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Pandemic Influenza A/H1N1 (pH1N1) in Hong Kong: Anatomy of a Response

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Abstract

Pandemic influenza A/H1N1 (pH1N1) spread rapidly from its origins in Mexico to affect Hong Kong as its first point of entry into Asia. In this paper, the different stages of government response from prevention to mitigation to vaccination and stand down are described and discussed from the perspectives of feasibility, pragmatism, effectiveness and population responses to offer insights into future influenza pandemic preparedness.

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Biography

Richard Fielding has been Professor of Medical Psychology and Public Health at the School of Public Health, University of Hong Kong, since 2006. His current responsibilities include Head of Behavioural Sciences Unit, Director of the Centre for Psycho-Oncology Research and Training, and Director of the Health Behaviour Research Group. As a Deputy Director of the School of Public Health in the University of Hong Kong, he has special responsibility for public health advocacy.

His research interests include smoking cessation, epidemiology, cardiac disease, psycho-oncology, risk in communicable diseases (HIV/AIDS, SARS and A/H5N1 avian and A/H1N1 influenzas) and environmental degradation, health communications and medical education. He has recently completed an international collaborative study to explore infectious diseases risk perceptions and risk communication needs across South East and East Asia from the perspective of human ecology relative to H5N1 avian influenza.

He is an outspoken advocate for a frankly ecological view of human health and has been an active environmental campaigner for over 30 years. In this area, his interests focus on the understanding the dynamics generated through industrial mechanisms of food production, microbial ecology, and their impact on human habitats and behaviour.

Background

Human influenza A pandemics probably occur, on average, every 30 years or so.[1] The 20th century has witnessed at least three human influenza pandemics, in 1918, 1957 and 1968. By the early part of the 21st century, there was a growing perception among the virology and public health community that another influenza pandemic was overdue. However, when the next influenza threat finally emerged, it did so not among humans but among birds in the form of H5N1 avian influenza (this influenza could, with difficulty, also affect humans, with serious consequences). That epidemic began dramatically in 1997 with an outbreak in Hong Kong during which 6 out of 18 people with confirmed infection died. The outbreak was traced to wet markets selling live poultry and waterfowl. Prompt culling of all Hong Kong's poultry is held to have stopped the outbreak but the virus remained in circulation probably within southern China flocks and shorebirds, and re-emerged in January 2004. By 2 February 2005, Thailand and Vietnam had documented 55 human avian influenza cases, which resulted in 42 deaths and the culling of many millions of birds. The virus appears to be endemic in many parts of the world, and particularly in Asia and North Africa. The low incidence but high mortality among humans infected with H5N1 – averaging around 60 per cent – coupled with rapidly developing molecular methods for tracking genetic changes in influenza genes, resulted in many predictions that H5N1 would be the next pandemic influenza among humans. Unsurprisingly, given the importance attributed to it by various health authorities, media reports initially speculated on the pandemic potential of H5N1 as it spread among domestic avian flocks in Asia, Europe and Africa with many doom-ladened articles heralding the new '1918 flu' that would decimate the world's population. At the same time, the Hong Kong government – caught unprepared by the 2003 Severe Acute Respiratory Syndrome (SARS) outbreak in which almost 300 people in Hong Kong died and several political 'lives' lost as a consequence – severely restricted live poultry imports and initiated a public education programme via the media, warning people to wash their hands and wear face masks if they have respiratory symptoms as well as avoid contact with all birds.[2]

Hong Kong's experience with SARS had two effects relevant to influenza response. It taught people, first, that they cannot rely solely on the government and need to take action to protect themselves against infection and, second, that better pandemic planning was needed from a public health perspective. Also, while it sensitised government agencies to the likely political fallout of such events and the potential for significant mortality, SARS may also have contributed to a more relaxed population response to subsequent disease outbreaks. Having survived SARS and the H5N1 avian influenza, when pH1N1 emerged, the Hong Kong population had adapted to the fact that epidemics had become a fact of life. Several structural changes in public health management were initiated as a consequence of SARS. These included the establishment of the Centre for Health Protection (CHP) that is tasked with pandemic planning and communications, and the Centre for Food Safety that is responsible for maintaining the integrity of Hong Kong's food supply, as well as a substantial increase in commissioned research on influenza. The government also increased and intensified its already established system of sentinel surveillance. Finally, strict import and market hygiene regulations, implemented to prevent further H5N1 outbreaks since 1997, were progressively tightened and poultry flocks were vaccinated against H5N1. As a result, except for two imported human cases of H5N1 infection in 2002 and a number of infected wild birds, Hong Kong has remained free of H5N1 despite its continuing endemicity.

Hong Kong's Response to pH1N1

The response of Hong Kong's government to pH1N1 can be divided into three phases: containment (primarily case isolation), mitigation (minimizing population impacts) and vaccination.

The historical context outlined in the previous section is important in understanding Hong Kong's responses to pH1N1. pH1N1 is a novel, triple-reassortment influenza A virus which most probably emerged from the intensive pig-rearing industry in the Mexican region of Veracruz in early 2009. Initial reports in the Western media were of desperate attempts by Mexico's government to limit the spread of infection once it reached the capital, Mexico City; and of an apparent high mortality rate from the infection, subsequently attributed to poor denominator accuracy. Images of masked people reminiscent of those during SARS[3], a re-awakening in the media of the 1918 pandemic mortality predictions, as well as politicians and public health figures predicting hundreds of thousands of deaths and even plans for mass graves added to the sense of alarm. However, the outbreak had probably been ongoing for a number of months before international awareness of the outbreak developed, and while it remains unclear why there was a peak in early mortality for pH1N1, it rapidly became apparent by mid-May 2009 that elsewhere outside Mexico mortality rates were very much lower than anticipated.

Phase 1: Containment

On Monday, 27 April 2009, the World Health Organization (WHO) raised its epidemic alert level to 4, two levels below 'pandemic' status. Hong Kong's Secretary for Health announced the enhanced surveillance of all points of entry to Hong Kong to monitor potential cases and took steps to ensure that there was a sufficient stock of antiviral medication.[4] Hospitals were placed on 'serious response level', the second stage of Hong Kong's three-tier alert system, and shortly thereafter, pH1N1 was made a notifiable disease.[5] Any feverish individuals arriving from infected countries – which at that time were Mexico, USA and Canada, and shortly afterwards Spain and the UK – were to be quarantined. People were also 'strongly advised' not to travel to infected countries.[6] At around 8 pm on Friday, 1 May 2009, Hong Kong's Chief Executive, Donald Tsang gave a press conference to announce that the first confirmed case to the city arrived the previous day from Mexico.[7] The unidentified man had checked into the Metropark Hotel before seeking medical help. The taxi driver who took the man to the hotel and about 300 hotel guests and workers were all quarantined within the hotel, and dramatic footage of fully-suited infection control officers carrying boxes marked 'Tamiflu' were widely shown in breaking news bulletins. The city authorities lifted their alert to the top tier, i.e., the 'emergency response level'. Demonstrating that important lessons in risk communication had been learned from the SARS episode, the Minister for Health Dr York Chow admitted that there was a lot that was unknown about this virus, but announced that HK$10 million was to be spent on enhanced cleaning in hospitals and public places and that quarantine centres were being set up. The hotel quarantine was reported worldwide. It caused significant distress to those affected and led to claims of over-reaction by the Hong Kong authorities.[8]

On 21 May 2009, the Under Secretary for Health, Dr G.M. Leung announced at a local conference on securitising infectious diseases that the Hong Kong government's policy for pH1N1 involved pursuing containment for as long as feasible in order to flatten the epidemic curve, thereby reducing the potential for the realisation of a worst-case scenario of massive numbers of hospital admissions which might overwhelm the system. Dr Leung said that upon occurrence of the first local case, Hong Kong will move to the mitigation phase.

Imported cases of the virus continued to accumulate over the ensuing month with all 49 cases subjected to the same seven-day quarantine regimen at special centres. However, on 10 June 2009, the first domestically acquired case (a domestically acquired case is defined as one which involves a person who had not acquired the infection (1) while overseas; or (2) through contact with an imported case; or (3) through contact with an infectious person who had himself or herself been in contact with an imported case) was reported at the same time as an announcement of an infected 16-year-old secondary student.[9] Immediately, the government responded by announcing a closure of all kindergartens and primary schools to protect the youngest, that is, the ones presumed to be the most vulnerable to the virus based on past influenza behaviour (influenza had in the past mostly affected the youngest and the oldest in the population), for a period initially of 14 days.[10] At that time, worldwide, there were about 26,000 cases in 73 countries, and 73 confirmed deaths. These cases were mostly from the early stages of the outbreak in Mexico, when pH1N1's tendency to infect teens and young adults was not yet clear (though there was a growing recognition of the mildness of the infection in most cases). A planned vaccination programme had been announced on 13 June at a projected cost of HK$300 million.[11] Within the span of two days, a cluster of infected cases in a secondary school had led to the progressive closure of a number of secondary schools in Hong Kong beginning from 15 June 2009. At this time government spokesperson, Dr Thomas Tsang, Controller of the CHP announced a shift in policy from containment to mitigation, heralding the start of the second phase. Secondary schools that were still open were advised to close once examinations concluded. There was a gradual shift away from containment over the following month, with the continued isolation of infected hospitalised cases. Contact chemoprophylaxis continued until the end of June.

However, in some ways the Hong Kong public had already moved ahead of the government in this regard. In a series of cross-sectional population telephone interviews, it was found that levels of population anxiety remained flat and lower than those during SARS across the duration of the epidemic except for the week prior to the announcement of the first imported case.[12] The population's lack of concern was reflected in the fact that intended pH1N1 vaccine uptake rates were projected to be less than desirable among both hospital workers, at >50 per cent, and the general public, at between 45 per cent to 26 per cent, as a function of increasing vaccine cost to the consumer, though this general population survey was based on a small sample.[13] Of concern is that this population survey of vaccination intent found that in the absence of safety trials and information, the numbers willing to receive pH1N1 vaccine could be as low as 5 per cent. However, this information was not available to government planners before August 2009. By mid-summer, it was clear that pH1N1, despite being classified by the World Health Organization as a pandemic, was far less of a threat to the person in the street than was initially believed.

School closures – a major strategy in Hong Kong's management of pH1N1– is controversial. Reports published during the 2008 influenza season showed that closing kindergartens and primary schools had undetectable effects on preventing community transmission[14] (this was believed to be due to the late implementation of the policy), though it might have helped to reduce the number of cases of infection among children in the more vulnerable school-age group.[15] In Hong Kong, a large number of households employ domestic helpers and school closures therefore did not have too much of an impact on parental work patterns, though there were families who needed to either leave the children at home alone or take time away from work.

Phase 2: Mitigation

The mitigation phase was characterised predominantly by the cessation of quarantining, and was implemented despite the rapidly growing number of local cases and despite the fact that exposed contacts were still required to visit local TB (Tuberculosis) and Chest clinics to receive chemoprophylaxis with oseltamivir (Tamiflu) under a directly observed therapy regimen. Conveniently, the introduction of school closures took place close to the end of the examination season and just two or three weeks prior to the onset of the summer vacation. If pH1N1 had occurred a month earlier, this policy would have been highly disruptive to the school examination process. The last week of June and the first week of July saw a drop in the number of new cases in Hong Kong, which was suggestive of a possible impact from school closures. However, the effect, if that is what it was, was short-lived as the number of new cases increased again over the subsequent two weeks. This suggests that the apparent drop may have been artefactual, arising from a change of case notification following the shift from containment to mitigation. If there had been any real effect, then one would say that the two-week hiatus bought potentially valuable time in smoothing out the epidemic curve in the early stages – probably the most intense phase of the pandemic in Hong Kong. But the evidence for this remains unclear. In any case, containment was always going to be a temporary measure with mitigation as the main strategy. By 30 June 2009, Thomas Tsang announced that Hong Kong would cease to admit pH1N1 infected persons to hospital (unless their condition warranted it). Over the course of the summer, the number of cases continued to rise. It was anticipated that there would be a surge in the number of new cases once schools reopened on 1 September 2009. However, surprisingly, the number of new cases reportedly dropped by about one-third for a week or so and spiked upwards thereafter. This probably reflected an apparent rather than real drop in the number of cases, likely attributable to the deferment of medical help sought by those affected as households adjusted their schedules to accommodate the new school term.

By early July, media attention shifted away from the number of infections to more controversial events, for example, the decision by Hong Kong to introduce a complete ban on indoor smoking in all restaurants on 1 July. However, only a few days later, stories regarding oseltamivir resistant strains of pH1N1began to appear in the local media. Two cases were identified in Hong Kong in early July. Over the course of the summer, four deaths occurred in Hong Kong. Despite this, it was highly likely that the low mortality rate from pH1N1 confirmed the increasingly widespread belief among the population that pH1N1 was a storm in a teacup. The global response shifted as well with attention increasingly being focused on vaccine development and acquisition. On 21 August, the WHO announced a recommendation that healthy pH1N1 patients should not routinely be given oseltamivir.[16]

Throughout September 2009, stories about vaccine development surfaced sporadically, culminating in the first USA Food and Drug Administration-approved pH1N1 vaccine in mid-September.[17] By the end of September, European agencies had licensed vaccines and Australia had begun mass vaccinations. Hong Kong had a total of nine pH1N1confirmed deaths. It was during September that the first wave of pH1N1 peaked in Hong Kong at more than 600 cases being reported daily. The figure dipped to around 200 just a fortnight later on 2 October 2009. Two weeks after that, by 16 October, there were just 50 notifications a day being made. By mid-November, just a few tens of influenza notifications were occurring daily. Earlier efforts to invite tenders for vaccine delivery to Hong Kong had to be withdrawn due to lack of interest by companies unwilling to accept the use or return clause the Hong Kong government had included in the contract. The Hong Kong government eventually placed an order with Sanofi-Pasteur for 3 million doses – half a million to be delivered in December 2009, and the remainder in January 2010. By late November there were about 30,000 infected cases and 39 deaths in Hong Kong, with very few new cases being recorded. On 24 May 2010, the Hong Kong government lowered its alert status for pH1N1 from 'emergency response level' to 'alert response level', the first such change in the alert status since 1 May 2009.

Phase 3: Vaccination

Hong Kong generally has a two-phase influenza season, with peaks in January and again in July.[18] The Hong Kong government's pH1N1 vaccination programme was implemented in two phases designed to precede the winter flu season. Recipients of the first phase of vaccination that involved the delivery of 500,000 vaccine doses in December 2009 included chronically ill patients and pregnant women, children aged 6 months to less than 6 years of age, older adults aged 65 and above, healthcare workers, pig farm and slaughterhouse workers, and residents of residential care homes. All of these groups were given vaccinations on demand, subsidised by the government to the amount of HK$129 per person, HK$50 for the injection and HK$79 for each vaccine dose. A group of private clinics were made available to administer the vaccinations. By 21 December 2009 when Phase I of the vaccination programme was initiated, 45 deaths from laboratory-confirmed pH1N1 had been recorded. Twelve months after the start of the pandemic, in early May 2010, Hong Kong had witnessed a total of 33,109 laboratory-confirmed cases and 67 deaths.[19] As of 16 May 2010, 190,919 members of the target groups for the Phase I vaccination programme (estimated to be around 1,000,000 people in total) had received the pH1N1 vaccination.[20]

Phase II of the vaccination programme was launched on 25 January 2010. During this phase, members of the public that did not fall into the high-risk categories targeted in Phase I of the vaccination programme were encouraged to receive the pH1N1 vaccination. Vaccinations were made available at selected private clinics at a minimum fee of HK$129 for each vaccination. This figure was agreed upon not without some controversy. Private medical practitioners expressed the opinion that the fee was insufficient to cover their costs and there was considerable opposition in the profession as a result. Consequently, not all private clinics agreed to offer the vaccine at this price and some refused to participate in the Department of Health's vaccination programme. Among those that participated, problems emerged. For example, vaccine phials that were distributed contained sufficient vaccine for several doses. However, there were reports that some doctors, when asked for the vaccine by patients, responded that the patient would have to pay for the full cost of a single phial, which costs more than HK$700. Another problem was that, once the phial was opened, the contents would have to be used within 24 hours and there was no guarantee that there would be other patients requesting the vaccination within that period. Some members of the general population reported that they were unable to locate a clinic where they were able to receive the vaccine.

Uptake of the vaccine was further inhibited by two other factors. The first of these is the low perceived need for vaccination among the population. In a series of cross-sectional telephone interviews of the Hong Kong general population involving over 13,000 subjects, persistent reports of low perceived risk associated with pH1N1 were observed, beginning from the first survey completed on the eve of the Hong Kong government's announcement of the first confirmed imported case on 1 May 2009.[21] Population anxiety levels remained consistently low over the duration of the pandemic. These data confirmed that most of the general population saw little incentive for protection against pH1N1, believing it to be for the most part a mild disease that does not threaten them or their family members. It is in the absence of this push factor that the second issue, the reported side-effects and unknown safety profile of the vaccine, takes on a far greater significance. The vaccine is then seen as a source of potential harm to a member of the public who weighs the costs and benefits of undergoing the vaccination.

The first adverse event that was linked with pH1N1 vaccination, and featured prominently in Hong Kong media, occurred just three days after the onset of Phase I of the vaccination programme. A 58-year-old man developed symptoms consistent with Guillain-Barre Syndrome (GBS), a characteristic but rare complication that has been associated with influenza vaccinations in past epidemics. However, Hong Kong encounters between 45 to 62 sporadic cases of GBS annually and the CHP was at pains to point out that among the many millions of vaccine doses given worldwide, pH1N1 vaccination did not seem to be associated with an increase in the background rate of GBS, suggesting that this particular case in Hong Kong was a sporadic one. Nonetheless, the media's response was already made. This was followed – just three days after the introduction of Phase II of the vaccination programme – by reports of two interuterine deaths. The deaths occurred a few days after both mothers went for pH1N1 vaccination. CHP press releases implied that the timing of the deaths and vaccination was a coincidence, and placed the emphasis on the number of sporadic cases of interuterine deaths that occur in Hong Kong annually. However, again, the media response was to emphasise the possible link between the deaths and pH1N1 vaccination. These most probably sporadic events that were nonetheless attributed to the vaccination programme by the media consequently raised the perceived risk associated with pH1N1 vaccination in the eyes of the general public.

The low perceived threat attributable to pH1N1 and the greater associated threat attributed to vaccination presents a classic example of risk distortion due to availability bias. Availability bias refers to the bias in probability estimations that arises when some high profile but low probability events are more readily recalled. In the case of pH1N1, most people's contact with pH1N1 infection would have been by way of their own family or friends, with most of them having had mild or sub-clinically symptomatic infection. The relatively few serious hospitalised cases were not available for recall by the majority of the population because they never knew about them. In contrast, the three high profile reports in local broadcast media on possible adverse reactions to the vaccine were readily available for recall although most people who received the pH1N1 vaccine had no significant reaction to it. The relative ease of recall availability means that probability estimates of harms are biased away from the potential hazards of infection and towards hazards associated with vaccination, thereby compounding the risk-benefit equation in favour of not vaccinating.[22]

Not surprisingly given this scenario, vaccine uptake was low. A telephone survey conducted on a general population sample size of over 1,400 immediately prior to the introduction of Phase II of the vaccination programme revealed that only 8 per cent reported their intent to be vaccinated as 'likely/very likely/certain'. Two months later when members of this sample were re-interviewed, only 7 respondents, i.e., 0.7 per cent reported that they had actually been vaccinated, just approximately 10 per cent of those who expressed their intent to be vaccinated.[23] The proportion that expressed an intent to get vaccinated corresponded to Lau et al.'s 5 per cent who would seek vaccination in the absence of information on the safety of the vaccine [24], but the proportion of those acting on their intention was only one-tenth of those that expressed such an intention. Across the general population (excluding the high-risk groups targeted in Phase I) a 0.7 per cent response to a vaccination programme must be considered a failure.[25] What is of interest is that similar low rates of vaccine uptake were reported worldwide, so this phenomenon is not unique to Hong Kong. Others have suggested that the refusal to be vaccinated was one of the only avenues open to the public to express their rejection of the health authorities' prognosis and strategy.

Moreover, the limited uptake of vaccination against pH1N1 was not restricted to the general public. Healthcare workers (HCWs) have also expressed reticence when it comes to being vaccinated. Their proximity to influenza-infected patients, and their potential for acting as vectors of infection to weak or immunocompromised and elderly patients mean that vaccination for HCWs is important. Chor et al. reported a survey from Hong Kong on influenza vaccination intent within a sample group of 2,255 HCWs. In January 2009, before the emergence of pH1N1, 28.4 per cent of the Hong Kong HCWs sampled said that they were willing to accept vaccination against H5N1 – a highly pathological avian influenza. At this time, the WHO had their pandemic alert at level 3. With regard to pH1N1, by the time the pH1N1 pandemic status was raised to level 5 by the WHO, 47.9 per cent of a sample of Hong Kong HCWs expressed willingness to be vaccinated against pH1N1.[26] However, the potential population benefits from the vaccination of HCWs are such[27] that even 50 per cent is a rather poor level of vaccination when around 90 per cent may be needed for the conferment of population-wide protection. There were also voices raised both outside and within the medical profession in opposition to the idea of the mass vaccination of healthy adults, with the opposition often citing the issue of personal choice and limited evidence of benefit.[28] In the USA, mandatory vaccination of HCWs was proposed in order to address this reticence on the part of HCWs. The proposal was legally challenged, and defeated.[29] Such reactions appear to be common, not just in Hong Kong, but elsewhere, such as the UK.[30]

One issue arising from the vaccination reticence among both HCWs and the general public has to do with the dilemma faced by an individual who is asked to adopt a practice that, while conferring benefit at the population level, may offer little or no benefit, and indeed possibly even a small risk of harm, at the individual level. From a policy perspective, vaccination is a good, usually cost-effective way to protect a community, provided the optimal number of vaccinated individuals can be maintained to prevent any infection from gaining access to sufficient numbers of susceptible individuals. Where the number of susceptibles is below a given threshold, this will limit the basic reproductive number R_0 (the average number of new cases of influenza that an infected individual generates). Few susceptibles equates to a lower probability that any one infected individual will encounter and infect a susceptible, and hence prevents the generation of a larger number of new cases. Low R_0 values in turn are associated with a less aggressive epidemic spread. Below a certain threshold (R_0=1) an epidemic will die out. However, a different set of criteria comes into play for an individual contemplating whether to undergo vaccination. In the case of pH1N1 where the impact of infection is generally mild, if every other person is vaccinated there is little, if any, gain in a person getting vaccinated. This is because the prior probability of infection is very low, as few susceptibles means few encounters with very contagious people. However, when the rate of vaccination falls and the number of susceptibles correspondingly rises, it becomes more beneficial for an individual to be vaccinated. But the low impact of infection also means that the costs of infection to the individual are correspondingly low, again working against the individual deciding to get vaccinated. Only if the costs of infection and the benefits of vaccination are high and any risks of vaccination-related harms are low does it make sense for an individual to get vaccinated. Rose described these issues of interventions which at the population level are beneficial, but where said benefit is diluted to invisibility for any individual recipient thereby generating population cynicism and opposition known as The Prevention Paradox.[31]

The individual's judgement about vaccination is likely to be informed by his perceptions of the risk-benefit trade-off inherent in the disease scenario. Because most individuals do not know the proportion of those vaccinated and hence the number of susceptibles in their district or neighbourhood, it is hard for them to 'game' the system to work out the best strategy for themselves or their family members. (This does not mean that individuals deliberately seek to cheat the system, but rather, seek to make the best decision that is in their interests.) As a consequence, proxy information sources are probably sought and these generally fall into two broad categories, which we categorise as formal and informal information sources.[32]

Formal information sources are usually official media-delivered announcements or programmes of public interest, news items or advertisements specifically addressing content from press conferences, and health education or promotion efforts or media stories related to these. Formal information includes government announcements about different developments in the pH1N1 episode, documentary programmes on broadcast media, news items on deaths and hospital admission rates, and newspaper articles about vaccine procurement strategies, for example.

In contrast, informal information sources are largely based on hearsay, opinion and belief expressed either directly or indirectly by others in conversations or other social exchanges that might be face-to-face during a social event, or through some electronic medium such as an internet chat room or blog. Informal information sources in their most fundamental form may comprise simple observations of the actions of others. Observational learning by looking at the behaviour of others and observing the consequences is a basic human learning strategy[33] but is seldom considered in public health research.

Nonetheless, research suggests that the degree of trust individuals place in different information sources differentiates the protective practices these same individuals would use during the emergence of a pandemic.[34] This in itself is not perhaps particularly surprising, but what is of interest is that individual protective practices, such as hand washing, face-mask use and social distancing appear to be linked to levels of trust in different sources of information by way of intervening levels of perceived susceptibility, worry, knowledge and self-efficacy (a belief in the ability to achieve desired future outcomes).[35] This set of relationships seems to hold for both H5N1 and pH1N1 influenzas, and possibly also varies according to age, gender and educational level. Greater reliance on informal sources of information is associated with more worry, greater perceived susceptibility and an increased tendency towards social distancing. Greater trust in formal information sources is associated with greater perceived self-efficacy to prevent influenza and greater influenza prevention-related knowledge, and in turn more hand washing.[36] If confirmed, then these findings would provide an added dimension to our understanding of how populations are likely to behave in adopting different preventive practices including hand washing, face-mask use and social distancing behaviours under different epidemic and pandemic conditions and at different stages of epidemics/pandemics of influenzas.

Finally, little research has systematically examined how population behaviours evolve and mature during epidemic and pandemic events. The study of these phenomena is still very much in its early stages. A significant amount of research has been carried out in relation to sexually transmitted diseases (STDs), particularly the prevention of the sexually transmitted Human Immunodeficiency Virus (HIV) that looks at risk perception and modification, and some attempts have been made to adapt this to inform pandemic planning. However, despite their being similar in that both diseases are socially mediated, the confounding variable of transmission by sexual activity, one of the most powerful drives influencing behaviour, likely creates a significant difference in the dynamics of population behaviour towards the two types of communicable disease.

What Worked, What Didn't: Policy and Planning Implications

The beauty of 20/20 hindsight is that it is often clear what, if anything, should have been done differently. However, as we all know, such clarity is not always obvious at the time decisions are made. Careful analysis of the episode can be valuable for the future management of epidemics and pandemics of influenzas. The following section addresses some of the key issues that arose from pH1N1.

The Importance of Accurate Incidence Data

The pH1N1 virus was infectious and population immunity was low in those below 60 years of age, (though it might be that immunity was in fact much higher, which accounts for the low attack rate), but in infected individuals it did not generate a particularly aggressive disease, and in many cases infection was asymptomatic. This left only the more serious cases visible and gave the impression that the likely impact of a pandemic spread was more serious and the virus more pathogenic than was actually the case. Excluding asymptomatic cases from the denominator inflates the apparent mortality rate and it appears that this was a major contributing factor that could account for why Mexico reported such a high case fatality rate (defined as the proportion of deaths among all confirmed cases of a disease) in the first weeks following the outbreak. This apparently high case fatality rate was in part responsible for generating the high levels of concomitant health authority alerts and media panic that were seen and which, through a process akin to social amplification, were fed back to governments and health agencies who believed they were facing an influenza with a lethality approaching that of H5N1.

In order to accurately determine the true number of cases, there is no real substitute for a well-implemented population serological survey to determine exposures and from this, to derive an accurate picture of the proportion of those infected, A; the proportion of A who show symptoms, $A_{(s)}$; the proportion of $A_{(s)}$ who are hospitalized, $A_{(s)}h$; and the proportion of A who die from their symptoms, M. The case fatality rate can then be accurately determined. This allows for a more precise estimate of the likely severity of the infection, not only in terms of deaths but also in terms of morbidity. This latter point is important in terms of estimating the likely economic impact of an epidemic or pandemic. Serological studies should therefore be performed as early on in the epidemic as possible.

Travel Restrictions

In late April 2009, the issuance of a travel advisory by the Hong Kong government strongly discouraged travel to infected countries, and was made in the full knowledge that it was probably only a matter of time before the virus arrived in Hong Kong from travellers returning from the states of California and even directly from Mexico. Travel restrictions were not recommended by the WHO in its updated travel advisory published on 27 November 2009.[37] During SARS, the WHO issued a travel advisory against travel to Hong Kong which was later criticised for causing significant economic impact to Hong Kong while not preventing the spread of SARS beyond the city. Consequently at the uncertain early stages of the outbreak in April 2009, the WHO held off from issuing travel restriction recommendations.[38] Modelling of epidemic spread from a single location indicates that travel restrictions that are 80 per cent effective (if this were possible) delay influenza spread by only a few days, while delaying the spread for more than two to three weeks requires an effective restriction of travel that exceeds 99 per cent,[39] a highly unrealistic scenario for any nation. However, this model assumed that exit screening would be implemented in the infected country and that this would be 100 per cent effective. In the case of pH1N1, this did not happen for people exiting either Mexico, or the USA, the two countries that were affected the earliest. Would restricting incoming visitors and returning residents from infected to uninfected countries have made a difference to the spread of pH1N1?

Border Controls and Traveller Screening

For a discrete territory such as Hong Kong that has a well-controlled border and which functions as a travel and trade hub, the imposition of border controls would carry massive economic costs and create significant social unrest. In the case of pH1N1, this measure would clearly have been severely criticised, if not before, then certainly after the event. However, would imposing entry screening make a difference to pandemic spread?

There is some evidence that exit screening of air passengers leaving a country where there are epidemic outbreaks may offer benefits to receiving countries if exit screening is implemented early.[40] When coupled with exit screening, entry screening may pick up as many as 50 per cent of infected individuals.[41] Exit screening seems to benefit the recipient country which has a lower false positive rate (and hence costs) as a consequence. Entry screening may also offer benefits, though these are marginal and the costs probably do not warrant the implementation for the at best few days' grace period gained.[42] For example, in Hong Kong only around one in three imported pH1N1 cases was detected by airport thermal scanning and subsequent investigations on entry during the first weeks of the outbreak and before a pandemic was declared. The remainder were detected through the local healthcare system after arrival.[43] Clearly, the 50 per cent detection figure is an upper limit, with most jurisdictions, like Hong Kong, achieving significantly lower detection. Even if 50 per cent could be achieved, that still leaves one in two infected persons undetected on arrival and so the possible benefits of entry screening are small.

In Japan, on-board screening of all arriving passengers was performed at Narita Airport, the main entry point to the country. More than 2 million passengers were screened, with the process turning up just 60 Polymerase Chain Reaction (DNA)-confirmed cases, while in Taiwan where 1.3 million passengers were screened, just four cases were detected.[44]

What about outbreaks other than influenzas? Theoretically, the utility of entry screening should increase as the infection and onset time for new infections decreases, all other things being equal. Assuming a screening test with very high specificity and sensitivity, then for diseases that are transmitted and that manifest in newly infected individuals within 12 hours or even less, (close to the upper time limit of most long haul flights), such a test would appear to offer some utility for detecting infected passengers arriving at destinations that require more than 12 hours of air travel. But even that guarantees nothing. A person infected during disembarkation would still be missed at entry screening and enter the country to spread the infection, unless the detection of one case triggers the full quarantining of all passengers on the aircraft.

This suggests that, for countries which have not already installed entry screening for passengers with fever, this mechanism may offer little in the way of value for money in terms of prevention unless countries are willing to enforce a strict quarantining approach in conjunction with screening. Thermal screening only picks up passengers with active symptoms but misses those who have yet to manifest symptoms. This will comprise the largest group of influenza carriers and hence entry screening is probably not going to be a cost-effective strategy, other than as a means of flattening the epidemic curve to reduce the peak demand on hospital services. However, this benefit is likely to last for only a few days at most as once the infection becomes established within the community, new incoming cases will add very little to the spread of the infection. Moreover, in this regard it should also be noted that different viral infections will present differently and, accordingly, an early fever cannot be presumed in all cases.

Quarantine

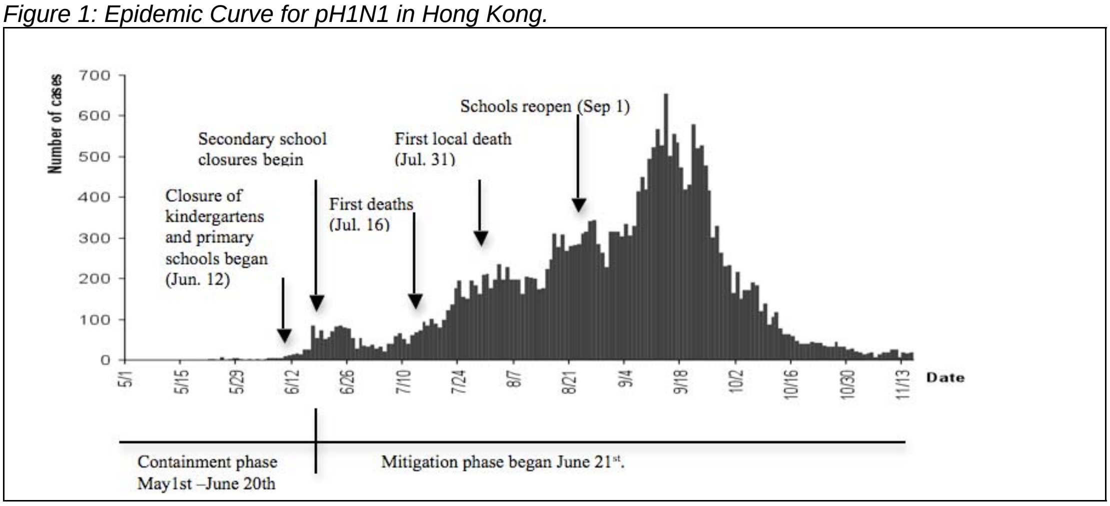
Quarantine is perhaps one of the oldest public health interventions still in practice, with the measure being recorded at least as early as the 14th century during the Venetian response to the Plague.[45] Quarantine is highly effective as a means of reducing infection spread where it can be humanely and logistically implemented. However, there is likely to be considerable opposition to the theory and practice of quarantining in the event of a high morbidity/mortality influenza emerging to epidemic or pandemic status. The opposition is likely to be twofold: first, like the people quarantined by Hong Kong in the Metropark Hotel, there will be considerable anger and fear among those people incarcerated against their will in the earliest stages of an outbreak. The modern expectations of the state to ensure freedom of movement and action will be seriously challenged when the state acts to forcibly restrain people against their will.

Voluntary quarantine at home is a more contemporary and acceptable alternative for most people, but does rely on individuals adhering to the policy. Sato et al. modelled three scenarios of a modified quarantine policy that required the population to stay at home, and assumed 10 per cent, 30 per cent and 50 per cent adherence to this policy.[46] Intriguingly, the most effective interventions were those that started between Days 6–11 following the day the first confirmed case was detected, provided that 50 per cent of the population were adherent. This model resulted in a 44 per cent reduction in the number of symptomatic cases and delayed the epidemic peak by 17 days. Interventions with 30 per cent adherence for the three days starting on Day 11 were more effective than those that were started on Day 6. Where all other scenarios showed a second peak in the epidemic curve following removal of the intervention, no second peak was seen for interventions that began on Day 16. Regarding costs, Sato et al. concluded that the most expensive intervention involved 50 per cent adherence for 14 days starting from Day 1, but that a 30 per cent adherence for 14 days starting from Day 11 resulted in the same reduction in influenza cases and used only half the amount of resources.

School Closures

In Hong Kong, school closures, which began on 15 June 2009, seemed to have had an impact on the epidemic curve (see Figure 1), although, as discussed previously, the time of the year – towards the end of the examination period – would have greatly facilitated this. The low school activity in the following three weeks then ran into the start of the school summer holidays that began on 10 July 2009 and lasted until 1 September 2009. Figure 1 shows that in the two weeks following school closures a decline in the number of new case notifications took two weeks to revert to pre-school closure notification levels, though this hiatus might be artefactual. Based on local research, there is evidence that this intervention probably reduced the number of cases by around 25 per cent.[47] The study estimated that the effective impact of this school closure policy was to reduce the reproductive number (R_0) from 1.7 prior to school closure to 1.1 for the summer holiday period.[48] This suggests that school closure was a very effective strategy for flattening the epidemic curve thereby reducing demand for both antiviral medication and hospital beds. Several studies suggested that more aggressive use of school closures could be more effective and help reduce the need for antiviral prophylaxis.[49] While this might reduce the direct costs of any epidemic/pandemic event, the consequence is that – unless there are caretakers who are permanently at home – either children must look after themselves or a parent must take time off work to care for the child (though as we observed in Hong Kong the employment of domestic helpers minimises this impact somewhat). The latter scenario is more likely for children that are less than 13 years old. As such the indirect costs of school closures to the community might be greater, possibly matching or even exceeding any savings accrued from reducing antiviral prophylaxis or from reduced healthcare resource consumption. Cost implications aside, school closures seem to offer clear benefits in terms of reducing the magnitude of an influenza epidemic/pandemic. This seems to be due to the fact that in the case of influenza A(H1N1), school-going and young adult populations appear to have the highest number of susceptibles and hence transmission rates.[50]

Figure 1: Epidemic Curve for pH1N1 in Hong Kong.



Source: Cowling BJ et al., Community Psychological and Behavioral Responses through the First Wave of 2009 Pandemic (H1N1) in Hong Kong. Journal of Infectious Diseases, 2010, 202, 867-876.

Antiviral Chemoprophylaxis

There is limited data on the effectiveness of antiviral chemoprophylaxis alone. Studies from Australia using computer modelling have claimed that in a small-town network, antiviral chemoprophylaxis offers improved protection if implemented aggressively.[51] Studies from Japan suggest that antiviral prophylaxis might help to slow transmission within households where there is an infected individual, but results were inconclusive due to small numbers of secondary infections.[52] In a randomised control trial (RCT) carried out in Hong Kong households, oseltamivir was associated with fewer symptoms in secondary household contacts of infected cases, but there was no clear evidence favouring a reduction in transmission or virus shedding.[53]

Antiviral chemoprophylaxis was used differently in different communities. In some places, such as Hong Kong, during the containment phase, antiviral chemoprophylaxis was offered to all infected individuals, but once the mitigation phase set in, this policy was gradually discontinued. In the UK by comparison, antiviral chemoprophylaxis was still being distributed to individuals who contacted the National Health Service (NHS) influenza hotline at the end of 2009; while in Australia antiviral chemoprophylaxis was released more guardedly.[54] There seem to be two reasons for this wide variation. In many places a concern about both the earlier warnings from Japan regarding unpredictable psychiatric side-effects in adolescents given oseltamivir and the high attack rate among teens plus the relatively benign impact of infection led to some resistance to oseltamivir prescription among younger adults. A second concern was prompted by early reports from Europe and then Hong Kong on the emergence of oseltamivir-resistant strains of the pH1N1 virus. There were fears that if oseltamivir were used excessively for milder infections in the first wave, then there would be no effective treatment available for severe cases should an aggressive second wave emerge.[55] A third concern seemed to involve conserving antiviral chemoprophylaxis stocks in order that there would be sufficient supplies for an expected second wave. Despite these concerns there is some evidence that antiviral chemoprophylaxis is both clinically and economically effective.[56] Regardless, the differing strategies adopted and pursued by each country also pointed to disagreements within the healthcare community as to the most effective way forward.

Vaccination

Vaccination is widely regarded as the most suitable strategy to manage influenza. The pH1N1 vaccine has been shown to be as efficacious as seasonal influenza vaccine. It has good tolerability and provides effective immunity in most age groups with one dose.[57] However, current methods of vaccine production require around six months for sufficient doses to be manufactured. This usually means that vaccines for novel influenza strains are unavailable for the first wave of the outbreak. What is the benefit of vaccinating against existing strains? Is there cross-immunity and if so how much? There is little reason to think that there would be substantial cross-immunity to a novel influenza strain, except among people previously exposed to one or more of the surface protein variants occupying the virus coat. Persons lacking prior exposure (either from vaccination or infection) should have little immunity to novel surface protein variants, on an a priori basis. Against the H5N1 virus, the normal seasonal influenza vaccine seems to provide no cross-immunity,[58] but there may be some cell-mediated immune response from previous priming by seasonal influenza vaccination.[59]

Combination Interventions

Most national responses to pH1N1 involved multiple interventions. In the case of Hong Kong this involved screening incoming visitors, quarantining suspected infected individuals and close contacts, and giving antiviral chemoprophylaxis to exposed contacts, which comprised a clearly defined containment phase. The subsequent emergence of local cases led to a shift in strategy to comprise school closures supplemented with the hospitalisation of infected cases until early September, by which time both policies were discontinued as the mild nature of the pandemic became apparent. Vaccination, introduced for high-risk groups in December 2009 and the general population in January 2010 was met with a relatively unenthusiastic response.

Some studies have contested the cost-effectiveness of school closures for a mild epidemic/pandemic such as that which characterised A(H1N1). Instead they argue for a combination approach of antiviral prophylaxis and 'mild' social distancing (staying away from unnecessary meetings, avoiding parties or shopping malls after school), but not school closure.[60] It is likely that the overall benefits of different strategies based on cost-effectiveness are going to vary as a function of the impact of an influenza strain, with more pathogenic strains justifying more radical interventions.

On-board flight screening and disembarkation screening generally have low effectiveness and are probably unwarranted unless accompanied by rigorous exit screening from the country of origin.[61] However, because this is not likely to benefit the country of departure as much as the country of arrival, there is less incentive for exit screening to be implemented and the costs are high.[62]

Based on the limited literature currently available, much of which is derived from computer models, it would seem that, in the event of a more pathogenic or aggressive strain of influenza becoming pandemic, efforts would be most fruitfully directed into three primary strategies: recommended home quarantine for up to 14 days beginning from Days 6–11 with an effectiveness of between 30–50 per cent; aggressive school closures; and effective, and prompt, use of antiviral chemoprophylaxis. The third strategy should be started within the first 48 hours after symptom onset at the latest. Thereafter there is probably little if any benefit to be gained by starting antiviral treatment.

In the event of a mild, less pathogenic strain of influenza, self-imposed mild social distancing methods should be advocated. School closures may or may not be warranted on the grounds of cost, but does seem likely to reduce the number of infections among school-age individuals.

There are a number of important surveillance strategies that should be in place at a national level. These include an adequate network of sentinel physicians who report weekly rates of consultation for influenza-like illness (ILI), and sufficient and technically capable virology and serology facilities to monitor influenza strains. This is particularly important if the country has a high concentration of pig and poultry farming; and where this is the case, sentinel monitoring of industry workers, poultry and pigs should be performed as part of routine monitoring of influenza viral activity.

Research should be a part of all national pandemic response plans. This should include: plans and funding for prompt seroprevalence studies to enable accurate determination of case fatality rate and other characteristics in the event of a new outbreak; reporting networks for case incidence and outcome notification by clinics, hospitals and doctors, particularly where these are provided by a broad mix of private and state facilities; and finally, population monitoring, ideally by well-constituted and representative sentinel cohorts, which can be polled periodically during the pandemic to monitor and provide feedback on population behaviour and responses to government initiatives and to better document impacts of population behaviour on pandemic evolution.

Conclusions

There appears to be no one ideal strategy to combat pandemic influenza. The characteristics of the influenza strain, the degree of preparation and resources available, the channels and effectiveness of pandemic-related communications and the level and preparedness of the public health infrastructure are all likely to modulate how effective strategies will be. Coupled with this is the reality that for many countries in the region, resources are limited or infrastructure lacking for the effective surveillance that is critical for early outbreak detection, and it is this which ensures prompt response and containment of new outbreaks.

Densely populated urban environments may benefit differently from formal social distancing interventions, such as school closures, than might rural areas. Travel and trade restrictions are unlikely to be effective and may generate significant hostility in the population if economic harms that affect the population directly arise from such interventions.

In the long run, however, economic development, to ensure that host societies are better equipped to cope with such problems, will probably be the only effective solution. The planning and testing of strategies for use in the event of pandemics might be the most effective long-term strategy for all countries to adopt.

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