

# Health diplomacy across borders: the case of yellow fever and COVID-19

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The measures deployed for halting the international spread of disease have varied considerably over time. The case of one disease – yellow fever – provides an insight into the evolution of public health interventions from which to see the health diplomacy implications of how global health and international relations interact and influence each other. Yellow fever is an infectious disease caused by a mosquito-borne flavivirus that occurs mostly in South America and sub-Saharan Africa. However, it used to be more widespread across the world, including parts of North America and could potentially spread to countries in Asia and the Caribbean. These countries are not currently endemic but the mosquito vector *Aedes aegypti* and non-human primate hosts are present.<sup>1</sup> In controlling yellow fever, the early application of quarantine later shifted to more co-ordinated approaches, which today include vaccine country entry requirements. Public health interventions directed at yellow fever have always been closely intertwined with economic and foreign-policy interests and frequently led to diplomatic tensions in the past, beginning with quarantines.

Quarantine measures of isolating people who may have been exposed to disease largely originated with Italian city-states in the 15<sup>th</sup> century.<sup>2</sup> They were soon adopted by other European powers and eventually most other international trading powers. However, regulating commerce using quarantines was often seen as a hostile act, leading to escalating tit-for-tat diplomacy and a pressure to continue the practice simply because others were doing so. As an early example, in the 1660s the English imposed a quarantine against ships coming in from the Dutch Republic, based on rumours about disease outbreaks in Amsterdam. The Dutch immediately banned English vessels and continued this ban once the original English quarantine had lapsed. After protesting in vain about these “obstructions upon our forygne (sic) trade”, the English restored their quarantine against ships from Amsterdam.<sup>2</sup> Lessons learned from such interactions meant that countries would later decide that there was a need for better international cooperation to control disease and harmonize decisions about quarantine.

The first international sanitary conference in 1851 was on plague, yellow fever, and cholera.<sup>3</sup> The findings of this conference would culminate eventually in the International Health Regulations in 1951 (replaced by and renamed the International Health Regulations or IHR in 1969). The WHO can apply the 2005 IHR to any disease considered a significant threat to international public health.<sup>4</sup> Cholera and plague both have treatments today, whilst yellow fever continues cause deaths up to 60,000 a year and has the potential to disrupt global trade and travel.<sup>10</sup> Therefore, yellow fever is currently the only disease for which proof of vaccination may be required for travellers as a condition of entry to a State Party under Annex 7 of the 2005 IHR.<sup>5</sup>

The reasoning for the IHR rules for yellow fever stemmed from the expansion of air travel and a vaccine becoming available. Population mobility increases have enhanced the speed at which infectious diseases can be introduced into new areas.<sup>6</sup> As air travel increased it was feared that yellow fever could be more easily spread across the world, leading to countries subjecting aircrafts to quarantine restrictions similar to ocean-going ships (administered by international health organisations, such as the Office international d’hygiène publique). Interventions were not very effective and so continued to cause tensions with those who saw them as restrictive to the development of commercial air travel. There was also a wide

country variation in the quarantines imposed on aircraft and isolation for individuals who arrived from an endemic country.

A yellow fever vaccine was more widely available by the 1940s and so vaccination became an additional public health measure when travelling to countries at risk of yellow fever. The Expert Commission on Quarantine, which was established at the WHO in 1948, produced the first global yellow fever risk map and made recommendations for permanent measures against arrivals from endemic areas.<sup>7</sup> The yellow fever vaccine itself has historically been considered one of the safest and most effective vaccines, although very rare but severe side effects do occur (anaphylactic or hypersensitivity reactions; YF vaccine-associated viscerotropic disease, and YF vaccine-associated neurologic disease).<sup>8</sup> Today travellers are advised to have the yellow fever vaccine if they are travelling to countries that are endemic for yellow fever and some countries have mandatory vaccine entry requirements.

Vaccine entry requirements either apply to all travellers (sometimes with age restrictions), or travellers arriving from countries with risk of transmission of the disease. The measures are intended both to protect travellers from contracting the disease and to prevent travellers introducing the disease into a vulnerable country. Any importation of yellow fever from risk countries by infected travellers could result in its propagation and establishment, leading to a permanent risk of infection for the population.<sup>10</sup> Decisions regarding the use of yellow fever vaccine for travellers must thus take into account, the risk of travel-associated yellow fever virus disease, country requirements, and the potential for serious adverse events following vaccination.<sup>10</sup> The most important factor influencing whether a country has yellow fever vaccine entry requirements recommended by the WHO is the presence or absence of the *Aedes aegypti* vector which transmits the virus. However, other factors include the capacity of countries to deal with potential yellow fever outbreaks and individual country histories also play a role. There are limitations to the increased use of vaccine entry requirements. Despite more widespread global cooperation, imposing restrictions on borders continues to lead to tensions and decisions about whether such measures are not just medical, but also a diplomatic act.

Diplomatic incidents are much rarer compared to 150 years ago, as shown by the stand-off between the English and the Dutch. Yet the potential for tensions persist today – most recently demonstrated in 2012. On arrival in South Africa, 125 Nigerians, including a Senator, were denied entry as they lacked the required yellow fever vaccination documentation and 75 of them were sent home.<sup>11</sup> Nigeria retaliated the next day by turning 28 South Africans away from an airport and deporting 56 illegal immigrants.<sup>11</sup> A vaccine entry requirement is still never just a health measure alone but needs to balance the interests of several different actors and may account for differences between countries in their requirements, which cannot be explained by the presence or absence of vectors alone. Even with numerous new vaccines in development – including those for yellow fever, which potentially will be associated with fewer side effects – other health measures will continue to play a role. Quarantine, for example, may still be used if there is no vaccine and effective treatment, or may be used alongside vaccination if there are constraints in supply. In the face of new outbreaks such as SARS in 2003, many countries most badly affected (e.g. China) reverted to quarantine to combat the disease.

The COVID-19 pandemic has also relied on quarantine or quarantine-like measures that amount to large-scale travel restrictions (lockdowns, stay-at-home orders/notices, isolation, travel bans, containment zones, social distancing, social gathering limits and closing of public places). Still, more sophisticated health measures at and between borders could be introduced on a widespread basis. These include health measures applied to planes and other cross-border transportation; responsible travel behaviour education; entry and exit screening and temperature checks; case finding and contact tracing; and mandatory isolation and quarantine for returning residents or travellers. One proposal has been the idea of immunity certificates or passports for those who have developed immunity to COVID-19 after becoming sick and developing antibodies to the SARS-CoV-2 virus. As shown with yellow fever vaccine entry requirements, these also will entail social and ethical dilemmas. As Kofler and Baylis describe, there are both practical problems and threats to individual freedom and principles of fairness.<sup>12</sup>

Furthermore, as research got underway within hours of the novel coronavirus being identified and there are now multiple vaccine candidates in development. While a return to older health measures has been a feature of the management of the COVID-19 pandemic, the rapid scientific advancement of new interventions presents the opportunity for combined strategies and the adoption of mixed approaches used for other diseases. Diseases in the past have confronted similar questions, adapting from quarantine to vaccination. What lessons then can be drawn from diseases such as yellow fever and where will the new health diplomacy lines be drawn?

If a vaccine is developed for COVID-19, applying vaccine entry requirements, as is used for yellow fever, may present an option to prevent the further spread of the disease and exemptions would also need to apply, at the least for medical reasons as per the IHR. The feasibility of vaccine entry requirements will be dependent on a number of factors that can be drawn from the yellow fever experience.

First the efficacy and safety of the vaccine raises many questions about what would be an acceptable protection rate and duration of protection to justify a vaccine requirement; second what to do about variation in the burden of disease across countries - what are the vaccination coverage rates and level of herd immunity is within a country and whether political motivations will be used to ask for vaccine requirements from certain countries; third whether a country already has mandatory vaccination for other diseases or for country entry; and forth how to respond to limited availability or other problems in assess or supply of a vaccine, including if multiple different types of vaccine are available. Also, legislation is one aspect, but robust enforcement will also be a consideration, as poor checks and forged documentation for yellow fever vaccination have demonstrated.

Since the 2005 revision of the IHR, the regulations to use vaccine entry requirements apply to "any event with the potential to be a public health emergency of international concern".<sup>13</sup> While yellow fever vaccine requirements would not constitute such an emergency, vaccine entry requirements may still be used as a public health tool with greater prominence in the future, particularly if a COVID-19 vaccine is developed. As a legally binding agreement between 196 UN states the IHR has two aims – to strengthen the reporting of infectious disease outbreaks as well as to deter states from imposing

unwarranted travel restrictions.<sup>14</sup> The WHO has not typically been in favour of travel bans and restrictions, seeing them as a disincentive for early outbreak reporting, disruptive for travel and trade with economic and social impacts, and as not always an effective health measure during an emergency, interrupting or diverting resources.<sup>14</sup> During the COVID-19 pandemic, the WHO has sought to achieve a balance between restricting travel or trade and appropriate protection when physical distancing is not feasible. Balancing health with travel, trade, and diplomatic considerations will continue to be an inherent part of disease control measures imposed on borders.

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