

Title:

Transmission and Prevention of Acute Viral Respiratory Tract Infections in Hospitals

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SUMMARY

Purpose of review: Transmission of acute respiratory tract viral infections in healthcare environments is a major problem worldwide. We review recent literature of viruses imported to hospitals from the local community and from abroad, their modes of transmission and measures required to reduce and contain them.

Recent findings: Common causes of outbreaks include Influenza viruses, Respiratory syncytial virus, Adenovirus, and Coronaviruses. Major lethal outbreaks of viral respiratory infections in hospitals have been caused by coronaviruses imported from abroad by travellers.

Summary: While viruses circulating in the local community are common causes of hospital outbreaks, major outbreaks have been caused by the coronaviruses imported from abroad by travellers. A high degree of clinical awareness and rapid enforcement of infection control measures are required to prevent transmission and spread.

Keywords: Viruses, Bacteria, AMR, Prevention, Infection control, Transmission, Coronavirus, influenza, parainfluenza

INTRODUCTION

Transmission of a range of common acute respiratory tract viral infections in healthcare environments is a major problem worldwide. This causes increased morbidity for patients, delays recovery, increases inpatient time, overwhelms available single room isolation facilities, causing ward closures and associated financial costs. Respiratory viruses are transmitted within healthcare facilities by other ill patients, visitors and healthcare workers, indirectly through contact with contaminated fomites, or from patient-to-patient spread. Transmission occurs through direct and indirect contact, as well as airborne routes. Air flows in and around people and during movement determines transmission. Long-range transmission occurs through infected respiratory droplets expelled by a patient or staff member which are eventually inhaled by a susceptible patient or healthcare worker. Exposure to droplet nuclei occurs as short-range transmission and exposure to deposited droplets is known as fomite transmission. [1] While viruses circulating in the local community are common causes of hospital outbreaks, major outbreaks have been caused by the coronaviruses imported from abroad by travellers.

TRANSMISSION IN THE HEALTHCARE ENVIRONMENT

Although face masks can be effective in preventing short range transmission, standard displacement ventilation in patient rooms may not be adequate to prevent transmission by expiratory droplets. [2**] Ventilation rates for isolation rooms are usually recommended as at least 12 air changes per hour. Airflow into single rooms helps prevent transmission by diluting the number of droplet nuclei in the air but is compromised by poor building maintenance. Overcrowding in enclosed environments also promotes airborne transmission. Airflow should pass from clean areas to dirty to prevent room to room transmission. Pressure differences between corridor and room are only maintained when doors and windows are fully closed and should be above 2.5kPa. Airflows are often found to be inadequate or incorrect. Large temperature differences and rapid movement of air increase the distance travelled of short range airborne particles. Droplets under 100 microns evaporate in 3-6 seconds limiting their range to 2 metres. However, droplet nuclei, formed by evaporation of droplets, and under 5 microns are readily inhaled into the bronchi and lung and can remain airborne for considerable distances protected by dry secretions.

RESPIRATORY INFECTIONS IN SPECIFIC PATIENT GROUPS

Patients having stem cell transplantation are extremely susceptible to acute respiratory viral infections and nosocomial outbreaks are common and associated with high rates of mortality and

morbidity. [3] A two-year study investigated patients having chemotherapy whether or not they had symptoms. Of 250 patients 79 had respiratory viral infections within 100 days, parainfluenza 3 accounting for 71%. One peak of infection occurred when there was little community prevalence and they were thought to have been acquired in hospital. Those with lower respiratory tract infections had longer periods of shedding and lower survival rate. Infection occurring before engraftment had the highest risk of developing lower respiratory infection. Some were infected despite being in single room isolation and members of staff or visitors were thought to be responsible. In another outbreak of parainfluenza virus 3, 13 of 19 patients had nosocomial infections in two clusters including one member of staff. The virus was detected in 43% of environmental samples up to 12 days after it was not detectable in the patient. [4] Respiratory syncytial virus caused outbreaks in consecutive years in another haematology unit. [5] In the first, the index patient was admitted from the community with symptoms, but asymptomatic shedders may have contributed. PCR was not always reliable in detection. Although infection control measures were applied to the whole ward on each occasion, most mildly affected staff were reluctant to stay off work.

Nursing home patients are another group highly susceptible to the spread of acute respiratory infections. In a study of patients with respiratory symptoms, 19% of 52 residents had parainfluenza, rhinovirus, RSV or influenza B. Examining high touch surfaces nearby, 2 of 10 showed environmental contamination with the same virus suggesting there was a significant risk of further spread. [6]

TRANSMISSION OF SPECIFIC VIRAL INFECTIONS IN HOSPITAL

Common causes of outbreaks include Influenza A, Influenza B, Parainfluenza, Respiratory syncytial virus A and B, Adenovirus, and Coronaviruses.

Influenza

Influenza viruses spread through aerosol or droplets as well as direct and indirect surface contact. Transmission routes in healthcare settings may be to determine because of the vectors involved, the vulnerable population and infection control interventions. In an investigation of a hospital outbreak of Influenza B, molecular characterization demonstrated sharing a room or bay was associated with an attack rate of 25% (19/75 patients admitted to ward). [7] However the data collection was retrospective, bed occupancy was not fully available, and infection control compliance and vaccination status were not known. In another study, compliance with use of personal protective equipment was observed in medical and surgical wards and intensive care units (ICU). In 325 observations, there were 283 failures, most often during personal protective

equipment (PPE) removal or unintentional contact with the face and clean surfaces. [8**] Entering a room with inadequate PPE to talk to the patient or deliver supplies was a common issue and often involved inadvertent contact with the environment.

Reliance on traditional epidemiological methods to track progress of a ward outbreak can be misleading. In one outbreak use of whole genome sequencing would have established a link between cases on opposite ends of a ward and avoided delay in infection control action and ward closure. [9] In another hospital outbreak of H3N2, modelling methods were applied. [10**] Infectivity was highest where virus aerosols were generated during respiratory therapy. There was air exchange across the door of the patient room which was under positive pressure. Infectivity declined with distance from the room. Transmission by healthcare worker hands and surfaces was rare in comparison but centred on common surfaces such as toilets.

Respiratory syncytial virus

In hospital, Respiratory Syncytial Virus was detected in 17% of symptomatic patients and 4% of asymptomatic. Asymptomatic caregivers had significantly greater risk of RSV than other healthcare workers (6.8% vs 2.0%). Children transmitting to caregivers had significantly higher viral loads than children who did not transmit. [11]

Measles

In a hospital outbreak of measles in Milan, epidemiological investigation suggested eight healthcare workers, three patients and one visitor were linked. [12] However, phylogenetic analysis showed none of the sequences to be identical. The root cause was inadequate vaccination rates in the staff.

CORONAVIRUS INFECTIONS

Two novel zoonotic coronaviruses are on the 2018 WHO blueprint list of priority pathogens that threaten global health security due to their epidemic potential and high mortality rates: Severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). [14]

Severe acute respiratory syndrome coronavirus (SARS-CoV)

One of the most notorious outbreaks of respiratory infection in hospitals was that of the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003. Using modelling of transmission of this coronavirus in Hong Kong, one ward outbreak was found associated with long range airborne or fomite vectors or a combination. For long range airborne route, the highest virus concentration in the air and the greatest risk of transmission was in the patient single room. The risk declined for

beds further away from the index patient. Healthcare workers' hands and surfaces were important vectors. The greatest risk to patients was for those visited by a healthcare worker immediately following an affected patient. The differences between patients were reduced by their contact with common shared surfaces.

Middle East Respiratory Syndrome Coronavirus

The Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in 2012 in a patient who died of severe respiratory disease in Jeddah, Saudi Arabia. [15] As of 16th October, 2018, there have been 2260 laboratory confirmed cases of MERS-CoV infection with 803 deaths (mortality rate 38%) reported to World Health Organisation from 27 countries.[16] The majority of MERS-CoV cases have occurred in the Middle East, particularly Saudi Arabia and the United Arab Emirates.[17] Cases of MERS-CoV reported from Europe, USA and Asia all had a history of travel to the Middle East [3]. With continuing reports of MERS-CoV transmission to humans in Saudi Arabia, the risk of global spread of MERS-CoV is ever present due to the estimated 10 million people who visit Saudi Arabia every year from 182 countries for Umrah and Hajj pilgrimages. [18**]

Dromedary camels are host animal species for MERS-CoV. Transmission to humans occurs directly or indirectly although the exact mode by which MERS-CoV infection is acquired remains undefined. [16-18] Confirmed cases of human-to-human transmission have been reported from hospital and family case cluster outbreaks among family visitors, patients, and health care workers. [17-19] Hospital outbreaks of serious respiratory tract infections have become a hallmark of MERS-CoV infection.[19] Hospital and healthcare associated outbreaks of MERS-CoV have occurred in several countries, with the largest outbreaks seen in Saudi Arabia, United Arab Emirates, and the Republic of Korea. [16] These MERS-CoV outbreaks in health-care settings occurred well before MERS-CoV was considered as a possibility by attending healthcare workers. [**19]

The clinical features of MERS-CoV infection are not MERS-specific [18] and patients have symptoms and signs that are common to other respiratory viruses. Thus, the diagnosis of MERS can easily be missed, unless the doctor or health-care worker has a high degree of clinical awareness and the patient undergoes specific testing for MERS-CoV. Clinical features of MERS range from asymptomatic to severe pneumonia, acute respiratory distress syndrome and multi-organ failure. MERS-CoV has been identified in clinical specimens such as sputum, nasal swabs, nasopharyngeal swabs, tracheal aspirate, bronchoalveolar lavage fluid, urine, faeces, blood, and lung tissue. [19-21] The precise modes of MERS-CoV transmission through direct or indirect contact, including transmission via airborne, droplet, or ingestion, are yet to be defined. [16,18,19**]

HOSPITAL OUTBREAKS OF MERS-CoV

To date there have been numerous small to large scale hospital outbreaks of MERS-CoV, mostly occurring in the Middle East, particularly in Saudi Arabia [16]. The largest outbreak of MERS-CoV outside the Middle East occurred in South Korea in May, 2015, resulting in 186 cases with 38 deaths. [16] This outbreak was caused by a Korean traveller returning from a visit to Saudi Arabia who became ill upon arriving in Seoul. He had sought healthcare at several hospitals, inadvertently transmitting MERS-CoV to many other people before a diagnosis of MERS-CoV was made. [20] This outbreak involved transmission within the hospitals and hospital-to-hospital transmission involving existing hospital patients, outpatients, visitors, and health-care workers. MERS-CoV spreaders (defined as an index patient who caused secondary infections of MERS-CoV) transmitted the infection from day 1 to day 11 of their illness (median 7 days, IQR 5–8), and the number of individuals infected by each index patient ranged from one to 84. MERS-CoV was detected in bed sheets, bed rails, intravenous fluid hangers, bed rails, tables and air samples of patients' rooms. [20, 21**, 22**]

Several risk factors are common to all hospital outbreaks of MERS-CoV.[18, 19**, 21, 22] The rapid spread of MERS-CoV is attributed to low health-care worker awareness of the possibility of MERS-CoV, the delay in diagnosis, with consequential slow implementation of infection control measures. MERS-CoV outbreaks in healthcare settings have been associated with poor compliance with infection control measures such as wearing of personal protection equipment while interacting with patients and application of AGPs, including intubation, manual ventilation before intubation, nebulized medications, and oxygen therapy. These underscore the importance of increasing awareness and infection control measures at first points of entry to health-care facilities.

A systematic review of 59 MERS-CoV studies [22] showed the duration from onset of symptoms to confirmation is 4–10 days, to hospitalization, 2.9–5.3 days, and 14–20 days to discharge from hospital. The elderly and those with other co-morbidities appear more susceptible to MERS-CoV infection, have more serious disease and increased mortality rates. There is no specific drug treatment for MERS and thus infection prevention and control measures are crucial to prevent spread of MERS-CoV in health care facilities. It remains unclear though, why MERS-CoV appears to be more transmissible in healthcare settings and continues to transmit in the Middle East. There is a large MERS-CoV camel reservoir. With no specific treatment or vaccine available, rapid case identification, isolation, infection prevention and control measures are essential to prevent the spread of MERS-CoV within households, the community, and health-care facilities.

PREVENTION AND CONTROL OF SPREAD OF CORONAVIRUSES IN HOSPITALS

Infection prevention and control measures are vital to prevent the spread of MERS-CoV in health-care facilities which provide care for patients with respiratory tract infections. Health-care workers should be educated and trained in infection prevention and control and should refresh these skills regularly. The SARS-CoV and the current MERS-CoV outbreaks led to important infection prevention and control recommendations. [24**, 25**] Prompt triage and isolation of patients with respiratory tract infection suspected of having MERS-CoV are critical to preventing spread. Droplet precautions should be added to the standard precautions and airborne precautions should be applied for aerosol generating procedures such as open suctioning or aspiration of the respiratory tract, intubation, bronchoscopy, or cardiopulmonary resuscitation. Airborne precautions should be applied in treatment rooms with at least 6 air changes per hour when performing aerosol generating procedures. CDC [24] recommend Standard, Contact and Airborne precaution for management of known or suspected MERS-CoV infection, these include the use of Personal Protective Equipment (PPE) such as gowns, gloves, eye protection (goggles or face shield), respiratory protection equivalent to a fit-tested NIOSH-certified disposable N95 filtering facepiece respirator. Health-care workers who have inadvertent exposure to patients with MERS-CoV must be quarantined, and if they are MERS-CoV positive should stay away from work until at least two upper respiratory tract samples taken at least 24 h apart are negative, over the full incubation period of 14 days. Each year an estimated 10 million pilgrims from 182 countries visit Saudi Arabia for the Hajj and Umrah pilgrimages. Watchful surveillance by public health systems, and a high degree of clinical awareness of the possibility of MERS-CoV infection are essential in any returning pilgrim with respiratory symptoms.

CONCLUSIONS

Nosocomial transmission is often due to a delayed diagnosis of acute respiratory infections in a patient shedding respiratory pathogens in a crowded health-care setting, such as an inpatient ward, emergency department, or renal dialysis unit. Early recognition of acute respiratory infections, improved compliance with internationally recommended infection control protocols, and rapid implementation of infection control measures are required to prevent outbreaks associated with healthcare facilities.

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Conflicts of interest

PW and AZ have a specialist interest in respiratory tract infections and serve as experts on several international and national advisory groups and committees

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