

## EDITORIAL

# IMPORT INFECTIOUS DISEASES IN BELGIUM

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### I. INTRODUCTION "DISEASES RESPECT NO FRONTIERS"

In 1997 the World Tourism Organization registered 613 million of people travelling across international borders, with about 30 % of the international tourist arrivals in developing countries and 4 % in Africa (1). In Belgium, about 650.000 persons above 15 years of age are estimated to travel to tropical-subtropical regions in 1997 (2). Although the overwhelming majority of travellers return without major health problems, (3) pathogenic micro-organisms may travel with them and be imported while coming home. Infections may be transported from one part of the world to another part within 36 hours, which is within the incubation time of many infectious diseases.

The pivotal role of the enormously increased mobility and movement of people in the last decades in the emergence of infectious diseases has recently been reviewed (4-6). Evidently, not only tourists, long-term residents and business men, but also immigrants, political refugees, asylum seekers, international students, migrant workers etc. may confront the physician from today with virtually every pathology existing anywhere in the world, diseases never or only rarely seen in our regions. Maybe, there exists nearly no infectious disease anymore for which there is not at least one case report of importation into the industrialised world.

Travel is nowadays not the privilege of adventurous or rich people only, but all social classes, all age groups, and also people with chronic diseases travel around the world. HIV-infection and other immunocompromising disorders may even enlarge the spectrum of rare diseases possibly imported by infected migrants or travellers. In this issue, Depraetere et al. describe *Penicillium marneffe* infection in two Thai HIV-infected women living in Belgium since some years (7). Infection with *P. marneffe* is but one among

the many potentially travel-associated opportunistic infections. The HIV infected traveller should not necessarily avoid travel, but the traveller and his physician should be aware of the increased risk for infections in general. The traveller will have to accept a certain risk, and he needs to keep that risk as small as possible. Physicians should be alert to early recognition of uncommon pathogens acquired in the tropics in case of post-travel medical problems (8).

### II. CLASSICAL INFECTIOUS DISEASES IN RETURNING TRAVELERS

Classical medical problems in returning travellers are fever, gastro-intestinal infections and dermatological problems, besides sexually transmitted diseases, eosinophilia due to symptomatic or asymptomatic worm-infestations (9) and many other possible diseases. Among the 17.042 sick travellers seen during a 45 month period (378 per month) in an university based clinic for tropical and infectious diseases in Munich, 95 % presented with either diarrhoea (70 %), fever (20 %) and/or skin alterations (11%) (10).

Although very suspect, fever in travellers returning from the tropics is not necessarily travel-related and has not necessarily a specific tropical origin. Cosmopolitan infectious diseases (e.g. respiratory or urinary infection, influenza, or even endocarditis, etc.) can also be the cause, although some diseases are present with a higher frequency in the tropics (e.g. leptospirosis, tuberculosis, acute HIV infection). Series reported from specialised centres may give some insight in the probabilities for the different causes of fever in travellers returning from tropical countries, as illustrated in a Canadian study: in 50% of all causes the origin of fever is not specific for the tropics; malaria, viral hepatitis, typhoid fever, and dengue accounted for 40% of all causes and 80% of tropical causes (11). This illustrates that, although there are many different diagnostic possibilities, most of the specific causes for fever after a stay in the tropics are within a relatively small group of infections.

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The clinical aspects of these classical topics on infectious diseases in returning travellers were recently summarised in this journal (12). The clinical suspicion for a specific infection is the most important factor for a rapid diagnosis. A good medical travel history and clinical examination are essential. As the diagnostic work-up and treatment of many of these pathologies may fairly often require expertise and not widely available diagnostic procedures, the non experienced clinician in charge should not hesitate to seek the support of a specialist. As a matter of fact, the majority of the classical tropical imported infectious diseases are well treatable, if treatment is administered timely.

### III. MECHANISMS OF IMPORTATION OF INFECTIOUS DISEASES

Most frequent is the direct transportation of infectious diseases from one part of the world to another by infected persons, but examples of other routes of importation (infected vectors, imported food or imported tools) will also be given below.

An *infected person* may be sick himself or be a healthy carrier, with in both cases the possibility of spread towards others. The threat of secondary cases and even a (mini-)epidemic is the main reason for the urgent obligatory reporting of cases to the national sanitary authorities. An area of concern are the cases of infections spread by faecal contamination. Among the many reported examples in the national and international literature we may cite cholera (13,14), typhoid fever (15), hepatitis A (16), amoebiasis and seemingly autochthonous cases of amoebic abscess (17), and even cysticercosis (18). Migrants and their children returning to their origins after prolonged absence may be at unappreciated risk of illness or disease acquisition and possible import (13,16,18). Well known other routes of transmission by persons are the respiratory route (droplet infection) and the sexually transmitted diseases (e.g. HIV). Among other ways of import by infected persons with subsequently secondary spread may be blood transfusion (19) and needle stick accidents. Recently reported examples of the latter, mainly occurring in nurses, are transmission of malaria (20) and dengue (21).

A hot topic which received much media attention during the last years, especially since the 1995 Ebola epidemic in Kikwit, Congo Kinshasa, is the threat of import of arboviral diseases and other viral haemorrhagic fevers. Although the risk for import of Ebola virus is considered very small, in two occasions it happened. A first imported case was a Swiss ethnolo-

gist who became infected in 1995 while dissecting a chimpanzee in Taï Forest National Park in Ivory Coast. She was repatriated, and recovered completely. The diagnosis was made after her recovery (22). There were no secondary cases. However, in 1996, during an ongoing Ebola epidemic in Gabon, a Gabonese physician suffering from a febrile illness travelled to South-Africa for medical care in a private clinic. He survived what was diagnosed afterwards as Ebola-infection, but one of the nurses caring for him died of haemorrhagic fever (23). Another recent report of arboviral disease is about a highly suspected case of fatal Crimean/Congo haemorrhagic fever in a 78 year old woman returning from Zimbabwe, where she stayed in a house near an ostrich farm (24). Ostriches are known to carry possibly infected Hyalomma ticks. Fortunately, no secondary cases were seen among the sixty-four health care worker contacts, including members of the resuscitation team.

Indirect secondary spread in laboratory workers is evidently also of concern. An experienced medical laboratory scientific officer became infected with a toxigenic strain of *Corynebacterium diphtheriae* while handling a sample originating from a patient with a severe sore throat who had recently returned from Russia (25). In our own institute we cared recently for a laboratory worker with acute sleeping sickness acquired from stored samples by needle stick accident. Finally the congenital transmission route of e.g. malaria, trypanosomiasis etc. may also be cited.

*Pathogen carrying vectors* may also be imported, and provoke totally unexpectedly exotic disease at a distance of their original habitat. In this issue a cluster of 6 cases of airport malaria are described, related to their presence in the airport of Zaventem in august 1995 (26). In case of fever of unknown origin in a thrombocytopaenic patient without a recent travel history, airport malaria should be considered if the patient lives near, works at, or has visited an airport recently, especially during hot summers. However, good anamnesis will not be helpful in the even more rarer cases of container or luggage malaria (27-29). Fortunately, in Belgium, the appropriate mosquitoes and climate circumstances are not present for the development of secondary cases by locally infected mosquitoes. However, in the USA mini-epidemics are described in some regions (30). This is the reason why in soldiers returning from Somalia (Restore Hope Operation) the cases of vivax malaria were sought for very carefully, and all returning soldiers received a preventive treatment with primaquine to kill possible hypnozoïtes or gametocytes of *Plasmodium* sp.(31). In the Mediterranean region of Southern Eu-

rope, the theoretical possibility of reintroduction of malaria (32) has been confirmed recently (33). Patients in non-endemic countries for Mediterranean spotted fever may become infected by tick, imported by dogs who visited endemic countries of the Mediterranean basin (34). Fortunately, the fear for importation of plague by fleas during the epidemic in India in 1994 has been unsubstantiated. An unusual example of import of infected animal reservoir, is the acquisition of schistosomiasis by unprotected skin contact by caring for imported African snails in a laboratory worker, who subsequently suffered from a Katayama-syndrome (35).

Recent examples of infections directly tributary to *contaminated imported commercial food* are the large outbreak of cyclosporiasis in the USA by raspberries imported from Guatemala (36) and the cases of cholera associated with imported crabmeat or coconutmilk in the USA (14) and probably with fresh vegetables in Paris.<sup>37</sup> However, there is no justification for an embargo on food exportation from cholera-endemic countries.

Finally to be cited as possible routes of importation are *contaminated objects* (as in the case of anthrax-contaminated souvenirs made from animal skin (38)), and probably even *wild trekking birds* (e.g. by their faeces contaminated with intestinal pathogens (39), or by their rickettsiosis carrying ticks (40)).

#### IV. EXPANDED SPECTRUM OF IMPORTED DISEASES

On discussing imported infectious diseases, one thinks first of all of the typical exotic diseases, which are not present at all or not anymore in our regions. For most of them, especially the vector transmitted tropical diseases, the risk for secondary cases is nearly inexistent (malaria, leishmaniasis, rickettsiosis, schistosomiasis) but the exceptions are described above.

Unfamiliar infectious diseases are not always imported from tropical countries. E.g. brucellosis, leishmaniasis, rickettsial diseases (fièvre boutonneuse) may well be imported from Mediterranean regions, as Rocky Mountain spotted fever, plague or coccidioidomycosis may be acquired during travel in the United States (41).

For some cosmopolitan diseases the incidence in the industrialised countries has strongly diminished, or is even reduced to zero (eradicated), so that almost all cases are imported. Typhoid fever is an example of rare infections in the industrialised countries. Of the 2445 cases of typhoid fever reported in the USA between 1985 and 1994, seventy-two percent were

travel-associated, with an increase from 33% in 1967-72, 62 % in 1975-1984, 65 % in 1985 till 75 % in 1994 (15).

The threat persists that by importation and subsequent secondary cases nearly-eradicated diseases may again be reintroduced, as exemplified by measles and poliomyelitis. The number of measles cases has spectacularly fallen in the Americas since the Pan American Health Organisation developed a measles-elimination strategy by intensified vaccination, associated with epidemiological and laboratory surveillance. In 1997 the USA reported a total of 138 cases, the lowest number of cases ever reported. In 59% of the reported cases there was epidemiological or virological (molecular tracing techniques) evidence of a foreign source, primarily from Europe and Asia (42). An outbreak of poliomyelitis occurred in the Netherlands between September 1992 and February 1993 in an unvaccinated religious group. Sequence analysis of the viral genome indicated that the wild poliovirus type 3 strain was very probably originating from the Indian subcontinent, although the genomic difference with the strain isolated in India was still too large to assume direct import (43). The wild poliovirus type 1 involved in the 1978 outbreak in the Netherlands travelled through contacts in Canada to members of the same religious groups in the USA (44). Those two examples illustrate the need for intensifying efforts to reach a high vaccination coverage, and to reach finally the WHO goal of global eradication, first for polio, but subsequently also for measles. Special WHO-directed and co-ordinated surveillance systems for diseases in advanced stage of eradication are needed, as for polio is the case. In every country an adequate surveillance of acute flaccid paralysis in children aged less than 15 years of age must be organised: all cases should be investigated clinically, virologically and epidemiologically. In the absence of poliomyelitis the reported incidence of acute flaccid paralysis should be around 1 per 100.000 children under 15 years of age.

Because of low incidence in our own regions, contribution of imported cases of other cosmopolitan diseases may be substantial and/or rising. The increasing incidence of viral hepatitis related to travel may be worrying. In one region of the United Kingdom travellers accounted for 6% of all reported cases of hepatitis B in 1981, for 8% in 1986, and for 12% in 1990-94 (45). Among 209 patients with acute viral hepatitis registered by 187 sentinel general practitioners in Belgium in 1991 and 1992, 41 suffered from hepatitis A and 11 from hepatitis B. Five cases in 41 (12 %) within the group of hepatitis A and 3/11 (27

%) within the group of hepatitis B had a travel to high-risk countries in the preceding months as only detectable risk factor (46). Parents of adoptive children carrying the hepatitis B virus A are also in a well known risky situation (47). In the industrialised countries, the estimated percentage of cases of hepatitis A related to travel may vary between 4 and 40 % (48).

The epidemiology of tuberculosis in industrialised countries has dramatically improved, while in low-income countries it has remained unchanged or even deteriorated. The proportion of tuberculosis cases that are foreign-born in industrialised countries has been dramatically increasing over just the last decade: in at least 4 countries in western Europe this proportion now exceeds 50% (49). Of 745 immigrants and refugees who sought medical evaluation in California from July 1, 1992 until December 31, 1993, 6.9 % had active TB and another 39.7 % were candidates for preventive therapy (50). Non-western allochtones from developing countries are responsible for up to one third of the new declared cases of tuberculosis in Belgium (51).

Another striking example of substantial contribution to the total number of disease cases is Legionnaire's disease. Of the 201 cases of Legionnaire's disease officially reported in the UK in 1996, almost half were linked with international travel to popular tourist destinations such as Spain, France, Greece, the Caribbean, Italy, the USA and Turkey (52). An European Working group for Legionella Infections was set up in 1986 and introduced the European Surveillance Scheme for Travel Associated Legionnaires' disease in 1987 (53).

Travellers may be a potential source of imported strains of antimicrobial-resistant *N. gonorrhoeae*, pneumococcal strains (54), meningococcal strains (55) or TB strains (56). Ten persons among a group of 69 Dutch servicemen tested positive on tuberculin skin testing after returning from a 3-month deployment in Turkey. They all stayed in the same hotel. One person developed multiple-drug-resistant TB 5 months later (57).

Genetic variants against whom nobody in the population has antibodies are responsible for recurring epidemics, especially the major antigenic shifts heralding pandemic influenza. The pandemics of the last decades began in mainland of southern China, the supposed "influenza epicentre", and spread both east and west (58,59).

## V. SURVEILLANCE

All these above mentioned examples underline the importance of notifying diseases to the national and international health authorities. Not all these diseases are notifiable, and for notifiable diseases notification is incomplete. Electronic information systems via internet (e.g. Promed) may play an important informal role. The WHO is updating the International Health Regulations, providing a mechanism for immediate notification of all outbreaks of communicable diseases representing an international threat (hence not only cholera, yellow fever and plague) (60). The "Division of Emerging and other Communicable Diseases Surveillance and Control" (EMC) is a special unit of the WHO, prepared to give advice on haemorrhagic viral diseases, and for ready to start operations, within 24 hours of notification to WHO. A "European network for imported viral diseases" (ENIVD) has recently also been established.

For the clinician, lastly, some books may be a useful guide as reminder of the geographical distribution of infectious diseases (61,62), as is the "Global Infectious Disease and Epidemiology Network" (GIDEON), a computer program designed to assist in the diagnosis of over 300 infectious diseases from over 200 countries, based on the symptoms, signs and laboratory findings (63).

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