Public Health History Corner

History of polio vaccination in Italy

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Jonas Edward Salk

Albert Bruce Sabin

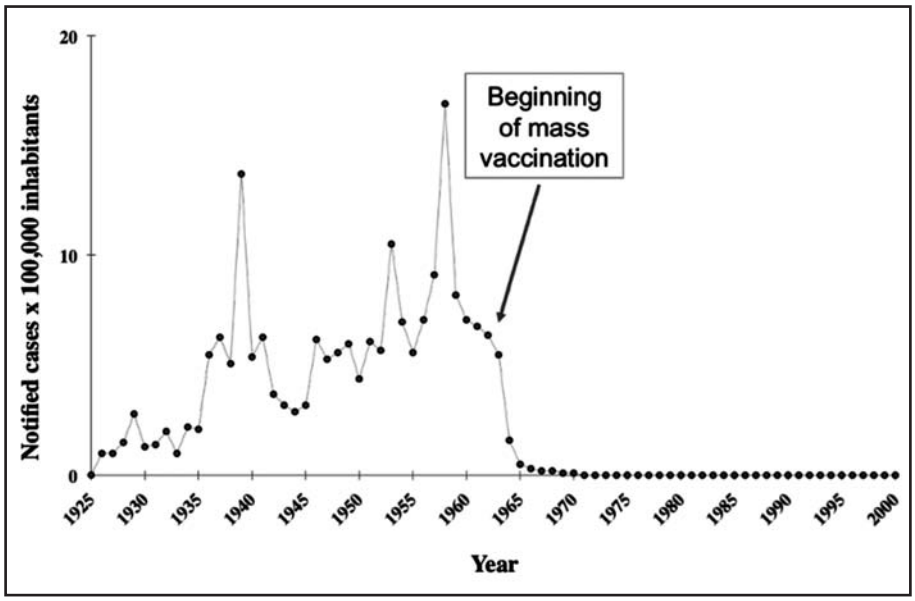
Polio, as a social disease, was first noted in Italy after the First World War (1915-18), with a consistent upward trend in the number of reported cases (Table 1, Figure 1). This situation has led to important research being undertaken in several National Hygiene Departments, in particular those located in Milan (Giovanardi, Monaci, Bergamini), Genoa (Petrilli, Agnese, Crovari), Palermo (D'Alessandro, Dardanoni), and Padua (Vendramini, Majori, Gasparini). Studies such as these, have examined the epidemiological and virological character of the illness in order to determine modalities for disease prevention. These studies demonstrated that all three poliovirus serotypes were circulating in Italy, with a higher prevalence (as a cause of paralytic disease) of poliovirus type 1 (about 80%), followed by type 3 (about 15%) and then type 2 (about 10 %). The presence of healthy carriers of the virus was very common in children (2-3%).The evidence of neutralizing antibodies in patients of different age groups confirmed that poliovirus infection was widespread. About 90% of the population over 14 years of age had antibodies against all three serotypes..

Research conducted mainly in the U.S., aimed at preparing a vaccine, was followed very closely by the Italian manifactures of vaccines that were equipped for the preparation of both inactivated (Institute Sieroterapico Italian-Naples) and live attenuated vaccines (Sclavo Institute -Siena and

Table 1. Incidence of poliomyelitis in Italy from 1921 to 1960.

Years	Average n. of cases per year	Average n. of cases per 100,000 inhabitants per year	Epidemic peak
1921-30	581	1,5	
1931-40	1941	4,5	6007 (1939)
1941-50	2140	4,7	
1951-60	4069	8,3	8377 (1958)

Figure 1. Polio morbidity in Italy from 1925 to 2000.



Institute Sieroterapico Milanese-Milan).

The first polio vaccine developed was an inactivated vaccine (IPV) developed by Dr. Jonas Salk and licensed in 1955. The Salk vaccine was approved in the U.S. after a large controlled field trial involving, , a total of 1,829,916 American, Canadian and Finnish children. The results were summarized in the report Francis presented on 12 April 1955. This report, which sanctioned the effectiveness of the vaccine, opened the doors to marketing the product by four American vaccine manufacturers that had used the experimental period for the production of the first batches of vaccine. The Salk vaccine in its first version was a mixture of three types of poliovirus (Mahoney, MEF1, Sauket) grown separately in primary cultures of monkey kidney tissue and inactivated with formalin. Unfortunately, when the enthusiasm to develop the new vaccine was at its peak, cases of polio occurred in the U.S. due to vaccine, manufactured by Cutter Laboratories containing virus that had not been completely inactivated. This incident affected the quality of the Salk vaccine. In fact, as a result companies intensified the process of inactivation with formalin thus reducing the antigenicity of the vaccine. In Italy, the Salk vaccine was approved in 1957. The Ministry of Health took charge of distributing free vaccine to community preschool children and schoolchildren. The product was also sold in pharmacies. Studies show that many batches of Salk vaccine used in Italy had low immunogenicity (Petrilli et al.), so, despite the availability of the Salk vaccine, it was not possible to stem the epidemic of polio in 1958 (8,377 cases).

The next years (1959-1962) were characterized by lively scientific debate. Following the U.S., some experts considered that they should still focus on the inactivated vaccine, improving its immunization. While others focused on live attenuated vaccines. The approach to this type of vaccine had taken off in parallel to that of inactivated vaccine but the time required for preparation and testing were obviously longer considering the delicate issue of "security" for a disease such as polio which involved a live virus vaccine, although attenuated. Strains attenuated by selection in the laboratory of viral clones with reduced neuro virulence were produced by different research groups (Sabin, Kroprowski, Cox) and numerous controlled clinical trials had been conducted or were in the pipeline especially in Eastern European countries (Poland, Czechoslovakia, East Germany, etc.). Even the Institutes of Hygiene in Milan and Genoa conducted pilot studies with strains of Sabin and Cox, respectively. Noting the results obtained using available vaccines and the prospects afforded by live attenuated

vaccine, in 1964 the Italian Ministry of Health decided to build a campaign of mass vaccination, using Sabin strains, with free offer of the vaccine to all children from six months to 14 years (above that age the majority of the population was already naturally immune, as mentioned earlier).

After a thorough process of carefully preparing healthcare workers and providing public information through the media, the monovalent vaccines were administered through Hygiene and Public Health outpatient services, as well as in kindergartens and primary schools. The preparation, Oral Poliovirus Vaccine (OPV), was given to children by dropping two drops of vaccine on a sugar cube. The Sclavo Institute supplied all the monovalent vaccines; supply of trivalent vaccine was divided evenly between the institutes Sclavo Institute and Sieroterapico Milanese. The vaccine was stored at -20 ° C and was thawed immediately before use. The preparation of the cold chain from producers to provinces and cities was one of the specific areas for which there were dedicated organizers. The month of March in 1964 was dedicated to the administration of the vaccine against type 1 poliovirus, the month of April to that of type 3 and the month of May to that of type 2. In October of that year, after the reopening of schools, children were given a dose of trivalent vaccine.

Each monovalent contained 300,000 TCID 50 of each virus. The trivalent vaccine contained 300,000 TCID50 of all three types. Accession to the vaccination was very good especially in the Centre-North, where immunization coverage often exceeded 90%. Subsequently, Polio morbidity declined sharply during the course of 1964 (Figure 1). Later, in 1965, using capillary action, non-vaccinated subjects was identified and, in 1966, in order to maintain thehigh level of vaccination, polio vaccination was made mandatory for newborns.

In 1972, monovalent vaccines were replaced by a more practical "balanced" trivalent vaccine (1 million TCID50 of type1, type2 and 300,000 of 100,000 TCID50 TCID50 of type 3). Morbidity relating to polio continued to decline after 1964, and remained at a low level throughout the seventies. Furthermore, since 1983, no index cases have been reported. In Italy, during 1964-2000, vaccination with OPV has resulted in a small number of vaccine associated paralytic polio (VAPP) cases being reported. Considering the ethical aspect of the problem and the favourable epidemiological situation, in 2000 a"sequential" schedule (IPV-IPV-OPV-OPV) was introduced and, in 2003, the use of live attenuated vaccine was suspended and IPV wasintroduced exclusively for polio vaccination during childhood. In conclusion, the campaign of mass vaccination with OPV in 1964, well organized and highly participatory, with forty years of brilliant vaccination policy have panned the alarming rise of polio in Italy in the first half of the twentieth century.

Sadly, the eradication of polio, which, perhaps, has prematurely been considered reachable, always presents new difficulties such as an epidemic reoccurence of the disease at the edge of Europe, a region declared by WHO to be "polio-free" in 2000.Therefore, we must remain vigilant and maintain surveillance for flaccid paralysis, which is a key observation for the early detection of polio.

Bibliographic material can be requested to the Author by e-mail.