SESSION 5

Policies and Planning to Minimize the Spread of Disease

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Transmission Patterns of Mosquito-Borne Infectious Diseases During Air Travel: Passengers, Pathogens, and Public Health Implications

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In addition to climatic, ecologic, and microbial factors, other significant factors that influence the emergence and reemergence of infectious diseases include international trade and air travel, globalization of agriculture and food production, exotic eating habits, lifestyle, and residential choices. The worldwide spread of the Asian tiger mosquito, *Aedes albopictus*, by imported tire shipments on container ships from Southeast Asia has introduced a new secondary (to *Aedes aegypti*) vector for dengue fever into the tropical Americas and Chikungunya fever in India, Bangladesh, and the Indian Ocean Islands, which are popular travel destination resorts (Figure 1).

FIGURE 1 The female *Aedes albopictus,* or Asian tiger mosquito, has been disseminated in coastal temperate zones worldwide by global trade and has genetically adapted to become a competent vector for dengue fever and Chikungunya viruses. (Source: CDC Public Health Image Library, Image No. 4735.)

Many models of climate change and vector–pathogen relationships now predict a significant expansion in potential malaria transmission cycles in the next few decades, with some studies predicting a 16% to 25% increase in person-months of exposure in malaria-endemic areas of Africa. Accessible airline connections now permit infected individuals to travel anywhere in the world in less than 24 h, delivering human reservoirs of malaria, dengue, West Nile virus, and Chikungunya fever to new temperate areas for autochthonous or local transmission by new and adaptable mosquito vectors, often recent air or sea arrivals themselves.

In 2008, Hochedez and coinvestigators in Paris reported their findings from a prospective study of 62 returning travelers who presented to their tropical diseases clinic with fever (above 38°C) and widespread rash over a 20-month period (*1*). The three main travel destinations were the Indian Ocean Islands (35%), Africa (21%), and Asia (18%). The three main tropical infectious disease diagnoses were Chikungunya (35%), dengue (26%), and African tick-bite fever (10%). Travel to the Indian Ocean Islands and South Africa was significantly associated with Chikungunya and ATBF, respectively. The authors concluded that arthropod-borne infectious diseases presenting with fever and rash were not uncommon among returning travelers and that travelers returning from endemic areas should be rapidly screened for tropical infections, some of which could be fatal, such as dengue and malaria. The mosquito vectors of infectious diseases that may be imported by infected passengers are compared by geographic distribution ranges and infectious disease transmission in Table 1.

History Repeats Itself: Why Is Dengue Fever a 21st Century Public Health Threat?

Yellow fever outbreaks claimed tens of thousands of victims in coastal and inland U.S. seaports and throughout Latin America and the Caribbean until stopped by a live virus vaccine developed in the early 20th century. Dengue virus, like yellow fever, is a flavivirus but it comes from a larger family of dengue viruses and there is no effective vaccine for it. Dengue fever and, in particular, its complications from subsequent dengue infections with other dengue serotypes, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome, may pose specific public health threats to the United States. Dengue is caused by four genetically related flaviviruses (DEN1 to -4); is transmitted by container-breeding, peridomestic *Aedes* species mosquitoes, preferentially *Aedes aegypti*; and can cause a spectrum of clinical manifestations ranging from asymptomatic initial infections to hemorrhagic fever with shock from microvascular plasma leakage.

Although an effective live vaccine is available for yellow fever (another flavivirus transmitted by *Aedes* mosquitoes), a dengue vaccine has proven very difficult to develop for several reasons: (*a*) the four dengue serotypes dictate a polyvalent vaccine, like the influenza vaccine; (*b*) a dengue vaccine must provide immunity against all four flaviviral serotypes at once by stimulating effective neutralizing antibodies; (*c*) the neutralizing antibodies must not cross-react and activate T cells, causing the cytokine reactions characteristic of DHF and DSS; and (*d*) multiple vaccinations every few years will likely be required to achieve long-lasting immunity against all four serotypes.

Dengue viruses are now endemic along the U.S.–Mexico border and have caused dengue fever outbreaks on both sides of the border and an autochthonous case of DHF in Brownsville, Texas, in 2005. Although yellow fever and dengue viruses historically have been confined to the tropics and transmitted by *Aedes aegypti*, a secondary *Aedes* vector, the Asian tiger mosquito *A. albopictus*, has now expanded its range globally in a warming ecosystem and is a competent vector of dengue viruses (Figure 1). The World Health Organization (WHO) considers dengue to be one of the world's most important reemerging infectious diseases, with 50 million to 100 million cases annually; 0.5 million hospitalizations, often requiring blood product transfusions; and 22,000 deaths annually, mostly in children. Even though the first dengue infection may be mild, the second could be lethal, even if it occurs years later. As there are no vaccines or specific drug treatments for dengue and because local *A. aegypti* and *A. albopictus* mosquitoes are capable of transmitting dengue in the United States, dengue poses a significant threat to the United States and a safe quadrivalent vaccine and better mosquito vector control along the U.S.–Mexico border are needed now.

TABLE 1 Mosquito Vectors of Infectious Diseases That May Be Imported by Infected Travelers or Vectors on Aircraft or in Airports

Mosquito Genera	Infectious Diseases Transmitted	Geographic Distribution Ranges	Causative Microbial Agents	Classification of Causative Agents
Anopheles spp.	Malaria	Africa, Asia, Central America, South America	*Plasmodium falciparum, P. vivax, P. ovale, P. malariae*	Protozoan parasites
Anopheles spp.	Bancroftian filariasis Brugian filariasis Timorian filariasis	Southeast Asia Southeast Asia Timor, Indonesia	*Wuchereria bancrofti* *Brugia malayi* *Brugia timori*	Filarial worms causing lymphatic filariasis
Anopheles spp.	O'nyong nyong fever	Africa	Alphavirus	Togaviruses
Aedes spp.	Yellow fever	Africa, Latin America	Flavivirus	Flaviviruses
	Dengue fever	Africa, Asia, Latin America	Flaviviruses DEN 1-4	Flaviviruses
	Chikungunya fever	Africa, Asia	Alphavirus	Togaviruses
	Eastern equine encephalitis	Eastern & Southeastern USA	Alphavirus	Togaviruses
	Ross River fever	Australia, Papua New Guinea	Alphavirus	Togaviruses
	California encephalitis	Western USA	Bunyavirus	Bunyaviruses
	LaCrosse encephalitis	Midwestern USA	Bunyavirus	Bunyaviruses
	Rift Valley fever	Africa	Phlebovirus	Bunyaviruses

Why We Could Not Stop the Spread of West Nile Virus Across the United States

Although dengue viruses are carried by mosquitoes or infected humans across the porous U.S.–Mexico border, West Nile virus was most likely imported to the United States in 1999 by international air travel. The West Nile virus arrived in New York City courtesy of an infected passenger or an infected *Culex* mosquito from an endemic region of East Africa or the Middle East. By 2002, competent local *Culex* vectors had initially established a mobile reservoir for West Nile virus in wild birds in wet, warming ecosystems that began to fly the virus rapidly across the United States from New York to the west coast. The initial wild animal reservoir for introduced West Nile virus in the United States was so specific that it targeted mostly birds of the family Corvidae, especially crows and jays. By 2005, West Nile virus infections were reported in other wild and domestic animals and humans across the continental United States and had caused more than 4,000 cases of meningoencephalitis with 263 deaths [case fatality rate (CFR) = 6.6%].

Why Are Mosquitoes Such Competent Transmission Vectors of Infectious Diseases in an Era of Climatic Change?

Only female mosquitoes seek frequent blood meals for their developing eggs from preferred nearby hosts. All female mosquitoes lay their eggs in standing water, either on or just below the surface. The anopheline vectors of malaria prefer to lay eggs in drainage ditches, marshy areas, and puddles. The culicine vectors of West Nile virus, dengue, and Chikungunya fever prefer to lay their eggs in containers that trap freshwater, such as flower pots, uncovered garbage cans, and even discarded tires. Climate changes, particularly warming nighttime temperatures and increased precipitation, offer selective advantages to all mosquito species, including (*a*) a longer reproductive life and a prolonged breeding season, (*b*) opportunities for more blood meals during gestation, (*c*) plenty of standing water surfaces for egg laying, and (*d*) a faster egg hatch over days and not weeks.

International Air Travel and Malaria

Malaria, a mosquito-transmitted parasitic disease, remains the most common cause of infectious disease deaths worldwide, followed by tuberculosis and AIDS. Although there are four *Plasmodium* protozoans capable of causing malaria in humans (*P. falciparum, P. malariae, P. ovale, P. vivax*), *P. falciparum* and relapsing *P. vivax* are the most common causative agents, with *P. falciparum* having a significantly higher CFR than *P. vivax*. According to the WHO's *World Malaria Report* (2005), 3.2 billion people live in malaria-endemic regions in 107 countries and territories, and there are between 350 million and 500 million cases worldwide per year, with 840,000 to 1.2 million deaths from malaria annually. Most malaria deaths occur in children under age 5 years, in pregnant women, and in nonimmune individuals, often travelers and expatriates returning to their malaria-endemic homelands to visit friends and relatives. About 60% of all cases of malaria worldwide and more than 80% of deaths from malaria worldwide occur in sub-Saharan Africa. Most malaria deaths worldwide are caused by *P. falciparum* transmitted by highly competent mosquito vectors, such as *Anopheles gambiae* in Africa, where transmission occurs year round.

The most common reasons for malaria to occur in the industrialized nations of North America and Europe where malaria was once endemic are also related to international air travel in a warmer and wetter climate and include airport malaria and, more significantly, imported malaria. Airport malaria is defined as the intercontinental transfer of malaria through the introduction of an infective anopheline mosquito vector into a nonendemic disease area with a changing ecosystem that supports the vector–pathogen relationship. The malaria-infected mosquito vector is a new arrival on an international flight from a malaria-endemic region. Airport malaria is transmitted by the bite of an infected tropical anopheline mosquito within the vicinity of an international airport, usually a few miles or even less. On the other hand, imported malaria is defined as the intercontinental transfer of malaria by the movement of a parasitemic person with malaria to a nonendemic disease area with locally competent anopheline vectors in a welcoming ecosystem. Climate change has now expanded the geographic distribution of malaria-endemic regions worldwide and extended the length of seasonal malaria transmission cycles in endemic regions, so more arrivals of malaria-carrying mosquitoes and malaria-infected travelers are anticipated. The greatest public health threats that imported malaria-infected mosquitoes and patients with malaria pose to nonmalarious regions include the reintroduction of *Plasmodium* species (especially *P. vivax* in the United States and Europe) into regions with competent anopheline vectors and the reestablishment of local or autochthonous malaria by local anopheline vectors.

Airport Malaria

How often do infected mosquitoes travel by air from tropical disease-endemic nations to capital cities in industrialized nations with disease-supporting warming ecosystems? In 1983, random searches of arriving airplanes at Gatwick Airport in London found that 12 of 67 airplanes from tropical countries contained mosquitoes. After the female mosquito leaves the aircraft, she may survive long enough, especially during temperate periods, to take a blood meal and transmit pathogens, usually in the vicinity of an international airport. After one or more blood meals, female mosquitoes seek a water surface to lay their eggs.

As international air travel between malaria-endemic nations and malaria nonendemic nations increased, cases of airport malaria have increased. In 1983, two cases of *P. falciparum* malaria were diagnosed in persons without histories of travel to malaria-endemic regions living 10 and 15 km from Gatwick Airport. Hot, humid weather in Britain may have facilitated the survival of imported, infected anopheline mosquitoes. During the summer of 1994, six cases of airport malaria were diagnosed in the vicinity of Charles de Gaulle Airport near Paris. Four of the patients were airport workers, infected at work, and the others were residents of Villeparisis, a small town about 7.5 km from the airport. To reach Villeparisis, the infected anopheline mosquitoes were thought to have hitched a car ride with airport workers who lived next door to two of the patients.

Imported Malaria

In addition to airport malaria transmitted by infected mosquito air travelers, many countries throughout the developed world are reporting an increasing number of cases of imported malaria because of the increase in long-distance air travel by infected passengers. Malaria cases imported from Africa to the United Kingdom (U.K.) rose from 803 in 1987 to 1,165 in 1993. By 2006, a total of 1,758 malaria cases were reported in the U.K. From 1990 to 1998, the annual number of imported malaria cases in Italy increased by 100% due to the rising rates of immigration and international travel, with immigrants currently accounting for most of the cases. In the United States in 2005, a total of 1,528 cases of imported malaria were diagnosed, an increase of 15% over the prior year. Today, imported malaria is the most common type of malaria in developed nations, with more than 10,000 cases reported annually; imported malaria remains the most common cause of fever in travelers returning from malaria-endemic regions.

In a retrospective analysis of 380 imported malaria cases in Verona, Italy, over the 5-year period 2000–2004 and 2008, Mascarello and coauthors reported that most cases occurred in adults (337 adults vs. 43 children), in immigrants (n = 181, 48% of adults), in patients returning from Africa (n = 359, 94.5%), and in travelers returning from visiting friends and relatives in malaria-endemic regions (n = 154, 40.5%) (*2*). Most cases were caused by single *P. falciparum* infections (n = 292, 76.8%), with few mixed *Plasmodium* infections (n = 23, 6%) (*2*). The authors concluded that malaria in travelers returning to Verona from Africa was not uncommon and targeted certain high-risk travelers, including adult expatriate immigrant travelers visiting friends and relatives, semi-immune children (recent immigrants), and nonimmune children (expatriates or born in Italy).

In a similar retrospective analysis of 109 travelers with malaria returning to Basel, Switzerland, over the period 1994–2004, Thierfelder and coinvestigators reported that *P. falciparum* was the most common causative parasite (84%); most infections were acquired in Africa in immigrants visiting friends and relatives (82%); and the mean incubation period was 4 days (range 0.5 to 31 days) (*3*). After their descriptive analysis, the investigators conducted three comparative analyses with two prior studies of malaria in travelers returning to Basel during the periods 1970–1986 and 1987–1992. The results of their comparative analyses included significant increases in the proportions of *P. falciparum* infections over three study periods (1970–1986, 49%; 1987–1992, 75%; 1994–2004, 88%) and significant increases (P < .001) in hospitalizations for *P. falciparum* malaria over the three decades studied. The authors concluded that there was a significant trend toward more serious malaria infections with *P. falciparum* in immigrants returning to Basel after visiting friends and relatives in their malaria-endemic native homelands.

In 2008, Rodger and coauthors reported a cluster of six cases of *P. falciparum* malaria at a British airport among 30 students returning to the United States after spending 2 months in East Africa in 2005 (*4*). Of the six patients, all were young (19 to 22 years of age) and in prior excellent health; five of the six exhibited features of acute cerebral malaria (disorientation, prostration) requiring urgent intensive care and therapy with intravenous quinine. The authors commended alert U.K. airport staff for recognizing the seriously ill travelers preparing to board a 9-h second-leg flight to the United States and for rapidly evacuating the patients to the nearest health care facility for intensive care, without which the five cerebral malaria cases would likely have been fatal.

Although many developed nations, such as northern Europe and the United States, do not have as efficient mosquito vectors for *P. falciparum* malaria as *A. gambiae* in sub-Saharan Africa, many nonendemic nations in southern Europe, the Middle East, and Asia do have efficient vectors for *P. falciparum*, and most have competent vectors for *P. vivax*, including the United States and Europe. The most disturbing recent trends in imported malaria today include the following: (*a*) an increasing proportion of *P. falciparum* infections capable of causing cerebral malaria and renal failure with the highest

CFRs; and (*b*) increasing immigration from malaria-endemic regions to malaria-free regions in developed nations, creating a unique set of high-risk travelers, especially expatriates (semi-immunes) and their children (often nonimmune) returning from visiting friends and relatives in their malaria-endemic native homelands.

In summary, imported malaria cases are increasing worldwide because of the ease and relatively low costs of international air travel to malaria-endemic regions worldwide. The world's malaria-endemic regions now have expanded distribution ranges for malaria transmission and longer mosquito vector breeding–feeding seasons due to global warming and increasing drought–monsoon cycles.

Autochthonous (Locally Transmitted or Reintroduced) Malaria

In the United States, 21 outbreaks of presumed locally transmitted or autochthonous mosquito-borne malaria transmission have been reported since 1950, all caused by *P. vivax*. Most of these introduced malaria outbreaks (n = 14), occurred in southern California, primarily among migrant Mexican agricultural workers. In 1986, a *P. vivax* malaria outbreak resulted in 28 cases of the disease, 26 of which were in Mexican migrant workers, over a 3-month period. In 1988, another outbreak of locally transmitted *P. vivax* malaria occurred in San Diego County, California, and involved 30 patients, again mostly migrant farm workers, and represented the largest reported outbreak of autochthonous malaria in the United States since 1952. Epidemiologic and microbiologic investigations of these malaria outbreaks later confirmed secondary spread from infected immigrants to other immigrants and local residents transmitted by local malaria-competent anopheline vectors.

Conclusions

Competent mosquito vectors for dengue, yellow fever, and Chikungunya virus are now present in the United States, including *A. aegypti* in the southern United States and *A. albopictus* throughout the country, and are awaiting an opportunity to transmit these imported arboviral diseases locally from arriving infected airline travelers to nonimmune citizens nearby. In addition, anopheline species have demonstrated their capacity to transmit imported *P. vivax* malaria along the U.S.–Mexico border and to transmit more serious *P. falciparum* malaria from arriving infected airline travelers and nonimmune individuals in southern Europe.

Prevention and control strategies for the imported arboviral infectious diseases (Chikungunya virus, dengue, and West Nile virus) and for airport, imported, and autochthonous malaria should include early case definition, case confirmation, and treatment; strengthened vector surveillance to detect the potential for autochthonous or local transmission; and drainage of potential mosquito breeding and egg-laying surface water sites. Although the relationships among infected vector importation, index case immigration, reclaimed disease ecosystems, and malaria transmission are complex, future attempts to control and eradicate airport and imported malaria should be based on an understanding of disease transmission mechanisms and an appreciation that climate and ecosystem changes can support reemerging local mosquito-borne infectious diseases in nonendemic areas, especially malaria, dengue, Chikungunya, and West Nile virus.

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Airline Policies and Procedures to Minimize the Spread of Diseases

Rose M. Ong (Presenter)

Faced with the outbreak of severe acute respiratory syndrome (SARS) in 2003, airlines found that they were generally ill prepared to deal with infectious diseases with public health concerns. Since that time, especially for an Asian-based carrier such as Cathay Pacific, there have been a number of other "novel" communicable diseases, including avian influenza and most recently the pandemic A/H1N1 influenza epidemic. Air travel is frequently cited as being responsible for the rapid spread of communicable diseases on a worldwide basis.

Since 2003, significant progress has been made among various commercial airline stakeholders to collaborate to minimize the spread of communicable diseases onboard flights.

Airlines followed guidance issued by major international organizations such as the International Civil Aviation Organization (ICAO), WHO, U.S. Centers for Disease Control and Prevention, International Air Transport Association (IATA), and Airport Council International (ACI) as well as local organizations such as the Hong Kong Centre for Health Protection. Many initiatives have been introduced by these organizations to promote better alignment and collaboration among key stakeholders in managing infectious diseases in air travel.

Airlines engage in routine baseline activities to manage infectious diseases, which include educating and training frontline staff, crew fitness to fly, cabin air conditioning and ventilation, cabin hygiene and sanitation, in-flight catering hygiene, and preparedness drills conducted in conjunction with airport authorities. Emphasis was placed on the aircraft ventilation system; it introduces fresh air at a rate of 50%, which is mixed with recirculated air and filtered through high-efficiency particulate air filters, with a 99.9% efficiency rate of removal of airborne biological contaminants. The entire cabin air volume is exchanged every 2 to 3 min with laminar airflow patterns, which minimizes longitudinal air movement, lowering the risk of in-flight transmissions in a forward-and-aft direction. The aircraft is cleaned and disinfected in accordance with maintenance schedules.

Other actions are taken in response to specific infectious incidents, including activation of the in-flight medical management systems (e.g., cabin crew training, in-flight aeromedical telephonic support, medical equipment including personal protective equipment, blood-borne pathogen barriers) and contact tracing of crew and passengers as appropriate. Crew have specific protocols to follow when a passenger is suspected of having a communicable disease; the individual is given a mask to wear, relocated to the rear of the aircraft if appropriate and possible, assigned a toilet if appropriate, and given tissues or a disposal bag to use. One crew member should be assigned to look after the sick passenger. The crew will communicate with the telephonic medical advisory and, if appropriate and indicated, the pilot will notify the en route air traffic control, who will advise health authorities in the arrival port.

During an infectious disease outbreak, additional measures are taken, including screening temperatures of all crew before operating an aircraft, providing refresher training and safety reminders for all crew at crew depar-