


**TABLE 88-6 COMMON CLINICAL FINDINGS AND ASSOCIATED INFECTIONS**

| CLINICAL FINDINGS   | INFECTIONS TO CONSIDER AFTER TROPICAL TRAVEL  |
|---|---|
| Fever and rash  | Dengue, chikungunya, rickettsial infections, enteric fever (skin lesions may be sparse or absent), acute HIV infection, measles, acute schistosomiasis                          |
| Fever and abdominal pain  | Enteric fever, amebic liver abscess   |
| Undifferentiated fever and normal or low white blood cell count | Dengue, malaria, rickettsial infection, enteric fever, chikungunya  |
| Fever and hemorrhage  | Viral hemorrhagic fevers (dengue and others), meningococemia, leptospirosis, rickettsial infections   |
| Fever and eosinophilia  | Acute schistosomiasis; drug hypersensitivity reaction; fascioliasis and other parasitic infections (rare)   |
| Fever and pulmonary infiltrates                                 | Common bacterial and viral pathogens; legionellosis, acute schistosomiasis, Q fever, melioidosis  |
| Fever and altered mental status                                 | Cerebral malaria, viral or bacterial meningoencephalitis, African trypanosomiasis   |
| Mononucleosis syndrome  | Epstein-Barr virus, cytomegalovirus, toxoplasmosis, acute HIV infection   |
| Fever persisting >2 weeks                                       | Malaria, enteric fever, Epstein-Barr virus, cytomegalovirus, toxoplasmosis, acute HIV, acute schistosomiasis, brucellosis, tuberculosis, Q fever, visceral leishmaniasis (rare) |
| Fever with onset >6 wk after travel                             | Vivax malaria, acute hepatitis (B, C, or E), tuberculosis, amebic liver abscess   |

Modified from Centers for Disease Control and Prevention: CDC health information for international travel 2012, New York, 2012, Oxford University Press.  
HIV, Human immunodeficiency virus.

categorized as classic FUO, health care–associated FUO, neutropenic (immune-deficient) FUO, and HIV-related FUO. Each of these FUO subtypes can have unique causes.

### Classic Fever of Unknown Origin

The most common causes of classic FUO are infections, malignancies, and noninfectious inflammatory disorders; miscellaneous causes and undiagnosed cases account for the remaining categories. Historically, infections have made up the largest category, representing 25% to 50% of cases. Abscesses, endocarditis, tuberculosis, complicated urinary tract infections, and biliary tract diseases have consistently been among the most important. Abscesses account for almost one third of infectious causes, and most are intra-abdominal or pelvic in origin. Perforation of a colonic diverticulum or appendicitis can sometimes lead to large, walled-off abdominal abscesses with few localizing signs.

During the past 50 years, the improvement of imaging studies and their greater accessibility have made abdominal or pelvic abscesses and malignancies more easily detected and less likely to be the cause of prolonged, undiagnosed fever. Malignant neoplasms can induce fever directly through the production and release of pyrogenic cytokines and indirectly by undergoing spontaneous or induced necrosis or creating conditions conducive to secondary infections. Endovascular infections are usually detectable by blood cultures, although slow-growing or fastidious organisms may make detection difficult.

**TABLE 88-7 COMMON CAUSES OF FEVER OF UNKNOWN ORIGIN**

| INFECTIONS   |
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| Abscesses  |
| Brucellosis  |
| Catheter infections  |
| Cytomegalovirus  |
| Coccidioidomycosis   |
| Histoplasmosis   |
| Human immunodeficiency virus (HIV) infection               |
| Infective endocarditis                                     |
| Intra-abdominal, subdiaphragmatic, and pelvic disease      |
| Liver and biliary tract disease                            |
| Lyme disease   |
| <i>Mycobacterium tuberculosis</i>                          |
| Osteomyelitis  |
| Sinusitis  |
| Toxoplasmosis  |
| Urinary tract infection                                    |
| AUTOIMMUNE CONDITIONS                                      |
| Adult Still's disease                                      |
| Familial Mediterranean sarcoidosis                         |
| Rheumatoid arthritis                                       |
| Systemic lupus erythematosus                               |
| Temporal arteritis   |
| MALIGNANCY   |
| Hepatocellular carcinoma                                   |
| Leukemia   |
| Metastatic cancers   |
| Pancreatic cancer  |
| Renal cell carcinoma                                       |
| MISCELLANEOUS CAUSES                                       |
| Deep vein thrombosis, pulmonary embolism                   |
| Hyperthyroidism  |
| Kikuchi's disease  |
| Periodic fever (tumor necrosis factor receptor associated) |

Infections, including tuberculosis, typhoid fever, malaria, and amebic liver abscesses, remain the most frequent causes of FUO in developing countries. The incidence of some FUOs vary in incidence according to geographic location. Classic FUO may occur as familial Mediterranean fever among Ashkenazi Jews; in Kikuchi's disease, which is an unusual form of necrotizing lymphadenitis seen primarily in Japan; and as TNF receptor–associated periodic fever (TRAPS), formerly called familial Hibernian fever, which is an inherited periodic fever syndrome described originally in Ireland.

The proportion of FUOs due to noninfectious inflammatory diseases and undiagnosed conditions has risen. Of the connective tissue diseases, juvenile rheumatoid arthritis (i.e., Still's disease), other variants of rheumatoid arthritis, and systemic lupus erythematosus predominate among younger patients. Temporal arteritis and polymyalgia rheumatica syndromes are more common among elderly patients.

Fever may be blunted or absent in up to one third of elderly individuals with serious conditions. Older people may more often have atypical clinical presentations of common infectious and noninfectious diseases. For example, elderly persons may have tuberculosis without cough or fever, infective endocarditis with fatigue and weight loss but without fever, abdominal abscesses with little abdominal tenderness found on physical examination. Leukocytosis and increased band forms are more