

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Gokhale V, Agarkar S. Persistent pupillary membrane. *N Engl J Med* 2017;376:561. DOI: 10.1056/NEJMicm1507964

Supplementary Appendix

Supplement to: Guy E. Thwaites and Nicholas P. J. Day. The Approach to the Returned Traveler Who Develops Fever.

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Table S1. On-line sources of information for physicians assessing febrile travelers and geographic risks of infectious diseases

Responsible agency/organisation	Website link	Description of information available
World Health Organization	http://www.who.int/topics/travel/en/	Provides advice on vaccinations and food safety for travelers and information on major current outbreaks.
United States Centers for Disease Control and Prevention	http://wwwnc.cdc.gov/travel	Authoritative and comprehensive advice on all aspects of travelers health for travelers and clinicians. Especially useful for current malaria and yellow fever geographic risks, outbreaks and other emerging health-related risks.
Public Health England	https://www.gov.uk/government/collections/viral-haemorrhagic-fevers-epidemiology-characteristics-diagnosis-and-management https://www.gov.uk/guidance/viral-haemorrhagic-fevers-origins-reservoirs-transmission-and-guidelines	Excellent source of information on all viral hemorrhagic fevers, including geography of past and current outbreaks.
National Travel Health Network & Centre, United Kingdom (NathNac)	http://travelhealthpro.org.uk	UK government organization providing authoritative advice and recommendations on all aspects of travelers health for healthcare professionals. Up-to-date information on malaria geographic risks and current outbreaks.
Travel and International Health Team of Health Protection Scotland (HPS) (travax)	http://www.travax.nhs.uk	On-line resource for health care professionals working within the Scotland's National Health Service who advise patients about healthy travel. Registration is required for access. Provides information on all aspects of travel and updates on latest outbreaks.
The Program for Monitoring Emerging Diseases (ProMed)	http://www.promedmail.org/	An Internet-based reporting system dedicated to rapid global dissemination of information on outbreaks of infectious diseases and acute exposures to toxins that affect human health, including those in

		animals and in plants grown for food or animal feed. Freely available electronic communications provide up-to-date and reliable news about threats to human, animal, and food plant health around the world.
HealthMap	http://www.healthmap.org/en/	HealthMap brings together disparate data sources to achieve a unified and comprehensive view of the current global state of infectious diseases and their effect on human and animal health. It disseminates freely available online information about emerging diseases in nine languages, facilitating early detection of global public health threats.
The Global Outbreak Alert & Response Network (GOARN)	www.who.int/csr/outbreaknetwork/en/	GOARN is a World Health Organization collaboration of existing institutions and networks which responds to outbreaks of international importance. Provides limited information on current outbreaks.
International Society of Travel Medicine	http://www.istm.org	A members-only online community offering access to special travel medicine alerts, links to important resources, members-only discussion groups including publications and educational products.
GeoSentinel	http://www.istm.org/geosentinel	A worldwide communication and data collection network for the surveillance of travel related morbidity. Current reports and data only available to members; but numerous scientific publications provide essential source of information on unwell travelers.
European Tropical Medicine and Travel Network of the International Society of Travel Medicine (EuroTravNet)	http://www.istm.org/eurotravnet	European network of clinical experts in tropical and travel medicine linked to GeoSentinel. Current reports and data only available to members.
Canadian Travel Medicine Network of the International Society of	http://www.istm.org/cantravnet	Canadian network of experts in travel medicine linked to GeoSentinel. Current reports and data only available to members.

Travel Medicine (CanTravNet)		
Fever travel: diagnostic algorithm	http://www.fevertravel.ch/	Swiss Practice Guidelines for Evaluation of Fever in returning Travelers or Migrants. Freely available Algorithm to create differential diagnosis for health professionals. Last updated in September 2012.
Institute for Tropical Medicine, Antwerp. Training tool and expert system for travel related fever	http://www.kabisa.be/	Freely available software for the diagnosis of imported fever, based on a prospectively generated database of over 2000 patients.
The Global Infectious Diseases and Epidemiology Network (GIDEON)	www.GIDEONonline.com	Advanced diagnostic software for fever in travelers. For clinicians; subscription only.

Table S2. Common and/or important causes of fever in the returned traveler, by presenting syndrome. Diseases mainly restricted to tropical or subtropical regions and cosmopolitan infections which have been shown to be particularly common in returning travelers are included. Within presentation categories diseases are ranked approximately by incidence in published series of returned travelers, with most common diagnoses listed first ^{1,2}. Common infections are colored in green; rare infections in orange.

Disease (pathogen)	Pathogen	Incubation period	Geographic regions affected	Vector / exposure	Common clinical and laboratory findings	Diagnostics	Initial or empirical treatment
<i>Systemic febrile illness</i>							
Malaria							
	<i>Plasmodium falciparum</i>	7-30 days (may be longer)	Africa, Asia, South America. Highest risk of infection in Sub-Saharan Africa	<i>Anopheles</i> mosquitos	Thrombocytopenia. Severe disease: coma (cerebral malaria); acidosis; renal impairment; hypoglycemia; jaundice; hypotension; pulmonary edema; retinal hemorrhages	Thick and thin blood smear microscopy; Rapid Diagnostic Tests (based on HRP2 or pLDH antigen detection); PCR	Uncomplicated: artemisinin-based Combination Therapy (ACT) Severe malaria: parenteral artesunate
	<i>P. vivax</i>	8-30 days (up to a year with long incubation strains)	South and Southeast Asia, South America, Horn of Africa	<i>Anopheles</i> mosquitoes	Severe disease uncommon; thrombocytopenia	Thick and thin blood smear microscopy; pLDH-based rapid diagnostic tests; PCR	Artemisinin-based combination therapy (except artesunate-SP) or chloroquine, + primaquine for radical cure High level chloroquine

							resistance in Indonesia/PNG)
	<i>P. ovale</i>	8-60 days	Widespread in the tropics, particularly Sub-Saharan Africa	<i>Anopheles</i> spp. mosquitoes	Severe disease rare; thrombocytopenia	Thick and thin blood smear microscopy	Artemisinin-based combination therapy or chloroquine, + primaquine for radical cure
	<i>P. malariae</i>	13-30 days	Widespread in the tropics	<i>Anopheles</i> spp. mosquitoes	Severe disease rare; thrombocytopenia	Thick and thin blood smear microscopy; PCR	Artemisinin-based combination therapy or chloroquine
	<i>P. knowlesi</i>	10-14 days	Southeast Asia, particularly Borneo	<i>Anopheles</i> mosquitos	Can be severe, with acidosis and renal impairment	Thick and thin blood smear microscopy	As for falciparum malaria. Also sensitive to chloroquine
Dengue	Dengue virus (flavivirus)	4-10 days	Extensive distribution in the tropics and sub-tropics	<i>Aedes</i> mosquitoes	Myalgia and rash; lymphocytosis; thrombocytopenia. Severe dengue: hypotension; narrow pulse pressure; hemorrhage (GI, intracranial)	NS1/IgM rapid diagnostic test, NS1 and IgM ELISAs, RT-PCR*	Supportive
Mononucleosis	Epstein-Barr virus, Cytomegalovirus, and <i>Toxoplasma gondii</i>	EBV: 28-56 days CMV: 28-60 days	Worldwide	Person-person contact (EBV and CMV); ingestion of contaminated	Pharyngitis; cervical lymphadenopathy; atypical lymphocytosis	EBV: heterophile and EBV-specific antibodies	Supportive

	<i>Occasionally other viruses</i>	Toxoplasmosis: 5-23 days		food or exposure to infected cat feces (<i>T. gondii</i>)		CMV and <i>T. gondii</i> : IgM ELISA, PCR	
Rickettsial infections	<i>Orientia</i> and <i>Rickettsia</i> spp.	2-20 days	Widespread, though scrub typhus (<i>Orientia tsutsugamushi</i>) mainly restricted to Asia and Northern Australia; <i>R. africae</i> common in southern Africa	Arthropod bites – ticks (e.g. <i>R. africae</i> and <i>R. conorii</i>), mites (<i>O. tsutsugamushi</i>) and fleas (<i>R. typhi</i>)	Rash; eschar (except murine typhus); thrombocytopenia; lymphadenopathy (especially scrub typhus). Severe disease: meningoencephalitis, pulmonary infiltrates	Serology, PCR	Doxycycline; second line antibiotics include azithromycin and chloramphenicol depending on species
Leptospirosis	<i>Leptospira</i> spp.	2-29 days	Widespread, particularly South and Southeast Asia and South America	Contact with urine from infected animals (rodents; many domestic and wild animals)	Conjunctival suffusion/subconjunctival hemorrhage; jaundice; renal impairment; coagulation disorders; pulmonary hemorrhage	IgM and IgG ELISA; PCR	Mild: doxycycline or azithromycin Severe: parenteral penicillin, doxycycline or 3 rd generation cephalosporin
Enteric fever	<i>Salmonella</i> Typhi and <i>S. Paratyphi</i> A and C	6-30 days	South and Southeast Asia	Fecal-oral transmission	Hepatosplenomegaly; relative bradycardia; lymphopenia; raised blood transaminases	Bacterial culture	Antimicrobial therapy (multidrug resistance common)
Chikungunya	Chikungunya virus (alphavirus)	1-12 days	Extensive distribution in the tropics and sub-tropics	<i>Aedes</i> mosquitoes	Myalgia; rash; thrombocytopenia	RT-PCR, IgM ELISA	Supportive
Zika	Zika virus (flavivirus)	3-12 days	South and Central America, Caribbean, Sub-	<i>Aedes</i> mosquitoes	Myalgia; rash; thrombocytopenia	RT-PCR on urine or serum /	Supportive

			Saharan Africa, South and Southeast Asia and Oceania			plasma, IgM ELISA*	
Schistosomiasis, acute (Katayama syndrome)	<i>Schistosoma haematobium</i> , <i>S. mansoni</i> , <i>S. intercalatum</i> , and <i>S. mekongi</i> ; <i>S. japonicum</i>	14-100 days (after primary exposure)	Africa, South and Southeast Asia, China	Freshwater exposure	Urticarial rash; cough; blood eosinophilia	Serology; generally positive before eggs are detectable in stool	Corticosteroids for Katayama fever, then praziquantel once acute symptoms have subsided
Acute HIV infection	Human immunodeficiency virus	5-70 days	Widespread, highest prevalence in Sub-Saharan Africa	Sexual contact, IVDA, blood transfusions	Rash; lymphadenopathy; lymphopenia	Combined HIV ab/p24 ag testing, plus HIV RNA	Anti-retroviral treatment
Amebic liver abscess	<i>Entamoeba histolytica</i>	Weeks to months	Sub-Saharan Africa, South and Central America, Asia	Fecal-oral transmission	Right upper quadrant pain; elevated blood alkaline phosphatase	Imaging; Serology; Abscess aspiration (microscopy, PCR)	Metronidazole or tinidazole, followed by paromomycin (or diloxanide furoate) to clear intraluminal cysts
Brucellosis	<i>Brucella</i> spp.	2-3 weeks	North Africa, Middle East	Unpasteurized dairy products, undercooked meat	Acute: arthralgia, myalgia; leucopenia and anemia. Chronic: hepatitis; arthritis; osteomyelitis; sacroiliitis	Serum agglutination test; Extended blood culture	Prolonged treatment with doxycycline + aminoglycoside, or doxycycline + rifampicin. Three drugs for complicated disease

Melioidosis	<i>Burkholderia pseudomallei</i>	Weeks or months	South and Southeast Asia, Northern Australia. Isolated reports from Africa and South America	Contact with contaminated soil or surface water	Cough; pneumonia; cutaneous and deep (e.g. lung / liver / spleen) abscesses; septic arthritis; severe sepsis with multi-organ failure. Parotid abscess in children	Bacterial culture	Ceftazidime or a carbapenem, followed by prolonged oral therapy with cotrimoxazole
Q fever	<i>Coxiella burnetii</i>	10-50 days	Widespread	Aerosol inhalation of contaminated animal waste; ticks	Myalgia; cough; hepatitis; meningitis; endocarditis; thrombocytopenia	Serology (IFA), PCR	Doxycycline. Alternatives include clarithromycin, azithromycin, and cotrimoxazole
Filarial fever	<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i> , and <i>B. timori</i> .	Months to years	Sub-Saharan Africa, South and Southeast Asia, Pacific Islands, Some areas of South America and Caribbean	Multiple species of mosquito	Rash; skin papules and nodules; blood eosinophilia	FBC for eosinophilia. Circulating filarial antigen assay, nocturnal blood smear examination, serology	Diethylcarbamazine (DEC); ivermectin + albendazole; doxycycline (kills <i>Wolbachia</i> symbiont)
South American Bartonellosis (Oroya Fever or Carrion's disease)	<i>Bartonella bacilliformis</i> , <i>B. rochalimae</i> and <i>B. ancashensis</i>	10-100 days	South America, particularly Peru	Phlebotomine sand flies	Hepatosplenomegaly; hemolytic anemia	Bacterial culture	Ciprofloxacin + ceftriaxone; chloramphenicol
East African sleeping sickness	<i>Trypanosoma brucei rhodesiense</i>	7-21 days	East and southern Africa	Tsetse fly	Chancre; arthralgia; lymphadenopathy; anemia; sleep cycle dysfunction; coma	Microscopy	Suramin (early stage); nifurtimox, or melarsoprol (late stage). Eflornithine +

							nifurtimox may be efficacious but clinical trial data absent
West African sleeping sickness	<i>Trypanosoma brucei gambiense</i>	Weeks to months	West and Central Africa	Tsetse fly	Indolent presentation; slowly progressive cognitive impairment; coma	Microscopy	Pentamidine (early stage); Eflornithine + nifurtimox (late stage)
Tick-borne relapsing fever	Various <i>Borrelia</i> species	3-18 days	Africa, Asia, Middle East, Southern Europe, Western US and Canada	<i>Ornithodoros</i> ticks	Myalgia; arthralgia; confusion; thrombocytopenia	Blood smear microscopy, multiplex RT-PCR	Doxycycline or ceftriaxone
Louse-borne relapsing fever	<i>Borrelia recurrentis</i>	2-15 days	Ethiopia, Eritrea and Sudan	Body louse (<i>Pediculus humanus</i>)	Chills; headache; myalgia; arthralgia; nausea; thrombocytopenia; elevated blood transaminases	Blood smear microscopy, IgM and IgG ELISA; PCR	Doxycycline. Jarisch-Herxheimer reactions common
Sandfly fever	Various Phleboviruses	3-5 days	South Asia, North and Central Africa, Southern Europe	Phlebotomine sand flies	Myalgia; abdominal pain; headache	RT-PCR, virus isolation	Usually self-limiting. Fever only lasts 3-5 days. Ribavirin
Japanese encephalitis virus infection	Japanese encephalitis virus	5-15 days	Asia, Western Pacific	<i>Culex</i> mosquitos	Confusion; coma; seizures; movement disorders; flaccid paralysis	IgM ELISA on CSF (preferred) or serum	Supportive
Rift Valley Fever	<i>See Table 1</i>						
Fever with rash							
Dengue	<i>See under 'Systemic febrile illness' above</i>						

Rickettsial infections	<i>See under 'Systemic febrile illness' above</i>						
Chikungunya	<i>See under 'Systemic febrile illness' above</i>						
Zika	<i>See under 'Systemic febrile illness' above</i>						
Enteric fever	<i>See under 'Systemic febrile illness' above</i>						
HIV seroconversion illness	<i>See under 'Systemic febrile illness' above</i>						
Acute schistosomiasis	<i>See under 'Systemic febrile illness' above</i>						
Meningococcal sepsis (with or without meningitis)	<i>Neisseria meningitidis</i>	2-10 days	Worldwide; meningitis belt of sub-Saharan Africa (from Senegal in the west to Ethiopia in the east) has highest rates of the disease.	Person-person contact	Non-blanching purpuric rash; neck stiffness; confusion and coma; disseminated intravascular coagulation	Blood and CSF culture; agglutination tests or PCR	3 rd generation cephalosporin
Disseminated gonococcal disease	<i>Neisseria gonorrhoeae</i>	2-30 days	Worldwide	Sexual transmission	Rash; arthritis; tenosynovitis	Blood cultures, synovial fluid microscopy and culture; urethral (men) and cervical (women) swab culture	Ceftriaxone, plus azithromycin or doxycycline

Syphilis	<i>Treponema pallidum</i>	3-90 days	Worldwide	Sexual transmission	Primary: painless genital chancre Secondary: rash; meningitis; alopecia; hepatitis	Serology, PCR on lesion swabs	Intramuscular penicillin G; doxycycline, ceftriaxone
Fever with diarrhea							
Classic 'traveler's diarrhea'	Enterotoxigenic Escherichia coli infection (ETEC)	Within 10 days of return	Widespread	Fecal-oral transmission	Watery diarrhea; abdominal cramps	Stool culture (usually unnecessary)	Hydration. Usually self-limiting, but antibiotics (fluoroquinolones or azithromycin) may reduce duration of symptoms
Giardiasis	<i>Giardia lamblia</i>	7-14 days	Widespread	Fecal-oral transmission	Diarrhea; abdominal bloating and cramps	Stool microscopy, antigen detection, PCR	Metronidazole, tinidazole, or nitazoxanide
Non-typhoidal Salmonellosis	Multiple serotypes of <i>Salmonella enterica</i>	6-72 hours	Widespread	Fecal-oral transmission	Watery diarrhea; abdominal cramps	Blood culture, stool culture	Fluid replacement; Fluoroquinolone or azithromycin
<i>Campylobacter</i> infection	<i>Campylobacter jejuni</i> and <i>C. coli</i>	1-7 days	Widespread	Fecal-oral transmission	Bloody diarrhea	Stool culture	Fluoroquinolone, azithromycin
Shigellosis	<i>Shigella flexneri</i> , <i>S. sonnei</i> , <i>S. dysenteriae</i> , <i>S. boydii</i>	1-7 days	Widespread	Fecal-oral transmission	Bloody diarrhea	Stool culture, PCR	Ciprofloxacin, azithromycin, ceftriaxone. Drug resistance an

							increasing problem
Cryptosporidiosis	<i>Cryptosporidium spp.</i>	3-28 days	Widespread	Fecal-oral transmission	Voluminous watery diarrhea	Stool microscopy, PCR, EIA	Usually self-limiting. Nitazoxanide if persistent symptoms or HIV positive
Intestinal amebiasis	<i>Entamoeba histolytica</i>	1-3 weeks	Widespread	Fecal-oral transmission	Bloody diarrhea	Stool microscopy, antigen testing, PCR. Serology	Metronidazole, tinidazole, or nitazoxanide, followed by paromomycin
Strongyloidiasis	<i>Strongyloides stercoralis</i>	Weeks to decades	Endemic in most tropical and sub-tropical regions	Fecal-oral transmission	Abdominal pain; diarrhea; cough; rash (larva currens); eosinophilia	Stool examination and PCR, duodenojejunal fluid sampling (string test), Serology, Endoscopy	Ivermectin, or albendazole
Fever with respiratory symptoms							
Upper respiratory tract infections	Wide range of respiratory viruses	1-3 days	Worldwide	Contact with contaminated surfaces, aerosols	Sore throat; coryza; dry cough	Clinical diagnosis	Supportive
Bacterial pneumonia	Typical (<i>Streptococcus pneumoniae</i> , <i>Haemophilus</i>)	Variable: 1-3 days (e.g. <i>S. pneumoniae</i>); 2-10 days	Worldwide	Aerosol inhalation, micro aspiration	Shortness of breath; pleuritic chest pain; cough; bloody purulent sputum;	Chest radiography, Legionella urinary	Beta-lactam antibiotic (e.g. ceftriaxone) plus a macrolide

	<i>influenzae</i> , <i>Staphylococcus aureus</i> , etc.) and atypical (<i>Legionella</i> spp, <i>Mycoplasma pneumoniae</i> , <i>Chlamydomphila pneumoniae</i> , and <i>C. psittaci</i>)	for <i>Legionella</i> spp; 7-21 days for <i>Chlamydomphila</i> spp; 1-4 weeks (<i>Mycoplasma pneumoniae</i>)		of upper respiratory flora	variable findings on chest radiography, including reticulonodular shadowing and consolidation	antigen testing, Nasopharyngeal swab multiplex PCR. Blood culture	antibiotic (e.g. clarithromycin)
Influenza	Influenza A, B and C viruses	1-4 days	Worldwide. Tropical transmission may not be seasonal	Exposure to virus in aerosols or on surfaces, or through direct contact with infected individuals	Sore throat; myalgia; arthralgia; dry cough; diarrhea and abdominal pain (children)	RT-PCR	Oseltamivir, Peramivir, or Zanamivir
Tuberculosis	<i>Mycobacterium tuberculosis</i>	Months	Widespread	Human to human respiratory transmission	Prolonged cough; bloody sputum; weight loss; lymphadenopathy; chest X-ray findings	Sputum microscopy and culture	Antituberculosis combination therapy
Viral pneumonia	Respiratory viruses including influenza, parainfluenza, RSV, Hantavirus, adenovirus, coronaviruses (including MERSCoV – see Tables 1 and 3)	2-14 days	Widespread, often seasonal.	Exposure to virus in aerosols or on surfaces, or through direct contact with infected individuals	Dry cough; wheeze; headache; myalgia	Chest radiography. Nasopharyngeal swab multiplex PCR.	Supportive. Oseltamivir, Peramivir, or Zanamivir for influenza
Q fever	<i>See under 'Systemic febrile illness' above</i>						

Fungal pneumonia	Fungal pathogens including <i>Histoplasma capsulatum</i> and <i>Coccidioides</i> spp.	Histoplasmosis 3-17 days Coccidioides 6 to 28 days	Histoplasmosis and coccidioidomycosis endemic in parts of US and Central and South America	Inhalation	Dry cough; myalgia; headache	Respiratory culture, PCR. Cytology and Ag testing for <i>Histoplasma</i>	Antifungal therapy
Strongyloidiasis	<i>See 'fever with rash' above</i>						
Filarial tropical pulmonary eosinophilia	<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i> , and <i>B. timori</i> .	Months to years	Sub-Saharan Africa, South and Southeast Asia, Pacific Islands, Some areas of South America and Caribbean	Multiple species of mosquito	Dry cough; wheeze; splenomegaly; blood eosinophilia	Chest radiograph. FBC for eosinophilia. Very raised IgE; confirmatory serology	Diethylcarbamazine (DEC); corticosteroids if strongyloidiasis excluded
Pneumonic plague	<i>Yersinia pestis</i>	1-3 days if transmitted by inhalation. 2-6 days if secondary to septicemic or bubonic plague	Remote areas of Africa, Asia and South America	Inhalation of infective droplets (primary), or rodent fleas (secondary)	Initial flu-like symptoms, followed by rapidly developing pneumonia. Shortness of breath; cough; chest pain; cough; bloody or watery sputum	Chest radiography. Sputum and blood culture	Aminoglycoside (streptomycin or gentamicin); doxycycline (second line)
<i>Fever with jaundice</i>							
Hepatitis A	Hepatitis A virus (<i>Hepatovirus A</i>)	14-45 days	Worldwide	Fecal-oral transmission	Fatigue; appetite loss; high blood transaminases	IgM RIA, EIA or ELISA	Supportive
Hepatitis E	Hepatitis E virus (<i>Orthohepavirus A</i>)	21-56 days	Africa, Asia and Central America	Fecal-oral transmission	Fatigue; appetite loss; high blood transaminases	IgM ELISA	Supportive

Leptospirosis	<i>See under 'Systemic febrile illness' above</i>						
Malaria	<i>See under 'Systemic febrile illness' above</i>						
Yellow fever	Yellow fever virus	3-8 days	South America, Africa	<i>Aedes</i> mosquitos; <i>Haemagogus</i> and <i>Sabethes</i> mosquitos in the jungle cycle	Headache; chills; myalgia; vomiting; bleeding; high blood transaminases	RT-PCR, IgM ELISA	Supportive
Viral hemorrhagic fevers	<i>(See Tables 1 and 3)</i>			Contact with infected individual or animal	Myalgia; headache; diarrhea; vomiting; petechial rash; bleeding; edema; hypotension. Lymphopenia; thrombocytopenia; raised hepatic transaminases; clotting disorders	RT-PCR	Supportive
<i>Fever with hepato- and / or splenomegaly</i>							
Malaria	<i>See under 'Systemic febrile illness' above</i>						
Amebic liver abscess	<i>See under 'Systemic febrile illness' above</i>						
Leptospirosis	<i>See under 'Systemic febrile illness' above</i>						
Brucellosis	<i>See under 'Systemic febrile illness' above</i>						
Melioidosis	<i>See under 'Systemic febrile illness' above</i>						
Q fever	<i>See under 'Systemic febrile illness' above</i>						

Visceral leishmaniasis	<i>Leishmania donovani</i>	3-10 months	South Asia, Horn of Africa, Mediterranean, Middle East, South America	<i>Phlebotomus</i> and <i>Lutzomyia</i> spp. sandflies	Weight loss; pancytopenia; splenomegaly; hepatomegaly	Serology (IFA, rK38 ELISA); KAtex test (urine) Histopathology, PCR and culture (Bone marrow aspirate or other tissue)	Liposomal amphotericin (first line); miltefosine, paromomycin
East African sleeping sickness	<i>See under 'Systemic febrile illness' above</i>						
<i>Fever with soft tissue infections / skin lesions</i>							
Impetigo, cutaneous abscess and cellulitis	<i>Staphylococcus aureus</i> ; Group A <i>Streptococcus</i>		Worldwide	Infected insect bites, toe-web intertrigo, wounds	Painful, red, hot lesions; pus	Pus/lesion swab culture	Antibiotic treatment. Drug resistance in <i>S. aureus</i> increasingly common in Asia, Africa and South America
Pyomyositis	Usually <i>S. aureus</i> (90% of tropical cases)		Widespread. Increased incidence in Asia and Africa	Hematogenous spread. Usually previous (often minor) injury to muscle.	Painful, red, hot lesions; pus	Pus culture	Operative drainage. Antibiotic therapy

<i>Fever with genito urinary symptoms and Sexually transmitted infections causing fever</i>							
Bacterial urinary tract infections	Cosmopolitan pathogens including <i>E. coli</i> , <i>Proteus mirabilis</i> , <i>Klebsiella pneumoniae</i> and <i>Staphylococcus saprophyticus</i>			Urinary tract infection by fecal flora. Sexual activity increases risk	Dysuria; frequency; blood in urine; abdominal pain	Urinalysis (microscopy or dipstick) and urine culture	Determined by local drug susceptibilities. ESBL-carrying Enterobacteriaceae common in South and Southeast Asia, Middle East and Africa
Primary genital herpes infection	Herpes simplex virus 1 and 2	2-12 days	Worldwide	Sexual transmission	Painful vesicular genital lesions	Serology,	Antiviral therapy with acyclovir, famciclovir or valacyclovir
HIV seroconversion illness	<i>See under 'Systemic febrile illness' above</i>						
Syphilis	<i>See under 'fever with rash' above</i>						
Disseminated gonococcal disease	<i>See under 'fever with rash' above</i>						
Hepatitis A	<i>See under 'Fever with jaundice' above</i>						

*Because of extensive cross-reactivity in Flavivirus serological assays, confirmation with plaque-reduction neutralization tests is recommended though may still not be definitive. Molecular detection methods should be used for infections <7 days post symptom onset

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