Epidemic poliomyelitis, post-poliomyelitis sequelae and the eradication program

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The author advises that on page 198 of their published article (*Microbiology Australia*, Volume 41, Issue 4, pages 196–200, doi:10.1071/MA20053), under the heading 'Late-onset sequelae of poliomyelitis (LOSP)', 'osteomyelitis' should read 'osteoporosis' in the fourth line from the end of the first paragraph. The correct text is shown here:

A broader category of sequelae, the Late Effects of Polio (LEoP), includes the consequences of musculoskeletal deformities and weakness such as scoliosis, osteoporosis, joint instability and pain, osteoarthritis and nerve entrapments[8].

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Abstract. **Epidemics of paralytic poliomyelitis (polio) first emerged in the late 19th and early 20th centuries in the United States and the Scandinavian countries. They continued through the first half of the 20th century becoming global. A major epidemic occurred in Australia in 1951 but significant outbreaks were reported from the late 1930s to 1954. The poliovirus is an enterovirus that is usually transmitted by the faecal–oral route but only one in about 150 infections results in paralysis when the central nervous system is invaded. The Salk inactivated polio vaccine (IPV) became available in Australia in 1956 and the Sabin live attenuated oral polio vaccine (OPV) was introduced in 1966. After decades of stability, many survivors of the earlier epidemics experience late-onset sequelae including post-polio syndrome. The World Health Organization launched the global polio eradication initiative (GPEI) in 1988 based on the easily administered OPV. The GPEI has resulted in a dramatic decrease in cases of wild polio so that only Pakistan and Afghanistan report such cases in 2020. However, a major challenge to eradication is the reversion of OPV to neurovirulent mutants resulting in circulating vaccine-derived poliovirus (cVDPV). A novel, genetically stabilised OPV has been developed recently to stop the emergence and spread of cVDPV and OPV is being replaced by IPV in immunisation programs worldwide. Eradication of poliomyelitis is near to achievement and the expectation is that poliomyelitis will join smallpox as dreaded epidemic diseases of the past that will be consigned to history.**

Epidemics of poliomyelitis

It was Easter 1951 and I was climbing the mango tree in the grounds of our family's Mareeba home in Far North Queensland when malaise and a headache forced me to bed. After a couple of hours, my leg was paralysed and I was taken to the Mareeba hospital, diagnosed with poliomyelitis (polio), placed in isolation and subsequently transported by ambulance to the Cairns Base Hospital where I remained until Christmas 1951.

I was one of the 1108 Queensland cases of paralytic polio among the peak number of 4940 Australian cases reported to the Commonwealth Director General of Health in the 1951 epidemic. New South Wales with 1608 cases and South Australia with 1488 cases also reported their peak numbers in 1951. Other Australian states reported maximum numbers of paralytic polio in different years, e.g. 1469 in Victoria in 1937, 704 in Tasmania in 1938 and 436 in Western Australia in 1954. For the period from 1951 to 1953, the incidence of polio per 100 000 of the Australian population was 32.30, exceeded only by Denmark with 59.90 incidence and Canada with 35.90[1].

Polio had been endemic in the human population for millennia. The first epidemics were reported from the Western world, e.g. Stockholm in 1887 with 44 paralytic cases and Vermont in the United States in 1894 with 132 cases. In 1905, a much larger epidemic occurred in the Scandinavian countries with more than 1000 cases[2]. A major epidemic was reported from the United States in 1916 with some 27 000 paralytic cases and 6000 deaths of which more than 9000 cases and more than 2000 deaths were reported from New York City alone[3]. These early epidemics mainly affected babies and young children but adolescents and adults were increasingly involved as the waves of epidemics became global and continued into the 1950s. The severity of the paralysis and the case-fatality rate also increased with age[4]. Ironically, improved public sanitation and personal hygiene meant that passive immunity, which was previously acquired by infants from their mothers when polio was endemic, no longer occurred to provide protection from paralytic polio[4]. Prior to the introduction of the US vaccination program in the mid-1950s, about 21 000 cases of paralytic polio were reported annually in the first half of that decade[3]. The year 1947 marked the largest and most widespread epidemic of polio in England and Wales, after which epidemics continued until vaccines became available[5].

Widespread fear gripped communities as parents faced the possibility of their children being crippled for life or even dying in these epidemics. In Australia, cinemas, swimming pools and playgrounds were closed and advice issued against attendance at large gatherings. Siblings of polio cases were placed in quarantine for 14 days and some schools were closed. For the protection of Queen Elizabeth and Prince Phillip during their 1954 Australian tour, handwashing was encouraged and indoor activities minimised. Most Australians viewed their Queen in open areas while she wore long white gloves.

Poliovirus and the disease

In 1908, Karl Landsteiner and Erwin Popper showed that a transmissible agent caused polio. The researchers' attempts to grow bacteria from the cerebro-spinal fluid and homogenate of brain tissue from a fatal case of polio proved negative. When the homogenate was injected intraperitoneally into monkeys, they developed polio and subsequently died[6]. Monkeys remain the only animals that are naturally susceptible to the disease.

Poliovirus is an enterovirus of the *Picornaviridae* family of small RNA viruses that are transmitted generally by the faecal–oral route. Australians, Sir Macfarlane Burnet of the Walter and Eliza Hall Institute and Dame Jean Macnamara, first showed that the poliovirus had at least two serotypes in comparative studies of immunity in monkeys to a Victorian isolate of poliovirus and one provided by the Rockefeller Institute in the United States[7]. Three serotypes of poliovirus (1, 2 and 3) have been identified and all can cause paralysis but type 1 is the most virulent and is the main serotype responsible for epidemics[4]. Seroprevalence of antibodies to the poliovirus indicate that only one in about 150 viral infections results in paralysis[4].

The virus multiplies in the oropharyngeal and intestinal mucosa and is shed from the oropharynx and in faeces. It spreads to the bloodstream via lymph nodes. Most infections end at this stage having caused a minor disease with non-specific symptoms and an antibody response. If the spinal cord is invaded, destruction of the motor neurons leads to weakness and temporary or permanent flaccid paralysis in muscles, especially of the limbs. Less often, the brain stem is invaded resulting in bulbar polio affecting swallowing, speaking and breathing. Life-threatening cardiac complications may also accompany bulbar polio[8].

Treatment of paralytic cases

Orthopaedic specialist Jean Macnamara championed the orthodox method of initial immobilisation to prevent deformity by bandaging and strapping the polio-affected body with legs spreadeagled to a cross-shaped Thomas splint. Some weeks later, physiotherapy was introduced. I was the recipient of this treatment. The alternative method of Sister Elizabeth Kenny involved the use of moist, heated wool packs to relieve muscle spasms and pain along with massage and gentle stretching and exercising of the muscles. She did not believe in immobilisation. Kenny had some followers amongst the medical profession in Australia but more detractors. In 1940, she introduced her method to the United States where it was better received and adopted but remained controversial[9].

Negative-pressure cylindrical or rectangular shaped 'iron lungs' enabled those with paralysed respiratory muscles to breathe again[8]. Most patients could be weaned off the iron lungs after a couple of weeks but a few spent their entire lives so confined. Death was the frequent outcome of paralysed respiratory muscles in the early epidemics.

Development of vaccines

Nobel Prize-winning research by John Enders, Thomas Weller and Frederick Robbins, which was published in 1952, showed that the poliovirus could grow in non-neural cell cultures from human tissues and in cultures of monkey kidney cells[10]. This paved the way for the production of adequate quantities of poliovirus for vaccine development.

American Jonas Salk developed the formaldehyde-inactivated polio vaccine (IPV) from cultures of poliovirus grown in monkey kidney cells. The culture fluids were first filtered to remove larger particles and then passed through a bacteria-retentive filter. Timing of the inactivation procedure required knowledge of the infectious titres of the culture fluids and control of the formaldehyde concentration, temperature and pH of inactivation. Final tests for safety were carried out by inoculation of monkey kidney tissue cultures and injection into monkeys. The latter were also subsequently tested for antibody responses[11]. Percival (Val) Bazeley of the Commonwealth Serum Laboratories (now CSL) left Australia in 1952 to join in the development of IPV and is a co-author of the relevant publication[11]. In 1955, he returned to Australia to direct production of IPV where it was used for routine vaccination starting in 1956.

Albert Sabin subsequently developed a live, attenuated oral polio vaccine (OPV) that was easily administered and cheaper to produce[12]. Oral administration of OPV meant that mass immunisation campaigns could be undertaken by untrained personnel. After multiplication in the intestinal tract of vaccinees, the attenuated poliovirus spreads through communities thus contributing to herd

immunity[4,12]. Although the live, attenuated vaccine was recognised as having the potential to revert to neurovirulence, this was considered to be an occasional and very rare event[3]. OPV was introduced into Australia in 1966.

As trivalent vaccines, IPV and OPV require multiple doses and usually a booster dose later to ensure immunity. OPV is also produced as a monovalent (mOVP) or bivalent (bOVP) vaccine. IPV is administered by injection and stimulates the production of serum neutralising antibodies. In addition to serum antibodies, OPV also produces local secretory IgA, which provides mucosal immunity in the intestinal tract.

Late-onset sequelae of poliomyelitis (LOSP)

After several decades of stability, many polio survivors – as well as some with no residual paralysis – develop LOSP including post-polio syndrome (PPS)[13]. These sequelae were not reported in the medical literature until the mid-1980s. The main symptoms of PPS are new muscle weakness and fatigability, joint and muscle pain and overwhelming fatigue. Other symptoms that may occur include cold intolerance, muscle atrophy and cramps, pulmonary dysfunction, sleep disorders and speech and swallowing difficulties[14]. A broader category of sequelae, the Late Effects of Polio (LEoP), includes the consequences of musculoskeletal deformities and weakness such as scoliosis, osteomyelitis, joint instability and pain, osteoarthritis and nerve entrapments[8]. No medication or dietary supplement has been shown to relieve the fatigue of LOSP[15]. I have now developed LOSP.

Post-polio support networks have been formed in most Australian states. The national organisation, Polio Australia Inc., provides health information and publishes resource material on LOSP for polio survivors. Polio Australia also conducts Clinical Practice Workshops to assist health-care providers in the diagnosis and management of polio survivors with LOSP.

Global polio eradication initiative

During his tenure as World President of Rotary International (RI) in 1978–79, Australian Sir Clement Renouf, inspired by the successful eradication of smallpox, asked American Rotarian and Paediatrician, Paul Severs, to suggest a vaccination program in which RI could participate. Dr Severs recommended vaccination against polio by the easily administered OPV. In 1985, RI started its PolioPlus program by immunising 6 million children in the Philippines[6].

In 1988, the World Health Organization (WHO) launched the global polio eradication initiative (GPEI) based on OPV[16]. Since then, the number of wild poliovirus cases has declined by 99.99%. The eradication of wild poliovirus type 2 was certified in 2015 and of type 3 in 2019[17]. By mid-2020, only Pakistan and Afghanistan are reporting cases of wild poliovirus type 1 (WPV1), as shown in Table 1[18–20].

Paralytic cases of polio due to circulating vaccine-derived poliovirus (cVDPV) as a result of reversion to neurovirulence of the serotypes of OPV are shown in Figure 1.

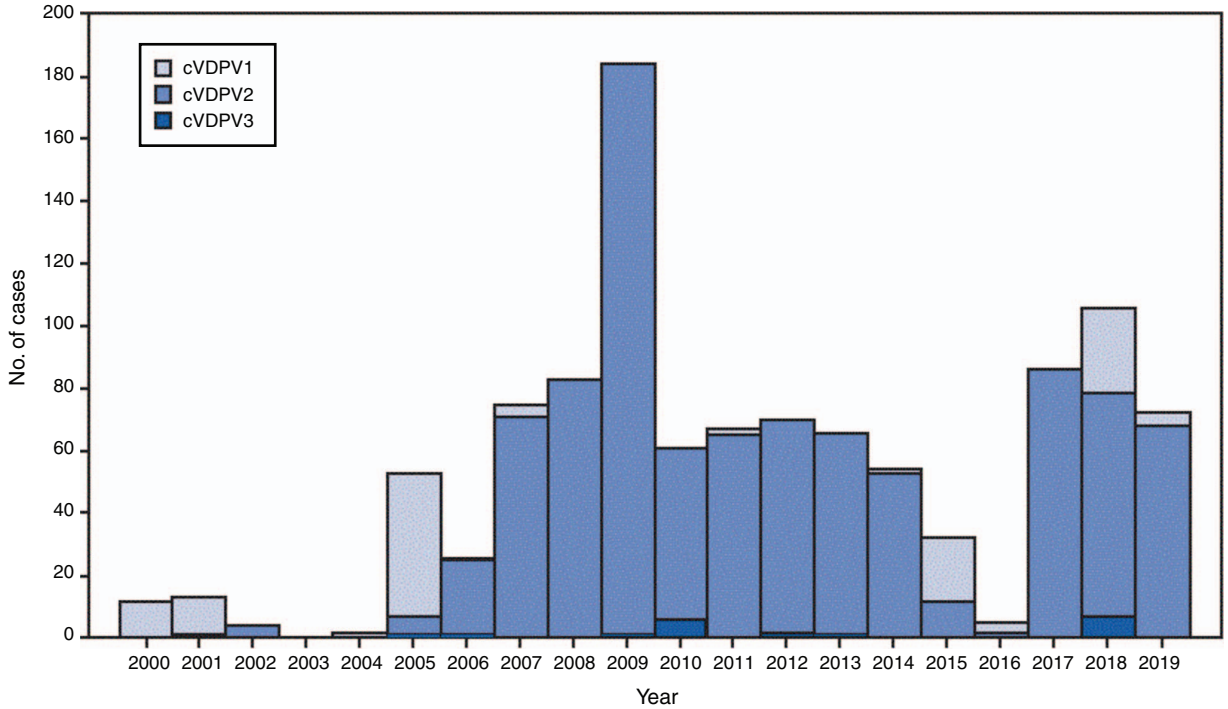

Figure 1. Cases of circulating vaccine-derived poliovirus (cVDPV) according to OPV serotypes[17].

Table 1. Cases of wild polio virus type 1 (WPV1) showing a significant upsurge in 2019 and 2020[18–20].

Country	Full year total					1 January to 30 June (half year)		Date of most recent case
	2015	2016	2017	2018	2019	2019	2020	
Pakistan	54	20	8	12	147	41	56	8 June 2020
Afghanistan	20	13	14	21	29	10	29	13 June 2020
Total	74	33	22	33	176	51	85	

Cases of circulating vaccine-derived poliovirus (cVDPV) occur in populations with low immunity[4,17]. Circulating VDPV2 has spread into multiple countries of four of the six WHO world regions: African, South-East Asia, Eastern Mediterranean and the Western Pacific[17]. One reason for low levels of immunity is the inhibitory effect of concurrent enteric infections on the OPV response in communities with poor sanitary conditions[21]. Other ongoing challenges to the eradication program are issues of inaccessibility in Afghanistan[19] and vaccine hesitancy and refusals, polio campaign fatigue and difficulties in reaching mobile populations in Pakistan and Afghanistan[20]. In addition, house-to-house vaccinations ceased for many months in 2018 and 2019 in both countries[20]. An outbreak of 26 cases of paralytic polio due to cVDPV1 occurred in Papua New Guinea in 2018[22]. Since January 2018, the frequency and geographic extent of cVDPV outbreaks have increased with transmission currently in 26 countries including Pakistan and Afghanistan[20].

In April 2016 after the eradication of poliovirus wild type 2 had been certified, a coordinated switch was made from trivalent OPV to bivalent OPV types 1 and 3 to prevent further emergence of VDPV2. Along with the switch, IPV was included in immunisation schedules to mitigate the loss of type 2 immunity[23]. As IPV does not confer intestinal immunity, the transmission of cVDPV is prevented by monovalent or bivalent OPV. A novel, genetically stabilised, monovalent nmOPV2 vaccine that is highly unlikely to mutate to neurovirulence has been developed recently to stop the emergence and circulation of VDPV2[24]. After the eradication of cVDPV, IPV will replace OPV in immunisation programs to eliminate the emergence and spread of all neurovirulent revertants. Australia and other countries in the WHO Western Pacific region were declared polio free in 2000[25] and OPV was replaced by IPV in Australia in 2005. By 2010, more than 50 countries were using IPV for their immunisation programs[6].

The WHO Polio Regional Reference Laboratory in the Doherty Institute in Melbourne is responsible for ongoing surveillance of the polio-free status of Australia and other countries in the WHO Western Pacific region. Faecal samples from cases of acute flaccid paralysis are investigated to exclude or confirm polio and sewage samples are investigated for the presence of poliovirus. The Reference Laboratory will also play a role in the final certification of polio-free countries in the region and the containment of laboratory stocks of poliovirus and destruction of any materials that might harbour poliovirus.

Apart from WHO and RI, the partners in the Global Polio Eradication Initiative (GPEI) are the US Centers for Disease Control and Prevention (CDC), UNICEF and the Bill and Melinda Gates Foundation. The Gavi Vaccine Alliance joined these partners in 2019 to promote the Polio Endgame Strategy 2019–2023. John Mackenzie is the Australian representative on the WHO Emergency Committee under the International Health Regulations (IHR) regarding the international spread of poliovirus. The risk has been assessed as a public health emergency of international concern (PHEIC) since 2014. At its meeting on 23 June 2020, the Committee agreed that, in view of the recent rise in numbers of WPV1 in 2019 and 2020 in Pakistan and Afghanistan and of the increasing frequency and geographic spread of cVDPV, the risk remains a PHEIC[26].

Because of the coronavirus pandemic, WHO suspended the Polio Endgame Strategy in March 2020 and the polio surveillance networks were diverted to help with COVID-19 tracking and tracing. In July 2020, Pakistan resumed house-to-house polio vaccination with vaccinators in personal protective equipment (PPE) administering the vaccine without touching the children.

To reach its goal of eradication, GPEI plans the safe resumption and scale-up of polio field activities, with the introduction of the genetically stabilised novel OPV2 to combat cVDPV2, when and where the COVID-19 pandemic allows[20]. Clem Renouf had hoped to live long enough to witness the fulfilment of his vision with the declaration of a polio-free world but he died on 11 June 2020 at 99 years of age.

Conflicts of interest

The author declares no conflicts of interest.

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Biography

Dr Margaret M Peel was the Principal Scientist at the Microbiological Diagnostic Unit Public Health Laboratory in the Department of Microbiology and Immunology at the University of Melbourne where she also gave lectures in microbiology to students as an Academic Associate. Margaret's first qualification was a Diploma in Medical Science, after which she obtained a BSc (Hons) from the University of Queensland (UQ). She then taught microbiology at the Queensland Institute (now University) of Technology. Margaret subsequently travelled to London to undertake the Academic Postgraduate Diploma in Bacteriology (Dip Bact) at the LSHTM, which she obtained with a mark of Distinction. She stayed on to receive a PhD from London University for studies on the immune response to vaccines. Her published contributions are in the areas of immunisation, public health microbiology and epidemiology, identification of bacterial isolates and sterilisation, disinfection and infection control. Margaret was awarded Doctor of Science (DSc) from UQ in 2009 for an annotated thesis of her published works. She is a Fellow of ASM (FASM).