**30.1 Introduction**

Experience with the recent viral pandemics has generated a renewed interest in the study of the transmission modes of respiratory pathogens. It not only provides better understanding of the pathogenesis of the disease but also of the rational design of infectious-control strategies. Hospital-acquired infections still account for many hospitalizations and deaths around the world, with many of these infections being transmitted via aerosolized microorganisms to patients and healthcare workers (HCWs).

The generation of such infectious aerosols of human respiratory pathogens can occur via three modes of transmission, which are not mutually exclusive: aerosol transmission, transmission by large droplets, and self-inoculation of the nasal mucosa by contaminated hands. The aerosol mode is arguably the most important because of its impact on hospital infection control, safety of the HCWs requiring specialized isolation rooms, personalized protective equipment, and caution with certain procedures.

Growing evidence supports that from the classic early studies by Wells regarding air borne transmission and spread of diseases in the hospital environment and its HCWs [1]. Many of these infections can be prevented. In this chapter, we discuss...
the biological and mechanical factors involved in the transmission of respiratory pathogens and their consequences. Chapter 31 discusses preventive measures to decrease airborne transmission of infections.

### 30.2 Definitions

- **Airborne transmission**: passage of microorganisms from a source to a person through aerosols, resulting in infection of the person with or without consequent disease.
- **Aerosols**: solid or liquid particles suspended in the air. The size of the particles (0.001 to >100 μm) allows them to remain airborne for a variable amount of time. Infectious aerosols contain pathogens.
- **Short-range airborne infection route**: transmission between an infected source and the susceptible host within a short distance, generally <1 m.
- **Long-range airborne infection route**: transmission of infected particles carried from the source for a long distance to the susceptible host by airflow (within rooms, between rooms, distant locations), generally >1 m.

### 30.3 Factors Involved in Aerosol Transmission

#### 30.3.1 Mechanics of Aerosol Transmission

When studying bio-aerosols generated by humans, it is important to distinguish between the initial particle diameter and the final diameter after evaporation of water in ambient air. These “droplet nuclei” are involved in the long-range transmission route but can also cause infection in the short range.

Once infectious droplets are released, the main factors that determine how they are transported are their size, type (with or without structural lipids), airflow patterns, humidity, and temperature. Humidity alters the evaporation rate of the droplets and therefore affects droplets’ size. Knight estimated the time taken for particles to fall to the floor in a 3-m height room. Particles of 1–3 μm in diameter remain suspended almost indefinitely, 10-μm droplets stay in the air 17 min, 20-μm droplets remain for 4 min, and 100-μm droplets fall to the ground after 10 s [2]. The droplet size thus affects how airflow patterns distribute their deposition. Temperature changes also greatly influence the exchange flows between rooms. Both temperature and humidity affect the lipid envelope and protein coat, affecting the period of survival. Temperatures above about 24 °C appear universally to decrease airborne bacterial survival. Transport of such airborne droplets is driven by various other environmental factors, such as the local ventilation airflow (windows, doors, ventilation systems), the movement of people and their clothing, and thermal and airflow gradients produced by various pieces of equipment.

Another important consideration for the pathogenesis of aerosolized transmitted infectious diseases is the penetration and deposition of these infected particles in the respiratory tract. Particles >20 μm rarely penetrate below the trachea, particles 5–10 μm have 50% penetration of the tracheobronchial tree, and particles <5 μm have
less penetration of the alveolar region (30 %) [3]. Receptors are required for some infectious agents to initiate successful infection and eventually disease. Whereas bacteria and fungi can exist independently of host cells, viruses require specific receptors to which they can bind before entering and replicating within particular host cells. This requirement has been offered as one of the explanations for why certain individuals were infected with avian influenza A (H5N1) and perhaps why others were not. Differing receptor distribution patterns in the upper and lower respiratory tracts among individuals can affect the ease with which inhaled airborne viruses can cause infection and disease [4, 5]. Finally, the nature of the infecting agent and the human respiratory activity itself may cause a different variety of organism to be expelled with differing effects on secondary cases. The physiology of a cough suggests that it is more likely to bring up and expel deep-seated organisms from the lower respiratory tract (e.g., influenza, Staphylococcus and Streptococcus bacterial species) than the sneeze or normal speech, both of which are more likely to expel organisms inhabiting the upper respiratory tract (e.g., rhinoviruses and coronaviruses).

### 30.3.2 Aerosol Infectious Dose

The infectious risk of transmission is critically affected by parameters such as the pathogenicity of the infectious agent, its infectious dose, rate of biological decay, and environmental interaction of the infectious agent (Table 30.1) [6, 7]. The infectious dose varies among individual pathogens and their hosts. Not only are immunocompromised hosts more susceptible to infection, even with low infectious doses they become more effective source spreaders because the pathogen is poorly controlled, leading to super-spreading events. Knowledge of the infectious dose can help estimate the number of air changes required in an indoor environment to reduce the pathogen concentration to a safe level.

Some organisms resist environmental degradation better than others. *Mycobacterium tuberculosis* has a thick cell wall and can survive for long periods in various environments. Nonlipid enveloped viruses (rhinovirus, adenovirus) survive longer in high relative humidity (RH), whereas lipid-enveloped viruses influenza, coronavirus, measles, varicella zoster virus (VZV) survive longer in low relative humidity. Minimal survival for both lipid and nonlipid membrane viruses occurs at intermediate RH (40–70 %) [7]. Data on human corona virus 229E indicate a half-life of 3 h at 80 % RH, 67 h at 50 % RH, and 27 h at 30 % RH, suggesting that if confronted with a coronavirus epidemic the room RH should be kept high (≥80 %) [8]. Influenza survives on nonporous surfaces for 24–48 h; 8–12 h on cloth, paper, or tissues; and 5 min on hands. It also has been shown that the severe acute respiratory syndrome–coronavirus (SARS-CoV) and the influenza virus can remain infectious in alkaline stool and respiratory specimens, respectively, up to 4–7 days at room air temperature.

### 30.3.3 Source of Infectious Agents

Infectious aerosols can be generated in many ways and in many settings. The infectious patient is the main source of aerosolized particles. During normal exhalation
Table 30.1  Diseases and pathogen characteristics associated with aerosol infectious transmission [6, 7]

| Disease/pathogen                     | Aerosol route | Large/medium droplet aerosol | Droplet nuclei | Basic reproductive number(R0)^a | Temperature Viability and infectivity | Relative humidity |
|--------------------------------------|---------------|------------------------------|----------------|----------------------------------|--------------------------------------|------------------|
| Chickenpox/shingles (varicella zoster) | Yes           | Yes                          | Yes            | 10–12                            | Decreased by higher temperature      | Stable at low (20–30 %) RH |
| Coronavirus (SARS-CoV)               | Yes           | Yes                          | Yes            | 2–3                              | Decreased by higher temperature      | Stable at low (20–30 %) RH |
| Gram-negative bacteria               | Yes           | Yes                          | No             | N/A                              | Decreased by higher temperature      | Lower at intermediate/high (50–90 %) RH except Klebsiella and Pasteurella |
| Influenza                            | Yes           | Yes                          | Yes            | 1.68–20                          | Decreased by higher temperature      | Stable at low (20–30 %) RH |
| Legionellosis (L. pneumophila)       | No            | Yes                          | No             | N/A                              | Decreased by higher temperature      | Stable at >65 % RH |
| Measles                              | Yes           | Yes                          | Yes            | 15–17                            | Decreased by higher temperature      | Stable at low (20–30 %) RH |
| Meningitis                           |               |                              |                |                                  |                                      |                  |
| N. meningitidis                      | Yes           | Yes                          | No             | 1.2–1.36                         | Decreased by higher temperature      | Lower at intermediate (50–70 %) RH |
| H. influenza                         | Yes           | Yes                          | No             | N/A                              |                                      |                  |
| S. pneumoniae                        | Yes           | Yes                          | No             | 1.4                              |                                      |                  |
| Whooping cough (B. pertussis)        | Yes           | Yes                          | Yes            | 15–17                            | Decreased by higher temperature      | N/A               |
| Pneumonia                            |               |                              |                |                                  |                                      |                  |
| S. pneumoniae                        | Yes           | Yes                          | No             | 1.4                              | Decreased by higher temperature      | Lower at intermediate (50–70 %) RH |
| M. pneumoniae                        | Yes           | Yes                          | No             | N/A                              |                                      |                  |
| C. pneumoniae                        | Yes           | Yes                          | No             | N/A                              |                                      |                  |
| Condition                                      | Rhinovirus | RSV | Staphylococcal disease | Tuberculosis | Fungi |
|-----------------------------------------------|------------|-----|------------------------|--------------|-------|
| Common cold                                   | Yes        | Yes | No                     | Yes          | No    |
| Decreased by higher temperature              | N/A        |     | Decreased by higher temperature | N/A          |       |
| Stable at high (70–90%) RH                   |            |     | Lower at intermediate (50–70%) RH | N/A          |       |
| Staphylococcal disease                        | Yes        | Yes | No                     | Yes          | Yes   |
| Decreased by higher temperature              | N/A        |     | Decreased by higher temperature | N/A          |       |
| Tuberculosis                                  | No         | No  | Yes                    | Yes          | No    |
| 1–10                                          |            |     | Decreased by higher temperature | N/A          |       |
| Fungi                                         | No         | Yes | Yes                    | N/A          |       |
| Increased by higher temperature              |            |     | Increased by higher RH   |              |       |

RH relative humidity, N/A not available or quantified, RSV respiratory syncytial virus

*R0* = the number of secondary cases arising from a single index case in an otherwise totally susceptible population
breathing, with individual heterogeneity, droplets can project up to 1 m in room air, whereas sneezing can project droplets several meters. Normal exhalation produces particles ≤1 μm, explained by the fact that aerosol particles are generated in the lower respiratory tract, where larger particles tend to be retained via impaction or deposition. A sneeze can generate up to 40,000 droplets 0.5–12.0 μm in diameter [9]. A cough can generate about 3,000 droplet nuclei—the same as talking for 5 min. More than 65 and 40 % of the droplets produced by talking and coughing, respectively, are <75 μm [10, 11].

### 30.3.4 Aerosol-Generating Procedures

Many aerosol-generating procedures (AGPs) are known to stimulate cough and promote generation of aerosols. The risk of infectious transmission is unclear, however, because of scarce scientific evidence to demonstrate the creation of aerosol-associated infections with these procedures, the burden of potential viable microbes within the created aerosols, and the mechanism of transmission to the host.

Several simulation studies with different AGPs have been published that tried to compensate for the lack of knowledge concerning airborne transmission with these procedures. Hui et al. studied aerosol particle production from various AGPs—oxygen mask, jet nebulizer, and noninvasive ventilation (NIV)—using a human patient simulator (HPS) and measurement of smoke particles. The aerosol particles exhaled using oxygen masks with flow at 4 L and 12 breaths per minute were captured by digital images showing that the exhaled air reached peak distances of 0.40 m [12]. The maximum dispersion distance of smoke particles through the nebulizer side vent was 0.45 m lateral to the HPS at normal lung condition but increased to 0.54 m in the presence of mild lung injury and beyond 0.8 m in the presence of severe lung injury [13]. Exhaled dispersion was also studied during NIV in the HPS simulating mild lung injury in an isolation room with negative pressure using different masks and increasing inspiratory positive airway pressure (IPAP) (10–18 cmH2O) and stable expiratory positive airway pressure (EPAP) (4 cmH2O). Using a ResMed Ultra Mirage mask, the dispersion was 0.40 m at an IPAP of 10 cmH2O and only increased to 0.45 m with an IPAP of 18 cmH2O [14]. The distance dispersion using the Respironics Image 3 mask, which requires an additional exhalation device to avoid CO2 retention, was 0.65 m with 10 cmH2O of IPAP and increased to beyond 0.95 m with an IPAP of 18 cmH2O. With the Respironics Comfort Full 2 mask, the distance was 0.65 m with IPAP at 10–14 cmH2O and increased to 0.85 m with IPAP at 18 cmH2O [15]. These studies used human simulator models or normal subjects mimicking respiratory distress, but the HPS may not closely reflect the behavior of sick patients. Also, the smoke particles measured were considerably smaller (<1 μm) than droplets generated by coughing and sneezing (5 to >10 μm). Therefore, the behavior of smoke particles may not accurately represent droplet dispersion.

Simonds et al. [16] evaluated the characteristics of droplet/aerosol dispersion around delivery systems during NIV, 60 % O2, nebulizer treatment, and chest physiotherapy by measuring the droplet sizes at <20 cm from the face or mask and at 1 m
distance. They also assessed the decay of droplets over time after discontinuing an intervention and the impact of modifying the NIV circuit by inserting a viral/bacterial filter in clinical practice. Three groups were studied: normal control subjects ($n=12$); subjects with coryzal symptoms ($n=11$); adult patients with chronic obstructive pulmonary disease (COPD) admitted because of an infective exacerbation ($n=21$). NIV using a vented mask without the filtered circuit and chest physiotherapy are droplet-, not aerosol-, generating procedures. They created droplets >10 μm in the COPD ($p=0.042$) and coryzal ($p=0.044$) patients but not in normal controls. Because of their large mass, most of the droplets landed on local surfaces within 1 m. O$_2$ did not increase droplet count in any size range. The only device that produced an aerosol was the nebulizer, consistent with nebulizer characteristics. (Nebulizers do not disseminate large droplets from patients.) These findings suggest that HCWs providing NIV and chest physiotherapy working within 1 m of an infected patient should have a high level of respiratory protection. Control measures designed to limit aerosol spread, such as negative-pressure rooms, may have less relevance.

Tran et al. [17] published a systematic review of AGP and the risk of transmission of acute respiratory infections to HCWs. They identified only ten studies of very low grade evidence by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evaluation (five relevant case–control studies and five retrospective cohort studies, with no relevant systematic reviews, meta-analyses, or randomized controlled trials identified) in China, Singapore, and Canada during the SARS outbreak. Procedures reported to present an increased risk of transmission in HCWs exposed versus nonexposed workers included pooled odds ratios (OR) with 95% confidence intervals (CI): for tracheal intubation, OR $6.6$; noninvasive ventilation, OR $3.1$; tracheotomy, OR $4.2$; manual ventilation before intubation, OR $2.8$. Other intubation-associated procedures, endotracheal aspiration, suction of body fluids, bronchoscopy, nebulizer treatment, high-flow O$_2$ administration, manipulation of O$_2$ mask, or bilevel positive air pressure/continuous positive air pressure (BIPAP/CPAP) mask, defibrillation, chest compression, insertion of a nasogastric tube, and collection of sputum were not associated with aerosol transmission. The studies evaluated only the risk of transmission of SARS-CoV and may not be generalizable to other acute respiratory pathogens. In addition, it is difficult to identify the specific part of a given procedure, which may be complex and involve several maneuvers that impart the greatest risk of transmission.

### Key Major Recommendations

- Generation of infectious aerosols of human respiratory pathogens can occur by aerosol transmission, transmission by large droplets, and self-inoculation of the nasal mucosa by contaminated hands.
- Main factors that determine how infectious droplets are transported are their size, type (with or without structural lipids), airflow patterns, humidity, temperature, local ventilation airflows, and thermal and airflow gradients.
• The risk of transmitting infection is critically affected by parameters such as the pathogenicity of the infectious agent, the dose, the rate of biological decay, and environmental interaction of the infectious agent including the host’s immune status.
• Aerosol-generating procedures associated with an increased risk of transmission to HCWs include tracheal intubation, NIV, tracheotomy, and manual ventilation before intubation.
• Endotracheal aspiration, suction of body fluids, bronchoscopy, nebulizer treatment, high-flow O₂ administration, manipulation of the O₂ mask or the BiPAP/CPAP mask, defibrillation, chest compressions, insertion of a nasogastric tube, and collection of sputum are not associated with aerosol transmission.

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