Pioneering Figures in Medicine: Albert Bruce Sabin- Inventor of the Oral Polio Vaccine

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Received 4 January 2005, accepted 25 July 2005

Summary: Over ten years after his death, the Sabin oral vaccine continues its profound influence on public health throughout the world. The annual incidence of polio has fallen dramatically since its introduction, with more than 300,000 lives being spared each year and an annual global saving in excess of 1 billion US dollars. In many ways, the development of an effective oral vaccine and its subsequent regulation by the World Health Organization can serve as a model for medical researchers. Our review describes the contribution of Albert Sabin as a medical researcher, and how his vaccine had a profound impact on the global reduction of polio infections. As many different factors influenced health-care last century, we describe Sabin’s involvement with respect to prevailing scientific paradigms and public health issues of the time. Our paper also outlines the basic epidemiology of poliovirus and the historical development of an effective vaccine, both with and without Albert Sabin.

Key words polio, vaccine, Albert Sabin, public health, medical history

INTRODUCTION

Communicable diseases have always represented one of the most significant threats to human health. Since the first eradication program began in 1915, much has been learned about disease treatment and prevention [1]. Arguably, one of the most successful campaigns in preventive medicine has been the development of an effective and affordable vaccine against poliovirus. Although it first appeared in the mid-twentieth century, the Sabin oral vaccine continues its profound influence on public health as we enter the new millennium. It has been estimated that 350,000 lives are spared each year, with an annual global saving of 1.5 billion US dollars. The annual incidence of polio has fallen by 90%, and by 2000 the disease was endemic in only 30 countries [1]. In many ways, the development of an effective polio vaccine and its subsequent regulation by the World Health Organization should serve as a model for health practitioners the world over. Given his significant involvement these achievements, the status of Albert Sabin as a pioneering figure in public health and preventive medicine, cannot be overestimated.

THE EARLY YEARS OF ALBERT SABIN

Albert Bruce Sabin was born on August 26th, 1906 in Bialystok, Poland [2]. In 1921, the Sabin family emigrated to the United States to avoid increasing persecution of Jewish citizens in what was then Imperial Russia [3]. Suspecting his future lay in academic pursuits, Sabin entered and later graduated from New York University in 1928. He subsequently enrolled in medical school at the same institute, and with financial aid from various fellowships and scholarships, graduated as a medical doctor in 1931. His early interest in experimentation yielded a new method for the rapid typing of pneumococci while still a medical student [2]. 1931 was also the year of a large polio epidemic within New York, which no
doubt influenced the young graduate and helped sow the seed for his lifelong interest in medical research [3].

After graduation from NYU, Sabin worked as a house physician at Bellevue Hospital in New York, between 1932 and 1933. In 1934 he moved to the Lister Institute of Preventive Medicine in London to take up a position as a National Research Council Fellow [2]. Sabin returned to New York in 1935, and subsequently joined the Rockefeller Institute for Medical Research. After four years in New York, he moved to the University of Cincinnati Children’s Hospital in 1939, and created a research laboratory which would later develop his landmark vaccine. Sabin served in the U.S. Army Medical Corps during World War II as a Lieutenant Colonel, during which time he studied various diseases that affected American troops stationed abroad [2]. From this work, Sabin developed vaccines against Dengue fever for troops in the South Pacific theatre and a vaccine against Japanese encephalitis virus. As a result, his encephalitis vaccine was administered to around 70,000 soldiers who were then preparing to invade Japan [2]. After the close of hostilities Sabin continued his interest in polio vaccines. This coincided with an interesting evolutionary phase for public health, as a large proportion of the international scientific effort which had previously focused on war-related activities, were now free to follow peacetime pursuits.

THE HISTORICAL DEVELOPMENT OF POLIOVirus KNOWLEDGE

Although sporadic Poliovirus cases have probably affected humans since the beginning of time, paralytic poliomyelitis began appearing in the medical literature by the mid-1700s. Clearly identifiable outbreaks were seen in the mid-1800s, which gradually began more frequent, more severe and more widespread [4]. Nevertheless, the epidemiology of poliovirus took some time to completely understand. In the early 20th century, although it was well known that epidemics usually radiated from a central point, polio’s pattern of spread was erratic and many infected people had no history of contact with a known source [5]. Part of the problem was early confusion regarding the biological infection route. In 1908 for example, it was thought that Poliovirus entered the human body via respiration [6], a hypothesis which had arisen via the demonstration of nasal lesions in infected cases. Nevertheless, 1908 also saw the first basic polio research being undertaken, with experimental transmission of the disease to monkeys [5].

In 1931, Albert Sabin contributed to poliovirus knowledge by publishing his first academic manuscript on the topic [7]. During the 1930s, the possibility of an oral-alimentary infection route for the virus was being considered by scientific researchers, and one which steadily began to develop momentum. One significant point occurred during 1932, when high levels of the virus were demonstrated in the feces of polio patients and healthy carriers [5]. The concept of alternative sites for transmission also began to simultaneously falter, when a 1936 publication showed that nasal lesions existed only in experimental monkeys who had contracted polio via a respiratory route [6]. Other animal models were also being developed for polio experimentation, with poliovirus first being grown experimentally in mice in 1939 [5]. In 1940, the Yale Poliomyelitis Study Unit began testing for polio among New York sewage and found it to be highly prevalent. Sewage testing not only showed that poliovirus was excreted from carriers in this manner, but that a large number of infected persons were probably asymptomatic. Melnick and colleagues later suggested a ratio of about 100 sub-clinical infections for every paralytic case [5]. By the 1950s, it had been established that poliovirus could be isolated from several species of flies during summer epidemics. However, flies emerging from maggots experimentally fed poliovirus were shown to be free from the agent [8], a finding which began to cast doubt on flies as a significant reservoir.

Research on poliovirus immunology was also developing during this period, and by 1952 it had been established that neutralizing antibodies for poliomyelitis virus were demonstrable in patients at or shortly after the onset of symptoms, and continued to increase during convalescence [9,10]. Experimental studies on poliomyelitis variants were also continuing in the Sabin laboratory [11]. As the 20th century progressed, the propensity for poliovirus to appear in community outbreaks, firmly entrenched it as an important issue for public health researchers. Furthermore, the implication of sewage as a possible vector suggested that public health interventions would need to be incorporated into any type of control program. Although some experts of the early 20th century had tried to define polio simply as a disease of the poor and unclean [12], large concentrations in sewage helped foster a new belief that it was a disease that could be contracted by any-
one, given the right exposure.

THE DEVELOPMENT OF A POLIOVIRUS VACCINE

During many of the experiments mentioned earlier, and for a variety of reasons, it had become apparent to Sabin that oral exposure might be a promising direction from which to develop a vaccine. Chief among them was the fact that although poliovirus was seemingly endemic in developing countries, not everyone suffered a paralytic attack. Similarly, the high titers found in first-world sewage indicated that gastric ingestion may not always result in paralysis. Sabin must have been considerably encouraged in 1952 when a large field-trial demonstrated that passive antibodies offered a short term protective effect against paralytic polio [5].

Interestingly however, Albert Sabin was not the only person to invent a poliovirus vaccine, nor was he the first. In 1955 an inactivated polio vaccine that had been developed by Jonas Salk was rapidly adopted throughout the United States [13]. Although an immediate decline in cases was noted, the trend leveled off and then turned around by 1959, despite the administration of approximately 300 million doses [14]. There were a few reasons for this, chief among them being that circulating antibody titers seemed to decline significantly within a few years of vaccination. Secondly, poliovirus had not been totally eradicated and wild types continued to circulate, causing localized outbreaks in partly immunized or non-immunized individuals. Tragically, 11 people had also died from vaccine-related poliomyelitis in a highly publicized incident [13]. It was later learned that poliovirus could still grow within the gut of vaccinated persons, before being transmitted to non-immunized persons [4]. Another disadvantage of the Salk vaccine was that approximately 1500 monkeys needed to be sacrificed to produce every 1 million inactivated doses [14]. As monkeys occupied an ever-increasingly important component of the medical research process, this large demand from a single branch of medical science began to cause a shortage of animals.

Throughout this time, Sabin maintained that intensive wide-spread vaccination with a live vaccine (as opposed to the inactivated ‘dead’ vaccine of Salk) could interrupt disease transmission at lower overall levels of vaccination coverage than ongoing or routine programs [15]. An oral vaccine could also be easily administered as a mass public health measure. Furthermore, live oral viruses would be effective at imitating natural infection as they could establish an asymptomatic infection within the gut, which would in turn, stimulate immune response and the excretion of local and systematic antibodies. Building on these theories, Sabin developed an oral vaccine consisting of three attenuated strains (one from each serotype) of live poliovirus [16].

PROFESSIONAL RECOGNITION FOR ALBERT SABIN

On August 6, 1960, Albert Sabin published his landmark article titled: Live, Orally Given Poliovirus Vaccine in the prestigious Journal of the American Medical Association (JAMA) [17]. In this manuscript, Sabin described the results of an impressive study conducted in South America. The experiment involved feeding his newly-developed trivalent oral vaccine to 26,033 children from a city of 100,000 people. The vaccine was fed to 86% of all children younger than 11 years over a period of four days. Due to the self-limiting nature of poliovirus, a second feeding was needed to achieve almost complete immunization coverage. This point was confirmed with increased understanding of poliovirus epidemiology in later years, as it was shown that transmission can be effectively interrupted by achieving high population immunity [1]. So important was Sabin’s article to medical science that it was actually republished by JAMA in 1984 [18], and later by the World Health Organization in 1999 [19].

In 1961, monovalent strains for the Sabin vaccine were licensed in the United States, with a trivalent vaccine following soon after in 1963. During this time in 1962, the world’s first nationwide polio vaccination campaign was undertaken in Cuba [14]. The significant Russian contribution to polio vaccine is also worth noting, as it followed a fortuitous meeting in 1956 between Albert Sabin and Mikhail Chumakov [20]. During this meeting Sabin provided experimental results and more importantly, his strains of polio vaccine to Chumakov, who subsequently began to produce it for use in his homeland. At that time, polio was a widespread public health issue throughout Russia, a fact which enabled Chumakov to trial the vaccine first in Estonia and later, in Lithuania. By 1959, 15,200,000 Russians, mainly children, had been inoculated with the Sabin vaccine [20].

The Russian success story constituted a large body of evidence considered by the Division of Biological Standards of the National Institutes of Health [USA], who eventually recommended all 3 strains of the Sabin vaccine for license. Between
1962 and 1964 around 100 million Americans of all ages received the new Sabin oral vaccine. Large, public health field trials were also conducted in Czechoslovakia, but it was the widespread use in Brazil in 1980 which demonstrated that polio eradication might be feasible on a worldwide scale. This prompted the World Health Organization in 1988 to adopt, a perhaps wishful policy of global Polio eradication [21]. Although their initial goal has not yet been reached, numerous public health achievements have nevertheless been made with respect to polio. By 1995 for example, around 80% of all children worldwide had received the 3 required doses of vaccine in the first year of life, and this was preventing at least 400,000 polio cases annually [4].

WHY THE SABIN VACCINE WAS SO IMPORTANT

Albert Sabin was not the first person to consider the eradication of a human pathogen, as major disease eradication schemes were being undertaken by public health researchers throughout the last century. Nevertheless, there were a few good reasons why Sabin’s oral vaccine was a scientific success, and why he was able to make such a significant contribution to public health. Firstly there was the issue of demand. Although poliovirus may be transmitted by various animals in certain situations (such as flies) [8], humans represent the only known reservoir [4]. It spreads rapidly through infected households and is often present in urban sewage, being most commonly spread from infectious feces by contaminated fingers. When Sabin was young, large polio epidemics were spreading across the United States and Europe. In the summer of 1916 for example, the United States experienced 27,000 cases of paralytic polio and 6,000 deaths [4]. People fleeing New York in the polio epidemic of 1931 were actually turned back at gunpoint by some residents of neighboring towns; such was their fear of the disease. Although it killed fewer children than other epidemics of the day, (such as diphtheria, whooping cough or measles) [12], polio certainly provoked more fear in the community. Therefore, the desire to find an effective vaccine was paramount in the eyes of not only public health experts, but also the general public and government officials.

Secondly, there was Sabin’s ongoing insistence that a live oral vaccine was superior to an inactivated one. Indeed, he once said that his mission was to ‘kill the killed [Salk] vaccine’ [2]. This was a shrewd scientific decision given the prevailing scientific paradigms of the day. An oral vaccine was easier to administer, and it provided longer lasting immunity from fewer doses. Importantly, the oral vaccine stimulated local and systemic immunity, which helped prevent its spread from asymptomatic people. Sabin, it seems, probably had a certain amount of luck when choosing his live strains. In 1950 for example, Koprowski and Cox began experiments with a slightly different, rodent-adapted Type 2 strain, which was subsequently fed to millions throughout the world. Unfortunately, the father of a child receiving Cox vaccination developed paralysis and died [4]. When properties of the Cox virus were recovered from his brain tissue, the strain was withdrawn, paving the way for the widespread adoption of the Sabin trivalent oral vaccine.

THE SABIN VACCINE TODAY

Over ten years after his death, the Sabin oral vaccine continues its profound influence on public health the world over. Aylward et al. [1] for example, estimates there are 350,000 lives saved each year by the oral vaccine, with an annual global saving of 1.5 billion US dollars. The annual incidence worldwide has fallen by 90% and by 2000 it was endemic in only 30 countries [1]. Despite these enormous savings in lives and dollars and the associated moneymaking potential, it seems that Albert Sabin’s motivation was not financial. In 1972 he donated his carefully devised strains of poliovirus to the World Health Organization. This unprecedented humanitarian gesture was intended to increase the availability of an effective vaccine for developing countries, and was remarkably successful from both a scientific and humanitarian point of view [22]. Nor was his legacy forgotten. Research has continued on the Sabin vaccine during recent years [23,24], and there has also been renewed interest in new and novel uses for it. Girard et al. [25] for example, have suggested using the Sabin strains of poliovirus as a possible vector in the engineering of new, recombinant vaccines. Meanwhile, the institute which bears his name continues to develop new vaccines for Guinea Worm and others.

EPILOGUE

Albert Sabin entered a world where the average lifespan of males was 47 years and females, 51 years. Tuberculosis, pneumonia and heart disease were the biggest killers, and ones for which adequate preventive measures were largely unavailable [World Health Organization. Basic Health Indicators by Region,
Online Resource: www.who.int]. Theories of disease causation were slowly being refined following the groundbreaking work of Pasteur and others, but the transition to a modern hygienic society had not yet been achieved. By the time of Sabin’s graduation from university in 1931, the average lifespan of human beings had risen to 60 years for men and 63 years for women. In the 29 year gap between the publication of Sabin’s first paper in 1931 [7] and his landmark JAMA article in 1960 [17], worldwide infant mortality had been reduced more than threefold and average lifespan had also increased by almost 150% in women. By the time of his death in 1993, male and female life expectancy had increased to 72 and 79 years, respectively [World Health Organization. Basic Health Indicators by Region, Online Resource: www.who.int].

Although Sabin never received the Nobel Prize, Sabin nonetheless received numerous well-deserved accolades for his work with the polio vaccine; including 46 honorary degrees, the US National Medal of Science, the Presidential Medal of Freedom, the Medal of Liberty, the Order of Friendship Among Peoples (Russia), the Ordem Cruzeiro do Sul Grande Oficial and the Gran Cruz da Ordem do Rio Branco (Brazil) [The Legacy of Albert Sabin, Online Resource: www.sabin.org]. By all accounts, Albert Sabin was a stubborn but eloquent speaker and therefore, difficult to defeat in scientific arguments. When asked about his prime competitor Jonas Salk, Sabin once declared that the Salk vaccine was ‘pure kitchen chemistry’ [2]. Sabin was not alone in this criticism, as many in the scientific community also felt that Salk had not really discovered anything new, rather he had simply produced a polio vaccine from techniques founded by others [13].

Albert Sabin retired from full-time work in 1986 at the age of 80, although he continued publishing [26], right up until his death from heart failure in March 1993 [27]. He was buried in Arlington National Cemetery as an honor for those who served in the United States military. Over the course of his life, spectacular achievements in public health (including the polio vaccine), had reduced infant mortality 10-fold. Infectious disease all but disappeared as the prime cause of mortality within industrialized countries. His early hypotheses on the theory and causations of large-scale public health epidemics would later be shown to be fundamentally correct [28]. Although Sabin was not alone in his desire to eradicate diseases; his achievements remain profound and far-reaching for public health, even when considering the continual advance of medical technology after his death. Sabin helped establish public health as a credible discipline by conducting rigorous scientific experiments and using his results to influence prevailing health care ethos. Given these facts, Albert Sabin can rightfully be listed as one of the true pioneers of this field, and there is much we can learn from his legacy as both scientists and physicians.

REFERENCES


