The accidental medical tourist

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Travel medicine may be defined as the area of medicine that deals with the prevention and management of health problems among international travellers. While travel-related illnesses may represent a wide range of infectious and noninfectious threats, travel medicine is frequently associated with individuals travelling to low-income tropical countries. As a result, immunization, chemoprophylaxis against malaria and other infectious diseases, and recommendations for preventive behaviours to reduce the risk for high-risk environmental, food and sexual exposures are key themes.

The explosion of medical tourism has added a new dimension to the field of travel medicine. Medical tourists are individuals who travel internationally for medical and surgical services. These services include, but are not limited to, joint replacements, ophthalmological procedures, cosmetic surgery, cardiac care, dental care, organ transplants, reproductive care and stem cell therapies (1,2). While this practice has been the source of considerable moral and ethical debate (3), a steady supply of customers frustrated with long wait times in publicly funded systems and noninsured or underinsured individuals in private systems are increasingly being catered to by the overseas health care market, in which services are readily accessible at relatively low costs (4). It has been difficult to quantify the global extent to which medical tourism occurs (5). However, estimates are that hundreds of thousands of patients are treated, and billions of dollars per year are spent by medical tourists in India alone (6). The practice of medical tourism is not without risk. The potential for medical tourism to cause widely geographically dispersed outbreaks of communicable disease was made clear in 2004, when multiple cases of postoperative *Mycobacterium abscessus* infections were identified in 12 individuals from New York, Massachusetts, North Carolina and Rhode Island in the United States, as well as Puerto Rico, who had undergone cosmetic surgical procedures in Santo Domingo, Dominican Republic (7).

The New Delhi (India) metallo-beta-lactamase (MBL), first reported by Yong et al (8), has thrown a far larger wrench into the cogwheel of medical tourism. These investigators reported a Swedish patient with a urinary tract infection who had recently travelled to and received medical care in New Delhi. The isolated multidrug-resistant *Klebsiella pneumoniae* strain produced a novel MBL that was related to, but distinct from, the previously reported MBLs VIM-1 and VIM-2. They found the gene for the enzyme *bla*(NDM-1) on a plasmid, both in the infecting strain and in a coisolate of *Escherichia coli* cultured from the patient's stool. Since this report, isolates carrying the *bla*(NDM-1) gene have been reported in Canada, the United States, Australia, Europe, Asia and Africa (8-11).

Kumarasamy et al (10) recently reported a series of patients with *bla*(NDM-1) from India, Pakistan and the United Kingdom. They identified *bla*(NDM-1) in 30 isolates of *K pneumoniae*, and in 19 *E coli*, seven *Enterobacter cloacae*, two *Proteus* species, and one each in *Citrobacter freundii* and *Klebsiella oxytoca*. Thirty-seven isolates with *bla*(NDM-1) were identified in the United Kingdom, which included 21 *K pneumoniae*, seven *E coli*, five *Enterobacter* species, two *C freundii*, and one each in *Morganella morganii* and *Providencia* species. Notably, among the 29 patients identified in the United Kingdom, 17 patients had travelled to India or Pakistan and 14 were admitted to hospital for a range of medical and surgical services. Overall, there was a high rate of observed resistance (greater than 95%) to a broad range of antimicrobial agents, with only tigecycline and colistin demonstrating significant rates of susceptibility at 63% and 93% of isolates, respectively. This publication has led to concern among the infectious diseases and medical microbiology community, and widespread attention by the media and the public at large.

The observation that multiresistant Gram-negative infections exist and can be spread through international travel, particularly to India, is well recognized (12-15). In addition, numerous multidrug-resistant Gram-negative infections including MBL-producing *Pseudomonas aeruginosa*, carbapenemase-producing *K pneumoniae* and multiresistant *Acinetobacter baumanii* have been circulating the globe in recent years (16-18). So, what has made organisms producing NDM-1 enzyme so concerning?

Unlike our previous experience with multidrug-resistant Gram-negative infections, in which typically a resistance determinant is observed at least initially within one or two species, from the outset, the NDM enzyme has been detected in a range of organisms. This is likely related, in part, to the fact that the *bla*(NDM-1) gene is carried on a plasmid that is readily transmissible among different species of Enterobacteriaceae. It is also noteworthy that NDM-associated infections have occurred as a wide range of different clinical foci with onset in both community- and hospital-based settings. Previously, multidrug-resistant Gram-negative infections have largely been associated with hospital-based outbreaks, often in critically ill and in other high-risk populations. Similar to some other resistant infections, NDM-associated infections have few treatment options. The only agent with a high rate of susceptibility is colistin, an antimicrobial agent associated with nephrotoxicity and neurotoxicity when used parenterally, and for which rates of resistance may be expected to increase (19,20).

Similar to other emerging infectious disease threats, such as severe acute respiratory syndrome and West Nile virus infection, NDM-associated infections underline the degree to which globalization of commerce and rapid international travel provide ready

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conduits for the dissemination of novel or mutated pathogens. Perhaps the most remarkable aspect of the emergence of NDM-associated infections is that they have raised public and medical community awareness of the practice and risks associated with medical tourism. For the medical community, this should mean greater attention to travel history in individuals with serious infections, and provides (yet again) a rationale for improved funding for surveillance and infection prevention and control activities. Pretravel counselling should include assessment of the potential for acquisition of resistant bacterial infections and recommendations for their prevention; although this, again, depends on the ability to adequately assess risk in locales that may have limited surveillance infrastructure and in overseas facilities, which may regard disclosure of such information as detrimental to their bottom line. The travelling public should be informed of the potential infectious diseases risks associated with hospital care abroad. On a much higher level, however, a larger societal discussion about the mismatch between system capacity and patient expectations that leads increasing numbers of individuals to travel abroad for advanced medical care is warranted.

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