IN-DEPTH REVIEW

Recent trends in infectious diseases for travellers

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In the early 1970s medicine was considered to have conquered infectious diseases. The following three decades have shown this optimism to be misplaced, with both traditional infections increasing in prevalence and novel diseases appearing. Many of these diseases have become major problems in developing countries, and coupled with the exponential growth in international traffic now pose a significant risk to the traveller.

The threat to the package tourist differs greatly from that to the businessman, soldier or backpacker. The latter groups may have little control over their food and water supplies and be exposed to vector-borne and zoonotic infections normally restricted to remote locations. However the package holidaymaker may be involved in mass outbreaks of food poisoning with novel pathogens or acquire unusual infections from close proximity to other tourists. All groups may be susceptible to diseases transmitted during travel, and these may be more common than is presently recognised. The common factor is that all such infections may be transported around the world within their incubation period, and that any disease can now present to any doctor.

Today more than ever before it is incumbent on any practitioner to ask not only 'where have you been?' but also 'what were you doing there?'

Key words: Infectious diseases; outbreaks; travel medicine; travellers.

INTRODUCTION

Infectious diseases, perhaps more than any other aspect of travel medicine, have grasped the imagination of the general public. The agents that cause these diseases possess the ability to travel themselves, either within patients or on inert vehicles of infection. It is a fact that virtually any infectious disease can be transported around the world within its incubation period, so that the concept of so-called 'tropical diseases' only presenting to centres of excellence is no longer relevant: they may now appear in the clinic of any general practitioner.

The changing patterns of travel in recent years have meant that not only are more people visiting foreign countries, but also that they are participating in different activities once they arrive. As a consequence they are exposed to an increasing variety of novel pathogens, related to both the geography and their behaviour. The diseases acquired have contributed to the worldwide interest in new and emerging infectious diseases, which in turn has led to a series of international initiatives to control their spread. It is also important to remember that a traveller with a communicable disease may not have been infected whilst overseas but instead during the journey home by air or sea, although this probably occurs infrequently.

There have been a small number of observational studies investigating the incidence and prevalence of different conditions in travellers, whilst the majority of recent papers report incidents and outbreaks of importance. In reviewing the latest published work, we have therefore concentrated on highlighting those reports of most interest and relevance to the practising physician.

INFECTIOUS DISEASE INCIDENTS OF INTERNATIONAL SIGNIFICANCE

In September 1994, the first television reports were broadcast of people fleeing from a city in northern India where cases of plague had been reported. Within days there was an international response, which was both extreme and inappropriate; borders were closed, travellers quarantined, and trade links suspended. The disease involved was one of the three covered by the
undertook a control programme which included not only public health measures but also culling of the poultry population, which was believed to be a reservoir for the virus. The campaign appeared successful, although the authorities in Hong Kong were either discouraged from travelling or else faced quarantine on return home.9 In 1999 a cluster of deaths from a haemorrhagic fever was reported from the Upper Congo region. Detailed investigation identified the aetiological agent as Rift Valley fever, which is both easily transmissible and potentially lethal. 10 A year later a large outbreak of Rift Valley fever affected several east African countries, all of which were dependent on international tourism for foreign exchange. Although no tourists were known to be affected, many were either discouraged from travelling or else faced quarantine on return home.9 In 1999 and 2000, over 170 people were affected and the threat to other countries has been sufficient to cause many (including the United Kingdom) to review their immunization programmes.15,16 Of arguably greater long-term significance, has been the surge in incidence of sexually transmitted diseases. Syphilis is now effectively uncontrolled, and cases have been exported to many countries.17 More worrying has been the associated rise in HIV infection, which in the future may have a similar impact in the former Soviet states to that of the disease in sub-Saharan Africa.18 Dengue has been well described as an uncommon arboviral infection in travellers for many years. In the last decade the epidemiology of the disease has changed markedly, as more efficient mosquito vectors have become widely distributed and the four different virus serotypes have appeared in new locations.19 The result has been a resurgence of disease, particularly in the Caribbean area, with cases of dengue haemorrhagic fever (DHF) being reported more frequently.20 The latter condition generally occurs as an immune manifestation of sequential infection by two different dengue serotypes, and its increased incidence is directly attributable to the appearance of strains in new locations.21 Travellers are commonly affected by dengue, but a recent report of possible DHF in a tourist suggests that the travel plans of people with proven past infection will in future need careful thought.22

NOVEL DISEASES AND TRAVELLERS

The threat of new and emerging infectious diseases to international public health was first described in 1992.2 There are numerous reasons for the appearance of new diseases and the resurgence of old infections over the last decade, but one of the major areas of concern is the importation of novel infections by travellers.3 This stems from both the difficulty of diagnosis in the index case, and the potential spread of disease amongst an immunologically naive population.

Hantavirus pulmonary syndrome is a new clinical entity, first described in 1993 in the south-western United States, when several outbreaks of severe respiratory infection affecting previously healthy young adults were reported. Over 170 people were affected and mortality was over 40%.23 The reservoir of the virus...
was found to be a type of mouse, whose numbers had rapidly increased following unseasonal rainfall: humans were infected following close contact with the rodents. 24 A worrying development is the demonstration of person-to-person spread of this infection, which, coupled with demonstration of its presence elsewhere in the Americas, suggests that it may soon prove to be a significant international problem. 25

Viruses related to influenza are known to be amongst the most easily transmissible of all agents. Two new viruses of this family have recently been described in Australia. Menangle virus, whose natural reservoir is a type of fruit bat, has been shown to spread to commercial piggeries (with economic impact), and then on to humans. Hendra virus probably also has a fruit bat as its normal host, but has spread to horses and their human handlers causing fatal respiratory infections in both. 26 A closely related new virus (Nipah virus) was the cause of several large outbreaks of febrile encephalitis affecting pig workers in Malaysia and Singapore, with over 100 deaths. These were eventually controlled by the mass culling of pigs. 27 Most cases had evidence of direct pig exposure, but up to a third may have acquired infection from other people.

Australian bat lyssavirus was first identified in 1996 and resembles classic rabies virus, although Australia has always been considered free of rabies. The infection has now accounted for at least two human deaths. 28 The importance of bats as a reservoir for rabies should not be underestimated, and they account for the majority of incidents requiring post-exposure treatment in the United States. Many of these incidents are in travellers returning home, particularly from South America. 29

INFECTION DISEASES IN TRAVELLERS

The diseases that cause the most concern are amongst the commonest. Malaria continues to present problems. The well-recognized difficulties surrounding pre-travel advice on chemoprophylaxis are now further complicated by the changing epidemiology of the disease. Drug resistance is increasing in both Plasmodium falciparum and Plasmodium vivax, whilst the range of parasite is extending reflecting migration of both vectors and human hosts. 30

Gastrointestinal infections may affect up to one third of all travellers, with bacteria being the most common aetiological agents. Antimicrobial resistance is now extremely common, particularly in countries where antibiotics are available as over-the-counter medicines, and there is evidence that travel-associated infections are becoming more difficult to treat. 31

The sexual behaviour of tourists has long been the subject of comment, and indeed an entire industry has been built around 'sex tourism'. Despite the enormous efforts now directed at behaviour modification and international legislation, recent work has continued to show that multiple sexual contacts are common in travellers. 32 HIV transmission generally attracts most international concern, yet the spread of multi-drug resistant organisms may cause more immediate problems. 33

Case reports of geographically unusual infections in travellers of different nationalities make the point that 'travel medicine' means just that, and that 'tropical medicine' is probably a misnomer for diseases seen out of context. Examples include the first reports of coccidiodomycosis in Korea, and murine typhus imported into France from Indonesia. 34, 35

TRANSPORTATION-ACQUIRED INFECTIOUS DISEASE

The nature of air travel means that diseases acquired during flight are extremely difficult to identify and investigate. There is a long-held belief in some circles that respiratory infections are commonly transmitted on-board aircraft but little evidence to support this hypothesis. Indeed, the microbiological quality of cabin air is probably better than that of most other comparable forms of transport. 36 Attention has focussed on the risk of transmission of tuberculosis following two case reports where this appeared to have occurred on aircraft during long-haul flights. 37 The WHO reviewed the subject and published its advice to operators in 1999. 38 Although there is no evidence to suggest that recirculated cabin air played any part in the reported incidents, there is a recommendation that all aircraft be fitted with high efficiency particulate air filters, which may cause major logistic problems for a numbers of operators.

A leisurely ocean cruise may seem a safer and more attractive alternative. Certainly, the recent growth in this commercial area would seem to reflect this view. Unfortunately, sharing of a closed environment with numerous other people for days rather than hours may increase the risk of disease transmission. There are now regular outbreaks of gastrointestinal disease at sea, especially when caused by small round viruses. 39 Legionella pneumophila has been associated with whirlpool baths on board ship, and one incident in the North Atlantic is probably the only recent outbreak where a communicable diseases epidemiologist has been parachuted into action! 40

Perhaps of most interest are recent reports of influenza A outbreaks at sea. Three cruises were affected in 1997–1998, in each case occurring outside the 'normal influenza season', when the index case originated from the other hemisphere. 41 These are particularly worrying when considering the global spread of influenza described above, but can also pose significant health problems to a group of passengers who are often elderly or have pre-existing disease.

SUMMARY

In contrast to the optimistic view expressed in the 1970s, infectious diseases are not defeated. New agents have
appeared, old diseases have been found to be caused by previously unknown organisms, and ancient plagues have returned. Travellers are the group most likely to be exposed to many of these diseases, and in whom a firm diagnosis will be made. They truly are the ‘sentinel chickens’ of the 21st century.

REFERENCES


2. Institute of Medicine. Emerging Infectious Diseases: Microbial Threats to the Health of the United States. Washington D.C.: National Academy Press, 1992. This document was the first to draw attention to the potential impact of new and emerging infectious diseases. It was instrumental in generating the international interest and funding necessary to meet the perceived threat.


4. PHLS Communicable Disease Surveillance Centre. Plague in India. Commun Dis Rep Wky 1994; 4: 183. Description of the first reports of possible plague cases in Surat, India. The incident had already attracted media attention by this time, coupled with inappropriate public health measures in a large number of countries.

5. Deodhar NS, Yemul VL, Banerjee K. The plague that never was: a review of the alleged plague outbreaks in India in 1994. Public Health Policy 1998; 19: 184–199. A discussion from the Indian perspective of the 1994 plague outbreak. The article is highly critical of the accuracy of diagnosis, and describes the international impact of the sanctions imposed on India as a result.


9. Centres for Disease Control and Prevention. Rift Valley Fever – East Africa 1997 – 1998. Morbid and Mortal Wky Rec 1998; 47: 261–264. Summarizes the investigation into an outbreak of RVF. It identifies the major risk factor to be contact with livestock, as opposed to general environmental factors. This probably indicates why cases were confined to the local population, and why no travellers were apparently affected.

10. World Health Organization. Viral haemorrhagic fever/ Marburg, Democratic Republic of the Congo. Wky Epidemiol Rec 1999; 74: 157–158. Summarizes the outcome of an investigation into a cluster of VHF, the majority identified as being caused by Marburg virus. All cases were amongst the local population, with no travellers implicated. A major risk factor was identified as being those involved in gold mining, suggesting a common source of infection.

11. PHLS Communicable Disease Surveillance Centre. Need for vaccination against yellow fever. Commun Dis Rep Wky 1999; 9(33): 289–292. Confirms that a fatality in a German traveller originally reported to be caused by Ebola, was in fact caused by yellow fever. The individual had not been vaccinated. This was the first yellow fever death in Germany since 1946, and reinforces the current recommendation for this vaccination for those travelling to west Africa.


13. Peiris M, Yuen KY, Leung CW, et al. Human infection with influenza H9N2. Lancet 1999; 354: 916–917. Reports the diagnosis and follow-up of two H9N2 influenza cases in children in Hong Kong and China (Guangdong Province), both of whom had mild symptoms and recovered with no medical complications. A linked survey of Hong Kong blood donors found evidence of old infection in a small number, suggesting that trans-species virus spread to humans from pigs and birds may not be uncommon.


15. UK Department of Health. Immunization against Infectious Disease. London: HMSO 1996. This booklet contains essential information for all practitioners considering immunization of any patient, but especially prospective travellers. There is a clear account of the background decision-making process within the UK, and a full description of most of the relevant practical procedures. It should be on the bookshelf of every medical centre.
Documents the first known imported case of adult diphtheria in UK from the newly independent states, and stresses the current recommendation for appropriate vaccination of adults visiting endemic and epidemic destinations, especially if living or working with local populations.

An account of heterosexually acquired syphilis presenting in travellers from eastern Europe returning to rural England. It illustrates that an inquisitive approach to patients presenting to any practice can identify problems of international importance.

A clear review of the global distribution of HIV as understood in 1997. It illustrates in a simple way that the virus continues to spread across the world, and how the varying modes of transmission are important in different countries. In a rapidly changing field, the article provides an excellent overview of the geographical extent of HIV infection from which travellers (and their medical advisers) can make their own individual risk assessments.

Summarizes the investigation into an outbreak of dengue. Positively identifies newly occurring serotypes amongst locally acquired cases. It raises the spectre of large numbers of patients with dengue haemorrhagic fever in the near future.

Discusses the risk factors involved in the re-emergence of dengue in Cuba. It especially highlights the breakdown in controlling the Aedes aegyptii vector population as being a major contributory factor.

A comprehensive review of the epidemiology and clinical features of illness caused by dengue viruses. There is a discussion of the latest theories about the pathogenesis of dengue haemorrhagic fever, which is understandable to the non-expert immunologist. This article highlights the importance of a globally important infection, which may be unfamiliar to UK practitioners.

A case report of a traveller returning from the Philippines which initially resembled dengue haemorrhagic fever. Although the clinical condition evolved into a benign condition, its serves as a reminder of the possibility of future problems in travellers.

The first description of the aetiological agent causing an outbreak of severe respiratory disease in the south-west of the United States. The people affected were characteristically previously healthy young adults, with many deaths despite early intensive medical support.

Reviews the virology and epidemiology of hantaviruses worldwide. It summarizes the appearance of hantavirus pulmonary syndrome, and confirms the direct link with certain rodent species populations.

Describes an outbreak of hantavirus pulmonary syndrome, in which some cases may have been infected by person-to-person spread. This raises the possibility that the disease may pose an even more serious threat to international health, as opposed to being an exclusively rodent-borne zoonosis.

Summarizes the current position of viral diseases in Australia. It discusses the spread of Hendra virus in both equine and human populations, but does not identify the mechanics of spread or the factors involved. There is also a useful concise description of various other important new viral infections in the Pacific region.

Concise summary of the outbreak in early 1999, affecting at least 257 people with over 100 deaths. Describes the various control measures employed, and the apparent interruption of virus transmission.

The first report of 'rabies' acquired within Australia. In fact the virus is a close relative, with fruit bats as the natural reservoir. However, as this case demonstrates, this virus can also be transmitted to humans and cause fatal encephalitis.

A full description of the measures recommended in the USA to control rabies. The catalyst for this revision to the preceding advice was the recognition of the importance of bats as a rabies reservoir, and the guidance now contains specific reference to the management of incidents of bat exposure.

A summary of the evolving malaria situation in Africa. The article discusses the disease itself and the reasons for the recent changes in epidemiology. An international approach is suggested to the problem, which although logical and intellectually attractive is probably politically unobtainable.

A review of the increasing resistance to an antimicrobial agent that is becoming one of the most important for treatment of serious sepsis and invasive gastrointestinal disease. The spread of EMRSA resistant to ciprofloxacin is a cause for concern.

In a selected sexually active population, this study demonstrated that between 20% and 40% of clinic attendees who had travelled overseas within a 3-month period had had a new sexual contact. Over half of these admitted intermittent or poor condom use.


Single dose regimens are commonly used in genitourinary medicine and rely on continuing sensitivity of the organisms to the antibiotics used. Fluoroquinolones are now the first-line drug of choice in many areas. Full fluoroquinolone resistance is now found in up to 10% of isolates from the Far East, with nearly 50% fully resistant in some countries.


A case report of a fungal infection common in the United States. It illustrates that travel medicine includes the export of 'normal pathogens' to areas where they may be geographically rare, and that diagnosis can be delayed for extended periods.


The first case reports of murine typhus imported into Europe from Indonesia. The article highlights the importance of making this diagnosis, since the condition requires specific therapy (usually tetracyclines).


A study that compared the microbiological quality of air in a commercial airliner with that of other representative locations, such as city streets and railway stations. It found that cabin air contained fewer bacteria than the other sites tested. The high efficiency filters now present in many locations, such as city streets and railway stations. It found that cabin air contained fewer bacteria than the other sites tested. The high efficiency filters now present in many aircraft systems mean that recirculated air is unlikely to pose a significant risk of infection.


Description of an investigation of a passenger who travelled on a series of long-haul American internal flights with open pulmonary tuberculosis. Of 925 passengers examined on four aircraft, six had evidence of recent infection that may have been acquired in-flight. All of these were seated close to the index case, and there was no evidence that recirculation of cabin air played a role. The article is important since it stimulated interest in the subject of airborne disease spread on aircraft, and led directly to the WHO guidance at reference 38.


A full review of the currently available information concerning transmission of tuberculosis on aircraft. It includes a series of recommendations to reduce the future risk of disease spread, although some of this may prove difficult to implement without legislation.


A summary of all outbreaks on cruise ships notified to Centres for Disease Control during the 8 year period. It concludes that at least one third of incidents could have been prevented by simple precautions such as avoidance of 'high risk' foods and excluding food handlers from working when ill.


An outbreak report describing Legionnaire’s disease affecting 50 passengers on a Caribbean cruise ship. Epidemiological investigation implicated a whirlpool spa, which was later found to be colonized with *Legionella pneumophila* of the same serogroup as that causing illness. New advice is given to reduce the risk of transmission of infection from these spas.


Summary of a large outbreak of influenza A occurring out-of-season in Alaska, almost exclusively affecting travellers. Tourists on cruise ships were thought to have introduced the virus from countries where influenza was 'in season', with secondary spread amongst groups undertaking land-based tours.