2011; 62, 3: 170–175
www.intmarhealth.pl

ISSN 1641–9251

VIA MEDICA

ORIGINAL PAPER

# Influenza and SARS: the impact of viral pandemics on maritime health

**Poh Lian Lim**

Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore

## ABSTRACT

*Global travel and transport play a critical role in the spread of infections. We see this clearly in the first two pandemics of the 21st century: SARS and influenza H1N1-2009. Although air travel contributed to dissemination in these two pandemics, the travel restrictions, quarantines, and heightened vigilance which resulted had an impact on maritime health.*

*Seasonal, pandemic, and avian influenza have some important differences with regards to exposure risks, infectivity, and severity. Most of the data for maritime influenza outbreaks focus on seasonal influenza on cruise ships, but influenza among crew members occurs due to close working conditions and is potentially preventable with staff vaccination programs. To date, avian influenza has low human-to-human transmission; infection typically requires close contact with poultry, but presents with severe disease and a high fatality rate. Pandemic (swine) influenza was readily transmitted between people, including young adults, and caused severe illness in high-risk groups including pregnant women, children, and those with co-morbidities and obesity.*

*In contrast, SARS had lower infectivity compared to influenza, and a longer incubation period. These characteristics slowed its propagation enough that outbreak control measures, such as isolation of infected cases and quarantine of exposed but well persons, were effective in terminating this pandemic. No effective vaccine exists for SARS at this time, whereas countries were able to deploy millions of doses of pandemic influenza vaccine within 7 months after the outbreak was first recognized in Mexico. The lack of a protective vaccine and the higher case fatality rate in SARS will mean that stringent quarantine measures may still be required for outbreak control if SARS ever occurs again. Compliance with international health regulations, and the ability to adapt these to maritime health needs, will be important in the shipping industry.*

*(Int Marit Health 2011; 62, 3: 170–175)*

**Key words: SARS, influenza, pandemic, maritime, ship, travel**

## INTRODUCTION

Global travel and transport play a critical role in the spread of infections. This was clearly demonstrated in the first two pandemics of the 21st century: SARS (severe acute respiratory syndrome) in 2003 and influenza A (H1N1) in 2009 (pH1N1). Although air travel contributed greatly to rapid worldwide dissemination through infected passengers, the travel restrictions, quarantines, and heightened vigilance which resulted had an impact on maritime health as well. This paper presents a focused review of the actual and potential effects of SARS and influenza in maritime health settings, incorporating two lectures given at the International Maritime Health Association conference in Singapore in December 2010.

Poh Lian Lim, MD, MPH, Department of Infectious Diseases, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433, Singapore, tel.: 65 6357 7919, fax: 65 6252 4056, e-mail: pllim@post.harvard.edu

## DISCUSSION

### INFLUENZA — SEASONAL, AVIAN, PANDEMIC

In preparing for influenza, it is helpful to differentiate between seasonal, avian, and pandemic influenza. These vary with regard to exposure risks, infectivity, and severity, as well as prevention and treatment measures (Table 1).

### SEASONAL INFLUENZA

Influenza is one of the most significant communicable diseases in maritime health, on passenger cruise ships as well as cargo ships. In a retrospective analysis of 49 medical logs from German cargo ships with over 1.5 million person-days of observation, 21% of medical visits were for communicable diseases, yielding a rate of 45.8 consults per 100 person-years [1]. Of the 68 outbreaks observed, 66 were acute respiratory infections (ARI), including 12 influenza-like illnesses (ILI). Attack rates ranged from 3–10 seafarers per ship (12–41% of the crew).

Influenza outbreaks on cruise ships are well-documented. A 12-day Baltic cruise (June 23–July 5, 2000) resulted in 45 crew out of 506 (9%) and 25 passengers out of 1311 (2%) developing ILI, and 2 out of 4 nasopharyngeal swabs tested positive for influenza B [2, 3]. Another cruise from Sydney to Noumea in September 2000 was affected by an influenza A and B outbreak. Of the 1100 passengers, 310 (37%) reported ILI afterwards, and 40 required hospitalization, with 2 deaths [4]. Passengers on cruise ships may include elderly individuals with co-morbid illnesses who would be at higher risk for severe illness and complications from influenza. One study documented that 994 of 1284 passengers (77%) on a cruise were over the age of 65; 215 (17%) of all passengers on that cruise developed ARI [5].

The particular vulnerabilities of cruise ships to influenza include: 1) large numbers of persons in close social contact; 2) cruise durations that are long enough to encompass 2–4 generation times for a short-incu-

**Table 1.** Comparison of SARS and influenza (seasonal, avian, pandemic)

| Characteristic | SARS | Seasonal influenza | Avian influenza | Pandemic influenza |
|---|---|---|---|---|
| Causative pathogen | SARS-CoV | Influenza A/H1N1<br>Influenza A/H3N2<br>Influenza B | Influenza A/H5N1 | Influenza A/H1N1 |
| Incubation (median)<br>Incubation (range) | 4 days<br>2–10 days | 2 days<br>1–6 days | 2 days<br>1–6 days | 2 days<br>1–6 days |
| Areas of transmission | Localized initially | Ubiquitous | Localized, poultry-related | Localized initially, now global |
| Routes of transmission | Human-human<br>Airborne or droplet | Human-human<br>Mostly droplet | Mostly poultry-human<br>Mostly droplet | Human-human<br>Mostly droplet |
| Who is at risk of infection | Healthcare workers<br>Contacts of cases | General population | Those in close contact with poultry | General population especially younger individuals |
| Groups at high risk for severe disease or death | Older patients | Elderly, persons with co-morbidities, pregnant | Delayed treatment | Pregnant, obese, elderly, persons with co-morbidities |
| Total deaths<br>Total cases | 774<br>8098 | 250,000–500,000<br>Millions | 325<br>556 | 18,449 (6 Aug 2010)<br>214 countries |
| Case fatality rate | 10% | < 0.5% | 58% | < 0.5% |
| Available vaccine | No | Yes<br>Trivalent (includes pH1N1) | Yes<br>Pre-pandemic H5N1 | Yes<br>Pandemic pH1N1 |
| Effective antiviral agents for treatment | No | Neuraminidase inhibitors | Neuraminidase inhibitors | Neuraminidase inhibitors |
| Effective antiviral agents for prophylaxis | No | Neuraminidase inhibitors | Neuraminidase inhibitors | Neuraminidase inhibitors |

bation disease like influenza; 3) mixing of persons from Northern and Southern Hemispheres where vaccination may not be available in the off-season for influenza transmission; and 4) fresh batches of susceptible passengers in subsequent cruises are then exposed to infected crew, resulting in onward transmission.

## AVIAN INFLUENZA

To date, avian influenza (A/H5N1) has demonstrated low human-to-human transmissibility [6] and is typically acquired through close contact with infected poultry. Clinical disease is usually severe, resulting in respiratory failure requiring mechanical ventilation [7]. Treatment includes early use of oseltamivir, but resistance to neuraminidase inhibitors (NI) has emerged and is associated with clinical failure and fatal outcomes [8]. A pre-pandemic vaccine is now available against H5N1 influenza, and it received Food and Drugs Administration (FDA) approval in the United States in 2007 [9].

Almost all the 556 confirmed human cases and 325 deaths from H5N1 influenza [10] have occurred among residents in affected areas, with very few, if any, among international travellers. The impact of avian influenza on maritime health is, therefore, relatively low although it still remains a disease of international concern due to high case-fatality rates (58%).

## PANDEMIC INFLUENZA

The H1N1 pandemic of 2009, initially dubbed "swine flu", was first announced by the WHO in April 2009. Beginning in Mexico and the United States, it spread worldwide over a period of weeks, with rapidly changing source countries as risk factors for introduction of the infection [11]. Initial figures suggested a higher case fatality rate (CFR), prompting the WHO to issue a pandemic alert, but subsequent studies have indicated this pandemic to be of mild severity with overall CFR of < 0.5% [12]. This strain, pH1N1, was nevertheless a novel strain, with younger individuals having greater risk of acquiring infection. However, risk of severe disease and mortality was seen in older patients as well as children under 5 years of age [13], pregnant women [13], and those with medical co-morbidities including obesity [14]. Early treatment with neuraminidase inhibitors such as oseltamivir was associated with reduced morbidity [15], mortality [16], and viral shedding [17]. However, resistance has emerged during treatment with oseltamivir [18] or intravenous peramivir [19] and prophylaxis with oseltamivir [20], with the H275Y mutation conferring high level resistance against oseltamivir, and a recently reported I223R mutation conferring multi-drug resistance against oseltamivir, zanamivir, and peramivir [21].

Both the WHO and the International Maritime Association issued interim guidance for sea travel [22, 23]. Within the past two years, more reports have emerged documenting the spread of pandemic H1N1-2009 influenza outbreaks on ships, including military vessels. One retrospective study of 237 crew on a military ship cruising in the Mediterranean (May––September, 2009) showed 52 reported acute respiratory infections (ARI), and of the 211 results available, 39% tested seropositive for pH1N1 [24]. The proportion of seropositives was associated with more crowded living conditions and younger age (< 40 years), in those with ARI symptoms. Another outbreak occurred on a Peruvian Navy ship carrying 355 crew in June–July, 2009 [25]. Of the 85 patients who developed febrile ARI, 78 (92%) tested positive for pH1N1 by RT-PCR, yielding an attack rate of 22% for confirmed influenza. Attack rates were highest among cadets and low-rank officers, as well as younger persons (aged 18–25 years).

The attack rates on these 2 military vessels were higher than in a civilian setting. An Australian study of a cruise ship with 1970 passengers and 734 crew showed 83 (3%) were infected with pH1N1 and 98 (3.6%) with H3N2 influenza [26]. This outbreak also indicated that two different strains of influenza can co-circulate onboard even in the midst of a pandemic. Military and cargo vessels typically have fewer individuals at high risk for influenza complications than cruise ships with elderly passengers, but close working and living conditions may lead to higher attack rates than on cruise ships, with adverse effects on crew members' ability to function effectively.

Given the risk of influenza among crew members due to close working conditions, and risk of complications among high-risk passengers on cruise ships, the data and experience outlined above should prompt a review of our approach to influenza preparedness. Control measures which maritime physicians should consider for implementation on ships include influenza vaccination programs for staff [27], surveillance and diagnostic testing, isolation, quarantine, hand hygiene [28], personal protective equipment (PPE) [28], antiviral agents for treatment, and post-exposure prophylaxis [29] (Table 2).

The composition of both Northern and Southern Hemisphere vaccines for seasonal influenza has remained stable from 2010–2012. As pandemic H1N1--2009 remains the dominant strain in circulation, the

**Table 2.** Influenza control measures for ships

| Influenza Control Measures | |
|---|---|
| Surveillance | Active and passive surveillance<br>Standardized case definition |
| Diagnostic testing | Rapid test kits<br>PCR or viral cultures for confirmation |
| Isolation of cases | If unable to isolate, provide surgical masks and encourage hand hygiene |
| Antiviral agents for treatment | Oseltamivir 75 mg oral twice daily × 5 days |
| Antiviral agents for prophylaxis | Oseltamivir 75 mg once daily for 10 days |
| Vaccination for passengers | Recommended for all high-risk passengers |
| Vaccination for crew | Attempt at least 80% coverage for crew |

seasonal influenza vaccine includes the pandemic H1N1-2009 strain in its trivalent composition, providing a wider spectrum of protective effectiveness. In tropical and equatorial regions, influenza may circulate with no distinct seasonality, unlike in temperate regions. Given potential mixing of passengers and/or crew from both northern and southern hemispheres as well as equatorial regions, the importance of influenza vaccination to prevent cross-infection in these congregate settings should be emphasized.

## SARS: A SINGAPORE PERSPECTIVE

The SARS pandemic of 2003 was disseminated primarily through air travel [30] rather than sea travel. However, the resulting changes in the WHO International Health Regulations (IHR 2005) apply to all points of entry and border controls including ports, in order to manage public health events of international concern [31]. Maritime physicians, therefore, need to be aware of IHR 2005 obligations, should SARS ever recur.

SARS transmission occurred on aircraft on several occasions. On one 3-hour flight with an ill index case and 119 other individuals, laboratory-confirmed SARS developed in 16 persons, 2 others were given diagnoses of probable SARS, and 4 were reported to have SARS but could not be interviewed [30]. Analysis of the 22 ill cases showed that being seated in the three rows in front of the index case conferred a 3-fold higher risk of infection, but 90% of the cases were seated more than 3 feet away, suggesting possible airborne rather than droplet spread. On another flight, only 1 of 246 passengers became ill despite 4 SARS cases on that 90-minute flight [32]. Using new techniques such as viral sequence variation (VSV) analysis, it was possible to determine retrospectively that the SARS-CoV infection of a German patient had indeed been acquired on a flight shared with a Singaporean SARS case (who had flown from New York to Frankfurt early in the outbreak), rather than from the patient's own stay in Hanoi, Vietnam [33]. Other flights with SARS cases did not result in any documented transmission [34], indicating that SARS is somewhat less transmissible unless patients are coughing with high viral burden.

The lessons learnt during the SARS outbreak bear re-visiting because SARS remains an emerging infectious disease (EID) caused by a novel pathogen, the SARS coronavirus (SARS-CoV), about which much is still unknown. Human-to-human transmission was the most common risk factor for acquiring SARS [35] but the originating animal reservoir for SARS remains elusive. Initially thought to be from the palm civet cat [36], more recent evidence indicates bats may be the original reservoir for SARS-CoV [37, 38].

Early detection of cases remains challenging because diagnostic tests for SARS such as SARS-CoV PCR on blood or respiratory samples can test negative in the first week of illness [39], and seroconversion may not occur until the third to fourth week after illness onset [40, 41]. Although researchers continue to investigate the pathogenesis and immunobiology of SARS, an effective vaccine for humans is not yet available. Neither is there any antiviral agent clearly demonstrated to be effective for treatment or prophylaxis, although preliminary data suggest some benefit from interferon [42]. The 10% overall case fatality rate for SARS [32] is also higher than for pandemic (H1N1) influenza, although it remains lower than for avian (H5N1) influenza.

Without a protective vaccine or effective specific treatment, the interventions for outbreak control will likely still be: 1) detection and isolation of infected patients; 2) quarantine of those who are well but exposed, for the duration of the incubation period (2–10 days from exposure [35]); and 3) supportive medical care for ill patients including access to mechanical ventilation. Within healthcare settings, use

of personal protective equipment (PPE) and restriction of hospital visitors will most likely be required again, and vigorous efforts at contact tracing in order to implement isolation and quarantine will be required in community settings. If or when another SARS outbreak occurs, all these heightened surveillance, isolation, and quarantine measures will probably cause travel restrictions that maritime physicians will have to grapple with. Good risk assessment, clear communications, and coordinated follow-through are critical to an effective outbreak response.

There are some important other differences between SARS and influenza. SARS had a lower infectivity ($R_0$) and longer incubation period compared to influenza. Patients were also not infectious prior to illness onset, unlike influenza. These characteristics allowed outbreak control measures such as isolation, quarantine, and social distancing to eventually slow down human-to-human transmission of SARS, and ultimately, end the pandemic.

Understanding the first two viral pandemics of this century allows us to scan the horizon for other potential emerging infectious threats. SARS remains quiescent currently, and it is unclear if, when, or where this virus will re-emerge to cause another outbreak. In contrast, there is a far greater burden of disease from seasonal influenza, and the risk of pandemic influenza remains a concern.

Mass gatherings continue to pose a hazard with large numbers of travellers from different regions gathering, being exposed through the respiratory route, and then dispersing to their respective countries. The Muslim Haj [43, 44] and the 2008 World Youth Festival in Sydney [45] have been venues for influenza outbreaks and dissemination of novel virus strains. The experience and perspectives gained from recent pandemics [46, 47] will strengthen our efforts as we seek to improve EID and pandemic preparedness in maritime health.

## KEY MESSAGES

1. Influenza is one of the most common health problems experienced in sea travel, for crew and passengers, with documented potential for outbreaks.
2. Influenza remains the most important vaccine-preventable respiratory infection in maritime health, and vaccination against seasonal influenza is 70––90% effective in preventing infection.
3. Maritime physicians should consider other influenza preparedness measures including surgical masks, hand hygiene, diagnostic tests, and antivirals for treatment and prophylaxis.
4. SARS remains an emerging infection without a protective vaccine or proven antiviral treatment; the mainstays of outbreak control will still be early detection and isolation of infectious cases, and quarantine of exposed individuals.
5. Good risk assessment, clear communications, and coordinated follow-through are critical to an effective outbreak response.

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