REVISÃO (REVIEW)

TRAVEL AND INFECTIOUS DISEASE

Roberto Chuit,[1] *Laura Mac Dougall,*[2] *Maria Cristina Evequoz,*[3] *Alicia Maria Bressan*[3] *and Maria Frías*[3]

ABSTRACT

Travel facilitates the physical transport of pathogens and vectors and increases the exposure of individuals and population groups to disease. Reciprocally, travel is affected by outbreak situations, particularly those occurring in areas of heavy tourism. In the individual, specific risk factors associated with travel-induced illness include the time of year traveled, travel destination and number of trips taken, age, predisposition to high risk behavior, pre-travel health, pre-trip counseling, and previous immunity. While the speed and frequency of modern travel facilitate the introduction of infectious diseases into new environments, disease emergence is dependent on the complex interrelationship of population immunity and genetic differences, behavioral patterns and cultural norms, environmental setting, the epidemiology of disease and the existing public health infrastructure. Travel-induced illnesses have serious economic, political and medical consequences including costs to health care systems in both home and host country, lost revenue to decreased tourism, increased health insurance claims, lost working days, issues of national security and the spread of antibiotic resistance. To minimize the impact of travel on infectious disease emergence, travel-acquired illnesses must be prevented through safe, effective immunizations, public and physician education programs, improved global sanitation and effective disease surveillance.

KEYWORDS: Travel diseases. Infectious diseases. Prevention.

INTRODUCTION

Contemporary advances in technology have dramatically increased the distance, speed and frequency of travel, revolutionizing the movement of people, animals and goods. Paralleling these advances in travel, outbreaks of

1 Academia Nacional de Medicina, Centro de Investigaciones Epidemiológicas. Pacheco de Melo 3130 (1425) Ciudad Autónoma de Buenos Aires. Argentina.
2 Organización Panamericana de la Salud/Organización Mundial de la Salud. 525 23rd Street, N.W. Washington, D.C. 20037 - 2895.
3 Ministerio de Salud, Provincia de Córdoba, Argentina

Address for correspondence: e-mail: chuit@aya.yale.edu

Recebido para publicação em 12/11/2001. Aceito em 27/12/2002.

infectious disease are occurring with greater speed and frequency and with less adherence to traditional endemic boundaries. A conduit for infectious disease transmission, travel facilitates the physical transport of pathogens and vectors and increases the exposure of individuals and population groups to disease. Reciprocally, travel is affected by outbreak situations, particularly those occurring in areas of heavy tourism.

The ease and low cost of travel today means that an unprecedented number of people are traveling for a wider variety of reasons. Traditional reasons for travel such as religious pilgrimages, war (military personnel; civilian refugees), seasonal migration (in search of food or work) and urbanization have been joined by an explosion in short-term business travel and tourism. According to the World Tourism Organization, the increase in world international tourist arrivals between 1950 and 1996 was over 2,000%. In 1996 alone, 593 million international tourist arrivals, estimated to generate 425 billion dollars in revenue, were reported (52).

In the individual, specific risk factors associated with travel-induced illness include the time of year traveled, travel destination and number of trips taken, age, predisposition to high risk behavior, pre-travel health, pre-trip counseling, and previous immunity (10, 25, 37). While infected travelers may introduce disease to new environments, disease emergence is not guaranteed. Rather, emergence is dependent on the complex interrelationship of population (immunity, genetic differences and behavioral patterns), environmental setting (land use patterns, climate, geography), the transmission of disease and the existing public health infrastructure (4, 32).

Travel-induced illnesses of an infectious nature have serious economic, political and medical consequences. Obvious costs involve the burden to health care systems in both home and host country while hidden costs include lost revenue to decreased tourism, increased health insurance claims, and lost working days. Infectious disease emergence introduces issues of national security involving emergency preparedness and policy planning as well as control and safety measures. International concern over the spread of antibiotic resistance is rising as travel increases the prophylactic and empiric use of antibiotics. Moreover, travel brings different strains into close physical contact, permitting the exchange of antibiotic resistant genetic material.

The prevention of travel-acquired illness through safe, effective immunizations, public and physician education programs, improved global sanitation and effective disease surveillance will serve to minimize the impact of travel on infectious disease emergence.

DISEASE TRANSMISSION

With any mode of transportation there is a risk of transporting pathogens and disease vectors as well as passengers. Disease causing organisms or their vectors can be found in or on airplanes, ships, trains, buses, etc. as well as in or on human and animal passengers, baggage and freight.

Air travel, especially, has increased the potential for international transmission of infectious diseases. In the first half of 1995 alone, the US Department of Transportation's Office of International Aviation reported 48.7 million passengers traveling by air between the United States and the rest of the world (49). Despite attempts at vector control, trapping studies have shown the presence of live mosquitoes on international flights (18, 42) and cases of dengue, yellow fever and malaria have been reported in non-endemic areas located near international airports (20). Confined air space and poor ventilation and filtration systems aboard aircraft increase the risk of in-flight transmission of airborne diseases such as tuberculosis (5, 13, 22) and influenza (23, 33). Outbreaks of food poisoning occur on international flights (14, 19) and may be exacerbated by non-traditional food preparation, storage and handling procedures.

The confined environment of ships offers suitable conditions for the rapid spread of disease. As well, *Vibrio cholerae* and other marine organisms can be transplanted from one area to another in the bilge water of ships (12). Other marine organisms can be found on ship's hulls, which if introduced into new environments, may disrupt the ecosystem causing indirect effects on human health. Ocean liners, cruise and cargo ships often harbor rodent reservoirs of disease, extending their ecological range and facilitating close contact with human hosts.

Infectious organisms or their vectors can also be transported with freight or cargo. Used tires shipped from Asia to the United States have been implicated in the introduction of *Aedes albopictus* (11, 39), capable of survival in both forest and semi-urban environments and able to act as a vector of dengue, La Crosse, yellow fever and other viruses (30, 31). The emergence of zoonotic diseases poses a growing threat as animals become increasingly transported, whether as domestic pets or animals intended for research, breeding or sale. In 1989, Ebola virus was isolated from cynomolgus monkeys imported from the Philippines into U.S. quarantine facilities in Virginia, Pennsylvania, and Texas (15, 21). Antibodies to one or more filovirus antigens were detected in persons routinely handling and managing quarantined non-human primates (17). Although no clinical evidence of infection was reported (17), proper inspection, handling, and quarantine procedures are required if transmission is to be limited (41).

With the globalization of food production and distribution, food-born illnesses are becoming international in scope, often affecting populations distant to the site of contamination. Recently in North America, imported raspberries, fresh basil, strawberries and mushrooms have been implicated as the source of cyclosporiasis, Hepatitis A and Staphylococcus outbreaks, respectively (6, 24, 34, 36).

In the last century, technology has lessened the time required to travel a given distance. In so doing, modern travel has extended the boundaries of infectious diseases beyond traditional national borders. Today, travel time is frequently shorter than the incubation period of most diseases; passengers incubating a disease may be infectious en route, but be scattered throughout the globe before symptoms appear. While traditional outbreak response has been to implement quarantine measures, the international nature, speed and frequency of air travel often hampers these efforts. For example, in 1994, Canadian authorities were notified of the Indian outbreak of pneumonic plague only hours before the first flight from Bombay was due to arrive at Pearson International Airport in Toronto (44).

RISK FACTORS ASSOCIATED WITH TRAVEL-INDUCED ILLNESS

In a cumulative review of 13,816 travelers returning to Scotland since 1977, 36% reported incidences of travel-related illness. At 18%, alimentary complaints involving diarrhea and vomiting were the most common type of illness, with an additional 10% reporting both alimentary and other symptoms (10). Another study of 10,884 staff and consultants of the World Bank reveals that infectious and parasitic diseases constitute the most common reason for filing a medical insurance claim. In addition, rates of medical insurance claims were higher among travelers than non-travelers and increased with frequency of travel (25).

Of all types of travel, those vacationing with package tours reported the highest rates of illness, and the probability of becoming ill increased with the degree of climatic and cultural disparity between home and guest country (37). Seasonal variations in sickness showed that travel during the summer months was associated with higher risk; travelers between the ages of 20 and 29 years were more likely to become ill, as were smokers (10, 37). High risk lifestyles in general, associated with both the 20-29 age bracket and smoking, may put travelers at greater risk of illness.

Antibody formation via immunization or previous exposure should reduce or eliminate the risk of secondary infection. However, a one-year serological study of patients hospitalized for travel-related reasons revealed that some patients showed no evidence of immunization for typhoid and hepatitis A, and incomplete immunity for poliomyelitis and diphtheria (10). Clearly, travelers are either not being vaccinated prior to departure or the vaccinations themselves are ineffective in certain cases.

Pre-travel health and pre-trip counseling play a determining role in traveler's health. In addition, poor nutritional status, pre-existing chronic or acute illnesses, and chronic fatigue can be exacerbated by the stress of travel, increasing the risk of infection. In a subgroup of Scottish travelers, the travel agent was the most commonly consulted source of pre-trip health advice and the physician the least (10).Therefore, travel brochures and other information available from the travel agent constitute an important source of preventive advice, although there has been concern over the quality and availability of such resources (38). Surprisingly, the incidence of disease was highest among those seeking pre-travel advice from their physician. However, this may reflect a bias related to an increased self-concern for health. Those already at heightened risk - travelers to high-risk destinations, those having previously experienced travel-associated disease or those with pre-existing illnesses (and therefore possibly predisposed to travel-associated disease) - might be more inclined to contact a physician for advice. In a study of travelers' diarrhea, patients receiving pre-travel health advice from their physician were indeed more likely to suffer diarrhea, however they were less likely to need medical assistance while abroad or upon their return (29).

FACTORS IN DISEASE EMERGENCE

Increasing travel and commerce facilitates the introduction of infectious agents into new host populations, however suitable circumstances must exist in order for disease to spread. In addition to travel, commonly recognized determinants of disease emergence include: population immunity levels, genetic differences, behavioral practices, environmental conditions, the epidemiology of disease and a breakdown in public health infrastructure (3, 32).

When they travel, people carry their individual genetic makeup, microbiologic flora and accumulated immunologic experience (51). Differences in these factors contribute to an individual's susceptibility to disease, and are important to the dissemination of disease in a given population. Severe epidemics can occur when new pathogens are introduced to an environment where there is little or no immunity from previous exposure or immunization. Exploration and colonization of the Americas brought smallpox, measles, influenza, malaria and yellow fever to the New World, with devastating consequences to Amerindian populations. European populations, in turn, were affected by syphilis, thought to have been introduced into 16th century Europe by sailors returning home from the New World (2). In addition to the pathogen itself, humans and animals also carry background flora that may offer opportunities for the recombination of genes encoding particular virulence or antimicrobial resistance (51).

Travel often brings different cultural practices, norms and traditions into contact. In a given population, human behavior patterns can lessen or exacerbate the dissemination of infectious diseases. Classic examples include hand washing in the reduction of dysentery and intravenous drug use and sexual practices in the spread of HIV infection. Unfamiliar with a given area, travelers may engage in risk behaviors avoided by local residents. Conversely, social conventions and accepted local practices may act to promote the dissemination of infectious diseases. In Zaire, for example, high-risk activities are associated with cultural traditions that involve women washing the dead, including washing out the mouths of corpses (26). Social stigma attached to the use of contraception has inhibited the control of STDs in many parts of the world. The risk of disease transference increases in communities that view disease as a product of black magic or a punishment from a higher power. Infected individuals are often shunned and denied early treatment that could reduce the risk of transmission. Occupational, domestic and cultural differences between and within population groups influence their respective risk of exposure to animal reservoirs, disease vectors and contaminated food and water sources.

Infection is often a result of the interaction between host, microorganism and environment. Pathogens as well as their vectors are greatly influenced by existing environmental conditions as well as the human actions that alter them. Proper climate conditions are necessary for pathogen survival and reproduction. In addition, for transmission and infection to occur, climate conditions must also support the survival of acceptable hosts and disease vectors. Travel, especially urban migration, causes changes in land use patterns and agricultural practices, increasing deforestation to accommodate housing, tourism, mass production and transportation systems. This can result in increased contact between agent and host or an increase in microbe or host populations, facilitating the emergence of disease. In effect, deforestation has caused shifts in the disease patterns of arboviruses, malaria, the leishmaniasis, filariasis, Chagas disease and schistosomiasis (50). Dam creation in particular creates reservoir-breeding sites for the mosquito vectors of malaria and filariasis as well as the snails hosts of schistosomiasis. Systematic studies of disease in local populations act as a necessary baseline from which to identify the effect of subtle shifts in the environment on host populations and vector dynamics. These are often the first indicators of disease and can be used to predict the relative risk of outbreak situations and identify possible avenues of control.

A lack of public health infrastructure or its temporary breakdown during periods of disaster makes it easier for disease emergence to occur. For example, deficiencies in water and sanitation standards and testing practices were responsible for a massive outbreak of cryptosporidium infection in Milwaukee in 1993 (27). Unsanitary conditions due to improper waste

disposal may attract rodent reservoirs of disease, increasing human exposure, while poor drainage provides breeding sites for a wide range of infectious disease vectors. Heavy influxes of people during catastrophic events such as war, drought, flood and technological disasters as well as mass urbanization movements place an unaccustomed strain on public health and sanitation systems. The crowded conditions of refugee camps provide environments conducive to the transmission of diarrheal diseases, measles, acute respiratory infections and malaria. The situation is frequently compounded by the malnutrition manifest in conflict-affected countries. In face of increased population density, maintenance of public health standards along with continued control efforts such as vector reduction programs and educational campaigns are critical in the prevention of possible epidemics.

Inadequate surveillance activities make outbreak detection difficult and can be compounded by a lack of equipment and trained laboratory personnel. In areas where tourism is a major industry, even if diseases are identified, political pressures and economic factors may delay control efforts and impede international reporting (41).

Certain inherent characteristics of the disease may also facilitate its spread. Given high population densities, airborne infections and those exhibiting a fecal-oral route of transmission are likely to spread more quickly. In addition, the incubation period and severity of disease affect the speed of disease detection and implementation of control measures.

CONSEQUENCES OF TRAVEL-ASSOCIATED DISEASE

Travel-acquired diseases may affect single individuals or, given suitable circumstances, may be implicated in the emergence or reemergence of disease and the creation of outbreak situations. In both cases, travel-associated diseases induce economic, political and medical consequences that impact both the individual and society.

The cost of travel-related illness in the UK is estimated to be in excess of £11 million, or close to 20 million dollars U.S. a year (37). Nevertheless, this figure is likely underestimated as it excludes the cost of specialists, primary care consultants, laboratory analyses, drugs, and lost working days. Unfamiliarity with many foreign diseases can lead to the late diagnosis of travel-acquired illnesses, further contributing to their cost. Currently, 1 in 5 travelers seek GP consultation upon return home (28). However, as travel becomes more frequent and the threat of emerging and reemerging diseases grows, travelers are bound to make more pre- and post-travel visits to family physicians with requests for baseline readings and follow-up examinations.

The frequency of travel related illness causes employers and health insurance companies to suffer economic losses in the form of increased sick

days and medical claims, respectively. In a one year study of 1,568 people reporting to a group medical practice, 26% required consultation with a doctor while abroad, 5% of ill travelers were admitted to hospital overseas and 48.4 % of those becoming ill required further consultation from general practitioners upon their return (28). It was also found that 8% of travelers presenting to the group medical practice did not have any medical insurance coverage (28).

Often, the threat of infection is enough to discourage travel to areas where disease outbreaks are occurring. This can have serious repercussions for countries financially dependent on travel and tourism. Lost revenue due to an outbreak of cholera along Kenya's coastline in 1997 was economically crippling for a country where revenue from the tourism industry represents more than 10% of its gross domestic product (GDP) (8). In addition, in an effort to prevent the spread of cholera, over 1,000 food kiosks, bars and abattoirs were closed down within a two month period in the province of Nyanza, leaving many people jobless (46). Travel to India was also affected by the 1994 outbreak of pneumonic plague: "several international airlines discontinued flights to India, some even turning back and returning their passengers to the subcontinent; major travel agents cancelled package tours to India. At least one country suspended postal links with India. The potential economic implications for India's tourist industry were therefore highly significant" (9).

Facilitated by increasing global travel, outbreaks of infectious diseases raise issues of national security. Countries must be prepared in the event that foreign infectious diseases are imported and disseminated within their national boundaries. As well, nations must endeavor to protect their citizens living, working or traveling in areas of endemic disease or areas affected by disease outbreak. Emergency preparedness planning, including effective surveillance strategy, contingency plans for outbreak prevention and control, functional national reference laboratories, and the availability and mobilization of human and material resources, is critical to the reduction of contemporary infectious disease threats. Effective planning demands multidisciplinary communication and cooperation between epidemiologists, clinicians, engineers, government officials, the media and the community.

National policies on immigration, environment, blood supply, health safety standards and immunization can impact travel-associated diseases. Not only must countries explore these issues at a national level, but must push other nations to consider the implications of these policies for infectious disease emergence and lobby for the creation and enforcement of international standards. For example, people traveling to certain countries of South and Central America are at risk for transfusion-acquired infectious diseases such as Hepatitis B and C, syphilis and Chagas disease. Roughly, one case of transfusion-related infection occurs every 43 to 1,072 donations,

depending on the infectious agent and country (43). Inadequate health standards and practices aboard cruise ships, involving whirlpool spa maintenance/decontamination as well as ill food handlers and undercooked foods, have been implicated in outbreaks of Legionnaires' and diarrheal diseases, respectively (16, 35).

Antimicrobial resistance is a further consequence of travel. The dissemination of pathogens provides the opportunity for different strains to interact, promoting genetic recombination and the transfer of antimicrobial resistance. Importation of drug-resistant strains of malaria, shigella, typhoid and other infectious organisms has been well documented; according to a specific study of shigella isolates in the United States, a history of foreign travel was the best predictor of clinically relevant resistance (45). In general, misuse of antimicrobials by both physicians and self-medicating individuals as well as overuse of antimicrobials contribute to resistance. In travelers, misuse of prophylactic measures can result from inappropriate dosage levels, improper or discontinued drug use. For example, travelers may reduce or discontinue antimalarial medication due to discomfiting side effects, reducing efficacy and promoting drug resistance. Resistance may also be incurred during 'trial and error' treatment of uncommon diseases with multiple antimicrobial/antiviral agents. This is of special concern when travel histories are not taken into account in the diagnosis of disease or when travelers are given to self-medication.

ILLNESS PREVENTION

Many of the most common travel-associated diseases are preventable through immunization or basic education. Travelers vaccinated against diseases they may encounter while abroad reduce the risk of illness both for themselves and for those they might infect upon return. While it seems intuitive that prevention is ultimately less costly than treatment, few cost-effectiveness analyses of travel prophylaxis have been conducted. Specific studies suggest that travel prophylaxis is economic in the case of malaria (1) and traveler's diarrhea (40), but disputed in the case of Hepatitis A (1, 47) and not cost-effective for typhoid (1). However, cost analyses must not only bear in mind the immediate costs of prophylaxis vs. treatment, but future costs associated with the emergence of new multi-drug resistant strains and the introduction of disease into non-immune populations. Each case should be considered individually, as risk factors such as travel to heavily endemic areas, rural visitation, etc. may change the relative risk of disease and the probability of treatment.

Traveler's health information is most often solicited from the travel agent (10), therefore specific educational efforts should be aimed at this group. In addition, accurate health advice for the traveler should be included

in travel guides and brochures available at travel agencies and other places (i.e. doctor's offices, banks, insurance agencies, airports, embassies etc.) frequented by travelers. General practitioners themselves are a valuable source of pre-trip health advice and Internet technology is becoming an effective way to reach an increasing number of travelers with accessible, up-to-date traveler's health information (a good example is the CDC's Travel Information web page) (5). Continuing education programs for physicians and health care providers should include instruction in travel medicine, emphasizing the importance of obtaining travel histories as well as providing training in foreign disease recognition and appropriate treatment practices. For their part, travelers must be aware of and avoid engaging in high risk activities including drinking from unpurified water sources, eating undercooked foods or those that have been left sitting out for long periods, consuming wild game, engaging in unprotected sex, and using contaminated needles or syringes.

Prevention strategies should also incorporate risk analyses, increased global surveillance, and the improvement of sanitation infrastructure and basic health practices. Specific programs such as the CDC's Vessel Sanitation Program, which conducts health inspections aboard cruise ships, help to develop international health standards and promote safe travel. Low inspection scores have been shown to correlate with increased disease risk (7), and since inspection scores are made public, pressure is placed on the industry to maintain health standards that minimize the risk of gastrointestinal and other diseases in their passengers and crew.

Strengthened global surveillance is particularly important given that travel contributes to the threat of emerging and re-emerging infectious diseases. Such diseases must be closely monitored so that change in disease patterns can be recognized and their spread controlled. International cooperation in surveillance activities and outbreak control is essential to rapid detection and response.

Improvements in hygienic practices and sanitation infrastructure help to decrease the number of travel related illnesses. Basic preventive health practices such as hand washing need reinforcement given that "restaurant, hospitals, nursing home and child/day care workers fail to wash their hands over 60 percent of the required time" (48). Safe cooking practices can be easily encouraged which prevent the spread of food-borne diseases like *E. coli*. Countries with active waste and water management as well as rodent and insect control programs not only protect their own citizens, but also make the area more attractive to travel and tourism.

CONCLUSIONS

Travel is an important factor by which infectious diseases are introduced into new environments. The speed and frequency of modern travel facilitate this critical first step, although disease emergence requires a more complex interaction of environmental, social, economic, and evolutionary factors.

Given suitable conditions, individuals acquiring travel-associated illnesses may spread infection to entire population groups. Individual travelers can reduce the risk of infection by following appropriate travel health advice, ensuring that they are properly vaccinated and abstaining from high-risk behaviors (i.e. engaging in unprotected sex, drinking or eating from unsafe food and water supplies). For their part, countries must step up surveillance activities, ensure adequate levels of sanitation and provide education in traveler's health and travel medicine for both the general public and the medical community. Emergency preparedness planning and policy considerations constitute additional and important preventive measures.

Travel associated illnesses can cost nations tens of millions of dollars per year. Health care systems, the health insurance and tourism industries, as well as public and private enterprises all incur direct and indirect costs of travel-related illness. In addition, increased travel is making it difficult for new research to keep pace with the rapid spread of disease. The reality is that many diseases, whether emerging, reemerging or the result of drug resistant pathogens are neither vaccine preventable nor curable with known medical treatments (i.e. AIDS). For this reason, effective prevention strategies, which can be implemented by both the individual traveler and by various levels of the health care sector, are of increasing importance.

Travel and the emergence or reemergence of infectious disease are connected; changes in one invariably affect the other. Any effort to understand and ultimately check emerging and reemerging disease requires international cooperation and multidisciplinary involvement in the research, prevention, surveillance and control of travel-related diseases.

RESUMO

Viagens e doenças infecciosas

As viagens não só facilitam o transporte físico de patógenos e vetores, mas também aumentam a exposição dos indivíduos e de grupos populacionais às doenças. Reciprocamente, as viagens são influenciadas por surtos, em particular em áreas de intenso turismo. Os fatores de risco específico individuais, associados a doenças relacionadas com viagens, incluem época do ano, destino, número de viagens, idade, condutas de risco, saúde prévia,

aconselhamento anterior à viagem e imunidade prévia. A introdução atual de doenças infecciosas em novos ambientes mostra que a emergência delas está associada a diferenças genéticas, aos padrões culturais e de conduta, ao meio ambiente, à epidemiologia dessas doenças e à existência prévia de infra-estrutura sanitária. As doenças provocadas por viagens acarretam conseqüências econômicas, políticas e médicas, incluindo custos nos sistemas de saúde – tanto no país visitado como no de origem –, perdas pela diminuição do turismo, aumento de reclamações perante as seguradoras de saúde, perda de dias de trabalho, gastos no seguro social e disseminação da resistência a antibióticos. Para diminuir o impacto das viagens na emergência de doenças infecciosas, estas devem ser prevenidas por meio de imunizações efetivas e de programas de educação sanitária tanto para a população quanto para os profissionais da área. A melhora global do saneamento e a vigilância efetiva das doenças também contribuirão para minimizar o problema.

DESCRITORES: Doenças do viajante. Doenças infecciosas. Prevenção.

REFERENCES

1. Behrens RH, Roberts JA. Is travel prophylaxis worthwhile? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid in travelers. *BMJ(London) 309*:918-922, 1994.
2. Berlinguer G. The Interchange of Disease and Health between the Old and New Worlds. *Am J Public Health* 82:1407-1413, 1992.
3. Center for Disease Control and Prevention. Travelers' s Health http://www cdc.gov/publication.htm
4. Centers for Disease Control and Prevention. Addressing emerging infectious disease threats: a prevention strategy for the United States. Atlanta: U.S. Department of Health and Human Services. 1994.
5. Centers for Disease Control and Prevention. Exposure of passengers and flight crew to *Mycobacterium tuberculosis* on commercial aircraft, 1992-1995. *MMWR 44*:137-140, 1995.
6. Centers for Disease Control and Prevention. Hepatitis A associated with consumption of frozen strawberries-Michigan, March 1997. *JAMA 277*: 1271, 1997.
7. Centers for Disease Control and Prevention. Vessel Sanitation Scores. *MMWR 37*:114-117, 1988.
8. Cholera Hits Kenya Tourism Hub. The Black World Today. Nov 1997. Http://www.tbwt.com/health/health17.htm.
9. Cook GC. Plague: Past and Future Implications for India. *Public Health 109*:7-11, 1995.
10. Cossar JH, Reid D, Fallon RJ, Bell EJ, Riding MH, Follett EA, Dow BC, Mitchell S and NR Grist. A cumulative review of studies on travelers, their experience of illness and the implications of these findings. *J Infect 21*:27-42, 1990.
11. Craven RB, Eliason DA, Francy P, et al. Importation of *Aedes albopictus* and other exotic mosquito species into the United States in used tires from Asia. *J Am Mosq Control Assoc 4*:138-142, 1988.
12. DePaola A, Capers GM, Moters ML, et al. Isolation of Latin American epidemic strain of *Vibrio cholerae* 01 from US Gulf Coast. *Lancet 339*:624, 1992.
13. Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of *Mycobacterium tuberculosis* associated with air travel. *JAMA 272*:1031-1035, 1994.

14. Eberhart-Phillips J, Besser RE, Tormery MP et al. An outbreak of cholera from food served on an international aircraft. *Epidemiol Infect 111*:9-13, 1996.
15. Ebola virus infection in imported primates – Virginia, 1989. *MMWR 38*:831-832, 1989.
16. Epidemiology of diarreal disease outbreaks on cruise ships, 1986 through 1993. *JAMA 275*:545-547, 1996.
17. Filovirus Infections Among Persons with Occupational Exposure to Nonhuman Primates. [Update] *MMWR 39*: 266-273, 1990.
18. Goh KT, Ng SK, Kumarapathy S. Disease-bearing insects brought in by international aircraft into Singapore. *Southeast Asian J Trop Med Public Health 16*:49-53, 1985.
19. Hedberg CW, Levine WC, White KE, Carlson RH, Winsor DK, Cameron DN, MacDonald KL & Osterholm MT. An international foodborne outbreak of shigellosis associated with a commercial airline. *JAMA 268*:3208-3212, 1992.
20. Isaacson M. Airport malaria: a review. *Bull World Health Organ 67*:737-743, 1989.
21. Jahrling PB et al. Preliminary report: isolation of Ebola virus from monkeys imported to USA. *Lancet 335*:502-505, 1990.
22. Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. *N Engl J Med 334*:933-938, 1996.
23. Klontz KC, Hynes NA, Gunn RA, Wilder MH, Harmon MW, Kendal AP. An outbreak of influenza A/Taiwan/1/86 (H1N1) infections at a naval base and its association with airplane travel. *Am J Epidemiol 129*:341-348, 1989.
24. Levine WC, et al. Staphylococcal food poisoning caused by imported canned mushrooms. *J Infect Dis 173*: 1263-1267, 1996.
25. Liese B, Mundt KA, Dell LD, Nagy L, and B Demure. Medical insurance claims associated with international business travel. *Occup Environ Med 54*:499-503, 1997.
26. Logan MH. Culture Affects Disease Outbreaks, UT Professor Says. Http://loki.ur.utk.edu/news/may95/disease.html.
27. MacKenzie WR, Hoxie NJ, Proctor ME, Gradus MS et al. A massive outbreak in Milwaukee of cryptosporidium infection transmitted through the public water supply. *N Engl J Med 331*:161-167.1994.
28. McIntosh IB, Reed JM and KG Power. The impact of travel acquired illness on the world traveler and family doctor and the need for pre-travel health education. *Scott Med J 39*:40-44, 1994.
29. McIntosh IB, Reed JM, Power KG. Travelers' diarrhoea and the effect of pre-travel health advice in general practice. *Br J Gen Pract 47*:71-75, 1997.
30. Mitchell CJ, Niebylski ML, Smith GC, et al. Isolation of eastern equine encephalitis virus from *Aedes albopictus* in Florida. *Science 257*:526-527, 1992.
31. Moore CG, Francy DB, Eliason DA, Monath TP. *Aedes albopictus* in the United States: rapid spread of a potential disease vector. *J Am Mosq control Assoc 4:356-361,1992.*
32. Morse SS. Factors in the emergence of infectious diseases. *Emerging Infect Dis 1*:7-15, 1995.
33. Moser MR, Bender TR, Margolis HS, Noble GR, Kendal AP, Ritter DG. An outbreak of influenza aboard a commercial airliner. *Am J Epidemiol 110*:1-6, 1979.
34. Outbreak of cyclosporiasis - northern Virginia-Washington, D.C.-Baltimore, Maryland, metropolitan area, 1997. *M M W R 46*:689-691, 1997.
35. Outbreak of Legionnaires' disease among cruise ship passengers exposed to a contaminated whirlpool spa. *Lancet 347*:494-499, 1996.
36. Outbreaks of cyclosporiasis in United States and Canada, 1997. [Update] *M M W R 46*:521-523, 1997.
37. Reid D & Cossar JH. Epidemiology of travel. *Br Med Bull 49*:257-268, 1993.
38. Reid D, Cossar JH, Ako TI, Dewar RD. Do travel brochures give adequate advice on avoiding illness? *Br Med J 293*:1472, 1986.
39. Reiter P, Sprenger D. The used tire trade: a mechanism for the worldwide dispersal of container-breeding mosquitoes. *J Am Mosq Control Assoc 3*:494-501, 1987.

40. Reves RR, Johnson PC, Ericsson CD, DuPont HL. A cost-effectiveness comparison of the use of antimicrobial agents for treatment or prophylaxis of travelers' diarrhea. *Arch Intern Med 148*:2421-2427, 1988.
41. Royal L, McCoubrey I. International spread of disease by air travel. *Am Fam Physician 40*:129-136, 1989.
42. Russell RC. Survival of insects in the wheel bays of a Boeing 747B aircraft on flights between tropical and temperate airports. *Bull WHO 65*:659-652, 1987.
43. Schmunis GA, Zicker F, Pinheiro F & D Bradling-Bennett. Risk for Transfusion-Transmitted Infectious Diseases in Central and South America. *Emerg Inf Diseases 4*:5-11, 1998.
44. St. John R. Preventing the Spread of Infectious Disease in the Modern World. *Can J Public Health 85*: 370-372, 1995.
45. Tauxw RV, Puhr ND, Wells JG, Hargrett-Bean N, Blake PA. Antimicrobial resistance of Shigella isolates in the USA: the importance of international travelers. *J Infect Dis 162*: 1107-1111, 1990.
46. The preventable epidemic that keeps coming back. Electronic Mail & Guardian. October 2, 1997. Http://www.mg.co.za/mg/news/97oct1/1oc-cholera.html.
47. Tormans G, Van Damme P, Van Doorslaer E. Cost-effectiveness analysis of hepatitis A prevention in travelers. *Vaccine 10 (Suppl 1)*:S88-S92, 1992.
48. Touch RJ. New, reemerging and drug resistant diseases: role of the sanitarian. Presented at the Fourth World Congress on Environmental Health, Environmental Health - A Global Challenge, May 27-31, 1996, Aberdeen, Scotland.
49. U.S. International Air Passenger and Freight Statistics: June 1995. Http://www.bts.gov/oai/international/junesum.htm#highlights
50. Walsh JF, Molyneux DH, Birley MH. Deforestation: effects on vector-borne disease. *Parasitology 106(Suppl)*: S55-S75, 1993.
51. Wilson ME. Travel and the Emergence of Infectious Disease. *Emerging Infect Dis 1*:39-46, 1995.
52. World Tourism Organization. *Compendium of Tourism Statistics, 1991-1995*. Seventeenth Edition, Madrid, 1997.