Review

Fever in travellers returning from the tropics[☆]

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A R T I C L E   I N F O

A B S T R A C T

The increase in international travel, the growing presence of arbovirus vectors in our country, and notifications of haemorrhagic fever such as the current outbreak of Ebola in D.R. Congo and the cases of Crimea-Congo haemorrhagic fever in our country have again cast the spotlight on tropical diseases. Isolating suspected cases of highly contagious and lethal diseases must be a priority (haemorrhagic fever, MERS-CoV). Assessing the patient, taking a careful medical history based on epidemiological aspects of the area of origin, activities they have carried out, their length of stay in the area and the onset of symptoms, will eventually help us, if not to make a definitive diagnosis, at least to exclude diseases that pose a threat to these patients. Malaria should be ruled out because of its frequency, without forgetting other common causes of fever familiar to emergency doctors.

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Fiebre en el viajero retornado del trópico

R E S U M E N

El incremento de los viajes internacionales, la creciente presencia de vectores transmisores de arbovirus nuestro país, las alertas de fiebres hemorrágicas, como el actual brote de ébola en la R. D. del Congo y los casos autóctonos de fiebre hemorrágica de Crimea-Congo en nuestro país, ponen de nuevo en primer plano las enfermedades tropicales. El aislamiento de los casos sospechosos de enfermedades de alta transmisibilidad y letalidad ha de ser una prioridad (fiebres hemorrágicas, MERS-CoV). Al valorar al paciente, una cuidadosa historia clínica basada en los aspectos epidemiológicos de la zona de procedencia, las actividades realizadas, el tiempo de estancia en el mismo y el inicio de los síntomas nos ayudarán finalmente, si no al diagnóstico definitivo, sí al menos a descartar las enfermedades que signifiquen una amenaza para él. Por su frecuencia y gravedad la malaria debe ser descartada, sin olvidar las otras causas habituales de fiebre con las que el médico de urgencias debe estar familiarizado también.

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Currently, the frequency of care required in the A&E by patients with a fever after an international trip to tropical countries, whether for tourism, work, family, voluntary work or immigration is on the increase. According to the World Tourism Organization, between January and August 2017, different destinations around the world welcomed 901 million international tourists which was 56 million more than in the same period in 2016,[1] with Africa showing the most outstanding increase. According to a multicenter study of the GeoSentinel surveillance network, fever is the cardinal symptom for which up to 23% of patients visit a doctor after returning from a trip, and it is the second reason for consultation[2] after diarrhoea. Globally, malaria was the most frequent cause of fever (29%), followed by dengue fever (15%), with the incidence varying according to the region visited. Other specific causes of fever to be highlighted in this study are typhoid fever, Chikungunya, rickettsiosis, viral hepatitis and HIV primary infection, with no significant difference to previous studies.[3,4]

The initial evaluation of patient from the tropics with fever in A&E should place emphasis on recognising or ruling out

diseases with high morbidity and mortality (malaria, typhoid fever, meningitis) and those that pose a public health danger[5] (viral haemorrhagic fevers, Middle East respiratory syndrome coronavirus [MERS-CoV], tuberculosis). The need for isolation should be evaluated as soon as possible so that health personnel may take appropriate protective measures and limit contact with other patients or relatives. It is therefore advisable that if the hospital triage detects a possible case that presents certain risks (haemorrhagic fevers and MERS-CoV), due to having taken into account the place from which the patient returns or originates, and the onset of fever within the considered incubation periods, then procedures should be followed to place the patient in isolation at that moment. Subsequent reassessment should be made ensuring the proper precautions of individual protection by the health personnel are followed, until the suspicion is confirmed or discarded. The possibility of haemorrhagic fever should be considered in patients with fever and haemorrhagic signs who have arrived within the last 21 days from a region where cases have been reported, or if they have had contact with patients, secretions or biological samples from infected patients.[6] MERS-CoV should be suspected in patients with fever and respiratory symptoms who have returned from countries in the Arabian Peninsula in the last 14 days or have been in close contact with patients from those regions under study.[7]

Additionally, principal emphasis should be placed on the detection of signs of clinical severity. In the latest international consensus of definitions of sepsis and *septic shock* qSOFA criterion were defined[8] (2 or more of the following criterion: altered level of consciousness, respiratory rate ≥ 22 bpm and systolic blood pressure ≤ 100 mmHg). This scale can be used as a tool to identify patients with a risk of sepsis and, who consequently require a more intensive evaluation. This scale may be useful for the detection of seriously ill patients with fever coming from the tropics.[9]

The evaluation should continue with the completion of a detailed clinical history, taking into account epidemiological aspects of the country and the region visited, the reason for travel (tourism, business, voluntary work, migration or visiting friends and relatives (VFR) and the activities carried out (Table 1). Questions must be asked about the vaccines received before the trip and the use of antimalarial prophylaxis and the degree of compliance.[10] The use of such prophylaxis does not completely rule out the possibility of developing malaria, with one of the most common errors being early suspension of the treatment once the trip has ended.[11] It is also common that the VFR traveller is unaware of the need for antimalarial prophylaxis when they are travelling to their native country.[12] Probably the most important information to obtain during the clinical interview, are the precise dates of the trip, the onset of fever and the evolution of other symptoms, since this allows us to infer the incubation period of the disease, delimiting the spectrum of possibilities and thus aiding the differential diagnosis (Table 2).

Often, we cannot know if in the country or the region where the traveller has been, was a malaria area or if there is an outbreak of any disease in that country. The CDC has updated *online* information regarding malaria (https://www.cdc.gov/malaria/travelers/country_table/e.html), and the International Society for Infectious Diseases has a portal which is updated daily with global epidemiological warnings (http://www.promedmail.org).

In addition to the aspects discussed, the presence of specific signs and symptoms can help to arouse diagnostic suspicion (Table 3).

Despite all of this, in up to 25% of cases of fever in travellers returning from the tropics the causes remain undiagnosed.[3]

Malaria

Malaria is the most frequent cause of fever in a patient returning from a tropical area,[2,4] and as this is a potentially serious disease any fever from an endemic area should be considered as malaria[13] until proven otherwise. It must be ruled out.

The World Health Organization (WHO) reported that in 2016 there were 216 million cases of malaria in the world and 445,000 deaths, with cases being notified in 91 countries.[14] In Spain in 2015, 583 cases were diagnosed.[15] Malaria is transmitted by the *Anopheles* mosquito, of wide global distribution, and it is produced by protozoa of the genus *Plasmodium* spp., which includes five species that cause the disease in humans. *P. falciparum* is the most aggressive species, producing more severe cases, and cerebral malaria. The clinical presentation occurs after an incubation period of between 7 and 30 days, with infection by *P. falciparum* being the shortest and *P. malariae* being the longest. Both *P. vivax* and *P. ovale* can present relapses years later, as they produce hypnozoites (schizonts that remain dormant in the hepatocytes and are not susceptible to drugs that eliminate the erythrocytic forms). *P. falciparum* and *P. malariae* may lead to recrudescences as parasites remain in the tissues, giving rise to new cycles of elevated parasitaemia. This usually occurs after untreated or poorly treated infections, presenting increasingly milder cases, especially in patients who live in endemic areas and have developed immunity against the infection. Usually the recrudescences occur quite soon after the initial infection, but they have been described up to 10 years later.[16]

The clinical condition produced by uncomplicated malaria consists of high fever, accompanied by malaise and musculoskeletal pain. In the laboratory, thrombocytopenia (80–85%, i.e. the most frequent disorder), anaemia (30%) and leukopenia (20%) can be observed. LDH and bilirubin may be increased; and metabolic acidosis and hypoglycaemia may appear in severe forms.[17]

According to WHO, it is considered as severe malaria if it meets at least one of the criteria listed in Table 4.[18]

The diagnosis will be made by thick film (high sensitivity) and thin film or smears (high specificity and identification of the species).[18] If there is a high suspicion of malaria but the thick film is negative, it should be repeated every 12 h for 3 days.[19] Another method, especially useful if no microbiologist is available to perform the thick smear evaluation, is the antigen detection test by immunochromatography. However, it is not recommended as a substitution to the thick blood film test, given the high number of false negatives for the other species except *P. falciparum*.[20] PCR techniques can also be performed, but given the time involved in the test and its cost, it is not practical in the A&E situation.[18]

In general, hospital admission is recommended in any case of malaria, especially when it is produced by *P. falciparum* in non-immune patients, even if they appear to be in a good overall state, as possible sudden deterioration can occur despite having started the correct treatment.[21] *P. vivax*, *P. ovale* and *P. malariae* tend to produce milder conditions and do not usually present complications. The treatment of malaria should be carried out according to the species and place of travel of the patient, as a way to consider the possible pharmacological resistance. Uncomplicated malaria can be treated orally with drugs if there is no digestive intolerance. Cases of complicated malaria should be treated in ICUs. IV artesunate has been shown to decrease parasitaemia and the length of stay both in the ICU and on the ward more rapidly, and therefore it has become the treatment of choice for the treatment of severe malaria, rather than quinine,[18] with little but growing drug-resistance described so far.[22] In Table 5 we review the treatment of malaria. In case of pregnancy, artesunate is contraindicated in the first trimester, so it should be treated with quinine + clindamycin.

Table 1
Exposure and activity carried out.

Contact with fresh water	Schistosomiasis, leptospirosis, free-living amebiasis
Direct contact with land (walking barefoot)	Ancylostomiasis, strongyloidiasis, cutaneous larva migrans, tungiasis
Contact with animals	Rabies, tularemia, Q-fever, anthrax, viral haemorrhagic fevers, plague, brucellosis
Dairy consumption	Brucellosis, tuberculosis, shigellosis
Untreated water consumption	Amebiasis, ulcer, hepatitis A and E, typhoid fever, shigellosis, cryptosporidiasis, cyclosporiasis, giardiasis
Consumption of raw or undercooked foods	Hepatitis A, bacterial enteric infections, trichinosis, amebiasis, toxoplasmosis, cestodiasis, hepatic dystomatosis
High-risk sexual contact	HIV, hepatitis A, B and C, herpes, gonorrhoea, syphilis, Epstein-Barr virus, cytomegalovirus
Caves	Histoplasmosis, rabies
Contact with ill-patients	Tuberculosis, meningitis, influenza, MERS-CoV, HF (Ebola, Crimean-Congo, Lassa)
Exposure to arthropods	
Mosquitoes	Malaria, dengue, yellow fever, other arboviriasis, filariasis
Ticks	Rickettsiosis, borreliosis, Q-fever, tularemia, encephalitis, Crimean-Congo haemorrhagic fever
Flies	African trypanosomiasis, leishmaniasis, onchocerciasis, bartonellosis
Fleas	Murine typhus, plague
Lice	Exanthematic typhus, relapsing fever
Mites	Shrub typhus

Table 2
Incubation periods.

Disease	Incubation periods	Geographic region
Malaria	7–30 days	Sub-Saharan Africa, Central and South America, India and Southeast Asia
Dengue	2–7 days	Southeast Asia, Central and South America, Africa
Haemorrhagic fevers	<21 days	Currently D.R. of the Congo, Uganda (Ebola) Nigeria (F. Lassa)
Crimean-Congo haemorrhagic fever	<9 days (sting) <13 (p-p contact)	Africa, the Middle East, Turkey, the Balkans and Asia (towards the west of China)
MERS-CoV	<14 days	Arabian Peninsula
Yellow fever	3–8 days	Africa, South America
West Nile encephalitis	3–6 days	Africa, Asia and Europe
Japanese encephalitis	3–14 days	Southeast Asia from Japan to India
Central European encephalitis	2–4 weeks	Central Europe, the Alps, Balkan countries and all of Russia
Typhoid fever	6–30 days	Cosmopolitan
Epidemic typhus	7–14	Cosmopolitan, epidemics
Leptospirosis	2–39	Cosmopolitan (Asia and South America especially)
Schistosomiasis	4–6 weeks	Africa, South America, Southeast Asia
Leishmaniasis	2–6 months	South America, Mediterranean, Africa, Asia

Table 3
Findings in the exploration and aetiological possibility.

Neurological disorder	Meningitis, malaria, typhoid fever, leptospirosis, rickettsia, viral encephalitis (Japanese, tick-borne, West Nile)
Jaundice	Viral hepatitis (A, B, C, E), malaria, leptospirosis, yellow fever and other viral hemorrhagic fevers
Localised adenopathies	Pyodermitis, *Bartonella*, TB, *Toxoplasmosis,* tularemia, trypanosomiasis
Conjunctivitis	Leptospirosis, Zika
Haemorrhagic manifestations (petechiae and ecchymoses)	Meningococcaemia, dengue fever, viral hemorrhagic fever, leptospirosis
Splenomegaly/hepatomegaly	Malaria, leishmaniasis, mononucleosis, dengue, schistosome, amoebic abscess, viral hepatitis
Rash	Dengue, Zika, Chikungunya, measles and other viruses, rickettsia, typhoid fever, HIV, Katayama fever

Arbovirus

Arboviruses are a set of RNA viruses transmitted by arthropods (mosquitoes or ticks) to numerous vertebrates that maintain their zoonotic cycle. Due to the increasing presence of new vectors that transmit these viruses in our country, such as *Aedes albopictus*,[23] it is possible that autochthonous cases also occur, as has happened with dengue.[21] Most arbovirus infections do not produce symptoms, or they produce a benign febrile nonspecific condition. When they do produce disease, this is manifested mainly by three clinical syndromes: fever-*rash*-arthralgia, haemorrhagic fever and encephalitis, with these symptoms sometimes overlapping each other. We explain the main ones.

Fever-rash-arthralgias (dengue, Zika, Chikungunya)

Dengue fever is the main virus that causes these symptoms, and the second most frequent cause of fever in the patient who has returned from the tropics.[24] There are 4 serotypes with different antigenic characteristics. Its incidence has increased in the last decades, with WHO estimating an annual incidence of 50 million cases.[25] It is considered a global public health problem, with a mortality of 2.5%. *The main vectors are principally Aedes aegypti,* and to a lesser extent *Aedes albopictus*. They present an incubation period of 4–10 days after the mosquito bite. Dengue and severe dengue are distinguished with or without signs of alarm.[26] It initially presents with a high fever (40 °C) and nonspecific symptoms (severe headache, pain behind the eyes, myalgias, arthralgias, nausea, vomiting, swollen glands). Petechiae and minor haemorrhages may appear. The tourniquet test (Rumpel–Leede sign) can be helpful in the diagnosis. It consists of the application of pressure by a sphygmograph higher than the mean arterial pressure for 5 min, to assess the appearance of petechiae after its withdrawal (being positive if there is more than 20 petechiae in a 5 cm diameter area). This febrile phase lasts between 3 and 7 days, followed by the critical phase, which begins when the temperature begins to normalise, below 37.5 °C. In these 48–72 h, the patients who improve after the fever subsides are considered cases of dengue without warning signs. However, there may be warning signs in relation to increased capillary permeability (severe abdominal pain, persistent

Table 4
Criteria for severe malaria.

Clinical features
Glasgow Coma Scale ≤ 11
Prostration (inability to sit or walk without help)
Seizures, more than two seizures in 24 h
Dyspnoea with acute respiratory failure
Shock
Jaundice (>3 mg/dl)
Spontaneous bleeding from the gums, nose, gastrointestinal
Analytical results
Hypoglycaemia, blood glucose < 40 mg/dl
Metabolic acidosis with bicarbonate < 15 mmol/l or base excess −8
Anaemia, Hb < 7 g/dl, Hct < 20%
Haemoglobinuria
Hyperlactacidemia: lactic acid > 5 mmol/l or > 45 mg/dl
Acute renal failure, serum creatinine > 3 mg/dl
Diuresis < 400 ml/24 h
Thrombocytopenia < 100,000 platelets
Disseminated intravascular coagulation
Radiological
Acute pulmonary oedema
Acute respiratory distress syndrome
Parasitological
Hyperparasitaemia (*P. falciparum*) (>2% in non-immune, >10% in any patient)

Source: World Health Organization, 2015.

vomiting, oedema, mucosal haemorrhage, lethargy, hepatomegaly), with analytical disorders such as increased haematocrit (due to the extravasation of fluids due to a decrease in protein), together with a rapid fall of platelets. Severe dengue (5%) is diagnosed if there is a significant loss of plasma that leads to haemodynamic *shock*, pleural effusion, severe haemorrhage or severe organ damage (elevation of transaminases > 1000, neurological or cardiac disorders). In the recovery phase the general condition improves, the gastrointestinal symptoms improve, the haemodynamic state is stabilized and diuresis is increased.

All the serotypes can produce a sever condition, although it has been observed that the maximum risk is DEN-2, followed by DEN-3, DEN-4 and DEN-1.[27] After a first infection, specific antibodies are formed against this serotype, with the risk of developing a more severe condition if re-infected by a different serotype.

The diagnosis will be made in the first 5–9 days by immunological techniques: PCR or viral antigen detection (NS1 protein). After this time period serological techniques should be used such as plaque or ELISA reduction neutralization.[28] In the most severe cases there is no specific treatment beyond the symptomatic and haemodynamic support.

Other arboviruses that, like dengue, produce fever *rash*-arthralgias, but which do not produce haemorrhagic fever, are Zika and Chikungunya, which share the same vector and practically the same geographical location. Zika usually produces a pruritic rash and conjunctivitis more frequently, and Chikungunya produces more painful arthralgias.

Only 15% of those infected with Chikungunya stop showing symptoms. The generalised arthralgias and polymyalgias begin shortly after the onset of fever, and arthritis and joint oedema may occur, predominantly in the distal joints. The acute phase usually lasts about a week. After the acute phase, up to 50% of patients present a chronic condition of arthralgia, arthritis, tenosynovitis and even symptoms similar to rheumatoid arthritis with joint erosion,[29] predominantly distal, which can last up to 5 years after infection, with a median of 20 months. There are also severe and infrequent complications, such as encephalitis, hepatitis, myocarditis and multiorgan failure. The treatment used is antipyretics and NSAIDs. Glucocorticoids should be avoided in the chronic phase.

The Zika virus was not considered as a particularly alarming disease because it produced mild and frequently asymptomatic conditions, until the 2015 outbreak declared in Brazil.[30] There, the association between the disease and cases of microcephaly and other brain malformations in the foetuses of mothers who become infected during pregnancy was observed,[31] as well as the increase of cases of Guillain–Barré syndrome after having the infection.[32] It has been confirmed that it can be sexually transmitted, even after a negative PCR result in blood,[33] as the virus can be detected in semen up to 3 months after having the disease.[34]

Haemorrhagic fevers

Different viruses produce these conditions, but all share a series of common symptoms in their pathogenesis, which are fever, increased vascular permeability, haemorrhagic phenomena and multiorgan damage that leads to death. With the exception of the Flaviviruses (yellow fever, dengue fever) and Rift Valley fever, all the other viruses that produce these symptoms can be transmitted person-to-person, which converts them into a potential public health problem due to their high risk of transmission. Their high fatality rate and easy transmission by contact, fomites and drops require strict isolation and the need to take protective measures with personal protective equipment (PPE). A general clinical suspicion would be the presence of a high fever (>38 °C) of less

Table 5
Treatment of malaria.

Severe malaria or oral intolerance
First line
Intravenous artesunate 2.4 mg/kg at 0.12 and 24 h and then every 24 h until tolerated via the oral route (at least the first 3 doses must be administered i/v before going onto oral treatment). Subsequently, complete the cycle with a complete oral regimen for uncomplicated malaria (oral artemisinins or atovaquone-proguanil)
Second line
Quinine gluconate[a]: initial loading dose 15 mg alkaloids base/kg i/v and, subsequently, maintenance dose of 8 mg alkaloids base/kg/8 h (infusing each dose in 4 h)
Quinine dihydrochloride[a]: initial dose of 20 mg/ and, subsequently, maintenance dose of 10 mg/kg/8 h (infusing each dose in 4 h)
Uncomplicated malaria
Plasmodium falciparum
First line
Atovaquone/proguanil 250 mg/100 mg: 4 tablets/day orally for 3 days
Dihydroartemisinin/piperaquine 40 mg/320 mg: < 75 kg 3 tablets/day orally for 3 days; 75–100 kg 4 tablets/day orally for 3 days
Second line
Quinine Sulfate 300 mg: 2 tablets every 8 h orally + 100% doxycycline mg/12 h or
Clindamycin 450 mg/8 h for 7 days
Plasmodium vivax, P. ovale, P. malariae or *P. knowlesi*: chloroquine 620 mg the first and second day and 310 mg the third day (it can be treated as P. falciparum *as an alternative or if chloroquine resistant* P. vivax *(Southeast Asia)*
P. vivax and *P. ovale*: primaquine 15 mg/day 14 days to eliminate hypnozoites at the end of acute treatment

  a To the treatment with quinine add doxycycline 100 mg/12 h orally or clindamycin 10 mg/kg/12 h i/v for 7 days.

than 3 weeks duration after exposure to a potential vector or an infected person or their fluids (laboratory manipulation, etc.) plus the presence of at least two haemorrhagic manifestations (purpuric or haemorrhagic rash, petechiae, epistaxis, haemoptysis, haematemesis, melenas or any other evidence of external or internal haemorrhage), once any cause that could predispose the patient to bleeding diathesis has been ruled out.[6] From the analytical point of view, it usually produces leukopenia, thrombocytopenia, elevation of transaminases and coagulation disorders.

After considering a case of suspected haemorrhagic fever in our environment, we must activate the protocol advising public health to confirm the suspicion and send a blood sample to the reference laboratory of the National Microbiology Center or to the center designated by each autonomous community. After confirming a case, the patient must be transferred to a High-Level Isolation Unit.[6]

Because of its relevance, we highlight the current outbreak of Ebola in the Democratic Republic of the Congo, in the province of Nord-Kivu.[35] The outbreak of 2014–2016 in West Africa, which affected Liberia, Sierra Leone and Guinea, has been the most important in history, with 28,616 suspected cases, of which 11,310 persons died.[36]

The recent detection of the Congo-Crimean haemorrhagic fever virus in Ávila, Spain, has resulted from the reference to the death of the patient in Ávila.[37] Two years after the first two autochthonous cases in Spain,[38] we remember that the criteria are fever >38 °C in the first 9 days after the bite of a tick, or 13 days after contact with blood or secretions of a patient (or a laboratory sample), plus the presence of at least one criterion of the following: profuse haemorrhagic manifestations, thrombocytopenia (<100,000 platelets/mm^3), prolonged prothrombin time. Leukopenia (<4000 leukocytes/mm^3) is also frequent, although it has been excluded as a criterion in the latest protocol.[39] The virus has been found circulating in Spain in ticks of cattle in the areas of Cáceres, Toledo, Ávila and Madrid.[40]

Yellow fever is widespread in Africa and South America. Fortunately, there is a vaccine, although there are still important outbreaks. After the mosquito bite, there is an incubation period of 3–6 days, after which sudden onset fever and musculoskeletal pain appear. This is followed by a period of apparent remission, and on the second day haemorrhagic fever symptoms appear, with the presence of jaundice, kidney failure and haemorrhagic diathesis (petechiae, gingivorrhagia, melenas, epistaxis), leading to death in 7–10 days in 30–60% of cases.[41]

Lassa fever is caused by an arenavirus (not an arbovirus) which is transmitted when the patient comes into contact with the urine, blood, saliva or stool of a rodent *(Mastomys natalensis)* through faecal-oral or inhaled route, as well as being a virus that is transmissible from person to person. This disease usually occurs in the form of outbreaks, mainly in rural areas. Between 100,000 and 300,000 cases per year are reported in Africa, producing 5000 deaths.[42] Nigeria is an endemic area, with occasional outbreaks in neighbouring countries (Liberia, Sierra Leone and Guinea).

Meningitis and encephalitis

- The Japanese encephalitis virus usually produces asymptomatic or paucisymptomatic infections (fever and headache), with an estimation that only one out of every 250 infected persons presents a severe condition. Approximately 68,000 cases are reported annually, with a mortality rate of 30%, producing sequelae in 50% of those affected.[43] It is transmitted by the *Culex* mosquito, which spreads through Southeast Asia from Japan to India. The incubation period is 7–21 days. There is no specific treatment, but there is a vaccine to prevent it.
- The Tick-borne encephalitis virus is transmitted by the bite of ticks of the genus *Ixodes* and by the consumption of unsterilized milk from infected animals. It extends from Central Europe, the Alps and the Balkan countries to all Russia.[44] Its incubation period is 1–4 weeks. It manifests as a two-phased illness, with a febrile period with myalgias, headache and non-specific symptoms during a week, after which two thirds of the patients recover. The other third of patients develop the neurological manifestations of encephalitis later in the week.[45] It leaves sequelae in 30–60% of cases (varying degrees of paralysis, ataxia, etc.).
- The West Nile virus is widespread in Africa, Asia and Europe. In 1999 it was detected for the first time in the USA and spreading throughout the country.[46] It is transmitted by *Culex* mosquitoes, and its reservoir are horses and birds. In Spain, autochthonous cases have already been detected in the region of Andalusia.[47] In 2018 there has been an alarming increase in cases in Italy and Eastern European countries, with more than 1300 cases and 90 deaths.[48] It has an average incubation period of 2–14 days. Up to 80% of those infected are asymptomatic; the other 20% develop fever, headache, arthralgia and even rashes. It is estimated that one out of every 150 infected persons develops a severe form encephalitis.[49] There is no specific treatment or vaccine.

With respect to bacterial meningitis, meningococcal meningitis in Europe and North America is mainly due to serogroups B and C, but in the tropics the serogroups A, C, Y and W-135 are more frequent, especially in countries of the African Sahel belt.[50]

Typhoid fever

It is caused by the *Salmonella typhi* and *Salmonella paratyphi bacteria*. Its reservoir is human, and the route of transmission is faecal-oral, through waters that are not well disinfected or the ingestion of contaminated food, with the sources of infection being the convalescent patient and chronic healthy carriers. It continues to be an important cause of fever in the traveller, with an estimated incidence of 27 million cases a year worldwide.[51] The amount of inoculum ingested (>10^6 bacteria) and the characteristics of the host are decisive in the development of the disease. Its incubation period is usually between 5 and 21 days, with lapses of up to 60 days having been observed. It presents in the form of fever, cough, headache, constipation or diarrhoea and abdominal pain. Its classic description is that during the first week there is a high fever; during the second week, abdominal pain, and maybe the appearance of maculopapular rose-coloured lesions in the abdomen and trunk (roseola); and from the third week onwards, possible hepatosplenomegaly and complications such as intestinal bleeding or perforation in relation to hyperplasia of the Peyer's patches. In is during this phase that the patient normally suffers septic *shock*. If there are no complications after the fourth week, the condition tends to improve progressively, leaving the patient in a chronic carrier state. Possible complications may appear in the form of endocarditis, osteomyelitis, arthritis and meningitis. The diagnosis is made by culture (50–70% of positive blood cultures in the first week).

In the choice of treatment, the severity of the clinical condition must be considered, as well as the geographical origin. Taking into account that strains resistant to fluoroquinolones have appeared in recent years (mainly in Asia, where the disease is more prevalent), the treatment of choice should be ceftriaxone 2 g every 24 h for 10 days. Other alternatives would be azithromycin or cefixime.[52] In Pakistan, cases of extremely resistant strains that are only sensitive to carbapenems have been described.

Table 6
Most frequent rickettsioses.

Rickettsia	Location	Reservoir	Peculiarities
R. africae	Sub-Saharan Africa	Great herbivores	Black spot, milder clinical picture
R. conorii (boutonneuse fever)	Europe, North Africa, Middle East, India	Dogs and rodents	Black spot, severe condition
R. rickettsii (Rocky Mountain Fever)	From Canada to Argentina	Dogs and rodents	No black spot, characteristic rash, very severe condition
Orientia tsutsugamushi (scrub typhus)	Japan, Southeast Asia, Australia, India and Russia	Mites	No black spot Transmitted by mites that live in scrubs and crops
R. typhi (murine typhus)	Africa, Asia, Mediterranean	Flea	Black spot, not frequent
R. prowazekii (epidemic typhus)	Worldwide	Body louse	Associated with overcrowding, disaster areas, refugees

Rickettsiosis

Different rickettsia of the genres *Rickettsia, Orientia, Ehrlichia* and *Anaplasma* can produce the disease in humans. All of them are transmitted by the bite of different types of arthropods (mites, fleas, lice and ticks), with those produced by the latter being the most frequent. The clinical manifestations are generally nonspecific, namely fever, malaise, headache, myalgia and cutaneous *rash*. Occasionally, a necrotic papule (black spot) appears at the site of the vector bite, which is very indicative of the disease *(R. conorii, R. africae, R. typhi)*. The incubation period is usually between 5 and 14 days. Rocky Mountain spotted fever, Mediterranean spotted fever, scrub typhus, and epidemic typhus produce very severe conditions, with an estimated mortality of 20–60% if no treatment is received.[53] African tick fever *(R. africae)* has been described in some case series as the second cause of traveller's fever after malaria in Africa.[54] The most frequent conditions are described in Table 6.

As for the laboratory diagnosis, it is based on the detection of antibodies, although it is also possible to perform PCR techniques, and an eschar biopsy sample is useful when it is available. The treatment with doxycycline should begin as soon as the suspicion arises, before having the results of the serological tests.

Middle East respiratory syndrome coronavirus

It is a zoonotic coronavirus that was first detected in 2012 in Saudi Arabia. It has a high mortality rate, close to 35–40% of detected cases.[55] The natural reservoir of the virus is the dromedary camel, but most of the infections occur person to person, as it is highly transmissible. This can be verified in the outbreak that occurred in South Korea when one single patient transmitted the disease to 82 people when he went to the A&E.[56] Clinical description varies from asymptomatic cases to febrile symptoms with cough and respiratory distress, pneumonia and respiratory distress. It can also be accompanied by gastrointestinal disorders and diarrhoea. The incubation period is from 2 to 14 days. A person who travels from the Arabian Peninsula and neighbouring countries or who has been in contact with suspected or confirmed cases of MERS, and who presents the aforementioned respiratory symptoms raises suspicion of infection, although strictly the current protocol in our country requires pulmonary parenchymal involvement (pneumonia or distress).[57] In case of suspicion, strict respiratory isolation measures should be taken, and the health personnel should wear PPE and an FFP2 mask. The treatment available is support treatment.

Schistosomiasis

Schistosomiasis affects millions of people, 90% of them in Africa, and produces up to 200,000 deaths per year, according to WHO.[58]

It is a trematode that lives in fresh water and is released by certain species of snails. While a person is swimming or bathing, the cercariae penetrate the human skin and can pass into the blood stream. In some cases, a localised dermatitis (swimmer's itch) is produced.[59] In the blood, they mature and move to the blood vessels (the mesenteric venules and the venous plexus of bladder, respectively), where the adult worms lay eggs. These eggs can be excreted in the faeces or in urine, infesting the waters where the miracidia are released that infect the snails, closing the cycle. Additionally, the eggs provoke an immune reaction in the organism that produces the clinical symptoms of the acute infection. Katayama syndrome or fever at 3–8 weeks is typical but not frequent. It presents as a fever, with respiratory symptoms such as cough, and urticaria, and frequently a skin rash and eosinophilia in 50% of cases. There are 5 species of schistosomes: *Schistosoma mansoni* (more frequent in Africa, the Middle East, the Caribbean, Brazil and Venezuela), *S. japonicum* (China, Philippines and Indonesia), *S. mekongi* (Laos and Cambodia) *S. intercalatum* (Central African jungle areas) which all produce intestinal disease, and *Schistosoma haematobium*, frequent in Africa and the Middle East, which produces genitourinary disease. The diagnosis is based mainly on the detection of eggs in urine or faeces, although serology with detection of antibodies in blood or urine can be used. The treatment is praziquantel, in a single dose, although it is advisable to repeat the dose 2–4 weeks later.

Conclusions

The early isolation of diseases that are highly transmissible and with a high fatality should be a priority in the A&E. Malaria is the most frequent cause of fever in the patient who returns from the tropics and due to its severity, it should always be ruled out. The A&E doctor should be familiar with the most frequent tropical diseases and be up to date with the most relevant international health warnings. He/she should be aware of any possible emerging diseases in our environment, such as dengue, which are already a reality in our country.

Conflict of interests

The authors declare that they have no conflicts of interest.

Appendix A.

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