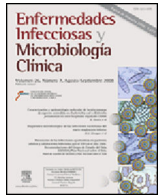




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Consensus statement

Executive summary of imported infectious diseases after returning from foreign travel: Consensus document of the Spanish Society for Infectious Diseases and Clinical Microbiology (SEIMC)



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ABSTRACT

Keywords:

International travelers
Imported infectious diseases
Returned traveler

In a global world, knowledge of imported infectious diseases is essential in daily practice, both for the microbiologist–parasitologist and the clinician who diagnoses and treats infectious diseases in returned travelers. Tropical and subtropical countries where there is a greater risk of contracting an infectious disease are among the most frequently visited tourist destinations. The SEIMC considers it appropriate to produce a consensus document that will be useful to primary care physicians as well as specialists in internal medicine, infectious diseases and tropical medicine who help treat travelers returning from tropical and sub-tropical areas with infections. Preventive aspects of infectious diseases and infections imported by immigrants are explicitly excluded here, since they have been dealt with in other SEIMC documents.

Various types of professionals (clinicians, microbiologists, and parasitologists) have helped produce this consensus document by evaluating the available evidence-based data in order to propose a series of key facts about individual aspects of the topic. The first section of the document is a summary of some of the general aspects concerning the general assessment of travelers who return home with potential infections. The main second section contains the key facts (causative agents, diagnostic procedures and therapeutic measures) associated with the major infectious syndromes affecting returned travelers [gastrointestinal syndrome (acute or persistent diarrhea); febrile syndrome with no obvious source of

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infection; localized cutaneous lesions; and respiratory infections]. Finally, the characteristics of special traveler subtypes, such as pregnant women and immunocompromised travelers, are described.

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Resumen ejecutivo de las enfermedades infecciosas importadas después de regresar de viajes en el extranjero: Documento de consenso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica

R E S U M E N

Palabras clave:

Viajeros internacionales
Enfermedades infecciosas importadas
Viajeros que regresan

En el mundo global, el conocimiento de las enfermedades infecciosas importadas es esencial en la práctica diaria, tanto para el microbiólogo-parasitólogo como para el clínico en enfermedades infecciosas que atiende a viajeros internacionales. Entre los destinos turísticos más visitados se encuentran muchos países tropicales o subtropicales, donde el riesgo de contraer una enfermedad infecciosa es más elevado. La SEIMC ha considerado pertinente la elaboración de un documento de consenso que sirva de ayuda tanto a médicos de Atención Primaria como a especialistas en Medicina Interna, Enfermedades Infecciosas y Medicina Tropical que atienden a viajeros que regresan con infecciones tras un viaje a zonas tropicales y subtropicales. Se han excluido de forma explícita los *aspectos de prevención* de estas y las infecciones importadas por *inmigrantes*, objeto de otros documentos de la SEIMC.

Varios tipos de profesionales (clínicos, microbiólogos y parasitólogos) han desarrollado este documento de consenso tras evaluar los datos disponibles basados en la evidencia para proponer una serie de datos clave acerca de este aspecto. Inicialmente se revisan los aspectos generales acerca de la evaluación general del viajero que regresa con una potencial infección. En un segundo bloque se señalan los datos clave (agentes causales, procedimientos diagnósticos y medidas terapéuticas) de los síndromes infecciosos principales en el viajero que regresa (síndrome gastrointestinal (diarrea aguda o persistente), síndrome febril sin foco aparente, lesiones cutáneas localizadas e infecciones respiratorias). Finalmente se describen las características en viajeros especiales como la viajera embarazada y el viajero inmunodeprimido.

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Introduction

Justification

According to the World Tourism Organization, there were around 1,184 million international tourist arrivals in 2015, some 50 million more than in 2014 (an increase of 4.4%). International tourist arrivals for the year 2016 were forecast to increase by 4%, both worldwide and regionally. Regional growth was expected to be highest in Asia and the Pacific (between 4% and 5%) and the Americas (between 4% and 5%), followed by Europe (between 3.5% and 4.5%), and Africa and the Middle East (between 2% and 5%).¹ *Familitur* data showed that international tourist movements made by Spaniards were 11.8 million in 2014, 1,140,000 of which were to the African continent, 764,000 to America (Central Caribbean and South) and 520,000 to Asia.²

The most frequently visited tourist destinations include tropical and sub-tropical countries where there is a higher risk of contracting an infectious disease.³ Travel to economically less developed countries frequently involves exposure to biological agents that cause infections or to infectious diseases transmitted by different routes (digestive, respiratory, mucocutaneous, vector, and so on). One point that should be highlighted from the outset is the possibility that an infection in the international traveler could also be caused by cosmopolitan agents found within our own country, an example of which would be sexually transmitted diseases (STDs), a set of infectious conditions that has been insufficiently studied among travelers. The differential diagnosis therefore should always include diseases that have a restricted geographic distribution as

well as those with a global presence. Furthermore, the severity of the clinical pictures presented here varies a good deal, so that a special section has been included on managing the seriously ill patient. Finally, there are certain situations that are physiological (such as pregnancy) or pathological in nature (for example, the immunocompromised patient, whether or not associated with HIV infection) that have special characteristics that warrant further discussion.

From a medical point of view, these guidelines will be useful to primary care physicians as well as specialists in internal medicine, infectious diseases and tropical medicine who treat travelers returning from tropical and sub-tropical areas with infections. The target population in this document is *adults* with infections imported after returning from international travel. The *prevention* of imported diseases and infections imported by *immigrants* are explicitly excluded here, since these have been considered in recent EIMC reviews. Also left out here in a general sense are other non-infectious illnesses among travelers, although certain aspects will be mentioned in particular sections.

Objectives of the document

Various types of professionals (clinicians, microbiologists and parasitologists) have helped produce this consensus document by evaluating the evidence-based information available and making recommendations about the following aspects:

- Definitions

- General evaluation of the returned traveler with a potential infection
 - The need to evaluate the asymptomatic traveler
 - The main syndromes associated with imported infectious diseases
 - Evaluation of the traveler with severe infectious disease
 - Evaluation of the traveler with potentially transmissible diseases and isolation precautions
- Main infectious syndromes in the returned traveler
 - Acute or persistent diarrhea
 - Fever of unknown origin
 - Localized cutaneous lesions
 - Respiratory infections
 - Eosinophilia
 - Neurological infections
 - Urinary tract infections
- Special characteristics of the pregnant traveler
- Special characteristics of the immunocompromised traveler

General methodology of the document

A systematic review of the bibliography was performed to evaluate all data concerning the causes, diagnostic methods and therapeutic options for infections imported by travelers. A search of the PubMed database was performed using the following selection criteria: articles published between 1968 and March 2016, in English or Spanish, and limited to humans only. The search terms used were “travel*” associated with each of the items explored (e.g. “fever”, “diarrhea”, and so on). This search was complemented with a review of the *Cochrane Database of Systematic Reviews*, using “travel*” as the key term, and also of the international guidelines dealing with each of the separate aspects evaluated. The search was conducted using PRISMA reporting criteria,⁴ and was reviewed by the contributors in the first instance, then by those coordinating the text version. A total of 436 publications were selected, eliminating those that were duplicated or not relevant. The specific set of references selected for each section may be requested from the contributors.

The recommendations were based on the international standards used in the consensus guidelines of the Infectious Disease Society of America (IDSA) and the Appraisal of Guidelines Research & Evaluation (AGREE) instrument.⁵ The coordinators and authors of the document issued a consensus version, which was published on the SEIMC web site between 13 November 2016 and 14 December 2016 for external review. The final submitted article was returned with approval for publication. The management board of the SEIMC will designate coordinators to review this document in the next 5 years.

Definitions

This section indicates the main internationally accepted definitions used by the World Tourism Organization. With respect to duration, three types may be distinguished: **short-term** (<3 weeks), **medium-term** (3 weeks to 3 months), and **long-term** (>3 months). Depending on the purpose of the trip, there are two main groups: trips **for personal reasons** and those undertaken for **professional reasons**. Trips for personal reasons can be further sub-divided into: (i) *leisure, recreation and holidays*; (ii) *visiting friends and relatives (VFR)*; (iii) *shopping trips*; (iv) *trips for educational/training purposes*; (v) *health tourism*; (vi) *for religious reasons and pilgrimages*, and (vii) *travel for cooperation and humanitarian aid*. Travel for professional reasons includes travel for *business/conferences* and *military purposes*.

General evaluation of the returned traveler with a possible infection

The selected key facts (KF) are indicated in the following sections.

The need to evaluate the asymptomatic traveler

KF1. Systematic evaluation is not indicated for all international travelers in the absence of clinical signs and symptoms (A-II).

KF2. Immigrant travelers visiting friends and relatives may benefit from evaluation, even if they are asymptomatic (C-II).

KF3. Long-term travelers (>3 months), those to high-risk areas and/or including high-risk activities may benefit from a directed evaluation (B-II).

KF4. Travelers who have been in contact with freshwater sources in endemic areas, or who have walked barefoot on contaminated soil may benefit from screening for schistosomiasis and strongyloidiasis respectively (A-II).

KF5. Any traveler who has engaged in risky sexual practice without protection may benefit from serological testing for the detection of STIs, HIV, hepatitis B and C and syphilis (A-II).

KF6. Health aid workers exposed to patients with active tuberculosis may benefit from the tuberculin skin test or interferon-gamma release assays (IGRAs) (B-II).

Principal syndromes associated with imported diseases by travelers

KF7. In overall terms, the most common syndromes affecting travelers who return home feeling ill are gastrointestinal (acute or persistent diarrhea), fever of unknown origin, localized skin lesions and respiratory infections (A-II).

KF8. The relative frequency of these syndromes varies depending on the geographic area or region visited (B-II).

KF9. The severity of these syndromes is variable. Fever of unknown origin or associated with other symptoms (such as diarrhea or respiratory problems) accounts for the majority of hospital admissions (B-II).

Evaluation of the traveler with serious infectious disease

KF10. The initial evaluation of the international traveler with severity criteria should be carried out at three levels: assessment of vital functions, syndromic evaluation and diagnostic strategy (B-III).

KF11. The immediate evaluation of hemodynamic stability should necessarily include blood pressure, respiratory rate, oxygen saturation, diuresis, heart rate and level of consciousness. Other variables to be taken into account are body temperature, the presence of edema, capillary refill and the presence of ileus (A-III).

KF12. The syndromic picture should be clearly established, since this will make it possible to select the most appropriate diagnostic tests and prognostic scales (B-III).

KF13. The analytical determinations that should be ordered for the seriously ill patient include blood count, biochemical tests including serum transaminase, bilirubin and blood coagulation, renal function, glycemia, arterial blood gas, and an analysis of urine. When possible, C-reactive protein and procalcitonin levels should also be requested (A-III).

KF14. The diagnostic strategy requires tests that are able to rule out malaria and dengue fever, and at least two sets of blood cultures, plus serological tests to detect rickettsial diseases, Q fever, HIV, HBV or HCV infection (A-III).

KF15. It is recommended that a specialist in tropical medicine or infectious diseases assess the patient as quickly as possible (C-III).

Evaluation and isolation precautions for travelers with potentially transmissible infectious diseases

KF16. In the returned traveler, the clinician should initially evaluate not only the individual disease, but also the possibility that it may involve a current public health alert (A-III).

KF17. The recommended methods (in Spain) are by phoning the *Departamento de Alertas de Salud Pública* (Department of Public Health Alerts) of the appropriate Autonomous Community, or by consulting the web page of the *Ministerio de Sanidad, Servicios Sociales e Igualdad* (Ministry of Health) (A-III).

KF18. Different isolation precautions will be applied depending on the clinical syndrome and the traveler's travel itinerary (B-III).

KF19. High-level isolation units (HLIU) for patient management are indicated for confirmed and suspected cases of specific viral hemorrhagic fevers, highly pathogenic emerging respiratory diseases, multidrug-resistant tuberculosis (MDR-TB) and outbreaks of potentially serious transmissible diseases (PSTD) caused by unknown agents (A-III).

KF20. A basic pillar of control of PSTDs involves the selection, education and training of staff. This should be regarded as one more isolation precaution (B-III).

KF21. Restricting the use of invasive tests is also an isolation precaution. The selection of tests and the staff involved should be agreed by protocols adapted to the center where the patient is being treated (B-III).

KF22. All travelers transferred from foreign hospitals should be regarded as potential carriers of multidrug-resistant organisms and should be proactively screened (by rectal smear) (A-III).

Main infectious syndromes in the returned traveler

Diarrhea (acute or persistent)

Causative agents

KF23. Most cases of acute traveler's diarrhea are caused by bacterial pathogens. Enterotoxigenic *Escherichia coli* (ETEC) is the most frequently identified causative agent worldwide (A-III).

KF24. In a significant percentage (30–50%) of cases of acute traveler's diarrhea, an etiological diagnosis cannot be made (A-III).

KF25. There are notable geographical variations with respect to the etiology of acute traveler's diarrhea, independent of the length of the trip (A-III).

KF26. For acute traveler's diarrhea, microbiological studies should be restricted to patients who present fever, dysentery, choleraform diarrhea, or who are dehydrated, immunosuppressed or have significant comorbidities (A-III).

Diagnostic methods

KF27. The diagnostic method of choice for acute traveler's diarrhea is the conventional stool culture or cultures on selective media (depending on clinical suspicion) together with serial blood cultures if there is fever, although the diagnostic yield is low (A-III).

KF28. For any traveler with fever and acute diarrhea arriving from an endemic area, malaria should be ruled out with the appropriate methods (B-III).

KF29. Before traveling, the patient should be given information about the main self-treatment measures to be taken in case of diarrhea, and told to seek medical care in the presence of high fever, severe abdominal pain, bloody diarrhea, uncontrolled vomiting, or if self-treatment is ineffective (A-III).

KF30. For previously healthy adults, rehydration with conventional liquids, especially associated with loperamide, should be enough in cases of mild diarrhea (A-I).

KF31. Rehydration and restoration of electrolyte balance with antidiarrheal drugs and non-absorbable antibiotics (rifaximin) is indicated for moderate diarrhea, and for the old or immunocompromised with no previous history of invasive disease (A-III).

Therapeutic measures

KF32. For severe diarrhea with obvious signs of dehydration, intravenous rehydration is recommended to restore the fluid and electrolyte balance (A-III).

KF33. The use of antidiarrheal agents is contraindicated in the presence of invasive disease (A-III).

KF34. The most useful drugs for the treatment of invasive diarrhea are fluoroquinolones or azithromycin, chiefly in single doses (A-I).

KF35. The pathogenesis of persistent traveler's diarrhea may fall into one of three major groups: persistent infection or co-infection; post-infectious syndromes (transient lactose intolerance, post-infectious irritable bowel syndrome, small intestinal bacterial overgrowth (SIBO) and tropical sprue); or an underlying gastrointestinal disease unmasked during or after the trip (A-III).

KF36. The most common infections in persistent traveler's diarrhea are due to protozoan pathogens, for which the diagnostic method of choice is the standard Comprehensive Parasitology profile, using specific stains based on clinical suspicion, and antigen detection methods and PCR, as available, for increased sensitivity (A-III).

KF37. Diagnosis of post-infectious irritable bowel syndrome is exclusively clinical (Rome criteria III–IV) and it is especially important to determine the state of digestive health before travel and to consider at an early stage whether there are clinical and analytical signs of alarm/organicity (A-III).

KF38. The incidence of tropical sprue may be underestimated. Its main differential diagnosis is with celiac disease. Upper endoscopy (EGD) to examine the jejunum and biopsy are frequently required to differentiate them (A-III).

KF39. Some authors recommend empirical therapy with nitroimidazoles if *Giardia intestinalis* is highly suspected, even if specific studies are negative (C-III).

Fever of unknown origin

Causative agents

KF40. The most common causes of fever of unknown origin in the returned traveler are, in order of frequency: malaria, arbovirus (e.g. dengue, Chikungunya, Zika) and bacterial infections (typhoid fever, rickettsial infections, Q fever and leptospirosis) (A-II).

KF41. Even though they are rare, serious diseases that are highly contagious, such as viral hemorrhagic fevers (e.g. Ebola, Lassa, Marburg, Rift Valley fever, Crimean-Congo hemorrhagic fever) should always be considered (C-III).

KF42. The traveler's provenance, period of incubation and specific risk exposures should provide guidance as to the etiology of the febrile process (A-II).

Diagnostic methods

KF43. Travelers who present with fever of unknown origin after visiting a tropical or sub-tropical area should seek immediate medical attention (A-II).

KF44. If there is any possibility of viral hemorrhagic fever (VHF), this should be investigated using appropriate biosafety measures and techniques that require the least handling possible (rapid tests or PCR) (A-II).

KF45. A significant proportion of fever episodes post-travel either do not lead to a specific diagnosis (A-II) or are due to cosmopolitan infections (A-II).

KF46. If there is no risk of VHF, malaria should be ruled out in the first instance using microscopy techniques and rapid diagnostic tests (A-II).

KF47. If the acute phase of an arbovirus is suspected (<10–15 days of clinical evolution), the patient should be tested for the presence of (NS1) antigens or viral RNA in blood and urine (A-II).

KF48. If arbovirus in later stages is suspected (>15 days of clinical evolution), the serologic response (principally IgM) should be studied and cases confirmed by neutralization tests (A-II).

KF49. The diagnosis of bacterial infection responsible for fever of unknown origin is based, in the acute phase, on isolating the bacterial organism or using molecular biology techniques, and in later phases, on serologic studies of paired serum samples (A-II).

Therapeutic measures

KF50. Treatment (etiological or symptomatic) should be based on identifying the causative agent (A-II).

KF51. If there is a high probability of malaria and a diagnosis cannot be made, or will be delayed for more than 3 h with no alternative diagnosis, administration of empirical antimalarial therapy is recommended (A-II).

KF52. Patients with a likely diagnosis of severe acute schistosomiasis or neuroschistosomiasis are treated with corticosteroids in combination with praziquantel (B-II).

KF53. In complicated or severe cases of malaria, use of ceftriaxone plus doxycycline is recommended while waiting for confirmation of diagnosis (C-III).

Localized cutaneous lesions

Causative agents

KF54. Various cosmopolitan infections, such as superficial mycoses (e.g. pityriasis versicolor, cutaneous candidiasis or dermatophytosis) and some ectoparasitic infections (such as scabies) are more frequent in travelers (A-II).

KF55. Classic bacterial infections constitute the leading cause of consultation for skin lesions and specifically, for those due to certain strains of methicillin-resistant *S. aureus* (MRSA) that produce Pantón-Valentine leukocidin (PVL) (A-II).

Diagnostic methods

KF56. The primary morphology of the lesion (e.g. papules, pustules, nodules, ulcers, blisters), configuration (e.g. linear) and distribution (exposed versus covered areas, specific parts of the body) are helpful for diagnosis (A-II).

KF57. In most cases, diagnosis is clinical, and dermoscopy is useful for some entities (scabies, cutaneous larvae *migrans*, furuncular myiasis and tungiasis) (B-III).

KF58. A helminth infection should be suspected if eosinophilia is associated with the skin lesions (A-II).

KF59. In an imported dermatosis that develops slowly, cutaneous leishmaniasis, mycobacterial infection or a subcutaneous mycosis should be suspected. Histological examination and identification of the causative agent with molecular biology techniques or mass spectrometry is essential (A-II).

Therapeutic measures

KF60. For many imported dermatoses, treatment is symptomatic with oral antihistamines (diphenhydramine, hydroxyzine, or loratadine), topical antipruritic therapy (calamine lotion) and topical corticosteroids (low potency for the genitals, medium potency for the trunk or extremities) (A-II).

KF61. The treatment of choice for the main imported dermatoses that are linear in pattern (cutaneous larva *migrans* (CTM), cutaneous larva *currens* and *gnathostomiasis*) is ivermectin, with albendazole an alternative option (A-I).

KF62. Surgical removal (associated with antibacterial tetanus chemoprophylaxis where appropriate) is the treatment of choice for furuncular myiasis, tungiasis, and *D. repens* infections (A-II).

Respiratory infections

Causative agents

KF63. The most common causes of respiratory infection in the local environment are also the most common among travelers, with exotic imported infections being much less frequent (A-II).

KF64. In general, viral and bacterial infections are more frequent than those caused by fungi and parasites (B-II).

KF65. Most respiratory infections in travelers are mild, affect the upper respiratory tract and are caused by viruses (A-II).

KF66. The most serious respiratory infection in travelers is pneumonia, and the most common causes of it in the traveler are similar to those in the autochthonous population, although with a greater incidence of infections due to *S. aureus* and *Legionella* spp. (A-II).

KF67. During short trips, the risk of tuberculosis is low and depends on the incidence of the disease in the countries visited (B-III).

KF68. The main causes of respiratory conditions associated with eosinophilia are acute schistosomiasis, Löffler's syndrome and paragonimiasis (B-III).

KF69. Travelers may also have non-infectious problems that have respiratory manifestations such as pulmonary embolism and mefloquine toxicity (B-III).

Diagnostic methods

KF70. Most respiratory infections during and after travel do not require diagnostic confirmation because they are mild, self-limited upper respiratory tract infections (A-II).

KF71. The diagnostic methods for pneumonia are no different from those used on autochthonous patients (B-II).

Therapeutic measures

KF72. In patients with pneumonia, the decision as to whether a patient with pneumonia should be admitted to hospital or the ICU should be based on severity scales used in the autochthonous population (A-II).

KF73. Procalcitonin levels can guide the clinical judgment of the attending physician in prescribing antibiotics for respiratory infections (B-II).

KF74. If tuberculosis is suspected, or any other infection transmitted via respiratory secretions (such as the MERS-CoV coronavirus), respiratory isolation and droplet precautions are recommended (A-I).

KF75. Most respiratory infections during and post-travel do not require specific treatment because they are mild and self-limiting. Treatment may be given for the symptoms (B-III).

KF76. For pneumonia in travelers, antibiotic therapy is initially empiric and should include drugs effective against the most common community-acquired pathogens, including *Legionella* spp. (B-II).

KF77. In travelers with influenza and severity criteria or risk factors, treatment with oseltamivir or zanamivir is recommended (B-II).

KF78. If the traveler with tuberculosis has come from a country with a high incidence of antimicrobial resistance, it would be reasonable to evaluate treatment with at least 4 drugs and rapid

DNA-based tests to detect mutations associated with resistance (B-III).

Eosinophilia

Causative agents

KD79. The causes of imported eosinophilia vary a good deal and depend on the characteristics of the patient, particularly whether the person is a traveler or an immigrant, and on the geographical destination, itinerary and length of exposure (B-II).

KD80. When a patient presents with imported eosinophilia of non-filarial etiology, it is important to rule out infection due to parasites, principally helminths (A-II).

KD81. In patients with imported eosinophilia, the cause is identified as a parasite in 60–75% of cases (B-II).

KD82. The three most frequently found parasitic infections are strongyloidiasis, schistosomiasis and soil-transmitted helminth infections, as well as filariasis in the case of Equatorial Guinea (B-II).

Diagnostic methods

KD83. All returning travelers with eosinophilia should request a stool examination to search for parasites using a concentration method and *Strongyloides stercoralis* serology (B-II).

KD84. Travelers returning from Africa should request tests for diagnosing schistosomiasis (examination of the urine sediment and feces), and *Schistosoma* spp. serology (B-II).

KD85. In cases where a diagnosis cannot be made with direct techniques, serological methods are a useful diagnostic tool, although their possible drawbacks should not be forgotten (B-III).

Therapeutic measures

KD86. When the cause cannot be identified, the empiric treatment for imported eosinophilia should be a combination of oral ivermectin plus albendazole. Praziquantel should be added for cases with possible epidemiological exposure to schistosomiasis (B-III).

KD87. Before starting empiric ivermectin therapy, the possibility of *Loa loa* infection should first be ruled out (A-II).

KD88. When empiric anthelmintic treatment is administered, the patient should receive clinical follow-up with monitoring of peripheral blood eosinophil counts, since some parasites, like *Trichuris* spp. and *Schistosoma* spp., have developed resistance leading to anthelmintic treatment failure (A-II).

Neurological infections

Causative agents

KF89. The most frequent causes of neurological disease in travelers are malaria, viral infections and bacterial meningitis (A-II).

KF90. Generally speaking, the main clinical manifestations affect the brain and/or meninges, and more rarely, the spinal cord and peripheral nervous system (B-III).

KF91. The main manifestation in the peripheral nervous system is Guillain-Barré syndrome, which is associated with infection due to *Campylobacter jejuni*, dengue and, more recently, the Zika virus (B-II).

Diagnostic methods

KF92. Any international traveler who returns with fever, severe headaches, sensitivity to light and/or a stiff neck should be evaluated urgently to rule out the presence of meningitis or encephalitis (A-III).

KF93. The cerebrospinal fluid (CSF) analysis can adopt four different patterns: normal, raised neutrophils, raised lymphocytes, raised eosinophils, which is useful for differential diagnosis (A-II).

KF94. Direct ophthalmoscopy is recommended for all patients with a diagnosis or suspicion of cerebral malaria, given its high prognostic and diagnostic value for malarial retinopathy (A-II).

Urinary tract infections

KF95. The possibility of infection with extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae should always be considered in travelers with urinary tract infections, principally those acquired in South and Southeast Asia (A-III).

KF96. In the presence of non-specific complaints and/or hematuria, urinary schistosomiasis (*S. haematobium*) should be considered in travelers returning from traditionally endemic areas (and other more recently reported ones, such as Corsica) (A-II).

The pregnant traveler

KF97. Pregnant women are much more susceptible to certain infectious diseases, such as traveler's diarrhea, listeriosis, typhoid fever and malaria (A-II).

KF98. Various diseases that are transmitted by eating or drinking contaminated food or water (traveler's diarrhea, hepatitis E, listeriosis and typhoid fever) are more severe in pregnant women (A-II).

KF99. Mother-to-child transmission of the dengue and chikungunya viruses can occur if the mother has fever in the days close to and during birth, while the main complications of Zika appear in the first trimester of the pregnancy (A-II).

KF100. Azithromycin is the antibiotic of choice for traveler's diarrhea and typhoid fever in pregnancy (B-II).

The immunocompromised traveler

KF101. The course of malaria in immunocompromised patients (especially those infected with HIV and with low CD4+ lymphocyte counts) tends to involve more severity criteria than in non-immunocompromised individuals. Early diagnosis and treatment is essential, therefore, if there is clinical suspicion (A-III).

KF102. Immunocompromised individuals who present with traveler's diarrhea should be given the parasitology stool test, including the modified Kinyoun stain for detecting coccidian species, such as *Cryptosporidium* spp, *Cystoisospora belli* and *Cyclospora cayetanensis* (B-III).

KF103. *S. stercoralis* hyperinfection syndrome and disseminated strongyloidiasis are more frequently found in immunosuppressed patients (corticotherapy, transplants, HTLV-1 coinfection) and have very high mortality rates. Early diagnosis and treatment with ivermectin at a dose of 200 µg/kg/per day for at least 7 days is required (A-III).

Conflict of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.eimc.2017.02.009](https://doi.org/10.1016/j.eimc.2017.02.009).

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