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Review

# Management of infections in critically ill returning travellers in the intensive care unit—II: clinical syndromes and special considerations in immunocompromised patients☆

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SUMMARY

This position paper is the second ESCMID Consensus Document on this subject and aims to provide intensivists, infectious disease specialists, and emergency physicians with a standardized approach to the management of serious travel-related infections in the intensive care unit (ICU) or the emergency department. This document is a cooperative effort between members of two European Society of Clinical Microbiology and Infectious Diseases (ESCMID) study groups and was coordinated by Hakan Leblebicioglu and Jordi Rello for ESGITM (ESCMID Study Group for Infections in Travellers and Migrants) and ESGCIP (ESCMID Study Group for Infections in Critically Ill Patients), respectively. A relevant expert on the subject of each section prepared the first draft which was then edited and approved by additional members from both ESCMID study groups. This article summarizes considerations regarding clinical syndromes requiring ICU admission in travellers, covering immunocompromised patients.


## 1. Introduction

Over the last 20 years, the increase in international travel, which has been intensified by the availability of low-cost flights, has facilitated the movement of an increased number of patients from areas with endemic diseases to distant regions. As a consequence, cities around flight hubs have been and are exposed to the rapid dissemination of imported infections, as was reported in the initial dissemination of HIV infection in North America, and more recently in the 2009 influenza pandemic. Similarly, outbreaks of cholera have been reported in travellers after long distance flights, and tourism has also been associated with the dissemination of infections such as measles, rubella, diphtheria, typhoid fever, and chicken pox, in addition to malaria and haemorrhagic fevers. Poor health conditions and crowding are associated with tuberculosis (TB), diarrhoea, tetanus, and other infectious events, which may be imported by migrants from areas devastated by war.

Immunocompromised patients encompass a growing population with increased susceptibility to infectious complications. Because they live longer and have a better quality of life than ever before, they may have more opportunity to travel and potentially encounter travel-associated infections. It has been estimated that up to one third of solid-organ transplant (SOT) recipients may travel to resource-limited countries within the first year post-transplant.[1] In a survey in North American transplant centres, up to 44% of haematopoietic stem cell transplant (HSCT) recipients reported travel outside the USA and Canada after transplantation.[2] A

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significant number of immunocompromised patients may also be migrants who may return to their countries of origin to visit friends and relatives, and may acquire travel-associated infections. The increased use of monoclonal antibodies for therapy in immunological and oncological diseases has created another at-risk population, although the actual risk of travel-associated infection in these patients is not well established.[3] Data on the real risk of infection in immunocompromised travellers relative to the general travel population are scarce,[4] and particularly the risk of developing an illness severe enough to warrant admission to an intensive care unit (ICU). The repatriation of immunocompromised patients from hospitals in destination countries also carries the risk of contamination of the receiving hospital with multidrug-resistant (MDR) microorganisms, which requires specific infection control measures.[5] This article also addresses certain specific syndromes, such as pneumonia and acute respiratory distress syndrome (ARDS) occurring after travel.

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## 2. Risk of infection in immunocompromised patients (Table 1)

### 2.1. Solid-organ and haematopoietic stem cell transplantation

The risk of infection in SOT recipients varies according to multiple factors, namely the type of organ transplanted, the time from transplantation, and the type and dose of immunosuppressive drugs received.[6] During the first month post-transplant, infectious complications are mainly healthcare-associated. The most profound immunosuppression occurs between months 2 to 6; historically, this is the period in which most opportunistic infections were diagnosed, including herpesvirus infections (cytomegalovirus), *Pneumocystis jirovecii* pneumonia, and invasive fungal infections.[7] However, with the use of universal antiviral preventive strategies and long-term co-trimoxazole prophylaxis, opportunistic infections are currently rarely seen. After 6–12 months, the risk of infection decreases significantly and infections over this period are usually community-acquired, except in the case of increased immunosuppression (due to allograft rejection or dysfunction) or in the case of chronic surgical complications. Because the incidence of infection is higher early after transplantation, it is recommended to avoid travel during the first year.[8]

HSCT recipients are at increased risk for bacterial and fungal infections during the engraftment period in the first month post-transplant. In the case of graft-versus-host disease, cellular immunosuppression is the mechanism responsible for the development of viral infections (particularly cytomegalovirus, adenovirus, and BK virus) and invasive fungal infections.[9] After the second year post-transplant it is considered that the degree of immunosuppression is non-significant if the patient has not developed chronic complications.

**Table 1**
Infectious risk according to type of immunosuppression

| | Infectious risk | Type of immunosuppression | Type of infection |
|---|---|---|---|
| SOT recipients | 1st month post-transplantation: risk related with surgery and ICU stay | Neutrophils: 0<br>B-cells: +<br>T-cells: ++ | Ventilator-associated pneumonia (Pseudomonas, enterobacteria), catheter-related infection, surgical site infection, invasive candidiasis |
| | 1st year post-transplantation: period of higher immunosuppression | Neutrophils: 0/+<br>B-cells: +<br>T-cells: +++ | Viral infections (cytomegalovirus, BK virus, HCV reactivation), fungal infections (Aspergillus, Pneumocystis) |
| | After 1st year post-transplantation: long-term immunosuppressive therapy | Neutrophils: 0/+<br>B-cells: +<br>T-cells: + | Community-acquired infections (pneumonia, urinary tract infection), community-acquired respiratory viruses (influenza, RSV), zoster, opportunistic infections in the case of chronic allograft dysfunction |
| HSCT recipients | 1st month post-transplantation: risk related with neutropenia | Neutrophils: +++<br>B-cells: +<br>T-cells: + | Bacterial infections (Gram-positive bacteria, enterobacteria, Pseudomonas), fungal infections (Candida, Aspergillus) |
| | 1st year post-transplantation: period of higher immunosuppression; immunosuppressive therapy for GVHD | Neutrophils: ++<br>B-cells: ++<br>T-cells: +++ | Viral infections (cytomegalovirus, adenovirus, HSV, BK virus), fungal infections (Aspergillus, Pneumocystis) |
| | After 1st year post-transplantation: non-significant immunosuppression >2 years | | |
| Oncological patients | After recent chemotherapy or radiotherapy (particularly in the case of neutropenia and anaemia) | Neutrophils: +++<br>B-cells: 0/+<br>T-cells: 0/+ | Bacterial infections (Gram-positive bacteria, enterobacteria, Pseudomonas), viral infections (HSV) |
| Splenectomized patients | Particularly during the first 2 years, but may persist several years after splenectomy | Neutrophils: 0<br>B-cells: +<br>T-cells: 0 | *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Capnocytophaga canimorsus* |
| Patients receiving anti-TNF therapy | During therapy and a month after discontinuation of anti-TNF drugs | Inhibition of macrophage activation, recruitment of neutrophils, and granuloma formation | Tuberculosis, skin and soft tissue infection, zoster |

GVHD, graft versus host disease; HCV, hepatitis C virus; HSCT, haematopoietic stem cell transplant; HSV, herpes simplex virus; ICU, intensive care unit; RSV, respiratory syncytial virus; SOT, solid-organ transplant; TNF, tumour necrosis factor.