International Journal of Infectious Diseases 48 (2016) 113–117

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Management of infections in critically ill returning travellers in the intensive care unit—I: considerations on infection control and transmission of resistance☆

Hakan Leblebicioglu [g], Alfonso J. Rodriguez-Morales [b], Gian Maria Rossolini [c,d], Rogelio López-Vélez [e], Jean-Ralph Zahar [f], Jordi Rello [a,*] on behalf of ESGCIP and ESGITM

[a] CIBERES, Vall Hebron Research Institute, Universitat Autònoma de Barcelona, Barcelona, Spain
[b] Public Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia
[c] Department of Medical Biotechnologies, University of Siena, Siena, Italy
[d] Department of Experimental and Clinical Medicine, University of Florence, and Clinical Microbiology and Virology Unit, Florence Careggi University Hospital, Florence, Italy
[e] National Referral Unit for Tropical Diseases, Infectious Diseases Department, Ramón y Cajal University Hospital, Madrid, Spain
[f] Infection Control Unit, Université d'Angers, Centre Hospitalier Universitaire d'Angers, Angers, France
[g] Department of Infectious Diseases and Clinical Microbiology, Ondokuz Mayis University Medical School, Samsun, Turkey

ARTICLE INFO

Article history:
Received 25 January 2016
Received in revised form 19 April 2016
Accepted 21 April 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:
Resistance
Infection control
Traveller
ICU
Migrant

SUMMARY

Depending on their destinations and activities, international travellers are at a significant risk of contracting both communicable and non-communicable diseases. On return to their home countries, such travellers may require intensive care. The emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), and more recently Ebola haemorrhagic fever, has highlighted the risks. Other well-known communicable pathogens such as methicillin-resistant *Staphylococcus aureus* and carbapenemase-producing *Enterobacteriaceae* have been described previously. However, malaria remains by far the most important cause of death. The issues related to imported antibiotic resistance and protection from highly contagious diseases are reviewed here. Surveillance strategies based on epidemiological data (country visited, duration of travel, and time elapsed since return) and clinical syndromes, together with systematic search policies, are usually mandatory to limit the risk of an outbreak. Single-bed hospital rooms and isolation according to symptoms should be the rule while awaiting laboratory test results. Because person-to-person contact is the main route of transmission, healthcare workers should implement specific prevention strategies.

1. Imported antibiotic resistance

Infections caused by multidrug-resistant (MDR) pathogens are typically associated with increases in morbidity, mortality, and healthcare-associated costs, and represent an increasing public health challenge of global dimensions.[1] The combination of a progressive loss of antibiotic efficacy due to the emergence and dissemination of resistance and the slow rates of discovery and development of new antibiotics active against MDR pathogens has led to what has been termed the 'antibiotic resistance crisis'. The situation has been further complicated recently by the emergence and dissemination of strains that remain susceptible to only a few antibiotics (extensively drug-resistant (XDR) strains), which are difficult to treat.[2]

The most challenging MDR pathogens include (1) methicillin-resistant *Staphylococcus aureus* (MRSA), (2) vancomycin-resistant enterococci (VRE), (3) *Enterobacteriaceae* producing extended-spectrum beta-lactamases (ESBLs) or carbapenemases (CPE), (4) XDR *Pseudomonas aeruginosa* that remain susceptible only to polymyxins, and (5) carbapenem-resistant Acinetobacter (CRA). Among these, CPE and CRA are currently the most problematic due to their XDR phenotypes, their propensity for epidemic diffusion in

DOI of original article: http://dx.doi.org/10.1016/j.ijid.2016.04.020
☆ ESGCIP is the ESCMID Study Group for Infections in Critically Ill Patients; ESGITM is the ESCMID Study Group for Infections in Travellers and Migrants.
* Corresponding author.
E-mail address: jrello@crips.es (J. Rello).

http://dx.doi.org/10.1016/j.ijid.2016.04.019

healthcare settings, and the high mortality rates associated with invasive infections.[2]

In principle, any of these pathogens can be encountered, either as colonizers or as infecting agents, in travellers returning from areas of endemicity and in patients repatriated from foreign healthcare facilities. Acquisition may be the consequence of exposure to contaminated food or environments, of close contact with colonized individuals, or of admission to hospitals and exposure to medical practices either for unexpected reasons (e.g., trauma, acute diseases) or for medical tourism (e.g., specialized surgery, organ transplantation). As has been clearly documented, the transmission of MRSA has increased with the growth of international travel, resulting in either asymptomatic colonization or clinically significant MRSA infections.[3,4] Some evidence is also available for the international dissemination of VRE via transfer/repatriation of patients from hospitals located in endemic areas.[5] Concerning Gram-negative organisms, the impact of international travel has been firmly established in the dissemination of MDR *Enterobacteriaceae*, including high-risk clones producing ESBLs (especially enzymes of the CTX-M type) and/or carbapenemases of various types (e.g., KPC, OXA-48, NDM, VIM).[6–8] The risk of the spread of MDR strains of *Enterobacteriaceae* in this situation includes not only *Escherichia coli*, *Klebsiella spp*, and *Enterobacter spp*, but also classical enterobacterial pathogens such as *Salmonella enterica* and *Shigella spp*, with evidence of imported cases of typhoid fever and shigellosis caused by MDR strains.[8,9] The transmission of MDR Acinetobacter has been documented following the international transfer of patients from intensive care units (ICUs) in countries with high-level endemicity,[10] and the repatriation of evacuees involved in military operations in endemic areas.[11] Less evidence is available for the travel-related dissemination of MDR/XDR *P. aeruginosa* strains, but this is clearly a possibility following the transfer of colonized patients from ICUs where these strains are endemic or are causing outbreaks.[12]

The admission to the ICU of patients colonized or infected by MDR/XDR pathogens is a matter of concern, since it may be followed by cross-infections and outbreaks in the ICU setting unless suitable infection control practices are enforced immediately. Moreover, infections caused by MDR/XDR pathogens may require different antimicrobial treatments from those routinely used in the ICU, which are based on the local epidemiology; this may result in inappropriate empiric treatment and thus increased morbidity and mortality.

Therefore, the possibility of carriage or infection by an MDR/XDR pathogen should always be considered for critically ill returning travellers admitted to the ICU. A risk assessment should be performed, considering the area of provenance, the history of the patient, and the presence of additional risk factors for carriage or infection by similar resistant pathogens.[2,12]

The epidemiology of MDR/XDR pathogens may vary according to geographical area. The proportion of MRSA among *S. aureus* isolates remains very high in some European countries, the USA, Latin America, and the Far East, but is considerably lower in other European countries such as the Netherlands and the Scandinavian countries.[13] ESBL-producing *Enterobacteriaceae* are now disseminated worldwide, with very high rates detected among ICU patients in Latin America, the Asia-Pacific region, and the Middle East.[14] For their part, CPE have achieved a notable level of endemicity in some areas of Europe (e.g., Greece and Italy), the Middle East (e.g., Turkey, Israel), South America (e.g., Colombia), and China.[15] Travellers/patients from areas of high endemicity for MDR/XDR pathogens have a higher risk of exposure to these pathogens, and the possibility of being infected or colonized by these agents at the time of repatriation should always be considered. When consulting sources of information regarding resistance and endemicity (such as ProMED-mail, http://www.promedmail.org), clinicians should consider that (1) for several countries (especially low-income settings) epidemiological information is scarce or lacking, and (2) the epidemiology of MDR/XDR pathogens can change rapidly. So this information should be considered partial and should be updated regularly.

Exposure to medical practices in facilities from endemic areas, either unanticipated or scheduled, is an additional risk factor for carriage/infection by MDR/XDR pathogens.[16]

Recommendations for ICUs, based on the current evidence, include the following:

(1) Carrying out a risk assessment for carriage/infection by MDR/XDR pathogens for all ICU admissions of patients returning from international travel or transferred from foreign hospitals.
(2) Enforcing infection control precautions upon admission for all patients returning from international travel or transferred from foreign hospitals with known risk factors for carriage/infection by MDR/XDR pathogens. The infection control precautions should cover the various types of MDR/XDR pathogens for which a risk was assessed, and should be kept in place until carriage/infection by MDR/XDR pathogens has been ruled out by the proactive surveillance and clinical microbiology diagnostic workup.
(3) Carrying out proactive surveillance for MDR/XDR pathogens for which a risk was assessed by culture and/or molecular methods.

2. Protection from highly contagious disease in critically ill returning travellers in the ICU

2.1. Introduction to potentially life-threatening travel-associated infectious diseases

Depending on their destinations and activities, international travellers are at a significant risk of contracting both communicable and non-communicable diseases.[17] The emergence of severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and more recently Ebola haemorrhagic fever, has highlighted the risks. However, other well-known communicable pathogens such as MRSA[18] and CPE[19,20] have been described previously. ICU patients, because of the severity of illness, the workload, and the antibiotic selection pressure, are important potential reservoirs of dangerous microorganisms. The most important challenges for ICU practitioners are first to identify admissions with the highest risk of communicable disease, and second to rapidly implement preventive measures in order to avoid nosocomial transmission.

Surveillance strategies for the early detection of unusual infectious disease events should be the rule. Syndromic surveillance can help to reduce the identification time. All patients transferred from hospitals in high-risk countries (Table 1) should be considered as potential carriers of MDR or highly drug-resistant microorganisms. All of these patients should be screened for rectal carriage at admission and a few days after any antibiotic therapy.[21] While awaiting screening results, the patient should be hospitalized in a single-bed room. Contact and body fluid precautions should be added. All patients with fever and clinical or radiographic evidence of pneumonia or acute respiratory distress syndrome, and with a history of travel from countries in or near the Arabian Peninsula (Bahrain, Iraq, Iran, Israel, the West Bank and Gaza, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, the United Arab Emirates, and Yemen) within 14 days before symptom onset, or close contact with a symptomatic traveller who developed fever and acute respiratory illness within 14 days after travelling from countries in the region, should be considered as potentially infected by MERS-CoV.[22] Viral haemorrhagic fever