

# Political will and international collaborative frameworks in infectious diseases

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## SUMMARY

The last few decades have been marked by a rapid expansion in the world's population, along with an increasingly dynamic mobility of individuals. This accelerated global inter-connectedness enabled microorganisms to reach virtually any location worldwide more rapidly and efficiently than ever before, reshaping the global dynamics of pathogens. As a result, a local infectious disease outbreak anywhere in the world may almost instantaneously assume global dimensions, and should therefore be considered a global priority. The history of several infectious diseases illustrates that in addition to prophylactic and therapeutic medical interventions, the interplay of social, economic, and political factors makes a fundamental contribution to the outcome of infectious disease outbreaks. Furthermore, this multi- and cross-disciplinary interconnectedness is a key determinant of the outcome of efforts to eradicate vaccine-preventable infectious diseases. A combined framework that incorporates teachings provided by previous outbreaks, and integrates medical and biomedical interventions with contributions made by social, economic, and political factors, emerges as vital requirement of successful global public health initiatives.

### Review criteria

Infectious disease eradication, political frameworks, international collaboration, smallpox, SARS, poliomyelitis, global mobility.

### Message for the clinic

Multi-disciplinary frameworks that incorporate medical and biomedical sciences, together with sociopolitical and economic perspectives, are instrumental for implementing successful global public health initiatives.

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None.

## Introduction

Between 1950 and 2012, the world population grew from 2.5 billion to over 7 billion, an approximately 2.8-fold increase (1,2) and, during the same time frame, the number of international tourists increased 41-fold worldwide, from approximately 25 million to 1035 million (1,3). A 10-fold increase in the spatial range of travel is thought to occur with every generation (4). This increasingly dynamic global mobility of individuals and, at the same time, of microorganisms, powerfully reshaped infectious diseases, and made local and national public health emergencies almost instantaneously assume global dimensions (5).

The increasing global mobility of humans is reflected in the dynamics of several recent pandemics. While the H1N1 virus that caused the first, spring wave of the 1918–1919 influenza pandemic, and the H2N3 influenza virus that caused the 1957 pandemic, each took about 6 months to spread throughout the world (6,7), the 2009 pandemic H1N1 influenza strain needed only 6 weeks to travel worldwide (8). It was estimated that the 1918 influenza virus would require only 4 days to spread around the world today (9,10). In 2002–2003, during another recent pandemic, the severe acute respiratory

syndrome (SARS) coronavirus spread from East Asia to North America and Europe within a few days and infected over 8000 people on five continents within a few weeks (7,11–13).

Particularly in context of this increased global mobility, social and economic factors together with political will and commitment are increasingly recognised as being at least as influential as biological and technical feasibility in preventing, controlling and eradicating infectious disease outbreaks (14–16). The 2002–2003 SARS coronavirus pandemic vividly demonstrated that prompt reporting and effective communication powerfully impact the course of an outbreak, and that local delays may escalate into national and global emergencies. Political will played a fundamental role in the global eradication of smallpox, which was announced by an independent committee of experts in December 1979 and ratified by the World Health Organization in 1980, after almost two centuries of challenges (Figure 1) (17,18). Only a few decades later, the poliovirus vaccination campaign provided a crucial lesson, when it revealed that stopping vaccination initiatives, even temporarily, may translate into local setbacks and, subsequently, global emergencies, such as the re-emergence of the virus in previously disease-free areas, compromising



**Figure 1** Parchment signed at Geneva on 9 December 1979 by the members of the Global Commission for Certification of Smallpox Eradication. Reproduced with the permission of the publisher, from *The Smallpox Eradication Programme – SEP (1966–1980)*. Available at: <http://www.who.int/features/2010/smallpox/en/> (accessed March 23, 2014)

and delaying global eradication efforts. The increased infectious disease morbidity and mortality in areas of conflict, which are characterised by reduced access to medication and vaccines, is an additional international and global concern that slowed past eradication efforts and promises challenges for the future.

### Severe acute respiratory syndrome

Severe acute respiratory syndrome, the first pandemic of the 21st century, was remarkable in several ways, the initially unknown aetiology and transmission routes being only two of these (19–21). One of the key lessons that emerged in the wake of the SARS pandemic was that social and political factors are powerfully shaping the outcome of the outbreak. As vividly reflected, an initial delay in reporting the initial SARS coronavirus infections in China exerted a major contribution on the global dynamics of the outbreak (22). In China, Guangdong officials first publicly reported about the disease on 11 February 2003, when provincial health officials informed about

305 cases of atypical pneumonia, and also indicated that the disease was under control. Nevertheless, the first case is thought to have started on 16 November 2002, and an investigation of the outbreak took place during this interval (23,24). Even though rumours about the disease were circulating during this time, and even after it became known that the infection was highly contagious, it was reported that local authorities in Guangdong did not alert the neighbouring provinces and Hong Kong officials (23,25,26). When the media first reported about the outbreak in February 2003, it conveyed the information that the outbreak was under control (23). The outbreak was hardly mentioned in the media until 20 April 2003, when it was announced to the public (27). The number of reported infections skyrocketed overnight, from 37 to 346, when a military surgeon publicly accused health officials of covering up the true extent of the outbreak. Subsequently, the President of China warned against a cover-up and requested an accurate report of the cases (23). Partially, this period of silence was explained by the

‘political mindset towards negative news’, and the 4-month media silence was important in shaping the course of the outbreak (23).

In contrast, in Vietnam, the prompt reporting and immediate actions taken by the government ensured that the disease was eradicated by the end of April 2003. As a result, the outbreak was considered contained on 28 April 2003, and Vietnam became the first country to achieve successful containment of the infection in the first phase of the outbreak (28). The quick recognition of the outbreak and the effective control of transmission in nosocomial settings, along with efficient international cooperation, the sharing of accurate information, and proper advice provided by the Ministry of Health were instrumental for successfully controlling the outbreak in Vietnam (29). Some of the contributing factors involved prompt steps that prevented the transmission from hospitals back into the community and the implementation of stringent infection control measures (30). Situated at the intersection of public health, political leadership and economic development, the SARS outbreak in China demonstrated that delays in reporting and in acting can translate into public health consequences within the country as well as beyond its borders (31). Once the virus was identified, its entire genome was sequenced by mid-April, allowing the first steps towards understanding its biology (20). In analysing SARS outbreak epidemic curves from several countries, it was reported that delaying control measures during the outbreak would have tripled the size of the outbreak, and would have increased its duration by 4 weeks, underscoring the importance of promptly implementing infection control measures (32). Collaborative public health networks and prompt communication were particularly critical during the SARS outbreak (33). A better understanding of the species barrier and cross-species transmission, and increased surveillance in animal reservoirs and humans emerge as fundamental aspects of these initiatives, and assume important roles for multiple zoonotic outbreaks (34–41). Subsequently, during the 2013 H7N9 influenza outbreak, China has gained international recognition for its effective response in handling the outbreak (42). The lessons provided by SARS made important contributions towards strengthening our capabilities in at least three areas: outbreak alertness, public health responses and international health (21).

## Smallpox eradication

Smallpox, which is thought to have caused 300–500 million deaths worldwide only during the 20th century (43), is to date the only human infectious dis-

ease that was eradicated through human efforts (44). To a large extent, this became possible through political will and determination. The smallpox eradication campaign was launched in the mid-1960s (45), and it represented one of the earliest examples when the medical community performed risk-benefit calculations, shaping the progress of medicine (46). Several characteristics of the virus contributed to the possibility to effectively eradicate the infection. These included the severity of the infection, the absence of an intermediate host, the known mode of acquisition, the short incubation period of 7–17 days, the existence of only one serotype, the absence of silent, asymptomatic, or recurrent infections and of a human carrier state and the absence of treatments except for supportive measures (44,47–50). The high mortality rates and the absence of a cure were additional incentives to generate a vaccine as soon as possible (44). The need for approximately 200 million vaccine doses annually, and for stable freeze-dried vaccines to ensure that individuals from remote tropical areas could be vaccinated, were some of the driving forces behind the technological developments associated with generating the smallpox vaccine (51). These also included the bifurcated needle, developed in 1966 and introduced into the vaccine program in late 1968, which used 0.0025 ml of vaccine per dose, one-fourth of what was previously required, and allowed an untrained person to learn within an hour how to use it, and to subsequently vaccinate up to 1500 individuals within a day (51).

Political and social factors played key roles in ensuring the worldwide eradication of smallpox (45,52), which was referred to as *a unique achievement in the history of international cooperation* (53,54). Political will is credited as one of the contributors to this, as it facilitated populations in remote places, sometimes engaged in military conflict, to be vaccinated. This was particularly challenging in countries where governments and health officials changed frequently (55). To be successful, political will had to be sustained and to involve all levels of the community (15). To eradicate smallpox, one of the requirements was to ensure that it will be eradicated in every country worldwide (54). Therefore, some countries that lacked the capacity to eradicate the disease depended on other countries for their success (53). To underline that a global infectious disease eradication campaign is contingent on the active participation of every country, including the countries with the weakest control programs, and the efforts of just one country can shape the benefits to all countries, eradication was referred to as a *weakest-link public good* (54,56).

During the immunisation program in India, which encountered one of the most challenging eradication efforts worldwide, and nearly collapsed on several occasions, one of the most important and gratifying aspects was the manner in which State Governments, the Government of India, and the WHO collaborated as a team (44,57,58). During the immunisation campaigns, 150,000 healthcare workers were involved in reaching over 600,000 villages, walking from house to house to vaccinate people (44). In several states, cash rewards were offered to the first person giving information about a new case and to the health worker receiving the information, an initiative that motivated the reporting of new cases and contributed to health education in the community (44). Often, vaccinators were inoculating themselves in front of the entire community, to demonstrate that vaccination was not harmful (51). In India, the eradication campaign was particularly challenging in the southern part of the state of Bihar, inhabited by tribes and characterised by a poor governmental health organisation. In this state, an industrial town harbouring a large steel company was found to export many smallpox cases to the neighbouring states. A key role in supporting the campaign was played by the chairperson of a local industrial corporate, the Tata Group of Companies, by providing crucial economic and political support, in the form of healthcare personnel and managerial and communication assistance. As a result, the southern part of Bihar became smallpox-free within a record time of 6 months (58,59). Until 1950, it is estimated that over 100,000 people died in India annually as a result of smallpox (44). While in 1951 India had 52% of the smallpox cases in the world, this percentage decreased in 1975 to 7.5%, and the country was certified to be smallpox-free on 23 April 1977 (60).

In Somalia, the almost complete absence of health services outside major towns, which required the WHO to establish almost the entire infrastructure, and the hostilities with neighbouring Ethiopia, opened significant challenges (61). While prior to 1977, the smallpox eradication program in Somalia was reported to be plagued by concealment, in February 1977, after the government allowed the WHO to search for smallpox outside Mogadishu, transmission was detected, and after the WHO assumed a leading role in the surveillance and containment, smallpox was eradicated, and Somalia was declared smallpox-free on 19 October 1979. It was reported that had the government been more open about the disease in Somalia (62), eradication would have happened sooner and at a lower cost. Smallpox eradication was particularly challenging in the Democratic Republic of Congo, formerly Zaire, the third largest country in

Africa, which was characterised by a particularly poor infrastructure and harboured 80% of the inhabitants residing in rural area and, at the time, had one of the most incomplete disease reporting systems in the world (63). In 1967, when the eradication program started, smallpox was widespread in the country, and the number of infections decreased to 3800 in 1968, with the last case being reported in 1971. The obstacles to vaccination in the DRC made it one of the more challenging countries during the smallpox eradication campaigns in Africa (63). This campaign provided important lessons for other infectious diseases, such as the need to increase vaccine coverage, enhance surveillance and establish collaborations within communities and across countries (63).

Another example of the tremendous challenges that were overcome during smallpox vaccination is portrayed by the situation from Ethiopia, a country that in 1970, when the eradication program started, had 25 million inhabitants but only 84 hospitals and 64 health centres, with less than 400 physicians and 2800 other health care staff (64). Additional challenges emerged in 1974, when the military revolution that overthrew the Emperor marked the beginning of a very difficult period for the country, and while all UN operations had to cease, vaccinations were allowed to continue; from 25,000 cases in 1971, the number of infections decreased to 915 in 1976, and August of that year saw the last case (64).

## Polio vaccination

The infectious disease that is poised to become the next target for global eradication is poliomyelitis. In 1998, the World Health Assembly declared its intention to eradicate poliomyelitis worldwide by 2000, by launching the Global Polio Eradication Initiative (GPEI) (65,66), and tremendous progress has been made worldwide towards this goal. The prevalence of global poliomyelitis declined by over 99% between 1988 and 2000, but the remaining 1% has turned out to be the most challenging aspect of the eradication (67,68). While in 1988 and in 1990 polio was endemic in > 125 countries, where it caused over 350,000 cases of paralytic disease, the number of endemic countries declined to six by 2003. The number of paralytic polio cases declined from 866 in 2008 to 223 in 2012, and became mostly restricted to three remaining endemic countries – Nigeria, Afghanistan and Pakistan (65,67,69).

While three decades ago, India was estimated to harbour at least half of the world's polio cases, with over 200,000 paralytic cases per year, or 500 cases per day, amounting to approximately one child developing paralytic polio every 3 min, its increasing

commitment during the late 1990s towards eradicating this disease led on 13 January 2013, after several milestones, to the announcement that the country has completed 2 years without any new polio cases. As a result, India is being viewed as a role model for the eradication of the disease in low-income endemic countries (66,70,71).

A few years ago, it was recognised that the key challenge to eradicating polio globally is not technical, but war (72). As a result of interventions that were implemented, poliovirus transmission was interrupted during conflicts in several countries, including Colombia, Sri Lanka, Cambodia, the Philippines, El Salvador and Peru (73). In some countries, such as Peru and El Salvador, vaccination efforts were so popular that guerrillas not only observed cease-fires but, in addition, often served as vaccinators (74). In El Salvador, between 1985 and 1992, during peace accords that were negotiated by the UNICEF, the Roman Catholic Church and several other organisations, fighting was suspended for 3 days annually to enable the vaccination of the children; as a result, the incidence of several infectious diseases decreased, and that of polio became zero (75).

One of the common features in the three regions where polio is still endemic, Nigeria, Afghanistan and Pakistan, is the fundamental role that is played by conflict and humanitarian emergencies; however, the contextual differences are significant and provide key teachings (69). At the Afghanistan/Pakistan border, the inaccessible populations are thought to bear the main responsibility for the persistence of the infection, while in Northern Nigeria, insurgents spreading antivaccination and anti-education philosophy are thought to play the major role (69). Moreover, the violence against and the murder of volunteer polio workers, such as the ones that occurred in Pakistan, threaten serious setbacks to the vaccination programs (76).

In some of these endemic regions, the persistence of polio recently led to national and international public health crises that extended far beyond the area initially involved. When some religious leaders in Northern Nigeria advised their followers not to allow their children to be vaccinated with the OPV, as a result of community pressure, federally sponsored polio immunisation campaigns came to a halt (77). One of the arguments was the belief that vaccines contained infertility drugs that were meant to sterilise young girls (77). As a result, between July 2003 and August 2004, five states in Northern Nigeria, Zamfara, Kaduna, Bauchi, Niger and Kano, initiated a boycott against polio vaccination (78–80). While vaccination campaigns resumed within a few months in the first four states, in Kano this only

happened about a year later (80). The end result was the increase in the incidence of polio in Nigeria from 202 in 2002 to approximately 800 by the end of 2004 and to 1143 in 2006 (80,81). As a result of the suspended vaccination programs from Northern Nigeria, polio spread to 20 countries in Africa, Southeast Asia and the Middle East (77), and led to 80% of the paralytic polio cases in the world (77), and DNA analyses of the virus confirmed that it originated in Nigeria (64). In Sudan, 105 cases of polio were confirmed in 17 of the 26 states as of 6 January 2005 (82). The disease spread to other polio-free countries, such as Indonesia, which had its last reported case in 1995, and where a case detected in April 2005 indicated that the infection has crossed the Indian Ocean (65). Ethiopia, another country where infections re-occurred, had at the time been polio-free for a year (65). In addition to the costs in human suffering based on the GPEI estimates, this boycott cost over \$500 million in subsequent expenses to control the outbreak, and also ended the hopes to eradicate the disease globally during this decade (77,81).

As of late 2013, polio remained endemic in Nigeria, Pakistan and Afghanistan (83). An important lesson from the Nigerian polio crisis was that it started at the subnational level, it affected a global eradication initiative that was orchestrated by national governments, non-governmental organisations and international organisations, and it required diplomacy across all these levels, to resume vaccination campaigns (77). These diplomatic efforts required the participation of the Centres for Disease Control and Prevention, the US government, GPEI, Organization of the Islamic Conference, and UN, along with other organisations (77). This example illustrates the global environment that currently shapes for any public health crisis and intervention. Another important teaching is the need to recognise that common factors, as well as the country-specific determinants, coexist and underlie the failure to eradicate polio in these countries (84).

## Days of tranquility

‘Days of tranquility’ are periods when a decision is made to cease military conflict, so that vaccination can proceed. Days of tranquility exerted an important impact on global public health in conflict-torn areas. One of the first such efforts, in recent years, started in 1985 in El Salvador. In the spring of 1985, when the Government and the rebel forces agreed to 3 days of tranquility annually, warfare stopped for three Sundays every year, to allow children to be immunised. This was repeated annually for 6 years,

until the early 1990s, when peace was achieved (85–87).

Similar initiatives took place in other regions engaged in civil war, as part of polio eradication initiatives, including Afghanistan, Angola, Lebanon, Somalia, Sri Lanka and Sudan (88). Between June 1996 and October 2000, the UNICEF negotiated cease-fires in civil conflict areas on at least seven occasions, in Sudan, Afghanistan, the Democratic Republic of Congo and Liberia (89). In 1999, Kofi Annan was able to negotiate 'Days of tranquility' in the Democratic Republic of Congo, to enable the immunisation of 10 million children under 5 years old between July and September 1999 (90).

Overall, at least 60 instances of 'Days of tranquility' were documented in 16 different countries (91,92). These initiatives contributed to what was referred to as the 'health-peace symbiosis', in which institutions that ensure peacemaking advance an important healthcare cause, while the healthcare intervention prevents progression of the armed conflict (93). Initiatives that improve health, thus, simultaneously have a role in advancing peace, whether within a group or between groups (94). In the Batticaloa District of Sri Lanka, it was reported that these initiatives also opened the path towards informal communication across political divides of the conflict-torn parties, allowing interests to 'converge across battle lines' and ensuring the immunisation of children (72,75,93).

## Displacement as a result of conflict

Since the end of World War II, over 150 major conflicts were reported, mostly in developing countries (73). Three patterns of conflicts were characterised: primarily international conflicts between countries; primarily internal conflicts involving two main forces, such as a government fighting with rebels; and primarily internal conflicts between several factions in countries without a recognised government. Of these patterns, the third one presents the most significant obstacles in delivering healthcare (73). A sixfold increase in the number of war refugees has been reported worldwide as compared with the 1970s, and refugees are currently thought to represent approximately 1% of the planet's population (95). Determining the exact number of refugees is in itself challenging, considering that approximately 75% of the countries from sub-Saharan Africa have become either the origin or the destination of refugee movements that involve millions of human beings, and most frequently the figures do not include people who have been internally displaced within their own countries, estimated to amount to 25–30 million individuals (96).

Military conflict shapes the risk of infectious diseases in multiple ways. Displacement of people, inadequate sanitation and resources (96), malnutrition (97), increased exposure to vectors (98,99), poor infrastructure and limited access to healthcare resources (100), including medications and vaccines (101–103), are only a few of the factors that contribute to the increased morbidity and mortality in areas of conflict and displaced populations, including refugee camps (96).

Between 1915 and 1916, tuberculosis mortality in the Netherlands increased from 154 to 180 in 100,000 people, and between 1916 and 1917 it increased by 50% in Berlin (104,105). Analyses of mortality in refugee camps from Thailand (1979–1980), Somalia (1980–1985) and Sudan (1984–1985) revealed crude mortality rates up to 40-fold higher than in non-refugee populations residing in the respective host countries. In 2011, a measles epidemic accounted for 17% of the deaths among Somali refugees to a camp in Kenya (106). A three-fold delay in diagnosing tuberculosis in conflict-affected regions from the Somalia Regional State of Ethiopia was reported, in comparison to regions of the country not affected by conflict (105). During military conflict in Guinea-Bissau, West Africa, patients with tuberculosis were over three times more likely to die because of irregularities in medical treatment as a result of the war, and each additional week of treatment before the war started led to a 5% increase in their probability to survive (107).

Between 1990 and 2001, 12 of the 18 countries with infant mortality rates exceeding 110 deaths per 1000 live births were engaged in a conflict, and no countries with infant mortality under six deaths per 1000 live births were at war at the time (89). The impact of military conflict on infectious disease outbreaks becomes even more relevant for the global community, if we consider that the profile of countries affected by conflict is shifting towards the ones with higher baseline incomes and higher life expectancies (108).

## Conclusion

In the current era of global mobility and connectivity, when local infectious disease outbreaks can assume national and global dimensions within days or weeks, social and political factors occupy a central position in epidemic and pandemic preparedness. The global spread of infectious disease outbreaks, just like the success of global eradication programs, is shaped to a great extent by the sociopolitical framework from the country that is the least prepared. The integration of active surveillance, prompt detec-

tion and reporting, and information sharing between the animal and human health sectors, within and across countries, at the local, regional and global levels, assume central positions during outbreak preparedness efforts. Through their inherent nature, airborne infectious diseases are strategically more powerfully positioned than any other medical condition, at the intricate and labile confluence shaped by several disciplines. Most importantly, there is an urgent need to combine medical and biomedical ini-

tiatives with interventions from the social and political arena, to establish a transnational multi- and cross-disciplinary framework. Capitalising on the teachings provided by previous epidemics and pandemics, this platform emerges as a fundamental facet of public health on the global stage that we all set through our interactions, and on which microbial choreography is unfolding faster and more dynamically than ever before.

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