

TABLE 26-2 ALL REPORTED CAUSES OF FUO^a

Infections	
Bacterial, nonspecific	Abdominal abscess, adnexitis, apical granuloma, appendicitis, cholangitis, cholecystitis, diverticulitis, endocarditis, endometritis, epidural abscess, infected vascular catheter, infected joint prosthesis, infected vascular prosthesis, infectious arthritis, infective myonecrosis, intracranial abscess, liver abscess, lung abscess, malakoplakia, mastoiditis, mediastinitis, mycotic aneurysm, osteomyelitis, pelvic inflammatory disease, prostatitis, pyelonephritis, pylephlebitis, renal abscess, septic phlebitis, sinusitis, spondylodiscitis, xanthogranulomatous urinary tract infection
Bacterial, specific	Actinomycosis, atypical mycobacterial infection, bartonellosis, brucellosis, <i>Campylobacter</i> infection, <i>Chlamydia pneumoniae</i> infection, chronic meningococcemia, ehrlichiosis, gonococcemia, legionellosis, leptospirosis, listeriosis, louse-borne relapsing fever (<i>Borrelia recurrentis</i>), Lyme disease, melioidosis (<i>Pseudomonas pseudomallei</i>), <i>Mycoplasma</i> infection, nocardiosis, psittacosis, Q fever (<i>Coxiella burnetii</i>), rickettsiosis, <i>Spirillum minor</i> infection, <i>Streptobacillus moniliformis</i> infection, syphilis, tick-borne relapsing fever (<i>Borrelia duttonii</i>), tuberculosis, tularemia, typhoid fever and other salmonellosis, Whipple's disease (<i>Tropheryma whipplei</i>), yersiniosis
Fungal	Aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, <i>Malassezia furfur</i> infection, paracoccidioidomycosis, <i>Pneumocystis jirovecii</i> pneumonia, sporotrichosis, zygomycosis
Parasitic	Amebiasis, babesiosis, echinococcosis, fascioliasis, malaria, schistosomiasis, strongyloidiasis, toxocarosis, toxoplasmosis, trichinellosis, trypanosomiasis, visceral leishmaniasis
Viral	Colorado tick fever, coxsackievirus infection, cytomegalovirus infection, dengue, Epstein-Barr virus infection, hantavirus infection, hepatitis (A, B, C, D, E), herpes simplex, HIV infection, human herpesvirus 6 infection, parvovirus infection, West Nile virus infection
Noninfectious Inflammatory Diseases	
Systemic rheumatic and autoimmune diseases	Ankylosing spondylitis, antiphospholipid syndrome, autoimmune hemolytic anemia, autoimmune hepatitis, Behçet's disease, cryoglobulinemia, dermatomyositis, Felty syndrome, gout, mixed connective-tissue disease, polymyositis, pseudogout, reactive arthritis, relapsing polychondritis, rheumatic fever, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus, Vogt-Koyanagi-Harada syndrome
Vasculitis	Allergic vasculitis, Churg-Strauss syndrome, giant cell vasculitis/polymyalgia rheumatica, granulomatosis with polyangiitis, hypersensitivity vasculitis, Kawasaki's disease, polyarteritis nodosa, Takayasu arteritis, urticarial vasculitis
Granulomatous diseases	Idiopathic granulomatous hepatitis, sarcoidosis
Autoinflammatory syndromes	Adult-onset Still's disease, Blau syndrome, CAPS ^b (cryopyrin-associated periodic syndromes), Crohn's disease, DIRA (deficiency of the interleukin 1 receptor antagonist), familial Mediterranean fever, hemophagocytic syndrome, hyper-IgD syndrome (HIDS, also known as mevalonate kinase deficiency), juvenile idiopathic arthritis, PAPA syndrome (pyogenic sterile arthritis, pyoderma gangrenosum, and acne), PFAPA syndrome (periodic fever, aphthous stomatitis, pharyngitis, adenitis), recurrent idiopathic pericarditis, SAPHO (synovitis, acne, pustulosis, hyperostosis, osteomyelitis), Schnitzler's syndrome, TRAPS (tumor necrosis factor receptor-associated periodic syndrome)
Neoplasms	
Hematologic malignancies	Amyloidosis, angioimmunoblastic lymphoma, Castleman's disease, Hodgkin's disease, hypereosinophilic syndrome, leukemia, lymphomatoid granulomatosis, malignant histiocytosis, multiple myeloma, myelodysplastic syndrome, myelofibrosis, non-Hodgkin's lymphoma, plasmacytoma, systemic mastocytosis, vaso-occlusive crisis in sickle cell disease
Solid tumors	Most solid tumors and metastases can cause fever. Those most commonly causing FUO are breast, colon, hepatocellular, lung, pancreatic, and renal cell carcinomas.
Benign tumors	Angiomyolipoma, cavernous hemangioma of the liver, craniopharyngioma, necrosis of dermoid tumor in Gardner's syndrome
Miscellaneous	
	ADEM (acute disseminated encephalomyelitis), adrenal insufficiency, aneurysms, anomalous thoracic duct, aortic dissection, aortic-enteral fistula, aseptic meningitis (Mollaret's syndrome), atrial myxoma, brewer's yeast ingestion, Caroli disease, cholesterol emboli, cirrhosis, complex partial status epilepticus, cyclic neutropenia, drug fever, Erdheim-Chester disease, extrinsic allergic alveolitis, Fabry's disease, factitious disease, fire-eater's lung, fraudulent fever, Gaucher's disease, Hamman-Rich syndrome (acute interstitial pneumonia), Hashimoto's encephalopathy, hematoma, hypersensitivity pneumonitis, hypertriglyceridemia, hypothalamic hypopituitarism, idiopathic normal-pressure hydrocephalus, inflammatory pseudotumor, Kikuchi's disease, linear IgA dermatosis, mesenteric fibromatosis, metal fume fever, milk protein allergy, myotonic dystrophy, nonbacterial osteitis, organic dust toxic syndrome, panniculitis, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes), polymer fume fever, post-cardiac injury syndrome, primary biliary cirrhosis, primary hyperparathyroidism, pulmonary embolism, pyoderma gangrenosum, retroperitoneal fibrosis, Rosai-Dorfman disease, sclerosing mesenteritis, silicone embolization, subacute thyroiditis (de Quervain's), Sweet syndrome (acute febrile neutrophilic dermatosis), thrombosis, tubulointerstitial nephritis and uveitis syndrome (TINU), ulcerative colitis
Thermoregulatory Disorders	
Central	Brain tumor, cerebrovascular accident, encephalitis, hypothalamic dysfunction
Peripheral	Anhidrotic ectodermal dysplasia, exercise-induced hyperthermia, hyperthyroidism, pheochromocytoma

^aThis table includes all causes of FUO that have been described in the literature. ^bCAPS includes chronic infantile neurologic cutaneous and articular syndrome (CINCA, also known as neonatal-onset multisystem inflammatory disease, or NOMID), familial cold autoinflammatory syndrome (FCAS), and Muckle-Wells syndrome.

can be nonspecific. Serologic testing for Q fever, which results from exposure to animals or animal products, should be performed when the patient lives in a rural area or has a history of heart valve disease, an aortic aneurysm, or a vascular prosthesis. In patients with unexplained symptoms localized to the central nervous system (CNS), gastrointestinal tract, or joints, polymerase chain reaction (PCR) testing for *Tropheryma whipplei* should be performed. Travel to or (former) residence in tropical countries or the American Southwest should lead

to consideration of infectious diseases such as malaria, leishmaniasis, histoplasmosis, or coccidioidomycosis. Fever with signs of endocarditis and negative blood culture results poses a special problem. Culture-negative endocarditis may be due to difficult-to-culture bacteria such as nutritionally variant bacteria, HACEK organisms (*Haemophilus parainfluenzae*, *H. paraphrophilus*, *Aggregatibacter* species [*actinomycetemcomitans*, *aphrophilus*], *Cardiobacterium* species [*hominis*, *valvarum*], *Eikenella corrodens*, and *Kingella kingae*; discussed below),