The Role of Influenza Vaccine in Healthcare Workers in the Era of Severe Acute Respiratory Syndrome

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The new coronavirus responsible for severe acute respiratory syndrome (SARS) found its first victims in healthcare workers with attack rates of more than 50% before infection control measures were instituted;[1,2] and this led to the near collapse of healthcare systems in some of the affected countries. In Singapore, healthcare workers accounted for 40% of the total number of SARS patients. The vulnerability of healthcare workers to this new respiratory disease should raise our awareness that this high-risk group may also be vulnerable to other well known respiratory diseases. One of these is influenza, but unlike SARS, influenza is vaccine preventable.

The rapid dissemination of sudden acute respiratory syndrome around the world should be considered a rehearsal for the next pandemic of influenza.[3] Even without an influenza pandemic, more people worldwide have died of complications of influenza during the SARS crisis than of SARS.

Influenza and SARS have a lot in common. Considerable morbidity, social disruption and economic loss occurred during past influenza pandemics and the very recent SARS epidemic. Transmission is by droplet or direct contact. The majority of infected persons have symptoms of disease – which, in turn, enhance the likelihood of contagion.[4] Mortality increases with age in both diseases. Both have non-specific early manifestations, with the most common early systemic symptoms being fever, malaise, myalgia and headache.[3] Because of the similar presentations, misdiagnosis is likely and this was mirrored in the Singapore experience: in the beginning of the outbreak (before even the term SARS was coined) the index patients admitted at Tan Tock Seng Hospital (which later became the designated SARS hospital) were initially thought to suffer from avian influenza. Vice versa, at the tail end of the epidemic, alarms were raised when a new cluster of healthcare workers from the Institute of Mental Health developed fever. Fears that this could be a resurgence of SARS led to major disruptions within the institute and quarantining of healthcare workers until influenza B was shown to be the causative agent.

Influenza and SARS also have a lot not in common. In addition to droplet and contact transmission, influenza is also associated with airborne transmission,[4] whereas all current evidence points towards the absence of airborne transmission for SARS. Therefore, the SARS epidemic does not appear to have the spreading potential which characterises an influenza pandemic, during which millions of people can be affected within months around the world.[5,6] The explosive nature of influenza outbreaks in groups aboard airplanes or cruise ships[4] has also not been observed in association with SARS.[7] The extent of infectiousness of influenza depends on the pre-existing immunity in the population, with high levels of immunity conveying protection, unless there was an antigenic shift or drift in the makeup of the virus. The SARS coronavirus hit a non-immune population, but at present it is unclear whether acquired antibodies to SARS (as demonstrated by a positive SARS serology) will lead to protection in the future or may be associated with a worse prognosis due to immune enhancement phenomena after repeated exposure. Unlike SARS, early laboratory diagnostic tests, an effective vaccine, proven antiviral therapy and chemoprophylaxis are available for influenza. Disease manifestation in influenza ranges from asymptomatic to severe disease and death with the majority having mild disease, whereas currently available data for SARS indicate that the vast majority of infected patients develop progressive pulmonary changes and around 15% die. The true range of clinical spectrum in SARS, however, remains to be established.

Experts predict that another influenza pandemic is highly likely, if not inevitable.[8,9] It is almost 35 years since the last pandemic, and the longest inter-pandemic interval recorded with certainty is 39 years.[10] More than 20 million people died during the pandemic 'flu season 1918-1919, the largest influenza pandemic of the 20th century. Whilst mortality on the scale

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experienced in 1918-1919 is probably unlikely, there was a high level of mortality among those infected with the A/H5N1 virus in 1997, so it cannot be assumed that a future pandemic will be as mild as those in 1957-1958 or 1968-1969.[10] There is likely to be more than one wave of infections. Health services in most countries will be hard pressed to provide vaccines or manage populations with clinical attack rates of approximately 25% to 30% and concomitant increases in demand for both primary and secondary healthcare services. The next pandemic virus is likely to emerge in Southeast Asia, as have 2 of the last 3 pandemic viruses.[10] To fail to prepare is to prepare to fail – this was a commonly used phrase during the WHO SARS conference in Kuala Lumpur in June 2003. Using a scenario analysis on pandemic influenza, authors in The Netherlands concluded that one of the most efficient approaches (in view of limited vaccine availability and resources) would be to target the elderly population and healthcare workers: the elderly population in order to reduce hospitalisation and death rates, the healthcare workers in order to keep the workforce to meet the demands influenza will have on the healthcare system.[8]

Even without the advent of SARS, there would be more than one reason to vaccinate healthcare workers against influenza:[11]

Healthcare workers are at higher risk of influenza compared to the general population, in particular those working in primary healthcare settings, paediatrics and emergency departments. In addition to its recognised health effects, influenza has socio-economic consequences, most notably sickness absence and associated work disruption.[12] It may account for 10% to 12% of all sickness absence from work.[12] In a large prospective randomised double-blind study on the impact of influenza vaccination on healthcare workers in the US, cumulative days of reported febrile respiratory illness were 28.7 per 100 subjects compared to 40.6 per 100 subjects in controls and days of absence were 9.9 per 100 subjects versus 21.1 per 100 subjects in controls.[13] Healthcare workers suffering from influenza who continue to work may pose a risk as a source of nosocomial infection. Serious outbreaks due to infected healthcare workers occur typically in elderly long-term patients, but have also been reported in renal, transplant and oncology units, neonatal intensive care and paediatrics.[14] Vaccination of healthcare workers has been shown to be a strategy for preventing influenza in elderly patients in long-term care: vaccination of healthcare workers was associated with reductions in total patient mortality from 17% to 10%.[15] Vaccination of healthcare workers in fact had a higher impact on reducing mortality in elderly patients than vaccinating the elderly themselves.[15] We need to keep in mind, though, that all these studies were conducted in the Northern Hemisphere which has a distinct annual influenza season. Although influenza is a major disease burden in Singapore and most parts of Southeast Asia, influenza does not have distinct seasons and tends to be an all-year-round problem.[16] The impact of influenza vaccine in healthcare workers on reducing febrile episodes, absenteeism and its protective effect on the elderly patient population therefore need to be urgently established in well-designed prospective studies for this region. The recent SARS crisis should add to the urgency of such studies.

Although the benefit of annual influenza vaccination for risk groups such as healthcare workers in the Northern Hemisphere is beyond doubt, a low acceptance of vaccine recommendations has been noticed to date.[17,18] Vaccine uptake rates have been reported to be no more than 40% and often between 20% and 30%. An evaluation of the performance of the UK National Health Service trusts, following a governmental directive to implement vaccination during the winter of 2000-2001, has shown a poor uptake of vaccine, and the authors conclude that there is a need for global leadership on this issue to promote the value of vaccination and to change the behaviour of healthcare workers.[19] Time will show whether the SARS crisis will contribute to a change in attitude and behaviour in healthcare workers towards influenza vaccine. In a survey amongst healthcare workers in Italy, results showed that a high proportion of the questioned healthcare workers showed a general lack of concern about the severity of influenza.[20] Doubts about vaccine efficacy and fear of post-vaccination side effects were also observed to have an important influence on the vaccination acceptance rates. These data underline the need for a systematic education and awareness program for healthcare workers before immunization programs are instituted. The facts are that influenza vaccines contain inactivated viruses and cannot cause influenza; respiratory disease after vaccination is coincidental and unrelated to influenza vaccination. The side effect reported most frequently is soreness at the injection site for up to 2 days. Fever, malaise and muscle pain may occur infrequently 6 to 12 hours after vaccination and persist for 1 to 2 days. Immediate allergic reactions rarely occurs; if they occur, they are most likely caused by residual egg protein. Influenza vaccination is contraindicated in persons with history of anaphylaxis or proven sensitivity to egg or egg protein. Guillain Barre Syndrome may occur in 1 out of 1 million vaccinated persons.[21]

Lessons need to be learned from the SARS crisis. The wrong lesson to be taken from SARS would be to pass new emergency regulations narrowly targeting funding for SARS research and control.[22] Research should also be targeted at identifying distinctive clinical and laboratory features of other viral respiratory diseases, as well as improving current early diagnostic tools. We need to expand hospital surveillance for all respiratory illnesses, inclusive of influenza. Reasonable

infection control measures should be maintained, especially diligent handwashing between patients and other droplet and contact precautions; and this is highly likely to result in reduced nosocomial transmission, not only of influenza.

On 31 May 2003, Singapore was declared SARS free. Will SARS return? It is too early to say. In addition to the abovementioned reasons for influenza vaccination, in the era of SARS or in the era of post SARS, there is now an even stronger rationale for influenza vaccination for all healthcare workers. Symptoms of influenza mimic early SARS and could potentially lead to a delay in the diagnosis of SARS which in turn would lead to late isolation and institution of infection control measures associated with enhanced transmission. Influenza vaccine for healthcare workers will minimise scenarios where new clusters of febrile illnesses in healthcare workers (due to influenza) would set off an alarm bell for a new outbreak of SARS and lead to unnecessary scare and disruption within the healthcare setting.

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