Influenza Transmission and the Role of Personal Protective Respiratory Equipment: An Assessment of the Evidence

The Expert Panel on Influenza and Personal Protective Respiratory Equipment

Council of Canadian Academies
Conseil des académies canadiennes

Science Advice in the Public Interest

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Don Low, Chair
Expert Panel on Influenza &
Personal Protective Respiratory Equipment

REPORT REVIEW

This report was reviewed in draft form by the individuals listed below who were selected by the Council of Canadian Academies for their diverse perspectives, areas of expertise, and broad representation of the academic, worker safety and clinical communities. The reviewers assessed the objectivity and quality of the report. Their submissions – which will remain confidential – were considered fully by the panel, and most of their suggestions have been incorporated in the report.

Although they have provided many constructive comments and suggestions, they were not asked to endorse the conclusions nor did they see the final draft of the report before its release. Responsibility for the final content of this report rests entirely with the authoring panel and the Council. We wish to thank the following individuals for their review of this report:

Robert Brunham, Provincial Executive Director and Scientific Director, BC Centre for Disease Control, Vancouver

John Conly, FCAHS, Professor and Head of the Department of Medicine, University of Calgary

Lewis Goldfrank, Chairman and Professor, Department of Emergency Medicine, New York University & Medical Director, New York City Health Department's Poison Center

Sergey Grinshpun, Director and Professor, Center for Health-Related Aerosol Studies, Department of Environmental Health, University of Cincinnati

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Jonathan Van Tam, Professor, University of Nottingham

The report review procedure was monitored on behalf of the Council's Board and Scientific Advisory Committee (SAC) by **Dr. Jean Gray,** a Fellow of the Canadian Academy of Health Sciences and a member of SAC. The role of the report review monitor is to ensure that the expert panel gives full and fair consideration to the submissions of the report reviewers. The Board of the Council authorizes public release of an expert panel report only after the report review monitor confirms that the Council's report review requirements have been satisfied. The Council thanks Dr. Gray for her diligent contribution as review monitor.

Peter J. Nicholson
President, Council of Canadian Academies

SUMMARY

Seasonal influenza and its complications send, on average, about 20,000 Canadians to hospital every year, and approximately 4,000 die. Pandemic influenza occurs when a new strain of the human influenza virus emerges for which people have little or no pre-existing immunity and that can spread efficiently from person to person and become geographically widespread. It is impossible to predict when the next influenza pandemic might occur or how virulent the virus will be.

Given the likelihood of another pandemic, governments and international bodies have developed various plans to help minimize the health, social and economic consequences of such an event. In the context of updating the Canadian Pandemic Influenza Plan for the Health Sector, the Public Health Agency of Canada asked the Council of Canadian Academies to appoint an independent expert panel to assess the current science that is relevant to the following questions:

a) How and where are seasonal influenza and pandemic influenza transmitted based on existing reviews, or where needed, original literature generated from seasonal influenza outbreaks and from previous pandemics?

b) Based on the conclusions of this review, what is your assessment of the contribution that N95 respirators or surgical masks will make to the prevention of transmission of seasonal and pandemic influenza?

This report represents the consensus findings of the panel.

Despite the seasonal occurrence of influenza and its clinical and economic consequences, definitive evidence is lacking regarding the transmission of influenza and the relative contribution of each of the possible modes of transmission. In the absence of definitive evidence, the panel sought to agree, where possible, on what was most likely.

MODES OF INFLUENZA TRANSMISSION

There are two primary routes by which influenza virus exits the respiratory tract of an infected person: (i) expulsion of the virus into the air through sneezing, coughing, speaking, breathing or through aerosol-generating medical procedures, or (ii) by direct transfer of respiratory secretions to another person or surface. The new host acquires the virus either by inhalation of the infectious particles from the air or by contact with infectious material directly or via self-inoculation through a contaminated hand.

Traditional infection control terminology has categorized influenza transmission as occurring either by "contact," "droplet" or "airborne" modes. Since both droplet and airborne transmission involve the inhalation of infectious particles into the respiratory tract, for the purpose of this report these two modes have been grouped together under the term *"inhalation transmission."*

A person emits respiratory particles in a wide range of sizes. Expelled particles can be categorized into two groups depending on how they travel – "ballistic" particles and "inhalable" particles. Ballistic particles are those with a mean aerodynamic diametre of greater than approximately 100 μm[1] and are predominantly affected by gravity, as opposed to air resistance. Their infectious range lies very close to the original point of departure – generally less than a metre. Inhalable particles are those with aerodynamic diametres falling approximately in the range of 0.1 to 100 μm and, depending on size and shape, they may remain in the air from seconds to days.

Where particles are deposited in the respiratory tract of the potential host depends primarily on their size. Ballistic particles can be deposited directly onto mucous membranes but have a low probability of being inhaled. The inhalable particles can be classified into three size categories that have different deposition behaviour. Nasopharyngeal-sized particles range from approximately 20 to 100 μm in diametre and tend to travel no further than the upper respiratory tract. Tracheobronchial-sized particles have a diametre ranging approximately from 10 to 20 μm and are capable of depositing as far down as the tracheobronchial region. Alveolar-sized particles are less than approximately 10 μm in diametre. They are the only particles capable of reaching the alveolar region but can be deposited anywhere in the respiratory tract.

Long-range and Short-range Transmission via Inhalation: There is accumulating evidence that, while the risk of acquisition of respiratory pathogens decreases with increasing distance, transmission of infection across distances of greater than one metre may occur. The U.S. Centers for Disease Control and Prevention (CDC) have recently reconsidered the traditional "short-range" distance benchmark (often referred to as the "three-foot rule") and expanded it to two metres. In this report, *short-range transmission* is defined as infection occurring within about two metres of the source, and *long-range transmission* as infection at distances greater than about two metres.

The persistent survival of influenza virus in ambient air under common environmental conditions suggests that long-range inhalation transmission of influenza is

1 A micrometer, also called a micron, denoted "μm", is 10^{-6} metre (m).

possible. However, direct evidence of its contribution to influenza transmission is sparse. The panel considered a number of studies that bear on the question of long-range transmission of influenza (including all of the most widely-cited), but was unable to draw any conclusions from them as to the presence, absence or relative importance of a long-range mode of transmission of influenza.

Previous reviews and reports have focussed discussion of short-range transmission on the concept of "droplet transmission." This, however, does not take into account the full range of particle sizes that are expelled from a potentially infectious individual. All particles of inhalable size, whether nasopharyngeal, tracheobronchial or alveolar, can contribute to short-range transmission of influenza. The panel concluded that there is evidence that influenza is transmitted primarily at short range.

Contact Transmission: Contact transmission involves transfer of virus either by direct contact (e.g., by kissing) or by indirect contact (e.g., by touching contaminated surfaces). Influenza virus has been shown to persist on external surfaces for upwards of 24 hours depending on the surface type, and on hands for up to five minutes after transfer from the environmental surfaces. It is thus reasonable to assume that mucous membrane inoculation of influenza virus via contaminated hands could subsequently occur. Once present on mucous membranes, viral particles must migrate to a region that contains appropriate receptors, such as the nasopharynx. Although the panel was unable to find evidence of experimental or natural infection of humans with human influenza virus via the mouth or eyes, there is a theoretical possibility that this could occur.

The panel concludes that although the occurrence and relative importance of the contact route for influenza transmission have not been demonstrated, or indeed studied in humans, contact transmission likely occurs. No evidence has been found that hand hygiene or other interventions that might prevent contact transmission (e.g., glove use in healthcare facilities) prevent the transmission of influenza.

Role of Setting: Evidence as to the effect of setting on influenza transmission is sparse. One setting in which transmission of influenza is of particular interest is healthcare institutions. Since healthcare workers care for patients with influenza, it may seem logical that they would be at higher risk than others of being infected. While the panel found some evidence that healthcare workers are at higher risk of contracting influenza than the general adult population, these data are not conclusive.

Seasonal and Pandemic Influenza: Although there is no evidence to suggest that the modes of transmission of influenza would differ between pandemic and seasonal influenza, there is evidence to suggest that lower inoculums may be

required to cause infection during a pandemic because of the absence of prior immunity. This may also mean that infected persons shed virus in higher concentration or for longer periods of time. These factors could increase the risk of transmission, but it is not known if they would alter the relative contribution of different modes of transmission as between pandemic and seasonal influenza.

Conclusions on Modes of Influenza Transmission

1. Ballistic, nasopharyngeal, tracheobronchial and alveolar-sized particles are all emitted from the human respiratory tract.

2. Evidence about the relative contribution of the different modes of transmission to the spread of influenza is sparse and inconclusive.

3. There is evidence that influenza is transmitted primarily at short range.

4. There is evidence that influenza can be transmitted via inhalation of tracheobronchial and alveolar-sized particles at short range.

5. There is evidence that deposition of nasopharyngeal-sized particles in the upper respiratory tract can cause infection.

6. There is evidence that contact transmission can occur. The current weight of evidence suggests that transmission of influenza by inhalation is more probable than by indirect contact.

7. The evidence is lacking to determine whether long-range transmission of influenza occurs, but it cannot be ruled out.

PROTECTIVE MEASURES AGAINST INFLUENZA TRANSMISSION

The only interventions that have been tried and shown unequivocally to reduce the spread, and to mitigate the impact, of influenza in populations are vaccines and antivirals. Other interventions are nevertheless needed because vaccination will not be 100 per cent effective, and because a vaccine is unlikely to be available during the first wave of a pandemic.

Public health, and occupational health and safety practitioners use a multi-component "hierarchy of control" when developing infection control measures for any disease. The hierarchy comprises three categories – engineering controls, administrative controls and personal protective equipment (PPE). No one category is intended to

be used alone. Each component works in conjunction with the others to provide a system of multi-layered protection.

Engineering controls include physical controls such as ventilation requirements, relative humidity and temperature controls, among others. Their biggest benefit is the fact that effectiveness is not dependent on individual practice. Administrative controls are procedural and behavioral measures – e.g., hand hygiene, respiratory etiquette, measures to identify individuals who are likely infected and require separation from others. Effective implementation of such controls has shown to be effective in preventing disease and controlling outbreaks from various pathogens in both healthcare and non-healthcare settings. Administrative controls have two important limitations: (i) individual adherence to preventive practices is needed for success; and (ii) the difficulty of identifying persons who are infectious. Personal protective equipment (PPE) – e.g., goggles, gloves, gowns, surgical masks and respirators – is considered the "last line of defense" against exposure and supplements engineering and administrative controls. Personal protective respiratory equipment (PPRE) is a sub-category of PPE designed to block inhalation of hazardous airborne contaminants.

Respirators: The charge to the panel specifically referenced "N95 respirators," a commonly used term in Canada that refers to NIOSH-certified, disposable, particulate filtering, half-facepiece respirators. Only this type of respirator is discussed in this report.[2]

Respirators are designed specifically to ensure capture of particles in the size range that can be inhaled into the respiratory tract, including the entire range of nasopharyngeal, tracheobronchial and alveolar-sized particles. Transmission of infectious material could nonetheless theoretically occur as a result of release back into the surrounding environment of particles that had been trapped in the respirator filter, or by the improper handling of respirators. While there are very few studies that examine particle release from the filter, those that have been carried out suggest that such release is insignificant and unlikely to be of concern. There might also be concern that inadvertent infection could result from improper handling of a contaminated respirator when it is being taken off ("doffing"). Since there are currently no published studies regarding the handling of used filters, it is unknown whether there is a risk associated with handling respirators that have been exposed to infected persons.

2 A filter marked N95 means that it is not resistant to oil and is at least 95 per cent efficient at removing test particulates at the most penetrating particle size of approximately 0.3 μm diametre. (NIOSH refers to the U.S. National Institute for Occupational Safety and Health.)

The major factor affecting the efficacy of a respirator in preventing inhalation of particles is the adequacy of the seal between the respirator and the user's face (the "fit"). N95 respirators vary substantially in the quality of fit that is provided to different facial structures. Adequate training of individuals in assessing the fit of the respirator each time it is used, and qualitative or quantitative fit-testing of individuals, have been shown to improve facial fit.

The response of individuals to the use of respirators involves both physiological and psychological factors. The dominant physiological effect is the increase in inspiratory resistance brought on by the airflow resistance provided by the respirator. For most healthcare work, physiological stress is not significant. However, physiology alone cannot adequately explain respirator tolerance. The interplay of various psychophysical sensations such as increased facial skin temperature created by a respirator can overwhelm the capacity of some workers to tolerate the device. Healthcare workers may also perceive that use of a respirator interferes with their ability to communicate with a patient, or otherwise provide patient care.

User compliance with institutional protocols for PPRE is known to be less than 100 per cent. Workers who have been engaged in the planning steps of institutional protocols and feel properly trained in the use of their protective equipment are far more likely to comply with institutional safety policies.

Surgical Masks: Surgical masks are not certified to serve as respiratory tract protection for their wearer and are not considered to be PPRE by occupational health and safety practitioners. They are intended to be worn by healthcare workers to protect patients during surgery. Surgical masks have, however, been used for decades to prevent the wearer from exposure to infectious large droplets and from contamination of oral/nasal membranes via the contact route. The relative importance and the effectiveness of surgical masks used to prevent exposure are unknown, as they are typically employed simultaneously with other control measures such as vaccination, antivirals, handwashing, and contact precautions.

Surgical masks worn by infected persons may play a role in the prevention of influenza by reducing the amount of infectious material that is released into the environment. If worn to prevent exposure, surgical masks offer a physical barrier to contact with contaminated hands and ballistic trajectory particles. Their biggest limitation is that they do not provide an effective seal to the face, thereby allowing inhalable particles access to the respiratory tract. In addition, the efficiency of the filters of surgical masks in blocking penetration of tracheobronchial or alveolar-sized particles is highly variable and their efficiency in blocking nasopharyngeal-sized particles is unknown.

Seasonal and Pandemic Influenza: The protective capacities of PPRE and other interventions apply to both seasonal and pandemic influenza. During a pandemic the absolute benefit of these interventions in preventing disease transmission may be greater than for seasonal outbreaks for reasons related to the previously-noted differences between seasonal and pandemic influenza – e.g., in a pandemic there will be no prior immunity; the disease may be more severe; and a vaccine is unlikely to be immediately available.

Conclusions on Protective Measures Against Influenza Transmission

1. The primary elements of protection against influenza transmission are engineering and administrative controls. When exposure to an infected person is required or unavoidable, PPRE is the final layer of protection.

2. N95 respirators protect against the inhalation of nasopharyngeal, tracheobronchial and alveolar-sized particles.

3. Surgical masks worn by an infected person may play a role in the prevention of influenza transmission by reducing the amount of infectious material that is expelled into the environment.

4. Both surgical masks and N95 respirators offer a physical barrier to contact with contaminated hands and ballistic trajectory particles.

5. The efficiency of the filters of surgical masks to block penetration of alveolar and tracheobronchial-sized particles is highly variable. When combined with the inability to ensure a sealed fit, these factors suggest that surgical masks offer no significant protection against the inhalation of alveolar and tracheobronchial-sized particles.

6. The efficiency of the filters of surgical masks to block penetration of nasopharyngeal-sized particles is unknown. The lack of a sealed fit on a surgical mask will allow for the inhalation of an unknown quantity of nasopharyngeal-sized particles.

CHAPTER 1 - INTRODUCTION

Human influenza is a respiratory disease caused by infection with influenza virus.[3] Seasonal influenza occurs annually throughout the world. Influenza and its complications send about 20,000 Canadians, on average, to hospital every year, and approximately 4,000 die (PHAC, 2006). The average person will be exposed to the influenza virus many times over the course of his or her life and will thus build up a degree of immunity toward similar strains of the virus. This increased protection can be attained either through natural exposure or regular influenza vaccinations. This acquired immunity, however, will not help in the event of a novel or "pandemic" influenza strain.

Pandemic influenza occurs when a new strain of human influenza emerges for which humans have little or no pre-existing natural or acquired immunity and that can spread efficiently from person to person and become geographically widespread. There were three pandemics in the 20th century: Spanish influenza in 1918-1919, causing an estimated 40 million or more deaths worldwide (Johnson, 2002); Asian influenza in 1957-1958 (about 1.5 million deaths worldwide); and Hong Kong influenza in 1968-1969 (about one million deaths worldwide).

It is impossible to predict where and when the next pandemic might occur or how virulent the virus will be. In light of the likelihood of another pandemic, governments and international bodies have developed various plans to help minimize the health, social and economic consequences of such an event.

The nature of pandemic influenza means that planning and response efforts need to be coordinated on local, national and international levels. Many countries have already developed recommendations or policies for public health measures including the use of personal protective equipment, by both healthcare workers and the general public, during a pandemic.[4]

3 In this report, "influenza" refers exclusively to the human form of influenza unless otherwise noted.

4 Annex B includes references and links to documents containing official recommendations and policies from various national and international bodies on matters relevant to the transmission of influenza and personal protective equipment.

TERMS OF REFERENCE

The Public Health Agency of Canada (PHAC) has been working with federal departments and provincial and territorial governments to develop effective pandemic preparedness strategies for both the general public and the healthcare communities. In particular, PHAC has developed the Canadian Pandemic Influenza Plan for the Health Sector which maps out how Canada is preparing for, and plans to respond to, pandemic influenza. There are, however, many challenges in planning due to gaps in scientific knowledge and understanding.

In February 2007, PHAC charged the following questions to the Council of Canadian Academies:

a) How[5] and where[6] are seasonal influenza and pandemic influenza transmitted based on existing reviews, or where needed, original literature[7] generated from seasonal influenza outbreaks and from previous pandemics? and

b) Based on the conclusions of this review, what is your assessment of the contribution that N95 respirators or surgical masks will make to the prevention of transmission[8] of seasonal and pandemic influenza?

PHAC requested an independent assessment of the current science and official positions on these issues as input to the working group on Annex F of the Canadian Pandemic Influenza Plan. This group is responsible for gathering and considering evidence to update this Annex which deals with "Infection Control and Occupational Health Guidelines During Pandemic Influenza in Traditional and Non-Traditional Health Care Settings."

5 e.g., aerosol (airborne), droplet, contact spread.

6 e.g., homes, health care facilities, schools, other workforce, and community at large.

7 As required, PHAC will provide copies of known key reviews which may not yet be published but have been submitted and accepted for publication, i.e., those by Canadian experts and other international experts and organizations such as the US Centers for Disease Control or UK Health Protection Agency or World Health Organization (WHO). These would serve to supplement the "review of reviews" which would be obtained through a comprehensive search of the existing literature (both health and non-health).

8 The contribution is to be assessed in the context of the infection control hierarchy; the components of which include, engineering controls, administration controls and personal protective equipment.

APPROACH TO THE ASSESSMENT

The design of effective infection control measures against a particular organism requires a fundamental understanding of how the infection is transmitted. Despite the seasonal occurrence of influenza and its clinical and economic consequences, definitive evidence is lacking regarding its transmission and the relative contribution of each of the possible modes of transmission. As a consequence, the debate continues within both the infection control and the occupational health and safety fields as to the relevance of each possible mode (Brankston, 2007; Goy, 2006; Janssen, 2005; Tellier, 2006). To answer the questions posed by PHAC, the panel's task was to evaluate the full spectrum of opinions and the evidence in support of each.

To this end, relevant reviews were compiled (see Annex B) and their bibliographies were combined in order to establish a preliminary literature pool for evaluation. This pool was then refined throughout the assessment process as information was obtained from expert witnesses, conference proceedings and individual interviews. The literature cited represents those articles the panel concluded were necessary for a full discussion of what is currently known about the transmission of influenza. The panel also canvassed the views of several experts – including members of the panel itself – who are currently conducting research or working in the relevant fields.

The literature and evidence were evaluated to determine what could be said definitively and what remains as speculation. It was noted that, not infrequently, a publication has been used to make the argument both *for* and *against* a particular mode of transmission (Brankston, 2007; Goldfrank, 2007; Goy, 2006; Janssen, 2005; Jefferson, 2007; Tellier, 2006). In the absence of definitive evidence, the panel sought to agree, where possible, on what was most likely.

An evaluation of the differences between surgical masks and N95 respirators was carried out in terms of fit, materials, intended use, and practical factors such as comfort, compliance and job performance. The panel drew conclusions from this evidence as to the potential contribution of surgical masks and N95 respirators to the prevention of influenza transmission.[9]

9 In this report, a "surgical mask" refers to an unfitted device intended to reduce transfer of potentially infectious bodily fluids from an infected individual and is designed to be disposable. A "respirator" is defined as a fitted device that protects the wearer against inhalation of harmful contaminants – i.e., it protects the wearer from others who are, or might be, infected. N95 refers specifically to the standards outlined by the National Institute for Occupational Safety and Health (NIOSH) where "N" means not resistant to oil and "95" indicates a 95 per cent efficiency level.

The primary focus of this report is the healthcare worker community in both traditional and non-traditional healthcare settings. This reflects the fact that the working group on Annex F of the Canadian Pandemic Influenza Plan will focus principally on the healthcare sector. But, when addressing the issue of "where" influenza is transmitted, both public and private settings are discussed, including those outside of traditional healthcare environments.

TERMINOLOGY

It became apparent to the panel that some existing definitions and terminology served to confuse, rather than clarify, an understanding of the modes of transmission. For example, the terms aerosol/airborne transmission, droplet transmission, and droplet nuclei blend issues related to size, particle behavior, and distance that ought to be kept distinct and treated systematically. Therefore, for the purposes of this report, the panel has adopted definitions as set out in the text box at the end of Chapter 1. A more comprehensive glossary can be found in Annex A.

The terms and their definitions incorporate language from both the infection control and the occupational health and safety fields.

Transmission of influenza requires that infectious material from one individual be transferred to a potential new host. This occurs primarily via expulsion of respiratory secretions from the respiratory tract of an infectious individual into the surrounding environment (e.g., sneezing or coughing). Traditional infection control terminology has categorized influenza transmission as occurring either by "contact," "droplet" or "airborne" modes. Both droplet and airborne transmission involve the inhalation of infectious particles into the respiratory tract.[10] For the purpose of this report, and in an attempt to avoid the often confusing use of the terms "aerosol/airborne" transmission, these two modes have been grouped together under the term "inhalation transmission." However, while airborne transmission occurs exclusively through inhalation of infectious particles, droplet transmission involves both inhalation and contact. In this discussion, those particles that fall outside of the range of inhalation (yet were included under the old "droplet" mode of transmission) are termed "ballistic particles" and are addressed in the short-range transmission section of the report. In this way, the factors that affect the likelihood of infection

10 Bloodborne and gastrointestinal routes of exposure to influenza virus have also been postulated for avian or pandemic influenza. However, in accordance with the terms of reference on the contribution of surgical masks and respirators to the prevention of influenza transmission, this report focuses on the respiratory contribution exclusively.

via inhalation of influenza virus can be examined in a manner that does not confuse issues such as the size, behaviour and travel distances of particles.

Infection control measures for the prevention of droplet transmission have been made with the assumption that droplets do not remain suspended in the air for significant periods of time, are affected primarily by gravity, follow a ballistic trajectory and travel no further than one to two metres from the infected person (Papineni, 1997). These measures are based primarily on epidemiologic evidence suggesting that close contact is required for transmission of most diseases of the respiratory tract, and on studies demonstrating that spacing beds in barracks or field hospitals or desks in schools at least three feet apart resulted in a substantial reduction in transmission of infection (Glover, 1920; Feigin, 1982). There is, however, accumulating evidence that, while the risk of acquisition of respiratory pathogens decreases with increasing distance, transmission of infection across distances of greater than one metre may occur (Xie, 2007; Wannamaker, 1954; Aintablian, 1998; Wong, 2004; Scales, 2003). Thus, the Centers for Disease Control and Prevention (CDC) have recently reconsidered this "short-range" distance benchmark (often referred to as the "three-foot rule") and expanded it to two metres (CDC, 2007).

In this report, *short-range transmission* is defined as infection occurring within about two metres of the source and *long-range transmission* is defined as infection at distances greater than about two metres.

It is clear that the risk of transmission of respiratory pathogens decreases as the distance from an infected person increases. However, there is no empirical evidence that increasing the recommended distance for control measures to two metres will result in lower influenza attack rates, and there are no data that permit the quantification of differences in risk as a function of distance from the infected person. The panel has nevertheless adopted the "two metre" definition of short-range as a precautionary decision based on the revised estimates of particle trajectories as described by Xie (2007).

Glossary of Key Terms Used in this Report*

Particle: Generic term for a small mass of either liquid or solid.

Droplet: A droplet is a specific type of particle. It refers to a small volume of liquid that is expelled during breathing, talking, sneezing or coughing and which contains assorted biological/biochemical components.

Droplet Nuclei: Particles that are formed by evaporation of droplets leaving non-volatile components.

Aerosol: The suspension in air (or in a gas) of solid or liquid particles that are small enough to remain airborne for prolonged periods of time.

Aerodynamic Diametre: Term used to standardize how particles of different shapes and densities behave in the air and how fast they will fall to the ground under the combined influence of air resistance and gravity (settling velocity). A particle has an aerodynamic diametre "d" if its settling velocity equals that of a spherical water droplet of diametre "d".

Ballistic Particles: Particles greater than approximately 100 μm in diametre. A "μm" or micrometer, is 10^{-6} m.

Inhalable Particles: Particles between 0.1 and 100 μm in diametre.

Nasopharyngeal-sized Particles: Particles having diametres in the range of approximately 20 to 100 μm in diametre. They tend to travel no further than the upper respiratory tract.

Tracheobronchial-sized Particles: Particles having diametres of approximately 10 to 20 μm. They are capable of depositing as far down as the tracheobronchial region.

Alveolar-sized Particles: Particles having diametres of less than approximately 10 μm in diametre. They are the only particles capable of reaching the alveolar region but can be deposited anywhere in the respiratory tract.

Fomite: Any inanimate object or substance capable of carrying infectious organisms (such as germs or parasites) and hence, of transferring them from one individual to another.

Inhalation Transmission: A mechanism of transmission via inhalation of infectious particles into the respiratory tract. This includes particles ranging in size from approximately 0.1 to 100 μm and therefore would encompass the classical airborne and droplet modes of transmission.

Contact Transmission: Transfer of virus from an infected individual to a potential host either by direct physical contact or indirect contact (e.g., by touching contaminated surfaces).

Long-range Transmission: Inhalation transmission of the virus at distances greater than approximately two metres.

Short-range Transmission: Contact transmission or inhalation transmission of the virus at distances of two metres or less.

** See also Annex A for a more complete glossary.*

CHAPTER 2 – MODES OF INFLUENZA TRANSMISSION

Transmission of influenza from an infected person to a new host requires release of the virus into the surroundings. Since influenza is a respiratory disease, there are two primary routes though which this can occur: (i) expulsion into the air through sneezing, coughing, speaking, breathing or through aerosol-generating medical procedures, or (ii) by direct transfer of respiratory secretions to another person or surface. Acquisition of the virus by the new host can then occur either by inhalation of the infectious particles from the air or contact with infectious material, followed by infection via self-inoculation through a contaminated hand. Inhaled particles may theoretically infect the host at any point in the respiratory tree, from the nares to the terminal alveoli, assuming that in the latter case the particles are small enough to penetrate below the trachea.

The current knowledge base regarding influenza transmission comes from observational and epidemiological studies augmented by a limited amount of clinical and laboratory research. To date, the following assumptions have been made regarding influenza transmission:

- the source of the virus is the respiratory secretions of an infected person;
- inoculation may occur by direct deposition of the virus onto respiratory mucous membranes, by self-inoculation of mucous membranes with contaminated hands, or by inhalation of particles containing viruses;
- transmission occurs predominantly at short range; and
- transmission by indirect contact can occur since influenza viruses can survive outside the human body for minutes to hours in the air and on various surfaces.

Reaching conclusions regarding the likelihood of the various possible modes of influenza transmission requires assessment of the evidence regarding the mechanisms by which the virus leaves the body of the infected person, enters the body of a potential host, and comes in contact with a site that permits replication of the virus, thus resulting in infection. Investigation of these steps in the transmission of influenza involves evidence as to:

- the various ways the virus can exit the respiratory tract – e.g., sneezing, coughing, talking, breathing, aerosol-generating procedures, or direct transfer of respiratory secretions;
- the size and relative volume of expelled particles and their eventual fate;
- the physical transmission through the air of expelled droplets containing the virus (e.g., in a cough). This involves analyzing the "physics of the cough" including expulsion, dilution and evaporation of the "droplet mist," as well as the effect of environmental conditions such as humidity and temperature;
- the viability and infectivity of the influenza virus once outside the body;

- the ways in which virus-containing particles within the inhalable size range (0.1 to 100 μm) may be inhaled by the potential host, or acquired by contact of the potential host with contaminated material that is not airborne;
- where inhaled or contact-transmitted viruses end up in the host's body and whether these locations harbor cells with specific receptors for the virus and are permissive for viral replication; and
- the relationship between risk of infection and number of viruses delivered to susceptible tissues (i.e., infectious dose).

In this chapter the evidence is reviewed, such as it is, regarding each of the preceding elements of potential influenza transmission pathways. Unfortunately, important knowledge gaps exist.

GENERATION OF INFECTIOUS MATERIAL

When an infected person coughs, sneezes, talks and breathes, particles – ranging from 0.1 to over 1000 μm in size – are emitted into the air. Both the number and size distribution of particles will depend on the mechanism of expulsion, with sneezing producing the most particles, and talking the least (Figure 1). However, a recent paper by Xie *et al.* (2007) noted that five minutes of talking can produce the same number of particles as a single cough.

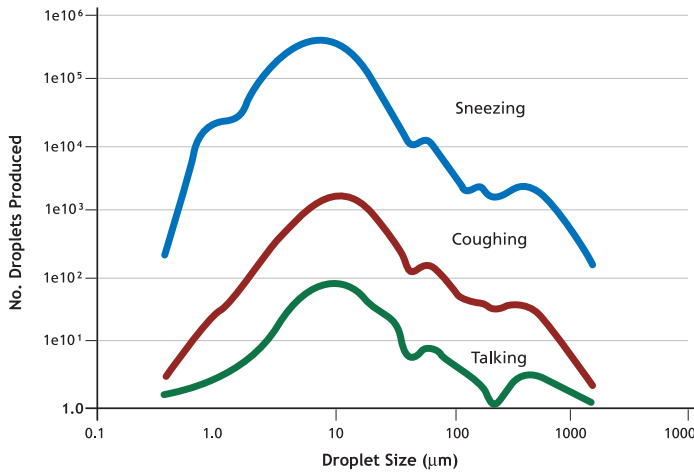


Figure 1

Size distribution of droplets formed upon sneezing (blue), coughing (pink) and talking (green) * Note: log scale (adapted from Kowalski & Bahnfleth, 1998)

If the concentration of virus in the particles is constant, the same volume of particles will have the same amount of virus. However, since the volume of a particle is proportional to the cube of its radius, a single 100 μm particle will have 1000 times the amount of virus as a single 10 μm particle. Thus, given a similar number of 10 μm and 100 μm particles the 100 μm particles would contain 1000 times more virus.

Data presented by Duguid *et al.* (1946) showed that particles ranging in diametre from 2 to 24 μm accounted for almost 90 per cent of the *number* of particles emitted. However, in terms of total *volume*, these particles accounted for a very small fraction. It is not known how influenza virus is distributed in particles emitted from infected persons. The viral concentration in emitted particles is expected to vary both among individuals, and over the course of their infection.

Effect of Particle Size

The route of an expelled particle depends on the physical and environmental factors that surround it. Expelled particles can be categorized into two groups depending on how they travel: "ballistic" particles and "inhalable" particles.

Ballistic particles – with a mean aerodynamic diametre of greater than approximately 100 μm – are predominantly affected by gravity (as opposed to air resistance) and follow so-called "ballistic trajectories" (Xie, 2007; Embil, 2003; Teleman, 2004; Langley, 2005; Wells, 1934; Duguid, 1946). These ballistic particles settle out of the air in seconds. Their infectious range lies very close to the original point of departure – generally less than a metre. Ballistic particles are capable of landing on any nearby surfaces, including people, and are thought to play a role in the contact mode of influenza transmission. However, at close range, these particles could also land on the mucosa of nearby individuals.

Inhalable particles are particles with aerodynamic diametres falling in the 0.1 to 100 μm range. The time during which a particle is likely to remain in the air is related to its overall size and ranges from seconds to days (Table 1). Some have diametres sufficiently small to allow them to be carried considerable distances depending on air currents and other factors (Evans, 2000). Particles near 100 μm in size deposit exclusively in the nasopharynx with thoracic and alveolar deposition occurring as the particles become smaller, especially less than 20 μm.

Table 1

Behaviour of Droplets in Still Air (adapted from Evans, 2000)

Diameter (μm)	Settling velocity (cm/sec) (Stoke's Law)	Time to fall 3 meters
100.0	25.0	10 sec
30.0	2.7	70 sec
10.0	0.31	17 min
3.0	0.028	3 hours
0.3	0.00042	8.4 days
0.03	0.000022	159 days

Effect of Evaporation

Particles, once ejected from the respiratory tract of an infected person, are subjected to the effects of evaporation. The rate of evaporation of the water in the particles is largely determined by the amount of water present in the air (relative humidity), the prevailing temperature, and the surface area of the particles (Lighthart, 1991; Duguid, 1946; Lidwell, 1967; Yassi, 2004). For a unit volume of water in air, the ratio of surface area to volume doubles as the droplet diametre decreases by one-half. For this reason, the evaporation rate is faster for smaller particles. The evaporation rate also increases with rising air temperature and/or falling relative humidity.

In a study that involved spraying a microbe-laden aerosol (i.e., mist) into the air and measuring the course of droplet size and downwind behaviour, Lighthart *et al.* (1991) showed that, at 49 per cent relative humidity and 21°C , droplets in the 80 μm diametre range evaporated before the droplets reached the ground; and the water in the particles with initial diametres less than 35 μm evaporated in less than one second. Lidwell re-evaluated Duguid's 1946 data and found that the water contained in the 5 to 50 μm particle size range quickly evaporated, reducing the particle sizes to the 1 to 10 μm range (Duguid, 1946; Lidwell, 1967). Therefore, because of evaporation, expelled particles do not remain the same size. Many of the larger ones very quickly end up as smaller particles as evaporation proceeds.

Effect of Humidity

The relative humidity affects not only how quickly evaporation occurs, but to what extent it will occur. The rate of evaporation decreases as relative humidity increases and is slowed by the presence of salts, proteins and other non-volatile components present in an ejected respiratory tract particle. As described by Yassi *et al.*(2004), while a droplet of pure water will evaporate fully if relative humidity is less than 100 per cent, a droplet that contains soluble material, such as sodium chloride, will reach

an equilibrium state which depends jointly on the concentration of the sodium chloride contained in the droplet and the relative humidity of the ambient air. Since respiratory secretions contain many different compounds as solutes or suspended material, the water in particles that contain microorganisms, will not always completely evaporate in ambient air. However, in an HVAC-equipped building,[11] located in a temperate climate, a relative humidity of 40 per cent or lower can be expected, particularly during winter months. Under these conditions, the water in a particle containing soluble material will evaporate completely, leaving behind a droplet nucleus that could contain any infectious agents that were originally present (Yassi, 2004). If these biological agents are not damaged by the drying process they can potentially infect a susceptible host if inhaled.

Effect of Distance

The physics of breathing, coughing, talking or sneezing plays an important role in determining how far and how quickly an ejected respiratory particle can travel. The average total volume of emitted material in a cough is approximately four microlitres at the moment of exhalation. Almost all of this volume is composed of larger particles that follow ballistic trajectories and land on "surfaces" within roughly one metre of the source (Duguid, 1946; Nicas, 2005; Loudon, 1967). The remaining volume remains in the air as an evaporating mist with the liquid particles converting to desiccated particles (droplet nuclei) at a rate inversely proportional to their size.

Figure 2
Particle mist created upon sneezing. (Davidhazy, 2007)

11 HVAC = heating, ventilation and air-conditioning

Figure 2 shows this mist of potentially virus-containing particles that is present within the immediate vicinity of a sneezing person. The average particle density of the mist rapidly dilutes as the mist expands into an increasing volume surrounding the sneezer (or cougher) so that, as the distance from the source increases, the relative concentration of particles in the air decreases in rough proportion to the distance cubed. Therefore, the likelihood of exposure, and the average number of particles inhaled, falls off rapidly with distance from the infected person in a way that depends on air flow patterns. In addition to this dilution factor, the effect of ventilation must be considered.

EXPOSURE TO INFECTIOUS MATERIAL

Respiratory secretions, once emitted by an infected person, can cause infection in another person if:

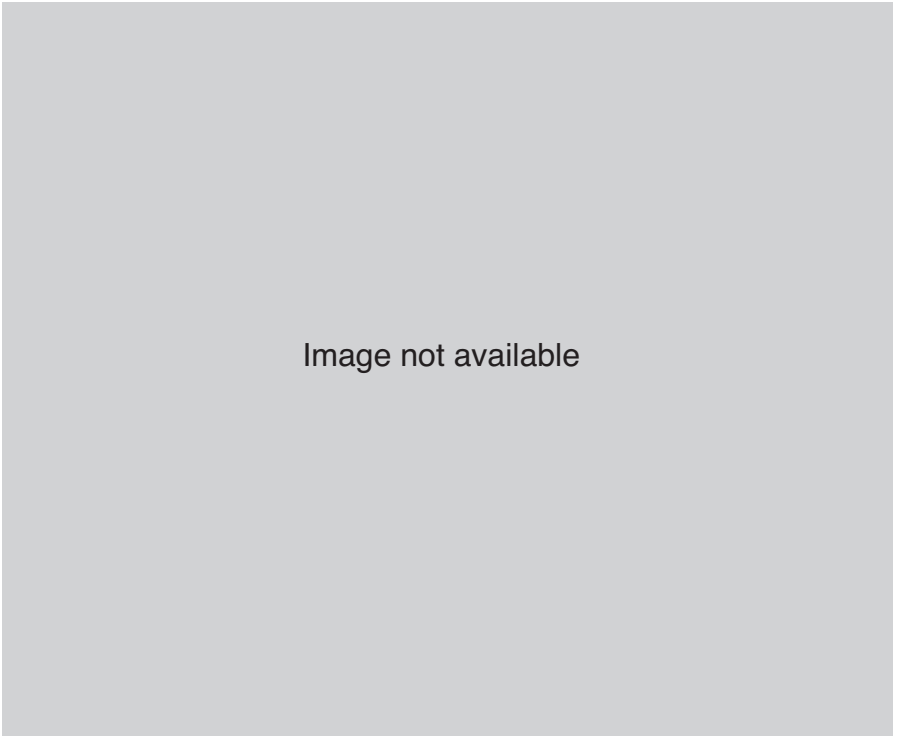
- infectious particles are inhaled;
- they are deposited directly onto the mucous membranes (e.g., by kissing, or by large particles from a cough or sneeze following a ballistic trajectory); or
- respiratory secretions deposited onto other surfaces are transferred to the mucous membranes (e.g., if the person's hands touch a contaminated surface and then touch their nose).

Inhalation

The human respiratory tract can be divided into three regions on the basis of structure, size and function:

(i) the upper respiratory tract, extending from just posterior to the external nares to the larynx;
(ii) the tracheobronchial region, defined as the trachea to the terminal bronchioles; and
(iii) the alveolar (pulmonary) region, comprising the respiratory bronchioles, alveolar ducts and alveolar sacs.

The thoracic region is defined as the tracheobronchial and alveolar regions combined (Figure 3).



A person emits respiratory particles in a wide range of sizes. Where particles are deposited in the respiratory tract of the potential host depends primarily on their size (Nicas, 1995; Vincent, 1990; Sattar, 1987; Lippmann, 1980; Stuart, 1976). While the size delineations for each category serve as effective discussion tools for planning purposes, it is important to note that, in actuality, particle behaviors fall along a continuum.

- Alveolar-sized particles are less than approximately 10 μm in diametre. They are the only particles capable of reaching the alveolar region but can be deposited anywhere in the respiratory tract.
- Tracheobronchial-sized particles have a diametre of approximately 10 to 20 μm. They are capable of depositing as far down as the tracheobronchial region.
- Nasopharyngeal-sized particles are from approximately 20 to 100 μm in diametre. They tend to travel no further than the upper respiratory tract.
- Ballistic particles have a diametre greater than approximately 100 μm. They can be deposited directly onto mucous membranes but have a low probability of being inhaled.

Figure 4 depicts the various regions of the respiratory tract along with the size classification of particles and their corresponding region of deposition.[12]

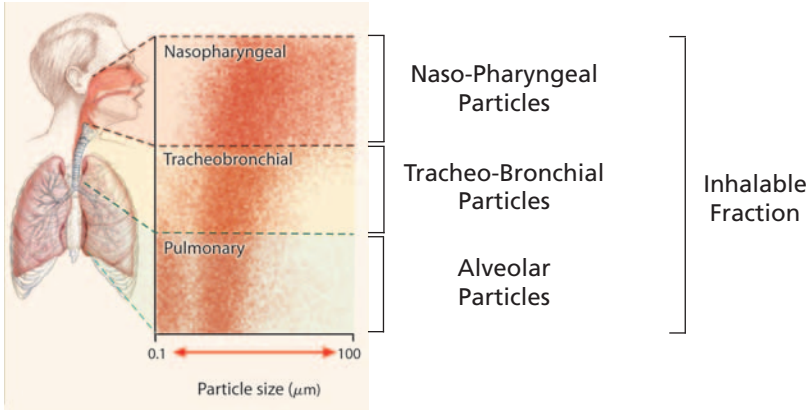


Figure 4
Deposition regions of the respiratory tract for the various particle sizes

The probability that inhalation of influenza virus will cause infection depends (among other factors to be discussed subsequently) on: (i) the presence of human influenza virus receptors and cells permissive to infection; and (ii) the infectious dose, or the average number of viable virions required to initiate infection.

The influenza virus must have access to receptors in the body of the host in order for viral attachment to occur. Although receptors used by influenza viruses are found in many tissues, and although many influenza strains can infect several animal species, there are several factors restricting tissue or species tropism. These include: cofactor mediation such as the availability of proteases[13] to cleave the haemagglutinin[13], whether or not the appropriate receptor is being expressed, the different receptors used by avian or human strains of influenza, and other intracellular factors.

There are two types of influenza receptors: the alpha-2,3-linked sialic acid receptor (utilized by avian influenza viruses) and the alpha-2,6-linked sialic acid receptor (utilized by human influenza A & B viruses). The alpha 2,6-sialic acids are found on cellular proteins in most tissues of the human body (Gagneux, 2003); however, viral replication in humans is restricted to the respiratory tract. Shinya *et al.* (2006) have demonstrated the presence of alpha-2,6 receptors on epithelial cells in both

12 These classifications are based largely on the American Conference of Industrial Hygienists report (ACGIH, 2005).

13 See Annex A – Comprehensive Glossary for definitions.

the upper and lower respiratory tract, and that human influenza viruses can infect epithelial cells in the nasal epithelium, the tracheobronchial tree and the alveolar epithelium. Mastrosovich *et al.* (2004) demonstrated that human influenza viruses preferentially infected non-ciliated epithelial cells, in correlation with the receptor density. This latter result was obtained on epithelial cells cultured in vitro and may not represent entirely accurately the situation in vivo. Shinya *et al.* (2006) and van Riel *et al.* (2006) have also shown that some epithelial cells in the alveoli and the respiratory bronchioles, identified as pneumocytes type II, express the alpha-2,3 receptor and allow for the replication of avian influenza A (H5N1).

A common means of evaluating the infectious dose for any given disease is by determining the amount of virus required to infect 50 per cent of a sample population (either in vitro or in vivo). This is referred to as the "tissue culture infectious dose 50 per cent" ($TCID_{50}$) for in-vitro studies or the "human infectious dose 50 per cent" (HID_{50}) for in-vivo, human studies. Alford *et al.* (1966) showed that for alveolar-sized particles the HID_{50} was in the range of 0.6 to 3.0 $TCID_{50}$. Couch *et al.* reported that the dose by intranasal drop inoculation (which initiates infection at the same site as nasopharyngeal sized-particles) required to cause infection was 100 times greater than that required to infect with alveolar-sized particles (Couch, 1971; Couch, 1974). The viral concentration from nasal washes in infected persons has been shown to be as high as 10^7 $TCID_{50}$ per ml. Since in a single sneeze, the volume of all the particles 10 μm or less (alveolar-sized particles) is estimated at 1.2×10^{-5} ml (Nicas, 2005), these alveolar-sized particles would contain 120 $TCID_{50}$, well above the HID_{50} calculated by Alford. Also, since 99.9 per cent of the volume in a sneeze is comprised of particles greater than 8 μm (Nicas, 2005), the infectious dose contained in nasopharyngeal-sized particles would also exceed the required dose for infection.

Long-Range Inhalation Transmission

For this report, long-range transmission has been defined as inhalation transmission of the virus at distances greater than approximately two metres. Once small particles have been produced by an infected person, the likelihood of long-range, inhalation transmission depends on the duration of viral viability in the air, the environmental conditions to which the virus is exposed, and the effects of dilution and air currents.

The persistence of the infectivity of influenza virus in aerosols has been studied in the laboratory. In experiments that used homogeneous aerosolized influenza virus suspensions (mean diametre of 6 μm), virus infectivity at a fixed relative humidity in the range of 15 to 40 per cent undergoes slow, exponential decay (Hemmes, 1960; Hemmes, 1962). These results are consistent with those of an older study in which infectious influenza viruses in an aerosol could be demonstrated to persist

for up to 24 hours at relative humidities of 7 to 24 per cent (Loosli, 1943). Virus infectivity decreases rapidly at relative humidity above 40 per cent.

The persistent survival of influenza virus in ambient air under common environmental conditions suggests that long-range inhalation transmission of influenza is possible. However, direct evidence of its contribution to influenza transmission is sparse. A commonly cited article for evidence of long-range transmission is the Moser *et al.* (1979) report of an influenza outbreak on an airplane (Gregg 1980). In this study, a single index patient developed symptoms while the aircraft was grounded and with the ventilation interrupted for a two to three hour period. Seventy-two per cent of other passengers and crew developed influenza over the next four days. The outbreak investigation established that the index case spent the waiting period on the ground (4.5 hours in total) lying down across two seats at the rear of the cabin, with no direct contact reported between the index case and other passengers. The authors state that "the high clinical attack rate among passengers aboard the aircraft was probably the result of their exposure to large aerosols of droplets produced by an ill patient in a confined, stagnant and dry airspace" (Moser, 1979).

Another frequently cited study supporting long-range transmission is that by McLean *et al.* (1959). This observational study, carried out during the 1957-1958 pandemic, showed that tuberculosis patients housed in a building with upper room ultraviolet radiation – which is known to inactivate influenza virus and to help control transmission via alveolar and tracheobronchial-sized particles – were less likely to become infected with influenza than tuberculosis patients housed in a building without ultraviolet radiation. The influenza attack rate was two per cent in patients in the building with ultraviolet radiation and 19 per cent in the patients in the non-irradiated building. The authors propose that the difference in infection rates suggests that control was achieved by air disinfection via ultraviolet light which would only have had an effect if infection via tracheobronchial or alveolar-sized particles was able to happen.

While the authors propose that these studies provide inferential evidence for long-range transmission, in both cases, infection could also have occurred via short range and/or contact transmission modes. The panel is unable to draw any conclusions from them as to the presence, absence or relative importance of a long-range mode of transmission.

Drinka *et al.* (1996) found significantly fewer cases of influenza during an outbreak season in a newly constructed building than in three older buildings (1.5 per cent of residents vs 12.5 per cent). The newly constructed building had

more square feet of public space per resident on each unit, did not contain office space that serves the entire four-building facility, and contained additional air filters with 100 per cent fresh air circulated back into the building. Drinka *et al.* (2004) updated their report and included five subsequent seasons with comparison of building attack rates of culture-confirmed influenza using an identical protocol. In retrospect, the authors admitted their initial report was based on a statistical outlier. In the subsequent five years, the building with more square feet of public space and less recirculated air had attack rates similar to the other buildings. Thus, these reports provide no evidence for long-range influenza transmission.

The issue of long-range inhalation transmission has also been raised in association with two other outbreak descriptions (Marsden, 2003; Klontz, 1989). The panel concludes that the arguments made by these authors were not compelling since the reported cases could also have resulted from short-range transmission.

Compelling evidence for long-range transmission is provided by experiments carried out with ferrets (Andrewes, 1941). In these studies, influenza infection was observed in ferrets placed greater than two metres apart. However, the relevance of such studies in human transmission remains unclear.

Seasonal influenza outbreaks occur every year in settings like long-term care homes, hospitals and schools. These outbreaks generally demonstrate outbreak patterns that are more consistent with short-range rather than long-range transmission. However, it should be noted that some diseases known to be transmitted, at least in part, by inhalation over long distance, also commonly have outbreak patterns suggestive of short-range, close-contact transmission (Panum, 1846). Identification of long-range transmission of measles and smallpox was only possible when these diseases had been controlled to the point where contact tracing could be carried out for individual cases, and a single exposure source confidently identified (Wehrle, 1970; CDC & WHO, 2003; MMWR, 1983; MMWR, 1987). Influenza remains too common in the community to permit definitive observational studies of the long-range transmission mode.

Short-Range Transmission

Previous reviews and reports have focussed their discussions of short-range transmission on the concept of "droplet transmission". This, however, does not take into account the full range of particle sizes that are expelled from a potentially infectious individual. Short-range transmission associated with respiratory particles expelled while talking, sneezing or coughing could occur by direct deposition of

ballistic particles onto mucous membranes or by inhalation of smaller particles. Ballistic particles will travel on a trajectory that generally extends no more than one metre from the source. In contrast, all particles of inhalable size – whether nasopharyngeal, tracheobronchial or alveolar – would be expected to remain airborne for at least two metres. Thus, *all* particles of inhalable size can contribute to short-range transmission of influenza, whereas only those with sufficiently small aerodynamic diametres to exhibit non-ballistic trajectories are candidates for long-range transmission.

Contact Transmission

Contact transmission involves transfer of virus from an infected individual to a potential host either by direct, physical contact (e.g., by kissing) or by indirect contact (e.g., by touching contaminated surfaces). Direct contact with the upper respiratory tract is not sufficient for influenza transmission to occur. Once present on mucous membranes, viral particles must migrate to a region that contains appropriate receptors, such as the nasopharynx where human influenza virus alpha-2,6-linked sialic acid receptors are present. There are no such receptors in the eye (Olofsson, 2005). Only alpha-2,3-linked sialic acid receptors (the avian type) are present in conjunctivae which may explain why avian H7 influenza infections in humans frequently manifest as conjunctivitis. Although human influenza viruses may not be able to infect conjunctival cells, they could migrate to the nasopharynx via the lacrimal duct and infect cells there. Orally deposited virus could reach the nasopharynx through swallowing. The panel concludes that while it was unable to find evidence of experimental or natural infection of humans with human influenza virus via the mouth or eyes, there is a theoretical possibility that this could occur.

Indirect contact transmission can only occur if the influenza virus remains viable outside of the body. Influenza virus has been shown to persist on external surfaces for upwards of 24 hours depending on the surface type, and on hands for up to five minutes after transfer from the environmental surfaces (Bean, 1982). It is thus reasonable to assume that mucous membrane inoculation of influenza virus via contaminated hands could subsequently occur.

Hand hygiene, which is the major mode of interrupting contact transmission, is a central component of essentially all influenza control protocols for both seasonal and pandemic disease. This assumption largely stems from several randomized controlled trials showing that routine hand hygiene (five times per day) will significantly decrease the risk of acquiring acute respiratory illness (Meadows, 2004; Ryan, 2001; White, 2003). While the great majority of acute respiratory disease is due to viruses, none of the studies performed microbiological testing, so that they

do not provide information about which viral illnesses were prevented or any information specific to influenza.

Given the large amount of virus contained in ballistic particles that would survive for prolonged periods of time in the environment (that could cause infection only by direct deposition onto mucous membranes or by surface contact followed by self-inoculation), it is reasonable to postulate that contact transmission might occur. In fact, preliminary data from a guinea pig model of influenza demonstrates that contact transmission of influenza occurs, but is less efficient than transmission via inhalation (Palese, 2007; Mubareka, 2007). However, no evidence has been found that hand hygiene or other interventions that might prevent contact transmission (e.g., glove use in healthcare facilities) prevent the transmission of influenza.

The panel concludes that although the occurrence and relative importance of the contact route for influenza transmission have not been demonstrated, or indeed studied in humans, contact transmission likely occurs.

THE ROLE OF SETTING IN TRANSMISSION

Evidence on the effect of setting on influenza transmission is sparse. One setting in which transmission of influenza is of particular interest is healthcare institutions. Because healthcare workers take care of patients with influenza, it may seem logical that they would be at higher risk than others of being infected. However, because most illness due to seasonal influenza is not severe, the majority of contact with, and care for, people with influenza occurs in the community. In addition, influenza is shed in highest quantities in the first days of illness – i.e., generally before hospitalization (Hayden, 1999). Thus exposure to influenza is widespread in the community.

A very limited number of studies provide evidence about whether healthcare workers are at higher risk of exposure to influenza than other adults. All studies have been of workers in acute care hospitals. The most frequently cited is that of Elder *et al.* (1996), in which 120 of 518 (23 per cent) unvaccinated British hospital workers had serologically confirmed influenza during the 1993-1994 influenza season. This annual rate of influenza infection (symptomatic and asymptomatic) is relatively high but not beyond the usual range (Fox, 1982; Monto, 1985). However these studies did not measure the rate of infection in other adults.[14] In another study, Wilde *et al.* (1999) reported overall rates of infection in unvaccinated healthcare workers ranging from 7 to 28 per cent (median 14 per cent) in influenza seasons

between 1992 and 1995. Again, the absence of comparator non-healthcare worker infection rates precludes conclusions about the relative risk associated with healthcare.

Hammond and Cheang conducted two studies of absenteeism in workers in an acute care hospital in Winnipeg during the 1980s (Hammond, 1984; Yassi, 1991). These authors report that the increase in absenteeism rates during influenza season compared to other times of year was higher in staff of clinical services likely to be exposed to patients with influenza than in other staff. However, no information is available to permit adjustment for potential confounders, and there were also substantial differences between absenteeism during the influenza season and at other times in non-high risk groups. A more recent analysis of absenteeism in UK hospital trusts (Ritchie, 1999) did not demonstrate higher rates of respiratory illness causing absenteeism in clinical staff, but does illustrate the differences in relative absenteeism that can occur when rates in different departments are age-adjusted. This analysis was from administrative data, and was not limited to the influenza season. Finally, a recent study from Japan reported on the results of active surveillance for influenza in patients and staff of a general hospital during three influenza seasons. Rates of symptomatic influenza were significantly higher in physicians, nurses and "technicians" than in administrative personnel (Kawana, 2006). However, rates of infection in administrative personnel were less than one tenth of one per cent in two of three years of surveillance, which suggests that surveillance may have been more intensive on in-patient wards than elsewhere in the hospital. In addition, it is not clear how the job titles correlated with exposure to patients, and adjustment for potential confounders was not performed. The panel concludes that there is some evidence that healthcare workers are at higher risk of contracting influenza than the general adult population, but that these data are not conclusive.

The following conclusions with respect to the role of setting are based on the evidence presented above and the inferential judgment of the panel.

- In settings where very close and frequent contact is likely (e.g., in a home, day care centers) the risk of transmission of influenza increases.
- Other factors being equal, outdoor settings should reduce the risk of transmission compared to most indoor settings, due to a dilutional effect on the densities of infectious particles and environmental factors, such as UV irradiation, on viral viability.

14 One proposed comparator is the cumulative population rate of medically-attended, laboratory-confirmed influenza illness in six general practices in the United Kingdom, which in that epidemic was approximately 13 per cent corresponding to a peak weekly rate of about 180 per 100,000 (Fleming, 1995). However, this rate underestimates infection because medically-attended illness is only a fraction of symptomatic illness, which in turn is a fraction of all infection, but overestimates infection in adults because children have higher rates (Fox, 1982; Monto, 1985). Thus, it cannot be used to estimate an overall adult rate of infection for comparison purposes.

- When care is provided to symptomatic patients, the risk of transmission increases because of close proximity. This increased risk will be present in all settings where care for sick people is provided, including home, ambulatory care and institutional settings. No evidence exists to assess differences in risk based on the particular setting where care is provided.
- Healthcare providers (if not protected by vaccination or antivirals) can also serve as vectors of transmission and infect other patients in their care as well as colleagues.
- No conclusions can be stated in respect of workplaces generally since conditions are so heterogeneous.

SEASONAL VS. PANDEMIC INFLUENZA

Although there is no evidence to suggest that the mode of transmission of influenza would differ between pandemic influenza and seasonal influenza, there is evidence to suggest that lower inoculums may be required to cause infection during a pandemic because of the absence of prior immunity (Alford, 1966). This absence of prior immunity may also mean that infected persons shed virus in higher concentration and/or for longer periods of time. These factors could increase the risk of transmission, but it is not known if they would alter the *relative* contribution of different modes of transmission.

CONCLUSIONS ON MODES OF INFLUENZA TRANSMISSION

The following summarizes the consensus opinion reached by the panel.

1. Ballistic, nasopharyngeal, tracheobronchial and alveolar-sized particles are all emitted from the human respiratory tract.

2. Evidence about the relative contribution of the different modes of transmission to the spread of influenza is sparse and inconclusive.

3. There is evidence that influenza is transmitted primarily at short range.

4. There is evidence that influenza can be transmitted via inhalation of tracheobronchial and alveolar-sized particles at short range.

5. There is evidence that deposition of nasopharyngeal-sized particles in the upper respiratory tract can cause infection.

6. There is evidence that contact transmission can occur. The current weight of evidence suggests that transmission of influenza by inhalation is more probable than by indirect contact.

7. The evidence is lacking to determine whether long-range transmission of influenza occurs, but it cannot be ruled out.

CHAPTER 3 – PROTECTIVE MEASURES AGAINST INFLUENZA TRANSMISSION

The second element of the charge to the panel is the following:

> Based on the conclusions of this review (of the various modes of transmission), what is your assessment of the contribution that N95 respirators or surgical masks will make to the prevention of transmission[15] of seasonal and pandemic influenza?

In light of the conclusions of Chapter 2, a surgical mask or respirator will mitigate the transmission of influenza only if it does one or more of the following:

- reduces the amount of infectious material that is introduced into the surroundings from an infected person;
- prevents ballistic particles from landing on the mucous membranes of a potential host;
- prevents self-inoculation of mucous membranes by contaminated hands;
- prevents nasopharyngeal, tracheobronchial and alveolar-sized particles from being inhaled by a potential host.

Surgical masks and respirators need to be evaluated and compared based on their design, function and ability to fulfill these criteria. This will establish what the theoretical role of each could be in preventing influenza transmission. These characteristics will then need to be examined within the context of a general hierarchy of control and practical mitigating factors in order to evaluate the incremental protective contribution of respirators and surgical masks respectively.

THE HIERARCHY OF CONTROL

The only interventions which have been tried and shown unequivocally to reduce the spread, and to mitigate the impact, of influenza in populations are vaccines and antivirals. The panel recognizes that the most important line of defense against influenza is vaccination, but that other interventions are needed because vaccination will not be 100 per cent effective, and because a vaccine is not likely to be available during the first wave of a pandemic. Prophylactic antivirals are an important adjunct to vaccine in the control of seasonal outbreaks of influenza in

15 The contribution is to be assessed on the context of the infection control hierarchy; the components of which include, engineering controls, administrative controls and personal protective equipment.

institutions (Hota, 2007; Monto, 2004), and it is likely that antivirals will be used during a pandemic for both treatment and prophylaxis. However, the possibility of antiviral resistance, the limitations in the size of antiviral stockpiles, and the fact that the prophylactic efficacy of antivirals is less than 100 per cent means that other measures need to be considered. The panel's charge was to consider the evidence for the contribution of surgical masks and N95 respirators to these other measures.

Beyond vaccines and antivirals, infection control, public health and occupational health and safety practitioners use a multi-component "hierarchy of control" when developing infection control measures for the prevention of transmission of any disease. The hierarchy is meant to address hazards through direct control at the source of the infection as well as along the path between the infectious source and a potential new host.

The hierarchy of control is made up of three categories: engineering controls, administrative controls and personal protective equipment (PPE). No one category is intended to be used alone; rather, each component works in conjunction with the others to provide a system of multi-layered protection. An understanding of the role played by each is needed in order to assess the incremental contribution of surgical masks and respirators.

Engineering Controls

Engineering controls include physical controls such as ventilation requirements, relative humidity and temperature controls (AIHA, 2003). In healthcare facilities, ultraviolet lighting and negative pressure rooms may also be used to interrupt long-distance transmission. Engineering controls also include measures to increase the space between people (e.g., how far apart desks are placed in schools (Feigin, 1982) or chairs in medical clinic waiting rooms); to prevent splashing from persons coughing or sneezing (e.g., glass enclosures in the triage area of emergency departments, or at cashiers' cubicles); and to facilitate hand hygiene (e.g., the placement of sinks outside patient rooms in hospitals). Engineering controls will minimize exposure to any infectious agent and are an important component of infection prevention programs in institutions.

The biggest benefit of engineering controls is the fact that their effectiveness is not dependent on individual practice. Many of these measures are most effectively implemented during the original design and planning stages for new buildings; however, the SARS outbreak in Toronto demonstrated that many can also be retro-fitted in emergency situations (Loutfy, 2004).

Administrative Controls

Administrative controls are procedural and behavioral measures such as hand hygiene, respiratory etiquette, and other basic practices to prevent the transmission of organisms (called Routine Practices in Canadian Healthcare Facilities) (PHAC, 1999; CDC, 2007). Administrative controls also include measures to identify individuals who are likely infected and who require separation from others; personal protective measures for caregivers; and education and training for all persons who must implement these measures. Effective implementation of such administrative controls has been shown to be effective in preventing disease and controlling outbreaks due to many pathogens, in both healthcare and non-healthcare settings (Christie, 1995; Rooney, 2004; Mayhall, 1996).

Administrative controls have two important limitations. The first is that individual adherence to preventive practices is needed for success. Achieving such adherence may be difficult. It requires, at a minimum, an institutional/societal commitment to a culture of safety, adequate education of individuals regarding necessary practice, and the engagement of users/practitioners in the design and implementation of preventive programs (Yassi, 2004; Possami, 2007). In some circumstances caregivers may choose to put themselves at risk. For instance, a healthcare worker who feels that personal protective equipment is preventing best patient care, or a parent caring for an infected small child, may chose not to wear their protective equipment in the interest of providing better care.

A second limitation of administrative controls is the difficulty of identifying persons who are infectious. Studies have repeatedly shown that, in outbreaks, most transmission of infection is from persons who are not recognized as having the disease (Huang, 2007), and modeling studies have suggested that improving identification of infectious persons is usually the most effective means of improving control programs (Nicas, 1998). Although it is often believed that influenza is relatively easy to diagnose, two surveillance systems in Canadian hospitals have recently shown that more than 20 per cent of patients with influenza are not believed at admission to have any infection (McGeer, 2007). In addition, transmission of infection from asymptomatic persons, and from persons incubating influenza but not yet symptomatic, has been described (Pettit, 1936; Sheat, 1992). Accounts of such transmission are very rare; however, it is important to note that, like long-distance transmission, detecting transmission from asymptomatic infection is extremely difficult for a disease as common as influenza. During a pandemic, the greatest limitation on control measures directed at barriers between infected and uninfected persons will be the recognition of those who are infected, and capable of spreading disease.

Personal Protective Equipment

Personal protective equipment (PPE) is considered the "last line of defense" against exposure. In general, the engineering and administrative controls are considered to be more important in preventing occupational exposures. However, these control measures may not be in place in all situations, or may not be 100 per cent effective. Therefore, PPE supplements engineering and administrative controls.

Personal protective equipment is traditionally defined as specialized clothing or equipment personally worn by an individual to protect against a hazard. It includes such things as goggles, gloves, gowns, surgical masks and respirators.

> *Personal protective equipment is not a substitute for good engineering, work practice, and administrative controls, but should be used in conjunction with these controls to provide for a safe and healthy workplace.* *CDC, 2007.*

The effectiveness of PPE will depend on the safety culture, supervision, and on an individual's willingness to properly wear the clothing or equipment as needed. These factors can be addressed through an effective health and safety program involving education and training. More than either of the other two measures within the hierarchy or control, PPE requires focused attention by the wearer on a day-to-day basis.

Personal Protective Respiratory Equipment

Personal protective respiratory equipment (PPRE) is a sub-category of PPE designed to block inhalation of hazardous airborne contaminants. Respiratory protection must be capable of preventing the inhalation of influenza viruses via the mouth or the nose. Many factors contribute to the effectiveness of PPRE in reducing influenza transmission and these must be assessed within the overall context of the hierarchy of control.

RESPIRATORS

Respirators protect the wearer by removing harmful contaminants from the air that might be inhaled or by providing a clean, independent source of air to the wearer. There are two types of filtering respirators: (i) for particulate matter, including liquids and solids; and (ii) for vapors and gases. Particulate respirators can be filtering facepiece respirators or elastomeric facepiece respirators with attached particulate filters. Examples of these are given in Table 2. The entire surface of a filtering facepiece respirator serves as the filter. The charge to the panel specifically referenced "N95 respirators," a commonly used term in Canada that refers to NIOSH-certified, disposable, particulate filtering, half-facepiece respirators. In order to remain within the charge, only this type of respirator will be discussed.

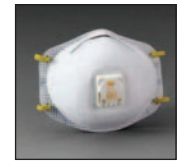
Classification of Protection Level

The criteria for the level of protection provided by a respirator are contingent upon four pre-requisites:

- the use of NIOSH-certified respirators in their approved configuration;
- individual fit testing;
- the respirator user understands and adheres to complete program requirements; and
- the respirator is always worn when exposure to infectious particles occurs.

The performance of a respirator depends on the filter efficiency (i.e., how well the filter collects airborne particles) and on fit (i.e., the amount of leakage between the facepiece and the face). NIOSH certifies the particulate filters according to three

Table 2
Examples of the Various Types of N95 Respirators
(©2000 Kimberly-Clark Worldwide Inc., used with permission)

Type of Respirator	Characteristic	
Particulate Filtering Facepiece	Cup Shaped, Non-vented	
Particulate Filtering Facepiece	Duck-Bill Shaped, Non-vented	
Particulate Filtering Facepiece	Cup Shaped, Vented	
Elastomeric Particulate Filtering Facepiece	Re-usable, Requires Cartridges	

classes: N-series (for "not resistant to oil"), R-series (for "resistant to oil"), and P-series (for "oil proof"). Each of these three classes of filters is also certified according to its level of filter efficiency (rated as 95 per cent, 99 per cent or 99.97 per cent efficient at removing particles 0.3 μm in diametre – the most penetrating particle size). For example, a filter marked N95 means that the filter is not resistant to oil and is at least 95 per cent efficient at removing test particulates at the most penetrating particle size. The specifics regarding filter efficiency are discussed in a subsequent section.

The level of protection afforded by a particular class of respirators for use by properly fitted and trained users is based on its "assigned protection factor" (APF). An APF is the minimum anticipated protection provided by a fit tested and properly functioning respirator. A NIOSH-certified N95 respirator is approved to provide a ten-fold level of protection – i.e., it carries an APF of 10 (OSHA, 2006). This means that the user will be exposed to no more than one-tenth of the outside concentration of airborne particles. A respirator with an APF of 50 (full facepiece, air-purifying respirator) means that a user could expect to inhale no more than one-fiftieth of the airborne contaminant. There are two methods by which respirator fit is assessed – qualitative fit tests and quantitative fit tests. APFs are based on data obtained through quantitative fit testing of respirators under actual use conditions in the workplace or under simulated conditions in a laboratory setting. These are termed workplace protection factors and simulated workplace protection factors, respectively (NIOSH, 2004).

Properties and Roles of Respirators

For particulate respirators, filters remove the contaminant particles from the air as they pass into the respirator. A common misconception regarding filter materials is that they act as sieves thereby eliminating particles based on particle size alone. In fact, filters are a "mat" of fibers. The air moves through the mat in a non-linear fashion, bringing the particles into contact with the fibers. Large particles will be collected either by inertial impaction – since large or heavy particles cannot follow the air streamlines – or by interception – i.e., particles brought into contact with the fibers. Small particles will be collected by diffusion, or random movements around the streamlines. Studies of filter efficiency have shown the most penetrating particle size to be between 0.1 and 0.3 μm depending on the air velocity through the filter (Figure 5). Electrostatic filters contain charged fibers that collect both large and small particles and offer advantages such as less breathing resistance and a more effective collection mechanism. Nearly all commercially available N95 respirators are constructed of electrostatically charged filter material.

It should be noted that when conducting certification tests, non-idealized (worst-case) conditions are used. This means that penetration is measured for neutral

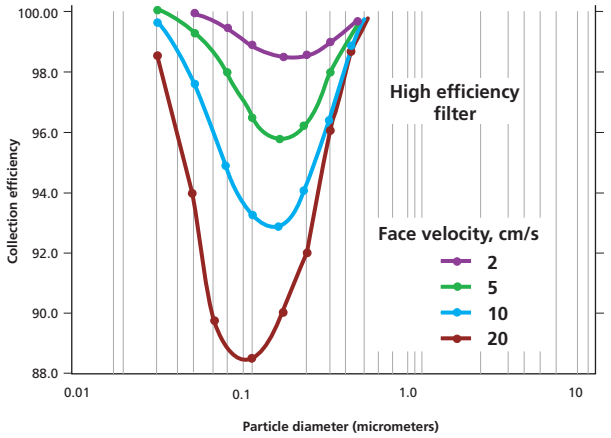


Figure 5
Effect of face velocity on collection efficiency and most penetrating particle size (NIOSH, 2006)

particles with the most penetrating particle size diametre. Thus an efficiency of 95 per cent means that for particles greater than or less than the most penetrating particle size, nearly 100 per cent of the particulate matter is collected by the filter.

A recent study by Balazy *et al.* (2006) explored the filter penetration in the nanoparticle range. The study raised the possibility that some N95 respirators would not filter at the required level particles in the 40 nm to 80 nm (going down to an efficiency of approximately 94 per cent instead of the required 95 per cent at a flow rate of 85L/min). Since influenza viruses are above that size range (80 nm to 120 nm) it appears to have little bearing on influenza control, but the study will have to be kept in mind when dealing with small viruses. Further studies will be required to clarify this issue.

Particle Release by Filters

Transmission of infectious material could possibly occur as a result of release of the trapped particles back into the surrounding environment or the improper handling of respirators. There are very few studies that examine particle release from the filter (Qian, 1997; Richardson, 2006). In one study, heavily loaded filters (10^5 particles/cm^2) showed extremely low release (0.002 per cent) at the low velocity that is characteristic of normal breathing. At higher velocities (sneezing or coughing), one per cent of particles 3 μm in size and six per cent of particles 5 μm in size were reported to be released. In general, it was shown that the percentage release of trapped particles increases in a way that is roughly proportional to the square of

both the particle diametre and the exhalation velocity. Release was shown to occur from the front layer of the filter with thicker filters exhibiting a lower percentage release. These studies suggest that particle release by filters is insignificant and unlikely to be of concern.

Respirator Doffing

A second area of concern is inadvertent infection resulting from improper handling of a contaminated respirator when it is being taken off ("doffing"). The concern with doffing involves the contact with the contaminated surface of the respirator while removing the device after use. There are currently no published studies regarding the handling of used filters. Therefore, it is unknown whether or not there is a risk associated with handling respirators or masks exposed to infected persons. The discussion of contact transmission in Chapter 2 concluded that the lack of studies regarding indirect transmission does not permit contact to be ruled out as a potential mode of transmission, nor is the panel able to rank the relative importance of contact transmission in the overall risk of influenza transmission.

MITIGATING FACTORS

The theoretical ability of a properly selected respirator to protect the wearer from inhalation of infectious material does not always equate with its "real world" effectiveness. Various factors can diminish PPRE's role within the overall hierarchy of controls. They need to be taken into consideration when evaluating the incremental contribution of respirators to preventing influenza transmission.

Design and Quality of Respirators

Because small particles are carried on air currents and can be entrained around respirators during inhalation, the major factor affecting the efficacy of a respirator in preventing inhalation of tracheobronchial and alveolar-sized particles is the adequacy of the seal between the respirator and the user's face (the "fit"). Disposable, half-facepiece filtering N95 respirators vary substantially in the quality of fit that is provided to different facial structures. The fit of some respirators to an average face without fit testing can be as good, and sometimes better than the fit of others after fit testing (Coffey, 2004).

Fit Testing/Checking

Achieving the best seal between a disposable, half-face respirator and the user's face requires training of the user, and checking that the overall shape of the respirator is adequate for that particular user. Because no one respirator will fit all types of faces, fit testing of users prior to stockpiling is needed in order to best

decide on the distribution of respirators in the stockpile. For infrequent users, or those who have not recently received training, re-training prior to use during a pandemic will be needed. Both adequate training of individuals in assessing the fit of the respirator each time it is used, as well as qualitative or quantitative fit testing of individuals have been shown to improve facial fit. Most regulatory agencies and jurisdictions mandate that fit tests be conducted on an annual basis.

Respirators are designed specifically to ensure capture of particles in the size range that can be inhaled into the respiratory tract, including the entire range referred to as "inhalable" which includes nasopharyngeal, tracheobronchial and alveolar-sized particles. A non-fit-tested respirator allows gaps between the PPRE and the user's face that inhalable particles can easily pass through, thereby bypassing the filter. Clearly, this would compromise the ability of the respirator to serve as a PPRE.

A recent publication by Duling *et al.* (2007) examined the level of protection afforded by fit tested and non-fit-tested respirators. This study reported an assigned protection factor (APF) of 4.6 when respirators that did not fit properly were included in the dataset. The APF increased to about 10 when respirators that did not pass qualitative fit tests were removed and the APF increased even further, to 14.5, when respirators that did not pass the quantitative test were removed.

User Adherence

A respirator cannot protect a wearer who does not know when to use it or how to wear it. Recent studies carried out in Canada, the United States and the United Kingdom have shown that user compliance within institutional protocols for PPRE is less than 100 per cent. Adherence is known to be associated with effective training programs and with workplace safety climate.[16] Workers who have been engaged in the planning steps of institutional protocols, and feel properly trained in the use of their protective equipment, are far more likely to comply with institutional safety policies (Yassi, 2004; DeJoy, 1996).

Comfort and Performance

The response of individuals to the use of respirators involves both physiological and psychological factors (Harber, 1988). The dominant physiological effect is the increase in inspiratory resistance brought on by the airflow resistance provided by the respirator. Relative to other types of respirators, the N95 particulate facepiece

16 The safety culture is the organizational commitment to safety (policies, training, provision of PPE). The safety climate is the collective employee perception of that safety culture (Gershon, 2007; Yassi, 2004). It is the safety climate that has been shown to be a far more reliable predictor of compliance.

respirators discussed in this document pose minimal physiological stress. NIOSH dictates that, for these respirators, the maximum allowable breathing resistance level is 35 mm water pressure for inhalation and 25 mm pressure for exhalation at a ventilation minute volume of 85 L/min (high work activity). As long as breathing resistance is maintained below these maxima, the physiological burden imposed by wearing a respirator is minimal (OSHA, 2006). Most healthcare work can be classified as "low level" work for purposes of respirator evaluation, with typical minute volumes averaging 15 L/min. At this level, physiological stress is not significant.

Physiology alone however cannot adequately explain respirator tolerance. The interplay of various psychophysical sensations such as increased facial skin temperature created by a respirator can overwhelm the capacity of some workers to tolerate the device (McLellan, 2000; Harber, 1989). Morgan *et al.* (1983) reported that 10 per cent of test subjects experienced dizziness, claustrophobia or anxiety attacks while exercising during respirator use. Psychophysical-related discomfort factors are expected to be more significant in workers who are only required to wear respirators occasionally. In healthcare, workers may also perceive that use of a respirator is interfering with their ability to communicate with a patient, or otherwise provide patient care, factors that may interfere with adherence.

SURGICAL MASKS

Surgical masks are not certified to serve as respiratory tract protection for their wearer and are not considered to be PPRE by occupational health and safety practitioners. Rather, surgical masks and other "medical" masks are intended, from an Occupational Health and Safety perspective, to be worn by health professionals during surgery and at other times to catch the bacteria shed in liquid droplets and aerosols from the wearer's mouth and nose – i.e., they are designed to protect the patient and not the wearer. Surgical masks may play a role in protecting against the spread of influenza by minimizing the amount of infectious material that is released into the environment. This can occur because covering the mouth and nose of an infected person will obviously reduce the amount of material expelled from the mouth and nose during talking, coughing or sneezing.

Surgical masks have also been used for decades to prevent the wearer from exposure to infectious large droplets and from contamination of oral/nasal membranes via the contact route. Indeed, essentially all current guidelines for the control of seasonal influenza recommend that surgical masks be worn by healthcare workers with the aim of preventing them from acquiring influenza (CDC, 2007). The

relative importance and the effectiveness of surgical masks used in this fashion as a control measure are unknown, as they are typically employed simultaneously along with other control measures such as vaccination, antivirals, handwashing, and contact precautions.

Surgical masks may provide an incremental benefit in reducing transmission of influenza by minimizing or preventing body fluid splashes and contact of contaminated hands to the mouth and/or nose.

The biggest limitation of surgical masks is that they do not provide an effective seal to the face, thereby allowing inhalable particles access to the respiratory tract. In addition, the efficiency of the filter of surgical masks in preventing penetration of tracheobronchial or alveolar-sized particles has been found to vary from 2 to 92 per cent under experimental conditions (Mitakakis, 2002; Brosseau, 1997; McCullough, 1997; Willeke, 1996; Tuomi, 1985; Cooper, 1983). The degree of protection against nasopharyngeal-sized particles is unknown. Some of these particles may impact on the filter and not penetrate, but others can be drawn through the gaps between the mask and the wearer's face.

SEASONAL VS. PANDEMIC INFLUENZA

Although the protective capacities of PPRE and other interventions apply to both seasonal and pandemic influenza, during a pandemic the absolute benefit of these interventions in preventing disease transmission may be greater than in seasonal influenza because:

- a high attack rate is anticipated in a pandemic because the majority of the population will have no immunity;
- this lack of immunity may also make people more susceptible to a smaller inoculum of virus;
- viral shedding by infected persons may be increased thereby contributing to transmission;
- pandemic disease severity, while unpredictable, is likely to be worse than most seasonal outbreaks;
- vaccine will not likely be immediately available; and
- the efficacy and availability of antivirals may be limited.

CONCLUSIONS ON PROTECTIVE MEASURES AGAINST INFLUENZA TRANSMISSION

The following summarizes the consensus opinion reached by the panel:

1. The primary elements of protection against influenza transmission are engineering and administrative controls. When exposure to an infected person is required or unavoidable, PPRE is the final layer of protection.

2. N95 respirators protect against the inhalation of nasopharyngeal, tracheobronchial and alveolar-sized particles.

3. Surgical masks worn by an infected person may play a role in the prevention of influenza transmission by reducing the amount of infectious material that is expelled into the environment.

4. Both surgical masks and N95 respirators offer a physical barrier to contact with contaminated hands and ballistic trajectory particles.

5. The efficiency of the filters of surgical masks to block penetration of alveolar and tracheobronchial-sized particles is highly variable. When combined with the inability to ensure a sealed fit, these factors suggest that surgical masks offer no significant protection against the inhalation of alveolar and tracheobronchial-sized particles.

6. The efficiency of the filters of surgical masks to block penetration of nasopharyngeal-sized particles is unknown. The lack of a sealed fit on a surgical mask will allow for the inhalation of an unknown quantity of nasopharyngeal-sized particles.

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APPENDIX A – COMPREHENSIVE GLOSSARY

administrative controls: Procedural and behavioral measures that include, for example: identification of individuals who are likely infected; hygiene procedures; education and training; medical surveillance of at-risk health care workers; and use of antivirals and vaccines.

aerodynamic diametre: Term used to standardize how particles of different shapes and densities behave in the air and how fast they will fall to the ground under the combined influence of air resistance and gravity (settling velocity). A particle has an aerodynamic diametre "'d" if its settling velocity equals that of a spherical water droplet of diametre "d".

aerosol: The suspension in air (or in a gas) of solid or liquid particles, small enough to remain airborne for prolonged periods of time.

aerosol-generating procedures: Medical procedures that facilitate airborne transmission of influenza. Such procedures may induce coughing, which increases the likelihood of droplet nuclei being expelled into the air. Examples of aerosol-generating procedures include: aerosolized medication treatments (e.g., salbutamol), diagnostic sputum induction, bronchoscopy, airway suctioning, endotracheal intubation.

airborne transmission: Traditional infection control term for transmission that occurs when bacteria or viruses travel on dust particles or on small respiratory droplets that may become aerosolized when people sneeze, cough, laugh, or exhale. They hang in the air much like invisible smoke. They can travel on air currents over considerable distances.

alveolar-sized particles: Particles having a diametre of less than approximately 10 μm which are usually deposited in the alveoli ("pulmonary or alveolar region").

assigned protection factor (APF): A measure of the anticipated level of workplace respiratory protection that would be provided by a properly functioning respirator, or class of respirators, to properly fitted and trained users.

ballistic particles: Particles with a mean aerodynamic diametre of greater than 100 μm. They are predominantly affected by gravity (as opposed to air resistance) and follow so-called "ballistic trajectorie."

contact transmission: Transfer of virus from an infected individual to a potential host either by direct physical contact or indirect contact (e.g., via touching contaminated surfaces).

droplet: A droplet is a specific type of particle. It refers to a small volume of liquid that is expelled during breathing, talking, sneezing or coughing which contains assorted biological/biochemical components.

droplet nuclei: Particles that are formed by evaporation of droplets leaving non-volatile components.

elastomeric facepiece: A reusable respirator where the facepiece is cleaned and reused but the filter cartridges are discarded and replaced when they become unsuitable for further use.

engineering controls: Physical controls put in place in an overall exposure plan; these include such things as ventilation requirements, ultraviolet lighting, relative humidity and temperature control and negative pressure rooms.

filter efficiency: The ratio of the number of particles trapped by a filter relative to the total number of particles found in the air upstream of the filter.

filtering facepiece: A negative pressure particulate respirator with a filter as an integral part of the facepiece or with the entire facepiece composed of the filtering medium.

fomite: Any inanimate object or substance capable of carrying infectious organisms (such as germs or parasites) and hence transferring them from one individual to another.

haemagglutinin: A protein found on the surface of the influenza viruses.

hierarchy of control: A range of hazard control methods arranged in order of implementation effectiveness.

HVAC: Heating, ventilation and airconditioning.

inhalation transmission: A mechanism of transmission of infectious particles via inhalation. This includes particles ranging in size from 0.1 to 100 μm and therefore would encompass the classical airborne AND droplet modes of transmission.

long-range transmission: Inhalation transmission of the virus at distances greater than approximately two metres.

micrometre (μm): 10^{-6} metres

mode of transmission: The method by which influenza is spread to other persons.

most penetrating particle size (MMPS): The size of the particles that achieve maximum penetration of the filter medium. Particles that are smaller or larger than the most penetrating size exhibit a lower rate of penetration.

nasopharyngeal-sized particles: Particles having diametres in the range of greater than 20 to 100 μm which are usually deposited in the upper respiratory tract above the larynx including the inner nasal passages ("nasopharyngeal region").

particle: A generic term for a small mass of either liquid or solid.

personal protective equipment (PPE): Clothing and other work accessories designed to create a barrier against workplace hazards. Examples include safety goggles, gloves and face shields.

personal protective respiratory equipment (PPRE): A sub-category of PPE designed to block inhalation of hazardous airborne contaminants.

prophylaxis: Prevention of disease or of a process that can lead to disease.

protease: An enzyme that hydrolyzes (breaks down a bond and adds water) proteins, especially to peptides.

qualitative fit test for a respirator: A pass/fail method that uses the wearer's sense of smell or taste to detect face seal leakage of a test agent during a set of test exercises.

quantitative fit test for a respirator: Quantitative tests that give an objective assessment of facial fit and provide a direct numerical result called a "fit factor."

respirator: A fitted device that protects the wearer against inhalation of harmful contaminants – i.e., it protects the wearer from others who are or might be infected. N95 respirators range in cost from $0.40 to $4.00.

short-range transmission: Contact transmission or inhalation transmission of the virus at distances less than and including two metres.

surgical mask: An unfitted device intended to reduce transfer of potentially infectious bodily fluids from an infected individual. Surgical masks range in cost from range in cost from $0.05 to $2.00.

tracheobronchial-sized particles: Particles having diametres in the range of 10 to 20 μm which are usually deposited below the larynx as far as the terminal bronchi ("tracheobronchial region").

virion: The complete virus particle that is structurally intact and infectious.

APPENDIX B – REVIEWS CONSIDERED & RELEVANT LITERATURE

Reviews Considered for Assessment of Evidence

Brankston, G., Gitterman, L., Hirji, Z., Lemieux, C. & Gardam, M. (2007) "Transmission of Influenza A in Human Beings". *Lancet Infectious Diseases*, 7, pp. 257-265.

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Janssen, R. (2005) *A Scientific Review - the Influenza Pandemic: Airborne vs. Non-Airborne Transmission and Considerations for Respiratory Protection*, Vancouver:WorkSafe BC.

•This report has not been published. For reproductions, please contact Bob Janssen at: Bob.Janssen@worksafebc.com

Jefferson, T., Foxlee, R., Del Mar, C., Dooley, L., Ferroni, E., Hewak, B., Prabhala, A., Nair, S., Rivetti, A. (2007) "Interventions for the Interruption or Reduction of the Spread of Respiratory Viruses (Review)" *The Cochrane Library*, 4, 1-56.

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Relevant Literature

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