REVIEW ARTICLE

Practical approach to a patient with fever who travelled to the tropics

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KEY WORDS

differential diagnosis, fever, public health, travel, tropics

ABSTRACT

By 2030, an estimated 2 billion international tourist trips are expected annually worldwide, with citizens of Poland as important contributors. Illness rates among returnees from developing regions range between 43% and 79%. Properly diagnosing fever in these travelers is vital due to potentially serious implications. After visiting tropical and subtropical zones, the main health complaints are diarrhea, fever, and skin lesions. A reliable diagnosis begins with taking a comprehensive travel history and identifying potential risks. In travelers returning from sub-Saharan Africa, malaria caused by *Plasmodium falciparum* is the main cause of fever, affecting 50 in every 1000 cases. Among returnees from Southeast Asia, dengue is dominant, occurring in 50–60 per 1000 cases, and its prevalence rises significantly nowadays. Other significant diseases include chikungunya, Zika, typhoid fever, amebic liver abscess, and occasionally viral hemorrhagic fevers. SARS-CoV-2 and influenza viruses are crucial pathogens as well. An in-depth assessment of the travel history, combined with knowledge on tropical diseases, are key to the diagnostic process, and algorithms may be helpful in selecting appropriate tests and treatment methods.

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Received: October 11, 2023.
Revision accepted: January 4, 2024.
Published online: January 11, 2024.
Pol Arch Intern Med. 2024; 134 (3): 16660
doi:10.20452/pamw.16660

Introduction Fever in a person returning from a trip to a tropical country is a frequent clinical scenario. In some cases, it can be a symptom, sometimes the only one, of a life-threatening disease,[1] necessitating urgent diagnosis and initiation of etiologic treatment.[2] In other situations, it may indicate a disease requiring patient isolation, which is significant for public health.

The incidence of diseases in individuals returning from developing countries falls within the range of 43% to 79% or 15% to 70%, depending on the study.[3,4] The most frequently diagnosed conditions associated with staying in the tropics include diarrhea, febrile conditions, and skin diseases.[2] Fever is reported by every fourth person seeking medical advice after returning from the tropics (eg, 23%,[5] 28%[1]), which makes it the second most common reason for a medical consultation, after diarrhea.[6]

Tropical malaria is the main cause of fever among travelers returning from tropical countries (50 per 1000 patients), although in persons who stayed in certain regions of Africa, African tick bite fever (ATBF) is also frequent. Among those returning from Southeast Asia, dengue is the most common (50–60 per 1000 patients),[7] according to a 20-year analysis of the EuroTravNet surveillance data.[8] Other febrile diseases of significant clinical importance include chikungunya, Zika, typhoid and paratyphoid fever, amebic liver abscess, visceral leishmaniasis, leptospirosis, and viral hemorrhagic fevers (VHFs; very rare in travelers).[9,10] Cosmopolitan diseases, such as influenza, COVID-19, pneumonia, and pyelonephritis should also be considered as a potential cause of fever.[11,12]

Generally, in patients with fever who travelled to the tropics, it is currently not recommended to initiate empiric treatment before first making an attempt to establish a diagnosis. This recommendation does not apply when the diagnosis can be made based on anamnesis and physical examination. For example, in the case of finding an eschar and fever in a patient returning from South Africa who reports having been bitten there by a tick, ATBF is the most likely diagnosis.[2]

Most cases of post-tropical fever associated with travel occur within a month of return,[12] and knowledge of the incubation periods of various diseases allows for a differential diagnosis.

TABLE 1 Infectious diseases requiring patient isolation

• Pneumonic plague
• Ebola fever
• Marburg fever
• Lassa fever
• Crimean-Congo fever
• Influenza A
• Middle East Respiratory Syndrome
• SARS-CoV-2 infection
• Avian influenza

TABLE 2 Post-travel patient interview protocol

1 Preparation for the trip: vaccinations received, use of vector protection measures, malaria chemoprophylaxis, and adherence to recommendations
2 Patient data: age, chronic diseases, intake of medications (regularly and during the trip), immune status, pre-existing diseases
3 Travel details: duration of the trip, date of return, countries visited, purpose of the trip, type of accommodation, activities undertaken, food hygiene
4 Date of fever occurrence in relation to the travel (exposure) time (significant in relation to the incubation period of different diseases)
5 Exposure to various environmental factors during the trip (related to the risk of contracting tropical diseases)
6 Disease symptoms other than fever, along with their onset time and dynamics of presentation
7 Self-treatment

For example, fever starting more than 21 days after returning from the tropics essentially excludes dengue, rickettsiosis, Zika, and VHFs, regardless of the exposure history. It is worth underlining that symptoms of malaria may present days, months, or even years after exposure. However, most of the dangerous febrile diseases manifest within the first weeks after returning from the tropics. Cases of a disease occurring months or years after a trip are less probable and sporadic.[13]

Malaria chemoprophylaxis and vaccinations significantly reduce, but do not eliminate, a risk of contracting malaria and various other diseases. The most common diseases occurring in travelers that can be prevented by vaccinations[14] include influenza, typhoid fever, and viral hepatitis.[15] According to the GeoSentinel database,[15] vaccine-preventable diseases occur relatively rarely in travelers (about 3% of cases) but are associated with frequent hospitalizations (60% of cases) in unvaccinated individuals.

Practical approach Fever, defined as a body temperature above 38 °C,[16] is an important symptom in a person returning from a tropical journey. Approximately one-third of individuals who experience fever after travelling to the tropics are diagnosed with a tropical disease; of those, 22% are diagnosed with malaria. In 36% of febrile individuals a nontropical infection is detected, whereas 17.8% remain undiagnosed.[17]

When a febrile patient presents to a physician, the first step is to assess their general clinical condition, for example, using the quick sequential organ failure assessment (qSOFA) scale.[17] If 2 or 3 of the following criteria are met: 1) Glasgow Coma Scale score below 12 points, 2) tachypnea (≥22 breaths per minute), and 3) systolic blood pressure lower than or equal to 100 mm Hg, urgent intervention is required, sometimes including intensive care. In addition to the qSOFA score, during a physical examination, attention should be paid to signs of a severe condition, such as petechiae, cyanosis, neck stiffness, symptoms of peritonitis, hematuria, icterus, oliguria / anuria, or distal necrosis.[15]

Probability of a disease posing a threat to public health (TABLE 1), such as VHFs, Middle East Respiratory Syndrome, or tuberculosis should always be considered, and the need for patient isolation should be assessed as soon as possible.[15] It should be noted that some diseases do not require patient isolation but rather special precautions, such as maintaining proper hygiene in the case of hepatitis A or typhoid fever.

Suspicion of VHF occurs in patients with fever or reporting febrile conditions in the last 24 hours, who stayed in an area of endemic or epidemic occurrence of hemorrhagic fevers in the last 21 days,[18] or those who had contact with sick people, their secretions, or biological samples within this time frame. High-risk situations include personal contact with an infected person, exposure to body fluids or secretions of a sick person, sexual contact with a sick person, and participation in a funeral of a person who died of VHF. Another risk factor is consumption or handling of bushmeat. If VHF is suspected, medical and laboratory staff should be informed, and diagnostics must be carried out in a biosafety level (BSL)-2+/BSL-3 laboratory.[15] Although the likelihood of an imported case of VHF is very low, the public health threat is significant enough that this hypothesis should be considered in the differential diagnosis. Patients with suspected VHF should be immediately isolated and subsequently transferred to a designated place. The medical staff needs to be informed of the suspicion and apply personal protective equipment when attending to the patient. Finally, health services and the Crisis Management Center have to be notified.[19]

To properly assess the risk of VHF, it is necessary to have up-to-date information about the currently ongoing epidemics,[15] which can be found on official websites, such as https://wwwnc.cdc.gov/travel/notices.

If a patient does not require urgent stabilization or isolation, further detailed interview should be conducted according to the protocol outlined in TABLE 2. Comprehensive explanations can be found in the subsequent part of the text.

1 Preparation for the trip: pretravel vaccinations, vector protection, malaria chemoprophylaxis, and compliance with recommendations.[20]

Among the available travel vaccinations, the effectiveness of various preparations varies. No vaccine completely protects against any disease, but they significantly reduce the risk of infection;

TABLE 3 Pathogens included in a differential diagnosis of tropical fever, depending on their incubation period

Incubation period	Bacteria	Viruses	Parasites
<14 days	• Anthrax • Bacterial diarrhea (*Campylobacter, Salmonella, Shigellosis*, cholera) • Legionnaires' disease • Leptospirosis • Melioidosis • Meningococcal disease • Paratyphoid fever • Plague • Relapsing fever • Rickettsioses • Typhoid fever	• Arboviruses (chikungunya, dengue, Japanese encephalitis, Rift Valley fever, West Nile fever, yellow fever, Zika) • Measles • Rabies • Viral gastrointestinal infections (noroviruses, rotaviruses) • Viral hemorrhagic fevers (Ebola, Lassa, Marburg, Crimean-Congo hemorrhagic fever) • Viral respiratory infections (influenza, COVID-19)	• African sleeping sickness • Malaria (*Plasmodium falciparum, P. knowlesi*)
14 days–6 weeks	• Bartonellosis • Brucellosis • Melioidosis • Q fever • Typhoid fever	• Acute retroviral disease • Hepatitis A virus • Hepatitis E virus • Rabies • Rubella	• Acute schistosomiasis • Amebic liver abscess • Malaria (*P. falciparum*, *P. vivax/ovale*, *P. malariae*)
<6 weeks	• Tuberculosis	• Hepatitis B virus • Rabies	• African sleeping sickness (West African variant) • Amebic liver abscess • Fascioliasis • Filariasis • Malaria (*P. vivax, P. ovale*) • Visceral leishmaniasis

for example, the efficacy of the yellow fever vaccine is over 99%,[12,13] while the hepatitis A vaccine protects nearly 100% of vaccinees. For cholera, the vaccine effectiveness is estimated at 79.5% after 90 days from administration.[21] With respect to malaria chemoprophylaxis, taking a preventive drug reduces, but does not eliminate, the risk of the disease.[22] It can also prolong the incubation period and modify the symptoms. During the medical history taking, it is important to establish whether the patient adhered to the scheme of taking the prophylactic drug, which needs to be used before, during, and after returning from a trip to a malaria-endemic region, or if they experienced severe diarrhea, which could reduce drug absorption.[23]

2 Patient medical data, including age, chronic diseases, medications taken regularly (both before and during the trip), and immune status.

Drugs taken by the patient can prolong the time of symptom onset or change the clinical picture of the disease; for example, doxycycline used for Lyme disease also has a prophylactic effect against malaria or ATBF. The patient's immune status, including a history of diabetes, steroid treatment, kidney damage, or past splenectomy, may be associated with additional indications for certain vaccines, or contraindications for the use of specific products (particularly live preparations). Altered immune status can also result in reduced effectiveness of vaccination and increase the risk of infection with specific diseases prevalent in tropical zones, such as those transmitted through foodborne routes, or of colonization with multidrug-resistant bacteria.[24]

3 Travel data: duration of the trip, return date, countries visited, purpose of the trip, type of accommodation, activities undertaken.

As a rule, the longer the journey, the greater the risk of infectious disease.[2] Knowledge on the geographic region of the trip allows for estimating the probability of contracting various tropical diseases. In febrile patients who stayed in sub-Saharan Africa, malaria should be suspected as the primary diagnosis, as it is most commonly diagnosed in febrile travelers returning from this region, although influenza and ATBF are more prevalent in certain African regions. After a stay in Southeast Asia, the risk of dengue is higher than that of malaria, whereas other tropical causes of fever are less likely. After a stay in Central and South Asia, especially in India, the risk of malaria, dengue, and paratyphoid and typhoid fever is significant. A visit to Nepal is associated with the highest risk for typhoid fever worldwide. After a stay in Central America and the Caribbean, dengue is the most likely, followed by malaria; other infectious causes of fever are much less frequent.[2]

The type and purpose of the trip are associated with the probability of exposure to certain infectious agents. The risk of cholera, for example,

TABLE 4 Most common diseases associated with particular types of exposure (continued on the next pages)

Type of exposure	Most common diseases associated with the type of exposure
Improper food hygiene (eg, consumption of untreated water, unpasteurized milk, undercooked or raw food)	Amebiasis Brucellosis *Campylobacter* infection Cholera Clonorchiasis Cryptosporidiosis Cyclosporiasis *E.coli* infection Fascioliasis Giardiasis Hepatitis A virus, hepatitis E virus infection Listeriosis Paragonimiasis Salmonellosis Shigellosis Toxoplasmosis Traveler's diarrhea Trichinellosis Typhoid fever
Consumption of unpasteurized dairy products	Brucellosis Salmonellosis Shigellosis Tuberculosis
Contact with freshwater, eg, swimming, kayaking	Acute schistosomiasis *Aeromonas* infections Amebiasis Atypical mycobacteriosis Legionnaires' disease Leptospirosis Melioidosis
Contact with seawater	Infections with *Aeromonas*, *Erysipelothrix rhusopathiae*, *Mycobacterium marinum*, *Vibrio vulnificus*
Contact with soil, eg, walking barefoot	Cutaneous larva migrans Hookworm disease Melioidosis (caused by *Burholderia pseudomallei*) Strongyloidiasis Tungiasis
Tattoos, piercings, parenteral drug administration, blood transfusions	Acute HIV infection Babesiosis Cytomegalovirus infection Hepatitis B virus infection Hepatitis C virus infection Malaria West Nile virus infection
Unprotected sexual contact, using paid sexual services, multiple partners	Chlamydial infections Cytomegalovirus infection Epstein–Barr virus infection Gonorrhea Hepatitis A virus infection Hepatitis B virus infection Hepatitis C virus infection Herpes simplex virus infection HIV infection Lymphogranuloma venereum Syphilis Viral hemorrhagic fevers Zika virus infection

TABLE 4 Most common diseases associated with particular types of exposure (continued from the previous page)

Type of exposure	Most common diseases associated with the type of exposure
Visiting relatives in tropical countries	Ebola virus infection Hepatitis A virus infection Malaria Meningococcal disease Tuberculosis Typhoid fever
Mosquito bite	Chikungunya Dengue fever Filariasis Japanese encephalitis Malaria Rift Valley fever West Nile fever Yellow fever Zika virus infection
Tick bite	African tick bite fever (caused by *Rickettsia africae*) Babesiosis Crimean-Congo hemorrhagic fever Lyme disease Q fever Rickettsiosis Tick-borne encephalitis Tick-borne relapsing fever Tularemia
Mite bite	Rickettsialpox (caused by *R. akari*) Scrub typhus
Flea bite	Murine typhus (caused by *R. typhi*) Plague Spotted fever (caused by *R. felis*)
Lice bite	Epidemic typhus (caused by *R. prowazekii*) Louse-borne relapsing fever (caused by *Borrelia recurrentis*) Trench fever (caused by *Bartonella quintana*)
Fly bite	African sleeping sickness (or African trypanosomiasis) Bartonellosis Leishmaniasis Onchocerciasis (also known as river blindness)
Kissing bug bite	Chagas disease
Chrysops/mango fly bites	Loiasis (*Loa loa* infection)
Animal bite	Cat scratch disease (caused by *B. henselae*) Monkeypox Rabies Sporotrichosis
Contact with animals	Anthrax Brucellosis Ectoparasites Hantavirus infection Hendra virus infection Lassa fever Middle East respiratory syndrome Nipah virus infection Plague Psittacosis (or parrot fever) Q fever Rat-bite fever Toxoplasmosis Tularemia (or rabbit fever)

TABLE 4 Most common diseases associated with particular types of exposure (continued from the previous pages)

Type of exposure	Most common diseases associated with the type of exposure
Contact with birds	Avian influenza Psittacosis (parrot fever)
Cave exploring	Histoplasmosis Rabies
Safari in East/Southern Africa	African tick bite fever African trypanosomiasis
Contact with sick people	Influenza Meningitis Middle East respiratory syndrome Tuberculosis Viral hemorrhagic fevers

is markedly different for a diplomat working in a tropical country who is accommodated in an air-conditioned house, than for a medical worker providing aid in an area of humanitarian crisis.

4 Date of the fever onset in relation to the time of exposure (important in the context of the disease incubation period).

In the case of malaria, 6 to 7 days must pass from the onset of exposure to the appearance of the first symptoms of the disease. In other words, occurrence of fever within a week from the first exposure to a mosquito bite in an area endemic for malaria is certainly related to a disease other than malaria. On the other hand, the incubation period of dengue is usually 5 to 7 days (range, 3–10 days), so fever occurring a few weeks after returning from the tropics cannot be associated with dengue.

Knowledge of the incubation periods of particular diseases[2] directly affects required diagnostic tests (TABLE 3). Performing the tests too early or too late can lead to false-negative results, and sometimes the tests need to be repeated.

5 Exposure to various environmental factors during the trip is related to the risk of tropical diseases.

It is worth remembering that the more detailed the interview, the greater the likelihood of obtaining information about the patient's exposure to an infection (TABLE 4). However, sometimes, the patient does not remember or has not noticed high-risk situations, such as a mosquito bite or consumption of untreated water. In other cases, the patient does not want to talk about important circumstances, such as undergoing alternative therapies in the tropics or engaging in high-risk sexual behaviors.[25]

6 Presence of symptoms other than fever (eg, influenza-like symptoms, cough, headache, rash, abdominal pain, and others) should be screened for, along with their time of onset and dynamics of presentation, as in the case of managing patients with no history of travelling to the tropics.

Some symptoms and signs are characteristic of particular diseases; for example, retro-orbital pain and measles-like rash of dengue, severe joint and muscle pain of chikungunya, as well as eschar of rickettsiosis and neck stiffness of meningitis. During a clinical examination, specific signs may suggest a diagnosis[15] (TABLE 5).

Investigative diagnostic procedures recommended for febrile travelers are available to a limited extent in outpatient settings (eg, at the primary care physician's office). Detailed laboratory tests can be performed at hospitals and clinics specializing in tropical medicine or infectious diseases. These tests are designed for cases with a suspicion of a tropical disease, supported by factors such as the geographic region of exposure, symptomatology, and incubation period.[26]

If malaria and other life-threatening diseases can be excluded based on the patient's travel route, the primary care tests that need to be performed include complete blood count, electrolyte, creatinine, urea, transaminase, γ-glutamyl transpeptidase, and C-reactive protein (CRP) levels, coagulation tests, urinalysis, stool tests, chest X-ray, and abdominal ultrasonography. In Poland, rapid diagnostic tests and microscopic examination of blood smears for malaria are available in selected laboratories; however, a family physician cannot refer patients for such tests free of charge, and waiting time for the results may be prolonged, especially on public holidays. In some cases, it may be preferable to refer the patient to a hospital; and if travel data indicate a possibility of malaria, the patient should be urgently admitted to an emergency department or emergency room, and then to a hospital ward.[27] The panel of recommended tests can be broadened to encompass blood and urine cultures, quick diagnostic tests for malaria and dengue (subject to a laboratory's diagnostic proficiency; including polymerase chain reaction [PCR] blood tests for malaria as well as serologic assessments), imaging examinations of the central nervous system, lumbar puncture, and computed tomography scans.

Discussion The issue of managing fever in a patient who stayed in the tropics has been widely discussed for years.[28] Fever in a returned traveler may be caused by a variety of diseases, and their diagnosis is often hindered by a lack of diagnostic capabilities.[15] However, even in referral

TABLE 5 Clinical manifestations accompanying tropical fever that may facilitate diagnosis (continued on the next pages)

Symptoms accompanying fever	Most common causes
Fever without local symptoms	• Dengue • Malaria • Rickettsial diseases (mainly from sub-Saharan Africa) • Typhoid and paratyphoid fever
Fever with rash	• Acute retroviral syndrome • Acute schistosomiasis • African sleeping sickness • Arbovirus infections • Chickenpox • Chikungunya • Cytomegalovirus • Dengue • Ebola virus infection • Epstein–Barr virus infection • Herpes zoster virus infection (shingles) • Marburg virus infection • Measles • Meningococcal disease • Rickettsial diseases • Relapsing fever • Rubella • Secondary syphilis • Strongyloidiasis • Typhoid fever • Viral hemorrhagic fevers • West Nile virus infection • Zika virus infection
Fever and respiratory symptoms	• Acute histoplasmosis • Coccidioidomycosis • COVID-19 • Influenza • Legionnaires' disease • Leptospirosis • Löffler syndrome • Melioidosis • Middle East respiratory syndrome • Plague • Pneumonia • Psittacosis • Q fever • Tropical pulmonary eosinophilia • Tuberculosis • Tularemia
Fever and diarrhea	• Amebiasis (bloody diarrhea) • Cryptosporidiosis (watery diarrhea) • Giardiasis • Malaria (watery diarrhea in 30% of cases) • Norovirus infections • Traveler's diarrhea (enterotoxigenic *Escherichia coli*, enteroaggregative *E. coli*, enteropathogenic *E. coli*, *Campylobacter*, *Salmonella*, *Shigella*, very rarely cholera) • Typhoid fever (after 2–3 weeks of illness duration)

TABLE 5 Clinical manifestations accompanying tropical fever that may facilitate diagnosis (continued from the previous page)

Symptoms accompanying fever	Most common causes
Fever and abdominal pain	• Amebic liver abscess (hepatomegaly) • Brucellosis • Cryptosporidiosis (upper abdominal pain, bloating, nausea) • Giardiasis • Malaria • Mononucleosis (splenomegaly) • Paratyphoid • Relapsing fever (hepatosplenomegaly) • Visceral leishmaniasis
Fever and jaundice	• Acute cholangitis (liver fluke) • Bartonellosis (Oroya fever) • Cytomegalovirus • Hepatitis A–E virus infections • Hemolytic uremic syndrome • Leptospirosis (Weil disease) • Mononucleosis • Severe malaria (hemolysis) • Viral hemorrhagic fevers (yellow fever, Crimean–Congo hemorrhagic fever, Rift Valley fever, severe dengue)
Fever and hepatitis	• Acute cytomegalovirus infection • Brucellosis • Dengue • Epstein–Barr virus infection • Hepatitis A–E virus infections • HIV infection • Leptospirosis • Q fever • Toxoplasmosis
Fever and neurologic symptoms	• African sleeping sickness • Angiostrongyliasis • Bacterial meningitis • Cerebral malaria • Dengue • Enteroviruses • Gnathostomiasis • Herpes simplex virus infection • Japanese encephalitis • Measles • Neurosyphilis • Rabies • Relapsing fever • Tick-borne encephalitis • Trench fever • Viral meningitis • Varicella zoster virus infection • West Nile virus infection
Fever and petechiae	• Hemorrhagic fevers • Leptospirosis • Meningococcemia • Plague • Rickettsiosis • Sepsis

TABLE 5 Clinical manifestations accompanying tropical fever that may facilitate diagnosis (continued from the previous pages)

Symptoms accompanying fever	Most common causes
Fever and eosinophilia	• Acute schistosomiasis • Ascariasis • Fascioliasis • Filariasis • Hookworm disease • Sarcocystosis • Strongyloidiasis • Trichinosis • Visceral larva migrans (toxocariasis)
Fever and joint/muscle pain	• Chikungunya • Dengue • Ross River fever • Sarcocystosis (Southeast Asia) • Trichinosis • Zika virus infection
Fever and localized lymph node enlargement, skin and subcutaneous tissue inflammation	• Bartonellosis • Toxoplasmosis • Trypanosomiasis • Tuberculosis • Tularemia
Fever and conjunctivitis	• Leptospirosis • Zika virus infection
Fever and bleeding symptoms	• Crimean–Congo hemorrhagic fever • Dengue • Leptospirosis • Meningococcal disease • Rickettsial diseases (spotted fever group 5) • Viral hemorrhagic fevers • Yellow fever
Fever and splenomegaly/hepatomegaly	• Amebic liver abscess • Dengue • Hepatitis • Malaria • Mononucleosis • Schistosomiasis • Visceral leishmanias
Fever and normal/low white blood cell count	• Acute HIV infection • Chikungunya • Dengue • Malaria • Rickettsial diseases • Typhoid fever • Zika virus infection

centers, about 25% of febrile patients remain undiagnosed[29]; therefore, a practical approach is recommended,[30] which involves case-by-case assessment of the probability that the fever is a symptom of a life-threatening disease, or a disease of significant importance for public health.[15] On the other hand, sometimes common, cosmopolitan causes of fever are overlooked, such as COVID-19,[31,32] measles, chickenpox, influenza, or tuberculosis.[2]

Special attention should be paid to diseases posing a risk of severe course and death, such as tropical malaria, monkey malaria, severe dengue, typhoid fever, VHFs, or Japanese encephalitis (TABLE 6), as well as nontropical diseases frequently encountered by travelers, including influenza, bacterial pneumonia, sepsis, and rabies.[33,34] Death among patients who travelled to a tropical region is rare, occurring in about 0.22% of cases.[17] Nevertheless, diagnosis should be made as soon as possible due to the risk of rapid deterioration of the patient's general condition, for example, during tropical malaria.[15]

Children, pregnant women, and immunocompromised individuals who develop fever after

TABLE 6 Potentially life-threatening tropical and infectious diseases

African trypanosomiasis (sleeping sickness)
Anthrax
Bartonellosis
Endemic typhus
Influenza
Japanese encephalitis
Leptospirosis
Melioidosis
Middle East respiratory syndrome
Plague
Rabies
Relapsing fever
Rickettsioses
Rift Valley fever
Scrub typhus
Severe dengue
Simian malaria
Spotted fever
Trichinellosis
Tropical malaria
Typhoid fever
Viral hemorrhagic fevers (Ebola, Crimean–Congo fever, yellow fever)

TABLE 7 Fever after travelling to the tropics: key points for a physician

1. Assess the patient's general clinical condition; eg, using the quick Sequential Organ Failure Assessment scale
2. Pay attention to signs of a severe condition of the patient
3. Consider the probability of a disease posing a threat to public health
4. Think about diseases potentially posing a risk of severe course and death
5. Ask about: • pretravel vaccinations, vector protection, malaria chemoprophylaxis, and compliance with recommendations • patient medical data, including age, chronic diseases, medications taken regularly (both before and during the trip), and immune status • travel data: duration of the trip, return date, countries visited, purpose of the trip, type of accommodation, activities undertaken • date of the fever onset in relation to the time of exposure (important because of the incubation periods of individual diseases) • exposure to various environmental factors during the trip (related to the risk of tropical diseases)
6. Look for the presence of symptoms other than fever
7. Pay attention to febrile conditions in children, pregnant women, and immunosuppressed individuals
8. Order laboratory and imaging tests, refer to a hospital if necessary

returning from tropical countries[2] require special attention, as the course of some diseases in these groups of patients may differ from that observed in the general population.[35-37]

Among the febrile patients who travelled to malaria-endemic regions, the priority is to exclude this disease, regardless of whether they have taken chemoprophylaxis.[38] Blood samples should be collected to perform microscopic examinations of blood smears (thick drop, thin smear).[39] If the results are negative, the smears should be repeated several times, for example, twice a day for 3 days, and during a fever spike (FIGURE 1). Treatment depends on the severity of malaria, which is caused by *Plasmodium* spp. infection. For uncomplicated malaria, the recommended treatment is oral artemisinin-based combination therapy. In the case of severe malaria, the initial treatment is intravenous artesunate, followed by a full course of oral antimalarial drugs. The choice of a specific antimalarial medication depends on the *Plasmodium* species causing the disease and the patterns of drug resistance in the region where the infection was acquired.[38]

Apart from malaria, in recent years, there has been a significant increase in arboviral infections among returned travelers, such as dengue, chikungunya, or Zika.[2,40,41]

In each case, establishing a specific diagnosis should be strived for, as diagnostics based on clinical symptoms alone are often unreliable. One of the exceptions is eschar, a characteristic skin lesion which, in the case of a history of stay in South Africa, allows for a probable diagnosis of spotted fever (caused by *Rickettsia africae*), while after a trip to Asia, it may indicate scrub typhus (potentially life-threatening, caused by *Orientia tsutsugamushi*). In the latter case, eschar is often overlooked as it develops on covered, moist parts of the body, which is where mites, the vectors of scrub typhus, typically bite.

Of note, travelling to tropical regions is associated with transient colonization of the gastrointestinal tract with drug-resistant bacteria, lasting about 3 months.[42] Patients who were treated in a medical facility in a tropical country and were then transported to another country should be initially isolated due to the possibility of colonization with multidrug-resistant pathogens.[1] Colonization occurs in about 30% of people, depending on the travel region; the highest risk (73%) is observed in India. Hospitalization abroad is a significant risk factor for multidrug-resistant bacteria colonization.[2,43]

With respect to patient age, people over 60 years more frequently develop severe malaria and lower respiratory tract infections.[44] Children, on the other hand, more often experience diarrhea, skin diseases, and upper respiratory tract infections.[15,44] In recent years, there has been an increase in the number of individuals aged 60 and above travelling abroad for medical purposes. Many of these individuals have coexisting medical conditions, and some have compromised immunity. This has a significant impact on the risk of infection with pathogens present in the destination region. It is also known that within this age group, there are more cases of infection with multidrug resistant infectious agents.[33]

In addition to infections, fever can also indicate other diseases. Fever of unknown origin is the first symptom of cancer (eg, lymphoma) in 2%–25% of cases, and of autoimmune diseases (eg, rheumatoid arthritis, giant cell arteritis) in 5%–32% of cases.[45] Drug-induced fever occurs in 3%–7% of people. Another potential cause of

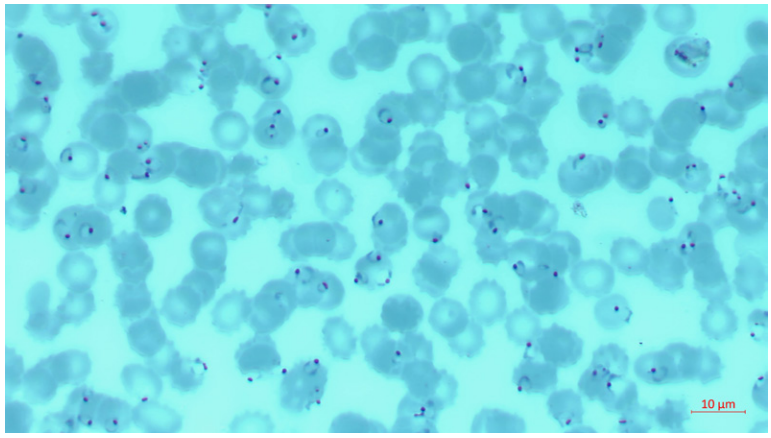

FIGURE 1 Thin blood smear (Giemsa staining) showing multiple trophozoites of *Plasmodium falciparum* (Zeiss AxioLab 5 microscope); photograph by M. Grzybek

fever is thrombotic disease, which may be related to a long flight (for flights lasting >8 hours, the risk is about 0.5%).[2]

Poland is a nonendemic country; therefore, significantly fewer cases of tropical diseases are observed here, which is to be expected. While tropical medicine remains a niche discipline, it sits at the intersection of infectious diseases and internal medicine. There are only a few dedicated tropical disease divisions and travel medicine clinics in the country. Yet, given the high interest in travelling among Poles, health care professionals should be ready to treat patients who become ill after returning from tropical regions.

Example of a diagnostic process A 45-year-old man presented to the emergency department (ED) due to episodes of fever up to 39.7 °C for the last 3 days. The patient also experienced severe headaches and chills, weakness, and muscle and joint pain. He reported a 4-week stay in Brazil, in the Rio de Janeiro region, where he had worked at a seaport as a crane operator. He returned to Poland the day before presenting to the ED; the fever episodes started on his last day in Brazil and continued during the return journey. The patient was vaccinated against yellow fever 7 years ago and did not use any insect repellents or malaria chemoprophylaxis. He did not consult the Travel Medicine Clinic before departure.

Upon arrival at the ED, the patient's condition was good. He scored 0 on the qSOFA scale. The attending physician ruled out diseases typical of the patient's area of residence that would pose a threat to the public health or require isolation. Physical examination revealed dry oral mucosa, body temperature of 38.7 °C, and tachycardia of 104 bpm. The liver was palpable 2 cm under the right costal margin, tender, soft. Laboratory workup showed a leukocyte count of 2.7 G/l (reference range [RR], 4.1–10.9 G/l), platelet count of 78 G/l (RR, 140–440 G/l), and CRP level of 23 mg/l (RR <5 mg/l).

A Combo test was performed for the influenza virus, SARS-CoV-2, and respiratory syncytial virus infection, with negative results. Given the patient's place of stay (Brazil) and febrile illness with influenza-like symptoms, tropical diseases should be considered in the differential diagnosis, along with cosmopolitan diseases. The patient had leukopenia, thrombocytopenia, and slightly elevated CRP levels. Due to occurrences of yellow fever in Brazil, it should be considered a possibility; however, the patient was vaccinated against this disease, and the vaccine has a very high efficacy. The most common cause of febrile illness in persons travelling to South America is dengue, followed by malaria. PCR tests were performed for 6 viral pathogens known as the tropical panel (dengue, Zika, chikungunya, West Nile virus, yellow fever, and Mayaro virus), as well as a rapid diagnostic test and blood smears for malaria. The result was positive for dengue.

The patient was started on symptomatic treatment (antipyretics, analgesics, fluids), and his vital parameters were monitored. A rash resembling measles appeared during body temperature normalization, lasting 1.5 days. No clinical signs of severe dengue were observed. Subsequently, the patient's symptoms subsided, and the laboratory parameters normalized.

Conclusions During their professional career, almost every doctor encounters a patient who experiences fever after staying in a tropical zone. Due to a continuously growing interest in travelling, the number of imported tropical diseases is likely to rise. It is important to consider tropical causes of fever, especially in the cases of potentially life-threatening diseases, such as malaria. The guidelines presented in the current review, summarized in **TABLE 7**, are intended to assist practicing physicians in the diagnostic process.

ARTICLE INFORMATION

ACKNOWLEDGMENTS None.

FUNDING None.

CONFLICT OF INTEREST None declared.

HOW TO CITE Kuna A, Grzybek M. Practical approach to a patient with fever who travelled to the tropics. Pol Arch Intern Med. 2024; 134: 16660. doi:10.20452/pamw.16660

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