



Review Article

Gu Fangzhou: A monument to polio elimination in China[☆]Fu-Min Huang^a, Rong Chai^b, Hai-Sheng Liu^a, Yun-Feng Wang^a, Guo-Xing Tang^c, Jing Liu^{a,*}^a Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China^b Institute of Medical Information & Library, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100005, China^c Peking Union Medical Audio-Visual and Electronic Publishing House, Beijing 100730, China

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ABSTRACT

Commemorating the centenary of Professor Gu Fangzhou's birth, this memorial article documents his landmark contributions to eliminating poliomyelitis in China. It details his strategic prioritization of the live attenuated oral polio vaccine (OPV) and his team's breakthroughs in overcoming logistical hurdles through the sugar-coated pill formulation and mass immunization campaigns. Furthermore, the review highlights his development of diagnostic reagents and a national surveillance network, which culminated in China's polio-free certification in 2000. Ultimately, the paper honors Professor Gu's legacy as a trailblazing scientist, demonstrating how his low-cost, high-efficiency research model provided a replicable template for global polio eradication and laid the institutional foundation for China's modern public health system.

1. A mission of return: from virologist to polio trailblazer

Following the founding of the People's Republic of China, the nation achieved remarkable successes in the prevention and control of infectious diseases, yet remained largely defenseless against poliomyelitis. Commonly known as infantile paralysis, polio left afflicted children dead or permanently disabled, with the disease spreading rapidly across the nation. Unlike many previously controlled infectious diseases, poliomyelitis was characterized by an acute onset and devastating long-term consequences; survivors often faced lifelong disability, with no cure available. The earliest records of polio in China date back to 1882, and by 1938, sporadic cases had been reported in 14 provinces and municipalities. In 1953, the Ministry of Health designated the disease as a legally notifiable condition, after which reported cases increased steadily and the affected areas expanded continuously. In 1955, polio epidemics erupted in Nantong, Jiangsu Province, and Qingdao, Shandong Province, with incidence rates reaching 32.1/100,000 and 37.6/100,000, respectively. Subsequently, reports of outbreaks continued unabated; by 1959, the incidence rate in Nanning City soared to a staggering 150.6/100,000. Given its high mortality and disability rates and the lack of effective treatment, polio caused considerable panic in epidemic areas.^{1,2}

After completing advanced studies in the Soviet Union, Gu Fangzhou returned to China in 1955 and launched poliovirus research in 1957. In March 1959, on a commission from the Ministry of Health, he was sent to the Soviet Union to investigate polio vaccine manufacturing technolo-

gies. He proposed a live attenuated vaccine strategy adapted to China's socioeconomic conditions, undertaking the historic mission of developing an indigenous vaccine to protect children's health. As one of the first government-sponsored students sent to the Soviet Union for advanced study, Gu was trained under Prof. Levkov, a renowned Soviet virologist at the Institute of Virology, USSR Academy of Medical Sciences. He mastered cutting-edge virological theories and experimental techniques and completed his dissertation on the pathogenesis and immunological mechanisms of Japanese encephalitis. His early work on viral crossing of the blood-brain barrier foreshadowed his later breakthroughs in polio vaccine development. Keeping his promise to serve the motherland, he worked intensively in the laboratory for four years, using thousands of murine models, did not take home leave during his overseas study, and finally graduated with distinction.^{3–5}

Upon his return, Gu initially led Japanese encephalitis research at the Encephalitis Division of the Institute of Microbiology and Epidemiology, Ministry of Health. He introduced the tissue culture technique pioneered by John F. Enders' team to successfully culture the Japanese encephalitis virus *in vitro*. This breakthrough overcame the long-standing bottleneck in propagating human viruses—including poliovirus—in non-human cells, laying the technical foundation for subsequent vaccine research and development. Faced with the scarcity and high cost of imported bovine serum, Gu led his team to a slaughterhouse in Changping County to collect neonatal calf blood and independently isolated and purified a replacement serum, easing the shortage of experimental materials.¹ In 1957, Gu collaborated with Soviet virologist Sokolov at the

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Academy of Military Medical Sciences in Shanghai to launch systematic poliovirus research. At that time, domestic research on poliovirus pathogenesis was still in its infancy, lacking standardized viral typing data and national epidemiological surveys—major obstacles to vaccine R&D. To map the domestic epidemiological profile of poliovirus, Gu established a rhesus monkey kidney cell-culture system and standardized protocols for immune serum preparation, viral isolation, and serotyping, addressing a critical domestic technological gap. During the 1957 Shanghai outbreak, he collected fecal specimens from epidemic zones at personal risk. Rigorous experiments yielded multiple poliovirus isolates, with type I as the dominant strain, providing the first systematic virological evidence for China's polio epidemiology.⁶ This work laid a solid foundation for targeted vaccine development. From then on, he devoted more than four decades to China's polio prevention and control.^{1,4,5} The inclusion of a centenary commemoration for Professor Gu Fangzhou in the agenda of the 43rd session of the UNESCO General Conference pays tribute to his seminal contributions to pediatric public health and the global eradication of poliomyelitis (or “polio”).

2. Overcoming technical barriers: development of China's live attenuated polio vaccine

In 1950s, the United States had developed the inactivated polio vaccine (IPV), secured its licensure from the U.S. Food and Drug Administration (FDA), and commenced commercial distribution; several Western countries subsequently adopted this vaccine for polio prevention. In March 1959, entrusted by the Ministry of Health, Gu was dispatched to the Soviet Union to investigate and learn about polio vaccine manufacturing technologies. As the head of the delegation, he was accompanied by Dong Dexiang from the Department of Virology at the Chinese Academy of Medical Sciences, Wen Zhongquan from Beijing Institute of Biological Products, and Jiang Jingwu from Chengdu Institute of Biological Products. To ensure the successful completion of the mission, specific assignments were allocated prior to departure: Dong focused on vaccine quality control and testing, Wen specialized in viral cultivation, and Jiang concentrated on cell and tissue culture, while Gu assumed overall command. Their objective was to acquire the complete suite of inactivated polio vaccine production technologies within a limited time-frame.

Although Gu's team gradually established a complete production workflow for IPV, Gu soon identified that this vaccine was poorly suited to China's national conditions at the time. IPV requires a massive dose of purified viral antigen, over 100 times the antigen dosage per dose of OPV. Its production relies on large-scale specialized equipment, sophisticated purification processes, high-grade biosafety workshops, and substantial expensive imported purification consumables, resulting in extremely complex manufacturing and vaccination procedures as well as exorbitant production costs — major flaws that made it unfit for large-scale national immunization. Financially, the IPV regimen required three doses, each costing tens of *yuan* — a sum that ate up the bulk of an ordinary urban worker's monthly wage at that time, and posed an even greater financial strain on rural families with much lower earnings. According to China's second national population census in 1964, the country had about 135.42 million children under the age of seven. Vaccinating hundreds of millions of newborns and susceptible young children would have placed an unaffordable fiscal burden on the state. Operationally, IPV's injectable administration required a huge team of professional medical staff for vaccination and safety management, which exceeded China's grassroots service capacity at that time. Technically, IPV also had inherent defects in epidemic prevention and control. While it could reduce individual infection rates, it failed to curb viral transmission effectively. The vaccine only triggers humoral immunity in the blood without building intestinal immune barriers. Since poliovirus invades the human body orally, replicates massively in the intestines before entering the blood and nervous system, unprotected intestinal mucosa leaves the population vulnerable to wild poliovirus in-

fection and transmission. Substandard vaccine quality, incomplete vaccination doses or declining antibody levels could also lead to new epidemic outbreaks, a risk verified by practical immunization data from the United States, Hungary, Canada, Israel and other countries. Based on the above analysis, Gu concluded that introducing IPV production technology would have little practical value for China's polio prevention and control work at that time.

In 1959, While Gu was in the Soviet Union, an international academic conference on the poliomyelitis vaccine was convened in Moscow, which he attended. The event brought together world-renowned scholars, where virologists debated fiercely and without reservation, airing their disagreements openly. There existed significant divergence among academic experts. One advocated for IPV, while the other championed the live attenuated vaccine. Advocates of IPV argued that the long-term safety of the live vaccine remained insufficiently observed. Some stressed that the live vaccine's non-adoption in the United States stemmed from concerns over potential virulence reversion—the fear that the virus might regain its toxic strength. As Gu listened to these debates, he pondered a critical question: Was this “reversion” merely a theoretical possibility, or an empirical reality? Off the conference floor, Gu consulted his Soviet mentors and classmates about the live vaccine challenges. Finally, he resolved to recommend the live attenuated vaccine to China. He submitted a formal report to the Ministry of Health of China, advocating for this technical route and urging the cessation of the existing IPV. This decision marked a significant turning point in modern Chinese epidemic prevention.⁷

At the time, the Soviet Union could not afford IPV either. Instead, using the viral strains provided by Sabin, they successfully mass-produced the live attenuated vaccine. In November 1958, the Ministry of Health of the Soviet Union initiated a population-level study to evaluate the efficacy of oral Sabin live vaccine. From January to June 1959, roughly 35 million people were immunized, with the results later presented at the All-Union Conference on Poliomyelitis. In June 1959, with the approval of professor Chumakov, director of the Poliomyelitis Research Institute under the USSR Academy of Medical Sciences, Gu's team obtained the original Sabin vaccine and 3,000 doses of live vaccine. To expedite domestic production of the live vaccine, Gu sought approval from Vice Minister of the Ministry of Health Qian Xinzong, who was visiting Moscow at the time, as well as from the Chinese Embassy in the Soviet Union. He then brought the vaccine samples back to Beijing.

Without hesitation, Gu and his colleagues decided to test the vaccine on themselves first. Risking possible paralysis, Gu took the lead and drank a small vial of the vaccine solution. One week later, none of them showed any abnormalities.

The next imperative was to prove the vaccine's safety for children. Gu and his colleagues volunteered their own children—five or six kids in total—for the experiment. The children were observed for one month, with particular scrutiny during the first and second weeks. Upon completion of the one-month observation period, none of the children developed any clinical symptoms. Phase I was a success. In July of the same year, the Department of Virology of the Chinese Academy of Medical Sciences collaborated with the Beijing Municipal Center for Disease Control and Prevention to conduct a trial administration among more than 2,000 children aged 0 to 7, so as to observe the immunogenicity and safety of the live vaccine. The trial results proved that the Sabin live vaccine had sound immunogenicity with no severe adverse reactions observed, laying a preliminary foundation for the independent production of live vaccines in China.^{5,8}

After Gu's team returned to China after completing its mission in September 1959, the Ministry of Health instructed the team to finish the trial production of 5 million doses of live vaccine as soon as possible. In October, under the leadership of the Ministry of Health, joint efforts were made by the Department of Virology of the Chinese Academy of Medical Sciences, the Beijing Institute of Biological Products of the Ministry of Health, the Chengdu Institute of Biological Products and other institutions. With strong support from the Beijing Institute of Biologi-

cal Products, the trial production was launched. In March 1960, China produced its first batch of attenuated live poliovirus vaccines.

On March 16, 1960, the Ministry of Health convened officials from health and epidemic prevention stations across ten provinces and municipalities to discuss the trial oral administration of live vaccines. The meeting decided to launch the use of the vaccine first in 11 cities including Beijing, Shanghai, Tianjin, Qingdao, Nanjing, Shenyang, Wuhan, Chengdu, Kunming, Nanning, and Jinan. The main objective was to evaluate the safety, immunogenicity, and epidemiological effects of the live vaccine when administered orally to large populations. To ensure vaccination was completed before the polio epidemic season, the immunization with Type I and Type II live vaccines was scheduled for April and May of the same year. Immunization with Type III live vaccine was carried out in May 1961. A total of 4.5 million children under the age of seven received the vaccine.

In 1960, multi-regional monitoring was conducted in China to evaluate the safety of domestically produced live poliovirus vaccine based on systematic follow-up observations of a large cohort of vaccinated children. Post-vaccination adverse reactions were mild and transient, with low-grade fever as the most prevalent symptom, along with occasional gastrointestinal discomfort, dizziness and mild rashes. All adverse events resolved spontaneously within a short duration without clinical intervention. Common seasonal infectious diseases were observed in both vaccinated and unvaccinated populations, which were unrelated to vaccination. Critically, no cases of paralytic poliomyelitis were detected among vaccinated children, demonstrating the satisfactory safety of the domestically produced live poliovirus vaccine.

Serological analysis was performed to assess the immunogenicity of the vaccine. The results showed that the domestically produced live poliovirus vaccine could efficiently induce neutralizing antibody responses in humans. Both Type I and Type II vaccines yielded high seropositivity rates, whereas Type III vaccine presented a relatively lower yet clinically acceptable positive rate. Collectively, the vaccine exhibited favorable immunogenicity and was capable of establishing effective immune protection in vaccinated children.

Epidemiological protective efficacy is an essential and critical indicator for assessing the practical effectiveness of vaccines. Large-scale immunization programs implemented in multiple Chinese cities markedly reduced the endemic incidence of poliomyelitis compared with the pre-vaccination level. In addition, widespread vaccination substantially altered the epidemic patterns of poliomyelitis. Historically, poliomyelitis outbreaks peaked seasonally in summer and early autumn. After the implementation of mass vaccination, such seasonal epidemic features were significantly weakened, and the traditional epidemic peaks disappeared in major immunized areas. These epidemiological evidences strongly indicate that the domestically produced live poliovirus vaccine has excellent protective efficacy and can effectively inhibit the transmission and prevalence of poliomyelitis.⁸

3. Innovative formulation and immunization strategies: sugar-coated vaccine and polio elimination

The liquid live attenuated vaccine required dilution and strict cold-chain transportation, making large-scale deployment highly inconvenient. Improper storage frequently led to spoilage and frequent waste. In May 1960, Gu attended the 4th Academic Conference of the Soviet Institute of Poliomyelitis and the International Conference on Live Polio Vaccines in Moscow, where he learned that the Soviet Union had successfully converted the liquid vaccine into a solid, sugar-coated pill, which effectively resolved the cold-chain transportation and storage issues and had already in mass production. However, given various constraints at that time, he was unable to obtain the sugar pill formula.

Upon returning home, Gu immediately reported this information to Shen Qizhen, Vice President of the Chinese Academy of Medical Sciences. Shen then leveraged his connections through the Shanghai Municipal Committee to identify the Shanghai Xinyi Chemical Pharmaceu-

tical Factory as a facility capable of undertaking this crucial task. Under Shen's direct coordination, Gu, Dong Dexiang, Wen Zhongquan, and others collaborated closely with the factory's technicians to overcome key technical challenges, including formulation, cold-processing, viral uniformity within the pill, and detection. Testing confirmed that the sugar pill vaccine remained stable far longer than the liquid version under various temperatures, while its immunogenic effect was identical to the liquid form, with no adverse reactions. The successful development of the sugar pill created the conditions for the large-scale use of the live vaccine and its promotion to remote areas. By the end of 1962, it was trialed in millions of people across Beijing, Shanghai, and Yunnan, before being promoted to major cities nationwide in 1963. Two years of practice proved its significant epidemiological efficacy. The success of the sugar pill laid the material foundation for controlling the polio epidemic in China.⁹

In 1968, the Institute of Medical Biology purchased equipment and, with assistance from Xinyi Pharmaceutical, began processing sugar pills to supply southwestern provinces while launching research into multivalent (combined-type) sugar pills. In 1975, after combining Type II and Type III pills into a bivalent formulation, they began researching a trivalent mixed sugar pill. Trials revealed a challenge: when Types I, II, and III live vaccines were administered simultaneously, the Type II virus interfered with the replication of Types I and III in the human intestine, compromising the immune effect. To address this, Dong Dexiang and others spent years studying the relationship between viral dosage ratios and immune efficacy. Finally, in 1985, they discovered the optimal ratio and successfully developed the I+II+III Trivalent Sugar Pill, which demonstrated excellent immunity upon administration and further optimized the national immunization schedule for polio vaccination.

There were no international precedents for the inspection methods of multivalent sugar pills. Researchers at the Institute of Biology worked tirelessly to establish China's own testing standards. The inspection laboratory conducted rigorous tests on the viral types and concentrations within the multivalent pills. Once certified, the multivalent vaccine was supplied nationwide.

The success of the trivalent sugar pill not only solved the supply problem of bulk vaccine liquid but also improved efficiency, reduced costs, and enhanced convenience. Following its nationwide promotion in 1986, it provided China with the highest quality, cheapest, most convenient, and most effective weapon for the ultimate elimination of poliomyelitis.¹

The isolation, typing, and antibody measurement of the poliovirus relied heavily on live cells—a process that was time-consuming, labor-intensive, and expensive, making it difficult to implement in grassroots epidemic prevention stations. Gu, along with Wang Shuhui, Sun Yueying, and others, conceived the idea of bypassing live cells and using the enzyme-linked immunosorbent assay (ELISA) for poliovirus detection. After more than two years of effort, they turned this vision into reality. In June 1983, they published "Application of Enzyme-Linked Immunosorbent Assay (ELISA) in the Screening of Type III Poliovirus McAb and Antigen Analysis", establishing a new methodology for polio research.¹⁰ In October 1985, they published another paper, "Screening of Poliovirus Monoclonal Antibodies and Antigen Analysis Using ELISA," highlighting the significance of having "the ability to distinguish between wild-type and vaccine-related strains of Type III poliovirus."¹¹ In April 1981, leading the team, Gu published a brief report titled "Establishment of hybridoma cell line E55 secreting monoclonal antibody against poliovirus type I."¹² The publication of this paper marked the successful application of monoclonal antibody technology to polio research and signified that polio research in China had entered a new historical stage, shifting from the cellular level to the molecular level.

In the mid-1980s, China's polio detection methods still followed decades-old cell culture techniques. These methods were technically complex, took 7–10 days to yield results, and were inaccessible to grassroots epidemic prevention stations. Therefore, a simple, rapid, and accurate detection method was urgently needed for rapid promotion across

both urban and rural areas. This critical subject was included in the National Seventh Five-Year Plan by the Ministry of Health. Leading a team of fewer than ten people, Gu once again accepted the urgent mission, launching a second charge against the poliovirus. In early 1991, Gu's team formally submitted their report "Preparation and Application of Poliovirus Monoclonal Antibody Diagnostic Kit" to the national administrative management and review agencies, and it received certification. In the great journey of Chinese scientists defeating polio, the Poliovirus Monoclonal Antibody Diagnostic Kit and the Live Attenuated Vaccine stand as two monumental milestones. In October 2000, official confirmation declared that the transmission of indigenous wild poliovirus in China had been interrupted, and China was certified as a polio-free country.

4. China's global contributions and far-reaching impact in polio prevention and control

The polio control program, in which Gu played a foundational role, has protected hundreds of millions of Chinese children. It established a "low-cost, high-efficiency" model for global eradication, offering a replicable pathway for developing nations facing resource constraints.

China's success rested on four key pillars: the indigenous development of the OPV, the innovative sugar-pill formulation, a tiered national immunization system, and robust acute flaccid paralysis (AFP) surveillance. The Manufacturing and Testing Guidelines for Oral Live Attenuated Poliovirus Vaccine, formulated under Gu's leadership, established an important technical benchmark. As of 2023, China had produced billions of doses and provided technical assistance to numerous developing countries and regions, thereby actively contributing to the Global Polio Eradication Initiative (GPEI). Through technology transfer, experience sharing, and vaccine aid, China helped mitigate operational barriers in low-income settings.

Beyond logistics, the polio elimination campaign redefined China's paradigm for infectious disease control. The national infrastructure built during this period established replicable models for addressing other major health threats. GPEI documents confirm that polio-derived infrastructure constitutes a core resilience mechanism for public health emergency response worldwide; the surveillance and response frameworks developed at that time provided vital references during the COVID-19 pandemic. Meanwhile, this campaign elevated the government's priority on public health, driving improvements in infrastructure, workforce training, and fiscal allocation, while entrenching the "prevention first" principle nationwide. These efforts laid the ideological groundwork for the Healthy China strategy.

5. An enduring monument

Professor Gu devoted his life to fighting the poliovirus and safeguarding children's health in China and beyond. With extraordinary dedication, wisdom, and innovation, he overcame successive technical barriers, ranging from the initial isolation of the virus in 1957 to the certification of its polio-free status in 2000. As the central figure in this monumental effort, he addressed a series of context-specific challenges, thereby writing a landmark chapter in the history of global public health.

The development of the polio vaccine represents not only a medical triumph but also a conceptual innovation in public health practice. Gu's legacy includes both tangible advances and an intangible scientific spirit, characterized by the pursuit of truth, pragmatic dedi-

cation, innovation, and selfless courage. His story, spanning from the public panic of the Nantong epidemic to nationwide polio-free status, and from technological constraints to the triumph of adaptive innovation, constitutes a magnificent chapter in China's public health history.

His contributions are forever engraved on the monument of China's public health achievements. He stands as a beacon, guiding the continued journey fight against infectious diseases toward the ultimate goal of "Health for All."

Authors' contributions

Huang FM: writing—original draft; Chai R, Liu HS, and Tang GX: writing—review and editing; Wang YF: resources; Liu J: conceptualization and writing—review and editing. All authors read and approved the final version of the manuscript to be published.

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During the preparation of this work, the authors used large language models to assist with language editing, translation, and figure formatting. After using this tool/service, the authors closely reviewed and edited the content as needed and take full responsibility for the final content of the publication.

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