ABSTRACT Infectious diseases are still among the leading causes of death worldwide due to their persistence, emergence, and reemergence. As the recent Ebola virus disease and MERS-CoV outbreaks demonstrate, the modern epidemics and large-scale infectious outbreaks emerge and spread quickly. Air transportation is a major vehicle for the rapid spread and dissemination of communicable diseases, and there have been a number of reported outbreaks of serious airborne diseases aboard commercial flights including tuberculosis, severe acute respiratory syndrome, influenza, smallpox, and measles, to name a few. In 2014 alone, over 3.3 billion passengers (a number equivalent to 42% of the world population) and 50 million metric tons of cargo traveled by air from 41,000 airports and 50,000 routes worldwide, and significant growth is anticipated, with passenger numbers expected to reach 5.9 billion by 2030. Given the increasing numbers of travelers, the risk of infectious disease transmission during air travel is a significant concern, and this chapter focuses on the current knowledge about transmission of infectious diseases in the context of both transmissions within the aircraft passenger cabin and commercial aircraft serving as vehicles of worldwide infection spread.

CABIN ENVIRONMENT, INFECTIOUS DISEASE RISK, AND CONTROL MEASURES

The air provided to passengers and crew on commercial jet aircraft is typically a combination of conditioned external (ambient) air that has been diverted to the cabin from the engine compressor stages, and air that is taken from the cabin, filtered, and recirculated. The first filter of recirculated air traps the largest particles. Then, on most modern aircrafts, the air passes through high-efficiency particular air (HEPA) filters before reentering the passenger cabin. The most efficient HEPA filters capture 99.97% of particles between 0.1 and 0.3 micrometer and 100% of the larger particles. In addition, the ultra-small contagion also gets captured by Brownian and electrostatic forces. The environmental control system is designed to minimize the introduction of harmful contaminants into the cabin and to control cabin pressure, ventilation, and temperature. Most commercial aircraft provide 10 to 15 air changes per hour of the passenger cabin depending upon the aircraft type, as the original cabin air is progressively diluted with incoming ambient air. Cabin airflow is principally side to side and compartmentalized into four- to seven-seat rows within the passenger cabin, thereby limiting longitudinal (front to back and vice versa) cabin contamination. However, although the principle is side-to-side airflow, evidence employing computational fluid dynamic modeling in a mockup full-sized aircraft cabin section suggests that airflow patterns can be influenced by many factors including seat and cabin geometry, occupancy density, and thermal loads of passengers and equipment.

Individual risk of infection within the aircraft cabin, or generally any enclosed space, involves many factors, including chance, source strength (generation rate of infectious agent), exposure (proximity to the source and duration of the exposure), and ventilation within the enclosed space (Fig. 1). Infections during flights can be transmitted not only by aerosols that remain airborne and can be inhaled, but also by large droplets that settle on surfaces or by direct contact with secretions, body fluids, or contaminated surfaces. Current risk assessment protocols used by public health authorities for in-flight infectious disease exposures are typically based
Determinants of risk of infection within a confined space. doi:10.1128/microbiolspec.IOL5-0009-2015.f1

upon the proximity of the fellow passenger to the index passenger and the duration of the exposure, exemplified by studies of transmission of Mycobacterium tuberculosis on board an air flight which is limited to close contacts and a flight time of >8 h. This protocol is based upon experiences with previous tuberculosis (TB) exposures/outbreaks aboard commercial flights and has become conventional wisdom for investigating most aircraft-related infectious disease incidents. However, it is fundamentally flawed since it does not consider ventilation—a key component of infection control, particularly for diseases with airborne transmission—and variation has been reported. For example, the largest in-flight SARS outbreak (Air China flight 112) involved passengers seated as far as seven rows from the index passenger, and the flight was only 3 h long. Multiple mathematical models of probability of infection are available, and perhaps the most commonly used is the Wells Riley calculation, which has been used to study both tuberculosis and measles outbreaks. A major limitation of the Wells Riley calculation is that it does not consider ventilation. Newer mathematical formulas developed by Sze To and later modified by Chu Lin take ventilation into account and might be the more accurate formula to be used for further risk analysis studies.

Proper ventilation within any confined space decreases the concentration of airborne organisms in a logarithmic fashion. In the case of recirculated systems, such as on modern commercial aircraft, where various fractions of air from the passenger cabin are recirculated and mixed with fresh air, this relationship holds only if the recirculated air undergoes filtration through HEPA filters. Although the practice of removing infectious airborne particles from recirculated air through HEPA filtering is well established as an effective infection control measure, the use of HEPA filters within commercial aircraft is neither required nor regulated by the Federal Aviation Administration or its British (Civil Aviation Authority) and European (Joint Aviation Authority) counterparts. A 2004 survey of major U.S. commercial air carriers by the U.S. Government Accountability Office found that 15% of large commercial aircraft within the U.S. domestic fleet did not routinely use HEPA air filtering and that nearly 50% of smaller regional commercial aircraft did not. Incorporating epidemiological data into risk assessment mathematical models may provide insight into how proximity and ventilation influence disease transmission aboard commercial aircraft.

A major public health challenge is created by the possibility of travel from one region or continent to another within a 24-h period, a period of time which is shorter than the incubation period of most contagious diseases. This allows for most travelers infected with a contagious disease to pass through entry screening undetected and reach their destination before they become symptomatic. Although many countries practice entry screening, studies reveal that this is very ineffective. Khan et al.’s retrospective evaluation of entry and exit screening of airline travelers during the 2009–2010 H1N1 pandemic states that entry screening is an anachronism and says interventions to mitigate the international spread of infectious disease—whether through preparedness or response—would have the greatest global impact if implemented as close as possible to the sources of any future epidemic threats (i.e., exit screening). Recent modeling for the current Ebola outbreak also found exit screening to be the most efficient and economical means of screening.

REPORTED OR POTENTIAL IN-FLIGHT AND FLIGHT-RELATED OUTBREAKS

Tuberculosis

One third of the world’s population are infected with TB. TB and, especially, the emergence of multidrug-resistant TB and extremely drug-resistant TB have raised much concern about international spread. TB is spread primarily through droplet nuclei (i.e., residual of large droplets containing microorganisms that have evaporated to a size of <5 mm) that are generated and released during talking, coughing, sneezing, vomiting, or aerosolization of feces. Unlike large droplets (which travel no further than 1 m), these nuclei become aerosolized, remain suspended in air for indefinite periods, and are capable of dispersing widely, depending on
environmental conditions. When inhaled, droplet nuclei are likely to bypass trapping mechanisms of the upper airways and are carried deep into the lungs, where in the case of TB, even a single microorganism has the ability to initiate infection. The risk of TB infection (defined as conversion from a negative to a positive tuberculin skin test) ranges from 1 in 100,000 people for casual social contact to 1 in 5 for dormitory contact to 1 in 3 for home and close work contact. There is currently little evidence to suggest that any particular strain of *M. tuberculosis* would be transmitted more readily than others. However, the consequences of infection with drug-resistant strains are potentially more complex in terms of treatment, outcomes, and cost.

There have been several incidents of TB exposure aboard commercial aircraft. A systematic review of TB and air travel published in 2010 found 13 published reports in which only two studies had evidence of TB transmission. Most flights investigated were longer than 8 h (range 2.5 to 14 h). A total of 38 index cases with pulmonary tuberculosis were identified: one rifampicin-resistant, one isoniazid-resistant, four cases with multidrug-resistant TB, and one with extremely drug-resistant TB. A total of 2,761 passengers and crew members were screened in the 53 flights investigated, but only 10 were shown to have tuberculin skin test conversion. No cases of active TB resulting from transmission during air travel have been reported thus far. The probability that a person transmits TB is determined by a number of factors including sputum-smear status, duration and nature of contact, shared air space or ventilation, and susceptibility of exposed people. Susceptibility to infection and disease is increased in immunocompromised people (e.g., HIV-infected), infants, and young children less than 5 years of age. Definitive assessment of transmission risk during flights and determination of the effectiveness of contact-tracing efforts will require comprehensive cohort studies. Although the risk of TB infection during a commercial air flight is low, an increase in travel and trade involving countries endemic for TB including multidrug-resistant TB and extremely drug-resistant TB could potentially increase this risk in the future.

**Influenza**

Influenza type A viruses are categorized into subtypes based on the type of proteins on the surface of the viral envelope: hemagglutinin and neuraminidase. There are 18 known types of hemagglutinin and 11 known types of neuraminidase, and although during the last few years only a few strains have been in global circulation, 198 combinations of these proteins are possible. Influenza A undergoes constant antigenic evolution, referred to as antigenic drift or shift that allows them also to re-infect individuals who have had previous infections. Influenza viruses are transmitted by the respiratory route, and small-particle aerosols are generated by infected humans; experimental studies in humans have shown that very small amounts (about 5 infectious particles) may be sufficient to infect humans by the aerosol route. Outbreaks while aboard commercial air flights are uncommon with modern ventilation systems. In 1979, a jet airliner with 54 people aboard was delayed on the ground for 3 h, during which the airplane ventilation system was inoperative. Within 72 h, 72% of the passengers became ill with symptoms of cough, fever, fatigue, headache, sore throat, and myalgia. The ill index case had influenza A N3N2, and the clinical attack rate among the others varied with the amount of time spent aboard. Since this outbreak there has been occasional human-to-human spread of influenza aboard commercial flights, and several cases during the influenza H1N1 outbreak in 2009–2010 were reported.

The current effective protection against influenza in general is hand washing/disinfectant after touching any potentially infected surface, receiving yearly vaccination of the current circulating strain, and potential chemoprophylaxis for exposed individuals in outbreak settings. The general advice of not boarding an aircraft while sick should be applicable for both crew and passengers. A study showed that crew members often fly while ill, and vaccination rates of crew members were only 20 to 27%. Wearing a face mask during a flight has been shown to decrease acquisition of influenza, but this is largely impractical, especially during long flights.

**SARS and MERS**

Severe acute respiratory syndrome (SARS) and Middle Eastern respiratory syndrome (MERS) are caused by two different coronaviruses and thought spread by droplet transmission and/or direct person-to-person contact. SARS was first identified in the southern People’s Republic of China in November 2002, with the last known case of person-to-person transmission in July 2003. Close to 800 deaths in 26 countries on five continents occurred during the 2002–2003 SARS outbreak. The World Health Organization (WHO) estimates that 6.5 passengers per million traveled on commercial flights originating from regions of active transmission while symptomatic with probable SARS during the height of the outbreak. A total of 40 flights carried 37 probable SARS index cases during the outbreak, resulting in 29 probable on-board secondary cases. Air China flight 112
represented the largest on-board transmission event, with 22 individuals developing a probable case of SARS as a consequence of being aboard the flight, and this incident was likely a consequence of the index passenger being a super-spreader, an individual able to spread the infection to a disproportionately high number of secondary contacts.

The MERS coronavirus (MERS-CoV) was first reported in Saudi Arabia in September 2012 from a patient with pneumonia. Within a few days, the same virus was detected in a Qatari patient receiving intensive care in a London hospital, and it has so far caused 178 laboratory-confirmed cases and 76 deaths. MERS-CoV has an epicenter in Saudi Arabia, and although cases have been reported from Italy, France, Germany, Tunisia, and the United Kingdom, it has not become a major pandemic outbreak. Although MERS-CoV has a low basic reproductive number, modeling suggests that as a result of in-flight transmission, one infectious individual could result in multiple simultaneous outbreaks in several different countries. No vaccine exists for either SARS or MERS, and prompt identification and isolation remain the most important actions available to prevent in-flight transmission should SARS reemerge or MERS surge.

**Measles and Rubella**

Measles transmission during commercial air travel is uncommon, but it remains a concern because it is a highly contagious viral infection that can be transmitted by direct contact with infectious droplets as well as by airborne spread. Another reason for measles being a high-risk virus for transmission during commercial air travel is the virus’s ability to transmit during the asymptomatic prodromal phase. Before the recent measles outbreak in the United States, most reported cases were a result of importations from developing countries. It is estimated that from 1996 to 2000, 30% of all imported cases occurred in people who flew while symptomatic. A case of measles transmission during a commercial flight in Brazil was reported, resulting in two secondary confirmed cases, and two clusters of measles associated with travel by air were described in The Netherlands in 2007.

Countries like Australia that have successfully interrupted local transmission of measles virus face repeated importation of measles by travelers who are infected overseas. A total of 327 measles cases were notified in Australia during 2007 to 2011. Forty-five people flew on a total of 49 flights (13 domestic and 36 international) while infectious. Most index cases were Australians who acquired their infection while traveling overseas, with a minority being overseas visitors who acquired their infection before traveling to or within Australia. Twenty secondary cases occurred among people on 7 of the 49 flights. Nine people identified as secondary cases were seated in the same row or within two rows of the index case; 11 were outside these rows, 1 of whom was a member of the cabin crew.

Measles transmission during air travel in the United States from 2008 to 2011 was investigated and included 74 case travelers on 108 flights. Information on 2,673 (79%) of 3,399 passenger contacts was provided to health departments; 9 cases of secondary measles were reported. Even in countries like Finland, which has vaccination coverage of >95%, and the 5% of unprotected citizens are protected by herd immunity, 47 cases occurred from 1996 to 2012 as a result of infection during traveling and resulting secondary cases in the nonimmune community, described by Kantele et al. This illustrates that lack of immunity is the greatest risk factor for contracting measles during travel, and therefore, adequate vaccination before international travel, particularly for children age 6 months or older, is critical.

Rubella transmits by person-to-person contact or droplets shed from the respiratory secretions of infected people. Rubella has not been reported to occur during in-flight transmission, but given that it is highly contagious, it is a disease of potential risk of spread and warrants contact tracing within two rows of the index case.

**Neisseria meningitidis**

*N. meningitidis* colonizes mucosal surfaces of the nasopharynx and is transmitted through direct contact with large-droplet respiratory secretions from patients or asymptomatic carriers. A case of air-travel-associated meningococcal disease is defined as a patient who meets the case definition of meningococcal disease within 14 days of travel on a flight of at least 8 h duration. In-flight transmission is of concern, and travelers flying to the haj pilgrimage or to the sub-Saharan meningitis belt are at particular risk for acquiring meningococcal disease. However, only two cases of probable air-travel-associated transmission have been described. The two cases were passengers on the same 14.5-h-long international flight from Los Angeles to Sydney. The investigation at the time could not identify direct contact between the two cases either before, during, or after the flight, but they were both serogroup B with the same allelic profile. In addition, there were no serogroup B meningococci with the same subtype and serosubtype detected among invasive isolates of *N. meningitidis* identified during the same year in Australia. Chemoprophylaxis was provided to fellow passengers seated within two rows of the index cases.
Ebola Virus Disease and Other Viral Hemorrhagic Fevers

On August 8, 2014, the WHO declared the 2014 West African Ebola epidemic a public health emergency of international concern given its potential for further international spread. The 2005 International Health Regulations (IHR) describe the guiding principles by which 196 participating countries are bound when responding to a public health emergency of international concern. The purpose and scope of the IHR are to “prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade.” In a recent *Lancet* article Bogoch et al. assessed the risks for international dissemination of Ebola virus via air travel during the 2014 West African outbreak. They used empirical data on global population mobility via commercial air travel and assessed the potential impact of flight cancellations and restrictions on risk of exportation and the efficiency of airport-based traveler screening interventions. Although the main countries of the current Ebola virus outbreak—Guinea, Liberia, and Sierra Leone—collectively account for only 0.04% of the world’s international air traffic, the majority of flights traveling to low- or lower-middle-income countries with low-resource medical and public health services may be unable to adequately detect and respond to an imported case of Ebola. Exit screening of travelers was found to be the most efficient mechanism to assess the health status of departing travelers, and widespread travel and trade restrictions were not recommended.

Only a few events of viral hemorrhagic fever cases during air travel are reported in the literature, with no documented infection in follow-up contacts. The CDC and European Center for Disease Control (ECDC) via the Risk Assessment Guidance for Infectious Diseases Transmitted on Aircraft project have published guidelines for risk assessment and tracing passengers with viral hemorrhagic fever who traveled on an airplane.

Diphtheria and Pertussis

Diphtheria is caused by infection with toxigenic strains of *Corynebacterium diphtheria* and is transmitted from person to person by respiratory droplets or direct contact with respiratory secretions, discharges from skin lesions, or rarely, fomites. Although diphtheria has not been reported in the United States since 2003, and no in-flight cases have been described, it remains a risk because it is endemic in many parts of the developing world, including some countries of the Caribbean and Latin America, Eastern Europe, Southeast Asia, and Africa, with a case-fatality rate of 10%.

Pertussis (whooping cough), caused by *Bordetella pertussis*, is highly contagious (attack rate of 80 to 90% of susceptible persons) and is transmitted from human-to-human contact via discharge from respiratory membranes or inhalation of infectious respiratory droplets that remain infectious for 3 to 5 days on fomites. Pertussis has a long incubation period (range of 4 to 21 days) and often nonspecific initial symptoms, making it difficult to report transmissions of the disease during flights—although it very likely occurs despite not being reported in the literature. With increasing incidence and widespread community transmission of pertussis, extensive contact tracing and broad-scale use of postexposure prophylaxis among contacts may not be an effective use of limited public health resources.

Mosquito-Borne Illnesses: Malaria, Dengue, Chikungunya, Yellow Fever, and West Nile Virus

Vector-borne diseases are very frequent causes of morbidity and mortality in many parts of the world, and the emerging and reemerging vector-borne infections can be transported globally by a commercial aircraft. Malaria cases occurring in and around airports all over the world in people who have not traveled to endemic areas, known as airport malaria, are evidence that malaria-carrying mosquitoes can be imported on aircraft. A case report of three *Plasmodium falciparum* malaria-infected patients in São Paulo during a 5-day period between August 31 and September 4, 1996, at a time and place where malaria transmission does not normally occur, led to an investigation that determined the infections were acquired as a result of an international flight from Lebanon to São Paulo. The flight included a 30-minute stop-over in Abidjan, Ivory Coast. During the epidemiological evaluation, it was found that each of the three patients had been seated in the first-class cabin, and the entomological investigation at the airport revealed the presence of four specimens of *Anopheles gambiae*, three in the first-class cabin and one in the luggage compartment. Attending physicians at the three hospitals where the patients were admitted did not consider malaria during their initial evaluation.

Rising rates of travel between malaria-free and -endemic countries has led to general patterns of increased rates of imported malaria over recent decades.
Due to infrequent encounters, imported cases can challenge health systems in nonendemic countries, with difficulties in diagnosis, misdiagnosis, and delays in treatment. Patterns in imported cases and airport malaria have been shown to be related to a combination of the numbers of travelers and the malaria risk at the destination, and these relationships will continue to evolve as new routes become established. In addition, we face a potential risk of spread of artemisinin-resistant malaria. Human movement via air travel is an important factor, and Huang and Tatem have published modeling of global air movement in relation to malaria-endemic areas. This important work can be used for risk prediction of imported malaria as well as to develop strategies for combating the disease.

The WHO has designated dengue a major international public health problem, and it is one of the most rapidly spreading mosquito-borne viral disease in the world. Dengue is transmitted between humans via the bite of infected *Aedes* mosquitoes, with humans serving as the main host. Even in the parts of the world where dengue is now rare, such as the United States and Europe, the mosquito vectors are still present. At least one of the two major vector species, *Aedes aegypti* and *Aedes albopictus*, is known to have established populations in 26 U.S. states. The ECDC gathered entomological and environmental mapping of the distribution and risk for *A. albopictus* in Europe and concluded that temperate strains of this species already exist and are likely to spread, with new populations becoming established in several parts of Europe. A published integrated quantitative model specifies the relative likelihood of the establishment of dengue in nonendemic areas based on infected passengers’ air travel patterns, and it also incorporates the principal mosquito vector distribution.

This model is also likely applicable to Chikungunya, which is transmitted to people through bites by *A. aegypti* and *A. albopictus* mosquitoes. Chikungunya is endemic in sub-Saharan Africa and South and East Asia, but has over the last years and months spread to having outbreaks in Southern Europe, the Caribbean, and very recently, the Americas. As of November 21, 2014, local transmission had been identified in 40 countries or territories in the Caribbean, Central America, South America, and North America, and it will likely continue to spread to new areas through infected people and mosquitoes.

Yellow fever virus (YFV) is found in tropical and subtropical areas in South America and Africa and is transmitted to humans primarily through the bite of infected *Aedes* or *Haemagogus* species of mosquitoes. In 2012 Johansson and Arana-Vizcarrondo et al. published a simulation of the global spread of YFV from a single urban outbreak started by infected airline travelers, based on the outbreak in Asunción, Paraguay, in 2008. By using simple probabilistic models, they found that local incidence, travel rates, and basic transmission parameters are sufficient to assess the probability of introduction and autochthonous transmission events. These models could be used to assess the risk of YFV spread during an urban outbreak and identify locations at risk for YFV introduction and subsequent autochthonous transmission.

West Nile virus is usually transmitted to humans by mosquitoes and is considered to be endemic in Africa, Australia, Asia, the Middle East, Europe, and in the past decade also in the United States. In 1999 a West Nile virus circulating in Israel and Tunisia was imported to New York, producing a large and dramatic outbreak that spread throughout the continental United States in the following years. The West Nile virus outbreak in the United States (1999–2010) highlighted that importation and establishment of vector-borne pathogens outside their current habitat represents a serious danger to the world.

“Disinsection” is a public health measure that is mandated by the IHR. It involves treatment of the interior of the aircraft with insecticides specified by the WHO. The IHR (2005) specify that states shall establish programs to control vectors that may transport a public health risk in the immediate vicinity of international ports, airports, and ground crossings. Although few countries now require that aircraft be disinfected, most countries reserve the right to do so and, as such, could impose a disinsection requirement should they perceive a threat to their public health, agriculture, or environment.

**MULTIDRUG-RESISTANT ORGANISMS**

With antibiotic resistance a worldwide concern, the potential risk of transmission of multidrug-resistant bacteria while aboard a commercial aircraft is of concern. In particular, travelers hospitalized during international travel and repatriated by commercial airlines could transmit multidrug-resistant organisms, for example, carbapenem-resistant *Enterobacteriaceae*, to other passengers or crew members. To date, there have been no published reports of commercial air travel–related outbreaks of nontuberculous multidrug-resistant bacteria.
BIOTERRORISM: SMALLPOX, ANTHRAX, AND PLAGUE

Smallpox poses one of the greatest risks as a biological weapon. Although the probability of an intentional release of smallpox may be small, were it to occur, the public health consequences would be considerable. Smallpox outbreaks have occurred from time to time for thousands of years, but the disease is now eradicated after a successful worldwide vaccination program. The last case of smallpox in the United States was in 1949. The last naturally occurring case in the world was in Somalia in 1977. After the disease was eliminated from the world, routine vaccination against smallpox among the general public was stopped because it was no longer necessary for prevention. Smallpox has been spread by virus carried in the air in enclosed settings, but generally, a direct and fairly prolonged face-to-face contact is required to spread smallpox from one person to another. Smallpox also can be spread through direct contact with infected body fluids or contaminated objects. Three cases of patients with smallpox while on board an aircraft was summarized in the ECDC’s risk assessment guidelines for infectious diseases transmitted on aircraft, but there have been no reported outbreaks or cases of secondary transmission. In 1970, a symptomatic index case that was thought to be suffering from dysentery had flown from Afghanistan to Denmark. After smallpox was diagnosed, a total of 550 contacts were isolated between day 8 and day 17 after the suspected contact. The patient eventually died, but no secondary cases occurred. In two other events dating back to the 1950s, passengers infected with smallpox were on board aircraft, but no transmission took place. Should such an event occur, the ECDC recommends comprehensive contact tracing, where all passengers and crew members should be traced.

Anthrax, Bacillus anthracis, is not transmitted by air from person to person but can act as a biological weapon if anthrax spores are deliberately released into the air. Inhalational anthrax is the most serious form of anthrax and carries a high mortality if not treated immediately. Other causes and routes of on-board transmission, e.g., through animal hides or other animal products brought into the cabin (not necessarily related to bioterrorism), may also lead to the infection of passengers with no history of animal exposure and should therefore be assessed when considering contact tracing, but no such cases have been described in the literature.

Plague, caused by Yersinia pestis, has historically been responsible for widespread pandemics with high mortality and was known as the Black Death during the fourteenth century, causing an estimated 50 million deaths. Since the 1990s, most human cases have occurred in Africa. In 2013 there were 783 cases reported worldwide, including 126 deaths. The three most endemic countries are Madagascar, the Democratic Republic of Congo, and Peru, and currently, Madagascar is having an outbreak with, as of 11 February 2015, a total of 263 cases of confirmed plague, including 71 deaths. There are three forms of plague infection, categorized according to the route of infection: bubonic, septicemic, and pneumonic. Only 2% of reported cases are the pneumonic form. Y. pestis used in an aerosol attack could cause cases of the pneumonic form of plague. One to six days after becoming infected with the bacteria, people would develop pneumonic plague. Once people have the disease, the bacteria can spread to others who have close contact with them.

AIRCRAFT AS VEHICLES OF WORLDWIDE INFECTION SPREAD

Air Travel Restrictions

The notion of restricting commercial flights to delay pandemics has been studied for several diseases. Several modeling studies concluded that flight restrictions would have little effect on the spread of pandemic influenza. One study shows that imposing a 90% restriction on all air travel would delay the peak of a pandemic wave by no more than 1 to 2 weeks, whereas halting almost all air travel (99.9%) would delay the pandemic wave up to 2 months. Simulation studies of the geographical spread of smallpox by air travel by Grais et al. from 2003 suggest that air travel restrictions instituted as soon as the first cases are recognized may still result in an epidemic seeding to other cities but may reduce the magnitude of the epidemic. However, if the air travel restriction is applied, it is important that it be done quickly, because a delay of a few days will likely result in cumulative forecast cases and in potential geographical spread, and therefore the consequences of halting domestic air travel may not be outweighed by public health benefits. The CDC has an established centralized electronic passenger database capability (e-manifest) to be used during infectious outbreaks for prompt passenger notification and contact tracing. The International Air Transport Association, in partnership with the WHO and other stakeholders, has established guidelines for the aviation industry for operations during pandemic influenza outbreaks to minimize commercial

Infectious Risks of Air Travel

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air travel spread. These include risk communication to the traveling public, establishment of national passenger exit screening from outbreak regions, and increasing airline preparedness (aircraft cleaning and procedures in case of in-flight illness). In light of the Ebola virus outbreak, the CDC and ECDC (not restricted to Ebola), via the Risk Assessment Guidance for Infectious Diseases Transmitted on Aircraft project, has published guidelines for risk assessment of trace-back of passengers with infectious diseases who traveled on an airplane.

**Risk-Based Border Screening**

The occurrence of epidemics and pandemics raises many public health questions regarding the application of international law in the context of preventing, protecting against, controlling, and providing a coordinated public health response to the international spread of disease. Many countries plan to use a risk-based approach during the early phase of a novel-agent pandemic to delay its spread within their borders as well as balancing between societal and economic disruption and public well-being. The goal of risk-based border screening is to identify the likelihood of infection in a traveler, and screening includes a brief interview and travel history. Individuals considered low to no risk for being contagious are given access to the country with no restrictions. Individuals failing the initial screening undergo a more extensive evaluation (Fig. 2). Once a pandemic disease is common

**FIGURE 2** Risk-based border screening of airline passengers during a novel-agent pandemic. Risk-based border screening of arriving passengers during a worldwide infectious outbreak involves a visual screening, brief interview, and travel history. Individuals considered to have low or no risk of being contagious are allowed access into the country with no restrictions. Individuals who do not pass the initial screen undergo more extensive evaluation, including a physical examination and testing. Individuals deemed low risk after being tested are allowed access, whereas high-risk individuals are either isolated or quarantined in addition to receiving antiviral treatment or prophylaxis. doi:10.1128/microbiolspec.IOL5-0009-2015.f2
in all countries, exit screening and border screening at points of entry will no longer be effective.

**International Health Regulations**

In December 2006, the United States formally accepted the revision of the WHO’s IHR, referred to as IHR 2005. IHR 2005 is currently the only international legal instrument that governs the roles of the WHO and its member countries in identifying, responding to, and sharing information about public health emergencies of international concern. The regulations are designed to prevent and protect against the international spread of diseases while minimizing interference with world travel and trade. The IHR regulations also contain routine requirements for disease surveillance and control activities at international airports, seaports, and border-crossings and make recommendations for the use of nonpharmaceutical interventions to mitigate the community impact of pandemic influenza and other novel infectious agents with pandemic potential.

**Closing Remarks**

The only way to eliminate virtually any risk of cross-infection within the aircraft cabin and to prevent the aircraft from serving as a vehicle for worldwide epidemic spread is to stop passengers from flying if they either have been exposed substantially to a communicable disease or are contagious. This is neither practical nor possible. Prevention is the most important means of control and requires a proactive approach. For individual air travelers, practicing hand hygiene remains the most effective means of minimizing risk of infection (see “Practical Tips” below).

Improved international regulations regarding the inspection, certification, and maintenance of aircraft environmental control systems are warranted. Regulations requiring HEPA filters for any aircraft utilizing recirculated air are needed to minimize the risk of infectious spread on and by commercial aircraft. Governmental, public health, aviation, and medical stakeholders should better educate the general public on health issues related to air travel and infection control.

Ultimately, humanity’s approach to emerging infectious disease threats of international concern and pandemic potential needs to shift from a containment or reactive strategy to a principally proactive or mitigating approach. This should include strengthening human and animal disease global surveillance in emerging infectious disease hotspots, greatly improving the global public health infrastructure, and expanding global vaccine development and production capacity. Only then can humanity respond to the challenges of novel microbial threats we will no doubt continue to face.

**PRACTICAL TIPS**

- Postpone travel if ill. Although it is recommended to postpone travel until one is no longer infectious, in reality this recommendation is not commonly followed by passengers, especially because few travelers purchase travel insurance.
- Minimize exposure while aboard aircraft. Sit near the front. Avoid window seats during the winter. Keep the air-conditioning nozzle on a low setting.
- Good hand hygiene is paramount to reducing the risk of disease transmission. Alcohol-based hand sanitizers are an excellent alternative to hand washing, especially when the hands are not visibly dirty or soap and water are not readily available, such as inside a crowded plane cabin. Every traveler should make good hand hygiene part of his or her travel routine.
- Seek travel advice in a travel clinic before international travel for appropriate vaccination, prophylaxis, and specific country recommendations and updated outbreak information as well as individual risk assessment.

**RECOMMENDED READINGS**


