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ANDREW B. SYMONS



Differential Diagnosis **OF** Common Complaints

SEVENTH EDITION

ELSEVIER

Differential Diagnosis of Common Complaints

SEVENTH EDITION

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Table of Contents

Cover image

Title page

Copyright

Dedication

Preface

Acknowledgments

1: Abdominal Pain in Adults

Nature of patient

Nature of pain

Location of pain

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

2: Abdominal Pain in Children

Nature of patient

Nature of pain

Location of pain

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

3: Backache

Nature of patient

Nature of symptoms and location of pain

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

4: Belching, Bloating, and Flatulence

Belching

Bloating and flatulence

5: Breast Lumps

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

6: Chest Pain

Nature of patient

Nature of pain

Associated symptoms

Precipitating and aggravating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

7: Colds, Flu, and Stuffy Nose

Nature of patient

Nature of symptoms and associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

8: Constipation

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

9: Cough

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

10: Diarrhea

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

Chronic diarrhea in children

11: Dizziness/Lightheadedness and Vertigo

True vertigo

Lightheadedness/Dizziness and Giddiness

12: Earache

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings and diagnostic studies

Less common diagnostic considerations

13: Facial Pain

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

14: Fatigue

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and exacerbating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

15: Fever

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

16: Forgetfulness

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

17: Headache

Nature of patient
Nature of pain
Headache patterns
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

18: Heartburn, Indigestion, and Dyspepsia

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

19: Insomnia

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

20: Menstrual Irregularities

Abnormal bleeding

Nature of patient

Nature of symptoms

Amenorrhea

21: Menstrual Pain

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

22: Nausea and/or Vomiting Without Abdominal Pain

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

23: Pain in the Foot

Nature of patient

Nature of symptoms

Precipitating and aggravating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

24: Pain in the Lower Extremity in Adults

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings and diagnostic studies

Less common diagnostic considerations

The leg and sports medicine

25: Pain in the Lower Extremity and Limping in Children

Nature of patient

Nature of symptoms

Associated symptoms

Physical findings

Diagnostic studies

Less common diagnostic considerations

26: Pain in the Upper Extremity

Shoulder

Elbow

Hand and wrist

Diagnostic studies

Less common diagnostic considerations

27: Palpitations

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

28: Shortness of Breath

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors other than medical therapy
Physical findings
Diagnostic studies
Less common diagnostic considerations

29: Skin Problems

Color Plate of Chapter 29

30: Sore Throat

Nature of patient
Nature of symptoms
Associated symptoms
Predisposing factors
Physical findings
Diagnostic studies

Less common diagnostic considerations

31: Swelling of the Legs

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

32: Urethral Discharge and Dysuria

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors

Ameliorating factors

Physical findings

Diagnostic studies

Less common diagnostic considerations

33: Vaginal Discharge and Itching

Nature of patient

Nature of symptoms

Associated symptoms

Precipitating and aggravating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

34: Vision Problems and Other Common Eye Problems

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

35: Voiding Disorders and Incontinence

Nature of patient
Nature of symptoms
Associated symptoms
Precipitating and aggravating factors
Ameliorating factors
Physical findings
Diagnostic studies
Less common diagnostic considerations

36: Weight Gain and Weight Loss

Weight gain

Weight loss

Index

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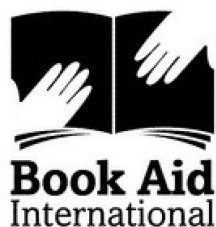
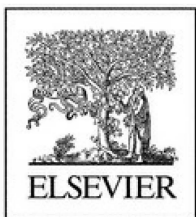
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Dedication



This edition of *Differential Diagnosis of Common Complaints* is dedicated to its senior author, Robert Seller, MD, who passed away in 2015.

Dr. Seller graduated the University of Pennsylvania with an MD degree in 1956. He was on the faculty at Hahnemann Medical College and Hospital from 1960 to 1974. In 1974 he joined the faculty of the State University of New York at Buffalo School of Medicine and Biomedical Sciences, where he chaired the Department of Family Medicine from 1974 to 1982, and remained on faculty until his death in 2015. Bob wrote the first edition of *Differential Diagnosis of Common Complaints* in 1986 while on sabbatical from the University at Buffalo.

On a personal note, Bob was my attending physician when I was both a student and resident at the University at Buffalo.

He instilled in us the importance of a careful physical examination and thoughtful consideration of differential diagnosis based on our findings. As a “new attending physician,” I was honored when Bob asked me to help him write the sixth edition of *Differential Diagnosis of Common Complaints*. I learned volumes just by meeting him weekly in preparation for publishing the book, and I valued his friendship, mentorship, and collegiality. I will forever be indebted to him for teaching me how to be a thoughtful physician and for allowing me to continue to author this important work to which he devoted so much thought, energy, and love.

Andrew B. Symons

Preface

The purpose of the seventh edition of *Differential Diagnosis of Common Complaints* remains the same as the first—to help clinicians accurately and efficiently diagnose common complaints. This book emphasizes a clinical approach to diagnosis rather than one that relies largely on diagnostic studies. Most medical school curricula, texts, and continuing education courses deal with diseases. However, patients usually come to their physicians complaining of headache, backache, or fatigue—not migraine, spinal stenosis, or depression. To address this reality, this book is organized around common presenting complaints—the patients’ symptoms rather than the disease. The 36 symptoms reviewed account for more than 80% of the chief complaints with which physicians are confronted. The clinician who has mastered the differential diagnosis of these symptoms will be able to diagnose accurately almost all the problems seen in a typical medical practice.

Each chapter deals with different common complaints, which are presented alphabetically. The chapters are organized to approximate the problem-solving process that most clinicians use to make a diagnosis. Initially, the presenting symptom suggests several diagnostic possibilities. Then, this diagnostic list is further refined and reduced by additional, more specific, historical findings; by the patient’s physical findings; and then by the results of diagnostic studies. The index lists all complaints, symptoms, and diagnoses noted in the text.

As with prior editions, this seventh edition has been revised to include suggestions by colleagues and students who appreciate the book’s clinical orientation and practical approach to differential diagnosis. Each chapter has been revised to include new information,

with an emphasis on the latest clinical and diagnostic studies. We also have added several clinical algorithms.

The text does not deal extensively with pathophysiology or therapy except in situations in which this information is particularly useful in the diagnostic process. The most useful and up-to-date diagnostic studies for differential diagnosis are reviewed. When available, evidence-based information is included. The text concentrates on the most likely diagnoses and common illnesses that include many serious illnesses. It also notes when the clinician must rule out extremely serious diagnostic possibilities.

The format of each chapter has remained the same:

Introduction

Includes relevant definitions as well as a list of the most common causes of the symptoms.

Nature of patient

Identifies those conditions that are most prevalent within a particular subgroup (e.g., children, the elderly, and premenopausal, diabetic, hypertensive, and immunocompromised individuals).

Nature of symptoms

Further identifies conditions by amplifying additional characteristics of the symptoms (how, when, where, radiation, acute/chronic, and others).

Associated symptoms.

Precipitating and aggravating factors.

Ameliorating factors.

Physical findings.

Diagnostic studies.

Less common diagnostic considerations.

Differential diagnosis table

A concise table located at the end of each chapter summarizes the

salient differential diagnostic features of the most common clinical entities that cause a particular complaint.

Selected references

Most articles represent an approach to the differential diagnosis of problems rather than a review of a specific disease.

Clinicians and students may use this book for general information about the many causes of common chief complaints. They can also use it as a reference text when treating a patient who is complaining of a specific symptom (e.g., facial pain, shortness of breath, fever) when the diagnosis is not apparent.

Differential Diagnosis of Common Complaints was written to be useful. We hope you find it so. Remember the adage: "If you don't think about it, you will never diagnose it."

Robert H. Seller; Andrew B. Symons

Fever

This chapter emphasizes fever as the presenting problem rather than fever of unknown origin (FUO). **Classically, FUO is a temperature greater than 101°F** that occurs on several occasions during a 3-week period in an ambulatory patient or during a 1-week period in a hospitalized patient. However, some experts suggest that the FUOs must persist for only 10–14 days in an outpatient. The cause of the fever should not be apparent, even after a complete history, physical examination, complete blood count (CBC) with differential, urinalysis, comprehensive metabolic profile (CMP), cardiogram, chest radiograph, monospot test, and intermediate-strength purified protein derivative (tuberculin [PPD]) test.

In most febrile patients, a diagnosis becomes evident within a few days. FUO is usually caused by a common disorder that displays atypical manifestations or is a benign, self-limiting illness for which no specific cause is found. Nevertheless, it is still important for the physician to search for occult sources of infection, especially if a response to antibiotics is possible.

Normal oral temperature is 98.6°F (37°C) plus or minus about 1°F. Body temperature shows normal diurnal variation; the lowest point is registered in the early-morning hours, and the highest is reached in the late afternoon. Infrared tympanic thermometry is a new and popular alternative for traditional measurement in the diagnosis of pediatric fever and has been demonstrated to have high accuracy.

Acute fevers are caused most often by *upper respiratory infections* (URIs), *tonsillitis*, *viral syndromes* (e.g., influenza, gastroenteritis), *drug reactions*, and *genitourinary tract infections* (e.g., cystitis, pyelonephritis, prostatitis). Less often, acute fevers accompany meningitis, intra-abdominal abscess, and other forms of sepsis.

Chronic low-grade fevers are caused most often by *hepatitis*, *tuberculosis* (TB), *infectious mononucleosis* (especially in children and

young adults), *lymphomas*, and *occult neoplasms* (especially in elderly patients). If the source of a fever is not apparent based on history, symptoms, or physical examination, the possibility of *drug fever* (particularly from penicillins, cephalosporins, antituberculosis agents, sulfonamides, macrolides, aminoglycosides, methyldopa, procainamide, and phenytoin), *sinusitis*, *dental abscess*, *prostatitis*, *TB*, *infectious mononucleosis* (especially with associated fatigue), and *hepatitis* (both anicteric and icteric) should be considered. Cocaine, ecstasy, and amphetamine abuse may also cause hyperpyrexia.

When recurrent fever occurs at *regular intervals* (21–28 days) in a child, the most likely cause is PFAPA syndrome (**p**eriodic **f**ever, **a**phthous ulcers, **p**haryngitis, and **a**denopathy). When recurrent fever occurs at *irregular intervals* in a child, the most common causes include repeated viral infections; repeated bacterial or occult bacterial infections, especially urinary tract infections (UTIs); and inflammatory bowel disease, especially Crohn's disease.

Less common causes of fever without an apparent cause from presenting symptomatology include neoplasms, abdominal abscess, multiple pulmonary emboli, diverticulitis, subacute bacterial endocarditis, osteomyelitis, and thrombophlebitis.

Nature of patient

The most common cause of fever in children is viral URI. Young children usually have signs or symptoms of a respiratory infection but may show only fever. Other viral causes of fever in children are chickenpox (varicella), “slapped cheek disease” (erythema infectiosum), roseola infantum, papulovesicular acro-located syndrome, and enteroviral infections. Common causes of fever in children who have no localizing signs or symptoms at the time of examination include *URIs, gastroenteritis, tonsillitis, otitis media, UTIs, measles, and roseola*. A true FOU in a child has serious implications. In one study, 41% of children with true FOU were found to have a chronic or fatal disease. Fever in children younger than 3 months may be the only indication of a serious disease. Unexplained fever in adolescents may be a manifestation of *drug abuse* or *endocarditis*. Severe, acute respiratory disease (SARS) seems to occur more frequently in young adults, for whom the average age is 40 years.

A history of UTI, sinusitis, prostatitis, and recurrent pneumonia on the same side increases the likelihood that the current febrile episode may be similar to those in the past.

In the absence of physical signs or symptoms suggesting the cause of fever, the physician should question the patient specifically about occupational history, exposure or contact with animals (e.g., bird flu, Lyme disease), chemicals, drug ingestion, and travel away from the patient’s usual residence (SARS, malaria, typhoid, and rickettsial infections). Fever from unusual infections is more common in immunocompromised patients and in those with human immunodeficiency virus (HIV) infection. In febrile, elderly patients who lack signs or symptoms that suggest a cause, *TB, occult neoplasm, temporal arteritis, and recurrent pulmonary emboli* must be considered. **Febrile response to infections is often diminished or absent in elderly patients.**

In the postoperative patient, fever may be caused by infection, atelectasis, or a reaction to anesthesia or medications.

Nature of symptoms

Contrary to common belief, studies have shown that the fever pattern is not likely to be helpful diagnostically, although the magnitude may help. Temperatures above 105°F (40.5°C) suggest *intracranial pathology, factitious fever, pancreatitis, or UTI*, especially with shaking chills. When severe hyperthermia is associated with muscle rigidity, the following causes should be suspected: ecstasy, cocaine, or other sympathomimetic agents; serotonin syndrome; antipsychotic drugs; drugs with strong anticholinergic properties; and inhalational anesthetics. Other causes are thyrotoxicosis, tetanus, strychnine poisoning, and central nervous system infections. A mild fever suggests *URI or a flulike syndrome*. Low-grade fever (especially when associated with fatigue) may be the initial manifestation of *tuberculosis, infectious mononucleosis, or hepatitis*. The fever range may also be helpful; e.g., a narrow range of fever, without spikes or chills, may be seen in lymphomas such as *Hodgkin's disease, lymphatic leukemia, and hypernephroma*.

A fever in an emotionally disturbed patient who is otherwise in good health and is employed in a health care–related position, has no weight loss, and demonstrates no related or proportional increase in pulse rate should make the physician suspect a factitious cause. Some investigators report that this situation is more likely in female patients. If a factitious cause is suspected, a simultaneous measurement of urine and rectal temperature should be obtained. **The temperature of the urine normally approximates rectal temperature, and a factitious cause should be suspected if the rectal temperature is significantly (usually more than 2.7 °C) higher than the urine temperature.** Other clues to a factitious cause include failure of temperature to follow a diurnal pattern, rapid defervescence without sweating, high temperature without prostration, and high temperature without weight loss or night sweats.

Drug fevers usually occur about 7–10 days after initial administration but reappear rapidly with subsequent administration.

Associated symptoms

The following clues may help the physician differentiate viral from bacterial infections. If the fever is high and there appears to be a sparsity of systemic symptoms (e.g., aches, pains, malaise, backache, and fatigue), with the more specific findings limited to the pharynx, abdomen, or chest, a *bacterial infection* is more likely. However, if a relatively low-grade fever of less than 101.5°F (38.5°C) is associated with systemic complaints (e.g., aches, pains, backache, fatigue, and headache) and the localizing findings are sparse, a *viral infection* is more likely. For example, the combined findings of a temperature of 103°F (39.4°C); a red, sore throat; hoarseness; and possible dysphagia suggest bacterial pharyngitis. A viral cause is more likely if the temperature is less than 101°F (38.3°C); the pharynx is injected and edematous but little evidence of follicular tonsillitis is present; and the patient complains of aches, pains, myalgia, and headache. Influenza syndrome is characterized by a sudden onset of cough and fever, headache, sore throat, myalgia, nasal congestion, weakness, and anorexia.

When a rash is associated with fever, the rash may be a viral exanthem (e.g., rubella, rubeola, or varicella) or a clue to a more serious illness (e.g., Rocky Mountain spotted fever, meningococcemia, thrombocytopenia, Lyme disease, infectious mononucleosis, erythema multiforme, or vasculitis).

Fever (>100.3°F), absence of cough, myalgia, diarrhea, absolute lymphopenia, low platelet counts, and travel to affected areas should suggest SARS.

Shaking chills suggest bacteremia frequently due to *pyelonephritis*. When fatigue is associated with a low-grade fever, *infectious mononucleosis* or *TB* is likely. Persistent fever after a URI, occasionally associated with a frontal headache, should suggest *sinusitis*.

When fever is associated with arthritis or endocarditis, the physician should suspect disseminated gonococcal infection, or *Lyme disease*. If fever is associated with generalized musculoskeletal pain,

the physician must consider rheumatologic or autoimmune disorders.

Precipitating and aggravating factors

Contact with people with URI or influenza or a local endemic increases the likelihood of *URI* or *influenza*. These two conditions are particularly common in the winter and late summer.

In women, a marked increase in sexual activity may precipitate *cystitis* or *urethritis*, sometimes referred to as *honeymoon cystitis*. In men, a sudden decrease in sexual activity, particularly after an increase in sexual relations (e.g., during a vacation), may precipitate *prostatitis*.

The pain of *sinusitis* may be exacerbated by bending forward, coughing, sneezing, or blowing the nose. Medications and over-the-counter drugs may also cause fever.

Physical findings

In addition to conducting a careful, thorough physical examination, the physician should pay special attention to certain areas when evaluating a patient whose chief complaint is fever. For example, *drug fever* should be suspected if the patient looks *inappropriately well* for the severity of the fever. The sinuses can be percussed and transilluminated for evidence of *sinusitis*. The throat should be examined for signs of *bacterial* or *viral infection* as well as the enanthema of *measles* or *infectious mononucleosis*. Carious teeth should be tapped for signs of *periapical abscess*. All lymph nodes should be palpated. Rectal examination may be performed for evidence of a *perirectal abscess* or *prostatitis*.

If an obvious source of fever is not made apparent through the history or physical examination, attention should be focused on sources of fever that initially manifest without any clue other than fever. This is particularly true in children. Because significant physical findings and symptoms other than fever may be absent in young children, the physician may use the following clues to assess the severity of the illness: decreased playfulness, decreased alertness, reduced motor ability, respiratory distress, and dehydration. Fever may be an early manifestation of many illnesses, ranging from *teething* to *roseola*. If the source of the fever in a child is not apparent, a urinalysis should be performed; pyuria and albuminuria may be the only manifestations of a UTI.

In teenagers and young adults, *infectious mononucleosis* should be suspected if the fever is associated with any one or more of the following: pharyngitis (either exudative or nonexudative), enanthema on the soft palate, posterior cervical or generalized adenopathy, hepatosplenomegaly, and exanthema. If these patients are given ampicillin, a rash similar to that seen after administration of penicillin may develop. If this occurs in patients with proven infectious mononucleosis, the likelihood of true penicillin sensitivity is small.

Diagnostic studies

Laboratory tests useful in determining the cause of a fever include CBC with differential. Attention should be given to monocytes and atypical lymphocytes as well as neutrophil counts and absolute lymphopenia. In addition, fever in patients with neutropenia may herald a life-threatening infection. Therefore, prompt recognition of patients with neutropenic fever is imperative. Other studies include thick and thin blood smears for malaria; a monospot test; measurement of erythrocyte sedimentation rate; urinalysis; blood chemistry analysis; antistreptolysin titer; a tuberculin test (PPD skin test); tests for antinuclear antibodies and febrile agglutinins; and cultures of blood, urine, pharynx, and stools. Computed tomography scans; sonograms; technetium Tc99m pertechnetate, gallium, and indium-111 scans; and special radiographic studies may also be helpful in some cases.

The procalcitonin test is very useful in separating bacterial infections from viral and invasive nonbacterial infections. It is particularly helpful in such infections in febrile children (between 1 and 36 months of age) and adults. The use of point-of-care rapid viral diagnosis testing and establishing a viral etiology to a fever may reduce the need for precautionary testing and antibiotic use for children presenting with fever and URI symptoms.

Less common diagnostic considerations

The many uncommon illnesses that cause fever include subacute bacterial endocarditis, acute bacterial endocarditis, bacteremia, meningitis, encephalitis, systemic lupus erythematosus, vasculitis, disseminated fungal infection, severe head injury (neurogenic fever), actinomycosis (including pelvic actinomycosis, which is often related to a retained intrauterine device), systemic calcium pyrophosphate deposition disease (pseudogout), myocarditis, lung abscess, osteomyelitis, encephalitis, neoplasms in any location, retroperitoneal lesions, lymphomas, connective tissue disorders, inflammatory bowel disease, diverticulitis, periodic fever, metal fume fever, factitious fever, malaria, rat-bite fever, and pulmonary emboli ([Table 15.1](#)). Periorbital edema associated with fever may be due to local or systemic infections or anaphylaxis.

Table 15.1

Fever of Unknown Origin: Classic Causes

Type of disorder	Common	Uncommon	Rare
Malignancy/neoplastic disorders	Lymphoma* Hypemephroma/RCC	Preleukemia (AML)* MPDs*	Atrial myxoma Multiple myeloma Colon carcinoma Pancreatic carcinoma Hepatoma CNS metastases Liver metastases Systemic mastocytosis*
Infectious diseases	Miliary TB Brucellosis*† Q fever*	Intra-abdominal/pelvic abscess* Intra/perinephric abscess* Typhoid/enteric fevers*† Toxoplasmosis* CSD* EBV CMV HIV Extrapulmonary TB (renal TB, CNS TB)	SBE* Periapical dental abscess* Chronic sinusitis/mastoiditis Subacute vertebral osteomyelitis Aortoenteric fistula Vascular graft infections* Relapsing fever* (<i>Borrelia recurrentis</i>) Rat bite fever* [†] (<i>Streptobacillus moniliformis</i> or <i>Spirillum minus</i>) Leptospirosis Histoplasmosis Coccidiomycosis Visceral leishmaniasis (kala-azar) LGV Whipple's disease* MCD* Malaria* Babesiosis* Ehrlichiosis/anaplasmosis* Chronic prostatitis Recurrent cholangitis* [†] (with Caroli's disease)
Rheumatologic/inflammatory disorders	Adult Still's disease (juvenile rheumatoid arthritis)* GCA/TA*	PAN/MPA* (LORA) SLE*	Takayasu's arteritis* Kikuchi's disease* Sarcoidosis (CNS) Felty's syndrome Gaucher's disease Polyarticular gout Pseudogout Antiphospholipid syndrome (APS) Behçet's disease* FAPA syndrome* (Marshall's syndrome)
Miscellaneous disorders	Drug fever* Cirrhosis*	Subacute thyroiditis* Regional enteritis* (Crohn's disease)	Pulmonary emboli (small/multiple) Pseudolymphomas* Rosai-Dorfman disease* ECD* Cyclic neutropenia* Familial periodic fever syndromes: FMF* Hyper-IgD syndrome* TNF receptor-1-associated periodic syndrome (TRAPS)* Schnitzler's syndrome* Muckle-Wells syndrome* Hypothalamic dysfunction Hypertriglyceridemia (type V)* Factitious fever*

From Cunha BA, Lortholary O, Cunha CB. Fever of unknown origin: a clinical approach. *Am J Med.* 2015;28(10):1138.e1–1138.e15.

AML, Acute myelogenous leukemia; *CMV*, cytomegalovirus; *CNS*, central nervous system; *CSD*, cat scratch disease; *EBV*, Epstein-Barr virus; *ECD*, Erdheim-Chester disease; *FAPA*, fever, aphthous ulcers, pharyngitis, adenitis; *FMF*, familial Mediterranean fever; *GCA*, giant cell arteritis; *HIV*, human immunodeficiency virus; *LGV*, lymphogranuloma venereum; *LORA*, late-onset rheumatoid arthritis; *MCD*, multicentric Castleman's disease; *MPA*, microscopic polyangiitis; *MPDs*, myeloproliferative disorders; *PAN*, periarteritis nodosa; *RCC*, renal cell carcinoma; *SBE*, subacute bacterial endocarditis; *SLE*, systemic lupus erythematosus; *TA*, temporal arteritis; *TB*, tuberculosis; *TNF*, tumor necrosis factor.

* May present as recurrent fever of unknown origin.

† If bacteremia suspected, obtain blood cultures.

Differential Diagnosis of Fever

Type	Nature of patient	Nature of symptoms	Associated symptoms	Precipitating and aggravating factors	Physical findings	Diagnostic studies
Acute						
URI viral	Any age	Oral temperature usually <101.5°F	Signs of URI Possible systemic symptoms	Contact with people with URI Local epidemic	Cough Oropharynx injected but not beefy red	Procalcitonin
Bacterial	More common in children	Often high fever, >101°F	Marked signs of URI Few systemic symptoms Children restless		Pharyngotonsillar exudate Pulmonary findings	Positive culture or rapid strep screen
Other Viral Syndromes						
Influenza	Any age	Usually mild fever	Muscle aches, cough, headache			Rapid influenza test
Gastroenteritis	Any age		Nausea Vomiting Cramps Diarrhea			
Viral exanthems	Children	Usually mild fever			Enanthem in some instances Rash Adenopathy	
Drug reactions	Taking prescription, recreational, or over-the-counter drug	Often high fever	Occasional rash Muscle rigidity with Ecstasy, cocaine, and methamphetamines		Fever abates when patient stops taking drug	
Urinary tract infection	More common in adults	Often high fever with chills	Backache Urinary frequency and urgency	Obstructive uropathy	Costovertebral angle tenderness	Urinalysis Urine culture
Prostatitis			Dysuria Backache	Marked change in sexual frequency	Prostate tenderness	Culture of prostatic secretions
Bacterial sepsis		Often high fever with chills				Blood culture WBC with differential count
Chronic						
Hepatitis	More common in IV drug users	Usually low-grade fever	Fatigue Jaundice Anorexia		Hepatomegaly Liver tender on percussion Jaundice	Liver function tests Hepatitis antigens
Tuberculosis	More common in diabetics	Usually low-grade fever			Chest findings	Chest radiograph Tuberculin test
Infectious mononucleosis	Teenagers Young adults	Usually low-grade fever	Fatigue		Enanthema Pharyngitis Adenopathy (especially postcervical) Splenomegaly	Monospot test
Neoplasm	Elderly adults	Usually narrow fever range	Weight loss			
Occult infection (sinusitis, dental abscess, prostatitis, fungal infections, diverticulitis, SBE, osteomyelitis, inflammatory bowel disease)		Usually low-grade fever	Depends on cause		Depends on cause	Many, including radionuclide scanning
Drug reaction	Taking prescription, recreational, or over-the-counter drug		Occasional rash		Fever abates when drug discontinued	CBC may show hematologic abnormality
Factitious fever	May be emotionally disturbed Associated with health care	Usually >105°F Can be low-grade fever	No weight loss Pulse rate not proportional to fever	Emotional stress	Disparity between rectal or oral temperature and urine temperature	

CBC, Complete blood count; *SBE*, subacute bacterial endocarditis; *IV*, intravenous; *URI*, upper respiratory infection; *WBC*, white blood cells.

Neuroleptic malignant syndrome (NMS) from antipsychotic medications (e.g., phenothiazines, risperidone, haloperidol) or anesthetic agents may present with fever or even malignant hyperthermia. The fever may begin at the onset of treatment or after

long-term administration. Other associated symptoms of NMS are severe muscle rigidity, tremors, diaphoresis, and elevated creatine kinase levels.

Fever may develop in patients (often of African, Eastern Mediterranean, or Southeast Asian descent) who have a *glucose-6-phosphate dehydrogenase deficiency* who have received sulfonamides, nitrofurantoin, phenacetin, antimalarials, or quinidine.

Cytomegalovirus disease, malignant histiocytosis, juvenile rheumatoid arthritis, Crohn's disease, and cryptic hematoma have been found to cause occult fevers.

Recurrent fevers can be caused by recurrent viral or bacterial infection, UTIs, inflammatory bowel disease, and (in children) PFAPA syndrome.

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