is an alternative term for the Salk vaccine).

- What factors allowed the USA to introduce mass polio vaccination after just one clinical trial, and without waiting to see whether the vaccine had long-term adverse effects?

- In the 1950s, there was a considerable real and perceived risk of contracting polio, particularly among children, and the consequences could be lifelong paralysis or death. The results of the pilot programme were very promising. There was a more general acceptance of medical authority, and of a role for the government in directing health promotion at that time, than there is now.

In 1962, a second vaccine was authorized for public use in the USA, named after its developer Albert Sabin. Like the Salk vaccine it was 'trivalent', i.e. it contained all three serotypes, but the Sabin vaccine consisted of live **attenuated strains** of the virus and it was administered orally (and is also known as the **o**ral **p**olio **v**accine, OPV). Attenuated strains have been treated (as described in Book 7, Chapter 3) to promote the acquisition of mutations, which ideally abolish their *pathogenicity* without affecting their *immunogenicity*. Thus, the aim of such a vaccine is to elicit a strong immune response without harming the recipient.

The attenuated virus strains in the Sabin vaccine replicate in the vaccinated person in the gut epithelium and lymphoid cells, just like the wild-type polio virus (see Figure 2.1), until a sufficiently strong immune response has developed to destroy them. Infants receiving their first series of OPV shed attenuated viruses in their faeces for a short period, and parents are advised to take particular care over hygiene to avoid spreading the attenuated strains to other people. (It will become clear in Section 6 why accidental spread of OPV strains poses a risk.)

Explain why the Sabin vaccine (OPV) is given by mouth, while the Salk vaccine (IPV) is administered by injection.

The Sabin vaccine is 'live' and is delivered by the same route as the wild-type virus in order to elicit a protective immune response in the gut. The Salk vaccine is a non-replicating antigen preparation that would be broken down in the gut if given by mouth, so the antigens are injected directly into the muscle.

The impact of the introduction of these two vaccines on cases of paralytic polio in England and Wales can be seen in Figure 5.1, curtailing a post-war polio epidemic which threatened to reach new and frightening levels. Note that in this period, polio case notifications were largely based on the clinical diagnosis of acute flaccid paralysis and relatively few cases of non-paralytic polio were recorded.

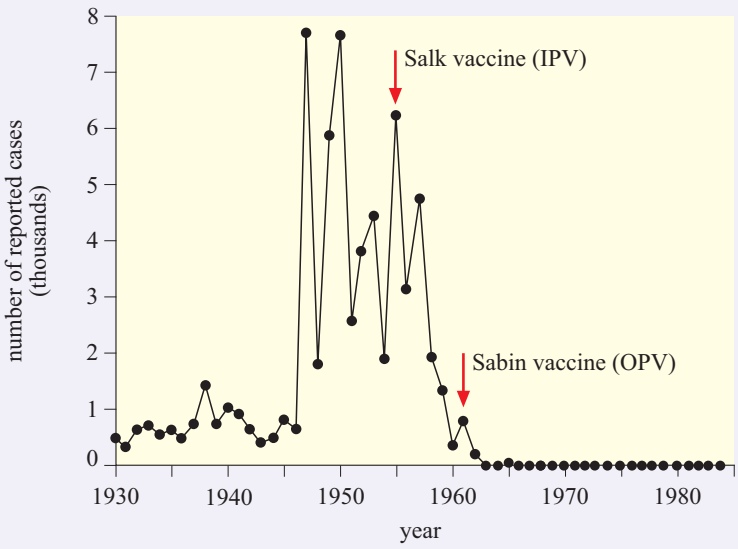


FIGURE 5.1
Effect of the introduction of mass polio vaccination programmes in the 1950s and 1960s on the incidence of paralytic polio in England and Wales.

- Explain why improved levels of personal and household hygiene may (paradoxically) have been a factor in the large rise in polio cases shown in Figure 5.1 around the end of World War II.

- Improved post-war levels of personal and household hygiene reduced the transmission of polio virus to infants and young children, resulting in an increase in the average age of infection with polio. The young are the most susceptible group because they have no prior immunity, but they are also less likely to develop paralysis than older individuals (the risk of paralysis rises with age), so most cases of polio in young children were not notified as such. As the average age of infection rose in the post-war period, so too did the proportion of cases who developed paralysis and appeared in official statistics. Thus, although changes in domestic hygiene may have contributed to a fall in polio incidence in the population, they may also have contributed to a rise in paralytic polio.

FIGURE 5.2
A child receiving oral polio vaccine (OPV).

Modern polio vaccines are based on viruses grown in bulk in tissue cultures derived from monkey kidney cells. Live attenuated vaccines such as OPV generally elicit a stronger and longer-lasting immune response than is provoked by 'killed' viral antigen preparations like IPV. The strong IgA response elicited by OPV in the gut also gives a high level of protection against subsequent infection with wild-type virus becoming established there. The low IgA response in people vaccinated with IPV means that wild virus may still replicate in the gut, with the result that these individuals are asymptomatic but infectious. The ease with which an oral vaccine can be given by drops into the mouth (Figure 5.2) or on a sugar lump, and its low cost (around US$1 per dose), are further reasons why OPV has replaced IPV in many countries.

However, the OPV has one drawback. It contains live virus, so there is always a possibility of **pathogenic reversion** in the vaccinated individual, i.e. the genetic changes that occurred in the attenuated strain are reversed, or new mutations are acquired, to produce a virus with similar properties to the wild-type strain. The closer the similarity between the wild-type strain and the attenuated strain, the greater the chance of pathogenic reversion occurring. For example, an attenuated P1 strain with 57 mutations has never reverted to wild-type, but reversion has occurred in attenuated P2 and P3 strains each with only two relevant mutations.

The risk of pathogenic reversion in the strains used in the OPV is very low, but cases of **vaccine-associated paralytic polio** (**VAPP**) have been reported at an incidence estimated at 1 case per 1.5 to 3 million OPV doses (it varies between countries). That risk is now higher in most parts of the world than the risk of contracting polio from wild-type virus, for the simple reason that (as Figure 1.2b showed) many regions are now certified as polio-free. Figure 5.3 traces changes in the incidence of VAPP and paralytic polio due to wild-type virus in the USA after mass vaccination with OPV was introduced in 1962. More recent data record a total of 144 cases of VAPP in the USA in the 20 years from 1980 to 2000, compared with around 20 000 cases of wild-type paralytic polio each year in the 1950s.

By contrast with OPV, the IPV has been responsible for only one instance of vaccine-associated paralytic polio in its 50-year history, when a batch of IPV was not fully inactivated and a proportion of recipients developed the disease. For this reason, several countries including the USA and the Netherlands have increasingly switched back to using IPV, or a combination of IPV followed by OPV to maximize the safety and effectiveness of each vaccine. The oral vaccine has not been

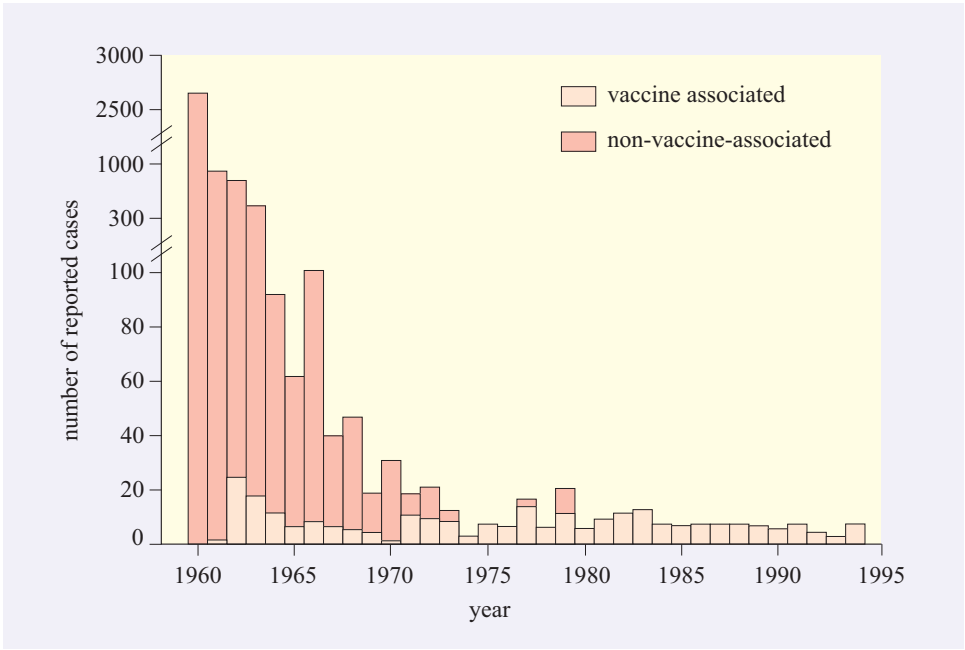


FIGURE 5.3
Annual incidence of vaccine-associated paralytic polio and paralytic polio due to wild-type virus in the USA, 1960–1994. (Note the breaks in the vertical axis of this diagram.) The danger of contracting vaccine-associated polio exceeded the risk of the natural infection by about 1980.

recommended for use in the USA since 2000. This switch in vaccine strategies illustrates the necessity to evaluate the changing risks of an infectious disease over time compared with the unchanging risks of intervention.

6 The global vaccination campaign

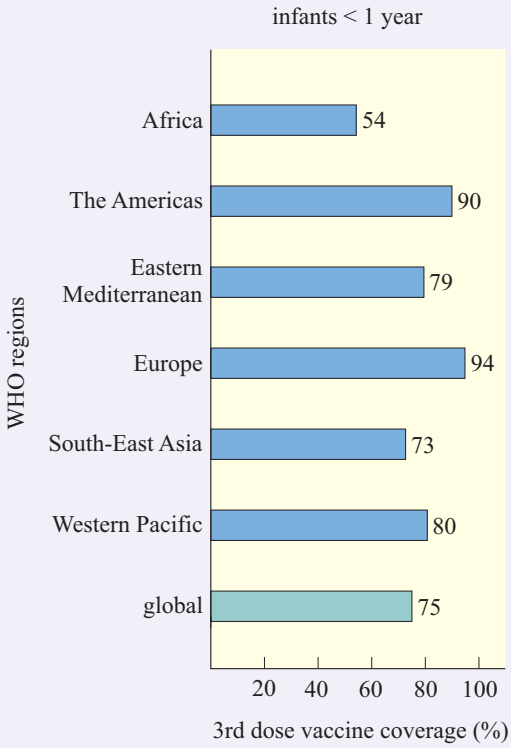
In those regions of the world where wild-type polio is still endemic, the very low risk of VAPP is far outweighed by the much greater risk of indigenous disease, so vaccination programmes use OPV for the reasons stated earlier. The goal of the global eradication initiative has been to achieve a high level of vaccine coverage in every country in the world, by whatever means are available. In polio-endemic countries, the key strategy has been to organize sub-national or **National Immunisation Days** (**NIDs**), followed up where possible by house-to-house visits to reach any children who were missed. NIDs involve massive advance publicity encouraging all parents to bring their children to vaccination centres throughout the country on specific dates.

- We noted earlier that children vaccinated with OPV shed live virus in their faeces for a few weeks. What risk is posed by accidental transmission of OPV strains by this route, and how could vaccinating a high proportion of children on the same day reduce this risk?

- Unvaccinated individuals who accidentally acquire OPV strains via the faecal–oral route may fail to develop a protective immune response, perhaps because the infective dose is too low and is not boosted by repeat vaccinations, or because their immune system is deficient. The OPV strains could become established in these individuals, and although they replicate without causing harm, over time they could spread to other susceptibles in the population. NIDs attempt to ensure that a high proportion of the population receives an immunising dose of vaccine at the same time, so there are too few susceptibles to support the OPV strains becoming established ‘in the wild’.

OPV strains are not harmful, so why is it a concern if they become established in the wild?

It is possible that an OPV strain could, at some point in the future, revert to pathogenicity and paralytic polio could emerge again as a major threat. It would also be impossible for the world to be declared 'polio-free' while vaccine strains of the virus are in still in circulation.



By scheduling a series of NIDs in a short period, a momentum is also created in which parents who did not attend one of the earlier dates are motivated by peer-pressure within their community to have their children vaccinated at a later NID. For example, in November 2002, sixteen countries in West Africa organized simultaneous NIDs with the aim of vaccinating 60 million children with OPV. The sharp rise in cases of polio in India in 2002 was attributed to a drop in vaccination coverage that year, and the response was to organize a series of six NIDs in February 2003 to vaccinate 160 million children.

The recommended polio vaccination schedule requires three doses of vaccine (OPV or IPV) to be given to each child in the first year of life, with a booster before the fifth birthday. Figure 6.1 shows the proportion of infants in each WHO region who were protected by three doses of polio vaccine in 2001 – a combined total of 575 million children in 94 countries.

FIGURE 6.1 Proportion of children in each WHO region in 2001 who received three doses of polio vaccine in their first year of life.

Think back to Book 6 and the discussion of the critical immunization threshold for polio (Table 4.1). How does the vaccine coverage in the various WHO regions shown in Figure 6.1 compare with this threshold?

Wild-type polio transmission can be expected to die out in a population that consistently exceeds a critical immunization threshold of 75–85%. Figure 6.1 shows that except in Africa and South-East Asia, this threshold has already been met.

The financial cost of the global eradication programme in the last 20 years has been huge – around US$2 billion – and the WHO has reported a funding gap of US$275 million to meet the target of certifying the remaining endemic countries as polio-free by 2005. And there are other challenges on the path to the eradication of polio. Stocks of wild-type polio virus must be maintained in secure laboratories as the basis for bulk production of vaccines. There must be a watertight system of detection of all cases of AFP in people aged under 15 years to ensure that the condition is accurately attributed either to wild-type polio virus, VAPP, or is unrelated to polio infection. And in the future, there are concerns that if vaccination

levels fall, then live oral vaccine strains may become established in the wild in populations with low immunity to polio-virus antigens, with all the risks discussed earlier.

We suggest that before returning to Book 7 to complete your study of vaccination in Chapter 3, you spend about one hour exploring the polio websites maintained by WHO and UNICEF, which give regularly updated information on the current global status of polio, specific country data on vaccination coverage and the latest news on the progress towards eradication. The websites can be located by following the appropriate links in the *Resources* section of the S320 website. If you have time, you may also find that the Public Broadcasting Service (PBS) website 'A short timeline of polio history' for the USA from 1916 to 1961 gives you a deeper insight into the severity and public perceptions of the disease (however this is optional). Seen together, the social history and the current epidemiology give an insight into the enormous progress that has been made against polio in the last 50 years. If you have a particular interest in the biology of the polio virus and its genome, you will also find a link to a website on Picornaviridae (run by the University of Leicester's Virology Department), which gives greater detail.

7 Learning outcomes

When you have completed this case study and explored the websites indicated in Section 6, you should be able to:

1 Define and use, or recognize definitions and applications of, each of the terms printed in **bold** in the text. (*Questions 1–3*)

2 Give a short description of the symptoms and progression of polio infection and its consequences, relating this to the biology of the polio virus and the cellular pathology it causes. (*Question 1*)

3 Describe the vaccines that have been developed to combat polio, their relative advantages and disadvantages, and their impact on the epidemiology of the disease. (*Question 2*)

4 Explain why the polio virus has been so susceptible to control by vaccination, and identify the problems that will need to be overcome in order to eradicate it completely. (*Question 3*)

8 Questions

Question 1

What are the principal cells of the body that become infected with polio virus and why do these cells become infected and not others? How does the distribution of susceptible cells relate to the symptoms of polio infection?

Question 2

What kinds of antibody response are induced by the oral polio vaccine (OPV) and the intramuscular polio vaccine (IPV), and how does this relate to the protection they offer?

Question 3

Suggest a number of biological and immunological factors that have contributed to the success of polio vaccination programmes. What are the principal barriers to eradicating the wild-type virus in those countries in which it is still endemic?

9 Answers to questions

QUESTION 1

The initial sites of polio virus replication are in monocytes and macrophages in the tonsils and the gut-associated lymphoid tissues (GALT), and subsequently in the gut epithelium and other lymphoid tissues. Neurons only become infected in 1–2% of individuals. The virus can infect these cell types because they express the polio virus receptor on their surface membranes. Most infected individuals develop no symptoms at all, but those who do generally experience a mild flu-like illness characteristic of an immune response against a viral infection, sometimes with gut-associated symptoms such as nausea and vomiting. If the virus spreads to the central nervous system (CNS), there may be transient stiffness in the muscles. Infection of motor neurons in the spinal cord or brain stem can lead to cell death and acute flaccid paralysis (AFP) usually in the lower limbs, and less often to asphyxiation through paralysis of the respiratory muscles.

QUESTION 2

The oral vaccine initiates a strong IgA response, which is long-lasting and can protect the epithelial surfaces of the gut against subsequent infection with wild-type virus. The intramuscular vaccine tends to favour an IgG response, which prevents viral spread during the viraemic phases, but is less effective at protecting the gut. Polio virus may still replicate in the gut of individuals who have been vaccinated with IPV, allowing transmission of viruses shed in the faeces, even though vaccinated people are protected from developing polio. A good antibody response to either vaccine is enough to prevent the virus from reaching the spinal cord, thereby protecting the person from serious pathology.

QUESTION 3

The success of the vaccination programme can be partly attributed to the fact that polio virus only infects people – there is no animal reservoir. However, it can be grown in bulk for vaccine production in tissue cultures derived from monkey kidney cells. Polio virus is stable and does not mutate under normal conditions (as do viruses such as influenza and HIV). There are only three different serotypes (strains) of polio virus to be incorporated into a vaccine. Killed or live attenuated strains have been developed which are highly immunogenic, eliciting a protective antibody response which is long-lasting if repeated doses are given in childhood.

Barriers to the final eradication of polio are primarily the huge financial cost (with a funding gap of US$275 million at the end of 2002) and the organizational difficulties in ensuring that more than 85% of children are vaccinated three times within a year of birth, and given a booster dose before they are five. Polio-endemic countries often lack the infrastructure and personnel to reach remote regions. Advertising campaigns for mass vaccination days may not have sufficient impact to persuade parents to travel long distances – perhaps on foot – to bring their children to the nearest vaccination centre.

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