Postoperative fever

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All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: May 2016. | This topic last updated: Jul 08, 2015.

INTRODUCTION — Fever above 38°C (100.4°F) is common in the first few days after major surgery [1,2]. Most early postoperative fever is caused by the inflammatory stimulus of surgery and resolves spontaneously [3–7]. However, postoperative fever can be a manifestation of a serious complication.

A thorough differential diagnosis of postoperative fever includes infectious and noninfectious conditions that occur following surgery. Fever may arise due to a surgical site infection (SSI), or from other hospital-related conditions, including nosocomial pneumonia, urinary tract infection, drug fever, and deep vein thrombosis (table 1). In evaluating a postoperative patient with fever, it is important to consider a broad differential, and not to assume that fever is due to infection.

Fever as a manifestation of infection may be reduced or absent in immunocompromised patients including those receiving glucocorticoids, cancer chemotherapy, post-transplant immunosuppression, and in some patients who are elderly or have chronic renal failure.

The evaluation of fever in immunocompromised patients is discussed elsewhere. (See "Fever and rash in immunocompromised patients without HIV infection" and "Approach to the immunocompromised patient with fever and pulmonary infiltrates" and "Overview of neutropenic fever syndromes" and "Diagnostic approach to the adult presenting with neutropenic fever").

PATHOPHYSIOLOGY OF POSTOPERATIVE FEVER — Fever is a manifestation of cytokine release in response to a variety of stimuli [8–10]. Fever-associated cytokines, including interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-alpha, and interferon (IFN)-gamma, are produced by a variety of tissues and cells (algorithm 1). There is some evidence that IL-6 is the cytokine most closely correlated with postoperative fever [11] (see "Pathophysiology and treatment of fever in adults").

Fever-associated cytokines are released by tissue trauma and do not necessarily signal infection. The magnitude of the trauma is correlated with the degree of the fever response. For example, laparoscopic cholecystectomy is associated with less tissue trauma and fewer episodes of postoperative fever than is open cholecystectomy [12]. Similarly, there is less postoperative fever when coronary artery grafting is performed without the use of a cardiopulmonary bypass pump [13].

Genetic factors may influence the magnitude of the cytokine release in response to tissue trauma, and thus the magnitude of self-limited postoperative fever. For example, children with osteogenesis imperfecta undergoing orthopedic surgery appear to have a greater and more sustained febrile response than matched controls [14].

Bacterial endotoxins and exotoxins can stimulate cytokine release and cause postoperative fever. Bacteria or fragments of bacteria translocated from the colon (eg, as a consequence of perioperative ileus or hypotension) may be responsible for some episodes of self-limited postoperative fever. Elevated levels of bacterial DNA have been demonstrated with polymerase chain reaction (PCR) testing of blood from surgical patients, even in patients whose blood cultures are negative [15].

Non-steroidal anti-inflammatory agents (NSAIDs) and glucocorticoids suppress cytokine release and thereby reduce the magnitude of the febrile response [16,17].

TIMING OF FEVER — The timing of fever after surgery is one of the most important factors to consider in generating a prioritized differential diagnosis of postoperative fever (figure 1). The timing of postoperative fever can be usefully described as:

- Immediate – onset in the operating suite or within hours after surgery
- Acute – onset within the first week after surgery
• Subacute – onset from one to four weeks following surgery
• Delayed – onset more than one month after surgery

**Immediate** — The potential causes of fever in the immediate operative and postoperative period are mainly limited to: medications or blood products to which the patient was exposed during preoperative care either in the operating room or in the recovery area; trauma suffered prior to surgery or as part of surgery; infections that were present prior to surgery; and rarely malignant hyperthermia.

Adverse medication reactions that produce immediate fever include immune-mediated reactions, such as reactions to antimicrobials and to transfused blood products. (See “Drug fever.”) The vasodilation that often accompanies these reactions makes hypotension a common presenting sign; rash may accompany fever in some patients with medication reactions.

The initial clinical signs (ie, hypercarbia) of malignant hyperthermia typically present within 30 minutes following the administration of a triggering agent (eg, inhaled anesthetics, succinylcholine), but have been reported later in the operative course and also following cessation of anesthesia. If the malignant hyperthermia response is not recognized and aborted with dantrolene, high fever may develop as result of hypermetabolism. (See “Malignant hyperthermia: Clinical diagnosis and management of acute crisis”.)

Fever due to the trauma of surgery usually resolves within two to three days. The severity and duration of these self-limited postoperative fevers depends on the type of surgery [18,19], but tends to be greater in patients with longer and more extensive surgical procedures [12]. Fever caused by severe head trauma can be persistent and may resolve gradually over days or even weeks [20].

**Acute** — There are many causes of fever in the first week after surgery. Nosocomial infections are common during this period. Occasionally, fever or other symptoms predate surgery and are manifestations of community-acquired infection, such as a viral upper respiratory tract infection.

While SSI and intravascular catheter infections can cause acute postoperative fever, other infections are more frequently identified, including pneumonia and urinary tract infection (UTI).

• Patients receiving mechanical ventilation during surgery are at risk for ventilator-associated pneumonia (VAP). The risk of VAP increases with the duration of mechanical ventilation [21]. The risk of pneumonia tapers to a stable, lower rate over the first postoperative week and with the discontinuation of mechanical ventilation. (See “Clinical presentation and diagnosis of ventilator-associated pneumonia”.)

• Patients with depressed mental status or gag reflex due to anesthesia and analgesia are more susceptible to aspiration if they vomit after surgery. A nasogastric tube also increases gastroesophageal reflux and the risk for aspiration [22]. (See “Aspiration pneumonia in adults”.)

• UTI is a frequent cause of postoperative fever in patients with indwelling urethral catheters. The risk of UTI increases with the duration of catheterization [23,24]. UTI is more common in patients who have undergone a genitourinary procedure and in those who have chronic, indwelling catheters prior to surgery. (See “Catheter-associated urinary tract infection in adults”.)

• SSI most often presents in the subacute period, one week or more after surgery. However, two organisms, group A streptococcus (GAS) and Clostridium perfringens, can cause fulminant SSI within a few hours after surgery. (See “Necrotizing soft tissue infections” and “Clostridial myonecrosis”.)

• Catheter exit site infections and bacteremia associated with intravascular catheters also tend to occur subacutely but should be considered as sources of fever in any patient with a catheter in place, especially if insertion was performed under emergent or nonsterile conditions. (See “Epidemiology, pathogenesis, and microbiology of intravascular catheter infections.”)

Acute fever can also be caused by noninfectious conditions. Pancreatitis, myocardial infarction, pulmonary embolism, thrombophlebitis, alcohol withdrawal, and acute gout can complicate the acute postoperative period.

**Subacute** — SSI is a common cause of fever more than one week after surgery; many patients have already been discharged from the hospital by this time [25-28]. (See “Epidemiology of surgical site infection in adults” and “Complications of abdominal surgical incisions.”)
Central venous catheters, if used, can be a source of infection and fever. (See "Epidemiology, pathogenesis, and microbiology of intravascular catheter infections").

Fever from antibiotic-associated diarrhea, typically attributed to Clostridium difficile, also occurs more commonly during this period. (See "Clostridium difficile in adults; Epidemiology, microbiology, and pathophysiology").

Febrile drug reactions are a frequent cause of subacute fever. Beta-lactam antibiotics and sulfa-containing products are commonly implicated, but other medications, such as H2-blockers, procainamide, phenytoin, and heparin, should be considered.

Thrombophlebitis should be considered as a cause of subacute fever in a patient with impaired mobility. Deep venous thrombosis and pulmonary embolism can cause fever and are more frequent in patients who are debilitated either by chronic medical problems or by the surgery.

Patients who require critical care after surgery are at higher risk for the development of subacute fever [29]. These patients typically develop a variety of postoperative complications. Nosocomial infections are more common in these patients because of their treatment with invasive medical devices. Device-related infections due to bacteria and fungi include intravascular catheter-related infection with or without bacteremia, VAP, UTI, and sinusitis. (See "Infections and antimicrobial resistance in the intensive care unit; Epidemiology and prevention").

Delayed — Most delayed postoperative fevers are due to infection, although fever due to postpericardiotomy syndrome should be considered in patients following cardiac surgery.

Viral infections from blood products, including cytomegalovirus (CMV), hepatitis viruses, and human immunodeficiency virus (HIV), can arise late in postoperative patients [13]. Parasitic infections (eg, toxoplasmosis, babesiosis, Plasmodium malariae infection) can also rarely be transmitted via transfusion [30-33].

SSIs due to more indolent microorganisms (eg, coagulase-negative staphylococci) can cause delayed fever, especially in patients with implanted medical devices or grafts. These devices generally need to be removed in order to cure the infection. Patients can also develop delayed cellulitis when surgery has disrupted venous or lymphatic drainage; this type of cellulitis can be recurrent [34,35]. (See "Cellulitis following pelvic lymph node dissection" and "Breast cellulitis and other skin disorders of the breast" and "Early noncardiac complications of coronary artery bypass graft surgery", section on 'Post-venectomy cellulitis'.)

Infective endocarditis due to perioperative bacteremia is also more likely to present weeks or months after surgery.

CAUSES OF POSTOPERATIVE FEVER — Although the list of causes of postoperative fever is extensive (table 1), the initial focus for most patients should be on a limited number of the more common infectious and noninfectious causes.

Infectious — SSI, pneumonia (especially VAP), UTI, and intravascular catheter-associated infection are the most common infectious causes of postoperative fever. Nosocomial bacterial and fungal pathogens are usually implicated. The infecting microorganisms generally are found as endogenous flora of the skin or bowel, but the flora change as patients are hospitalized for longer periods and receive antimicrobial therapy.

When patients are readmitted to the hospital, organisms acquired in the community may also be involved. As an example, Pasteurella multocida SSIs have been caused by pet cats and dogs licking a surgical site [36].

Viral infections in the postoperative patient are usually associated with the transfusion of blood products. As an example, West Nile virus was recognized to be transmitted both by blood products [37] and by organ donation [38]; nucleic acid amplification screening of donated blood has the potential to virtually eliminate this route of transmission [39]. The incubation period between blood product transfusion or organ transplantation and the onset of symptoms of West Nile virus infection ranged from 2 to 21 days. The median incubation period for blood product recipients was shorter than for transplantation recipients (10 and 13.5 days respectively) [40]. Donated blood is screened by immunoassay techniques for a number of viruses. (See "Blood donor screening; Laboratory testing", section on 'Infectious disease screening'.)
Viral infections in the postoperative patient can also be transmitted nosocomially, as has occurred with SARS [41]. Finally, postoperative viral infections, such as VAP can occasionally be caused by the reactivation of latent viruses, such as CMV or herpes simplex virus (HSV), especially in immunosuppressed patients [42-44].

Other postoperative infections include [45]:

- Sinusitis and, less commonly, otitis media, especially in patients with nasotracheal or nasogastric tubes. Mild sinusitis in a critically ill patient may not be clinically significant [46,47].
- Bacterial meningitis in patients after neurosurgical or head and neck procedures that inadvertently violated the subarachnoid space causing a "CSF leak".
- Parotitis, usually due to Staphylococcus aureus, in patients who have undergone manipulation of the oral cavity or are significantly dehydrated postoperatively. This postoperative infection is far less frequent with modern anesthesia and perioperative care [48].
- Acalculous cholecystitis can occur as a postoperative infection and recent surgery is second only to trauma as a cause of this complication [49].
- Toxic shock syndrome is uncommon, but can occur, particularly in patients with nasal or vaginal packing that may facilitate the growth of S. aureus or GAS [50,51]. (See "Staphylococcal toxic shock syndrome" and "Epidemiology, clinical manifestations, and diagnosis of streptococcal toxic shock syndrome".)

Noninfectious — Noninfectious causes of postoperative fever include underlying conditions that are unmasked by the stress of surgery (table 1). Other causes to be considered are:

Medication — Medications are the most common noninfectious cause of fever. Antimicrobials and heparin are the medications most commonly associated with postoperative fever, at least in part because they are used so frequently in the postoperative period (table 2). (See "Drug fever".)

Several medications commonly used in the postoperative period can interact with SSRIs or other antidepressants to precipitate fever as one manifestation of the serotonin syndrome. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Drug-drug interactions'.)

Additionally, antimicrobials and other medications incorporated into implanted materials may cause postoperative fever [52].

Malignant hyperthermia — Malignant hyperthermia is an inherited disorder most commonly manifesting as hypermetabolism during general anesthesia. MH-susceptible patients have genetic skeletal muscle receptor abnormalities allowing excessive calcium accumulation in the presence of certain anesthetic triggering agents. Prompt recognition of the initial clinical signs and treatment with dantrolene limits the morbidity and mortality associated with this disorder. (See "Susceptibility to malignant hyperthermia: Evaluation and management" and "Malignant hyperthermia: Clinical diagnosis and management of acute crisis".)

Inflammation — Surgical site inflammation without infection, including seroma and hematoma.

Gout — Gout and pseudogout in association with joint inflammation and effusion [53,54]. Oncologic surgery or concomitant cancer may be additional risk factors for postoperative gout and joint manipulation and hyperparathyroidism for pseudogout. (See "Clinical manifestations and diagnosis of gout" and "Clinical manifestations and diagnosis of calcium pyrophosphate crystal deposition (CPPD) disease".)

Pancreatitis — Pancreatitis can result from surgery involving the upper abdomen [55], an adverse reaction to perioperative medications, or preoperative alcoholism. (See "Etiology of acute pancreatitis".)

Deep venous thrombosis — Deep vein thrombosis (DVT) and pulmonary embolization are more common after procedures either directly or indirectly resulting in venous stasis, such as oncologic, pelvic, orthopedic, and neurosurgical. (See "Overview of the causes of venous thrombosis", section on 'Surgery' and "Overview of the causes of venous thrombosis", section on 'Trauma'.)

Fat embolism — Fat embolism occurs most frequently after surgeries for major blunt trauma or major orthopedic surgery (particularly those involving long bone and pelvic fractures) [56-59]. It can also develop after liposuction [60] and is part of the differential diagnosis in postoperative patients suffering from acute sickle cell chest syndrome [61]. (See "Fat embolism syndrome".)
**Cardiovascular and stroke** — Myocardial infarction, stroke, and subarachnoid hemorrhage can cause postoperative fever [62-64].

**Transfusion reaction** — Transfusion reactions, such as delayed serologic and hemolytic transfusion reactions (DSTRs, DHTRs), are more common in patients previously sensitized to foreign antigens through prior transfusion or multiple pregnancies [65]. (See "Immunologic blood transfusion reactions".) Complement activation due to antibody incompatibilities can also cause acute lung injury in the syndrome of Transfusion Related Acute Lung Injury (TRALI) [66]. (See "Transfusion-related acute lung injury (TRALI)".)

**Endocrine** — Hyperthyroidism or thyroid storm can occasionally cause postoperative fever. Although hyperthyroidism is more common in patients undergoing thyroid or other neck surgeries, it can also occur after other surgeries [67-69]. Acute adrenal insufficiency or Addisonian crisis has also been reported to occur after surgery, usually due to bilateral adrenal hemorrhagic infarction from coagulopathy [70,71]. The diagnosis can be obscure but is important because treatment with glucocorticoids can be lifesaving [72,73]. (See "Clinical manifestations of adrenal insufficiency in adults".)

**Atelectasis (not causal)** — Atelectasis is often used as an explanation for otherwise unexplained postoperative fever. Both atelectasis and fever occur frequently after surgery, but their concurrence is probably coincidental rather than causal. (See "Atelectasis: Types and pathogenesis in adults").

- In one study of 270 consecutive patients after abdominal surgery, the sensitivity and negative predictive value of fever as a predictor of atelectasis were both less than 50 percent, and the specificity and positive predictive value were 68 and 66 percent respectively [74].
- In another study, there was also no association between fever and the presence of, or the degree of, atelectasis [75]. Therefore, ascribing a postoperative fever to atelectasis is probably false reassurance and may mislead the clinician from pursuing the true cause of the fever.

**Neuroleptic malignant syndrome** — Neuroleptic malignant syndrome causing high fever and rigidity can develop perioperatively in patients receiving antipsychotic agents, especially haloperidol [76]. (See "Neuroleptic malignant syndrome".)

**CONSIDERATIONS FOLLOWING SPECIFIC SURGERIES**

**Cardiothoracic surgery** — Fever is common in the first few days after cardiothoracic surgery; additional investigation in febrile but otherwise clinically unremarkable postoperative patients is probably not indicated until the third postoperative day [77,78]. Individual indicators of infection, including fever, are unreliable in the immediate postoperative period. Aggregate measures of physiologic instability such as a persistently poor APACHE score can identify patients more likely to have serious infectious complications [79]. (See "Predictive scoring systems in the intensive care unit", section on 'Acute Physiologic and Chronic Health Evaluation (APACHE)'.) Pneumonia is a common cause of fever after cardiac surgery and may occur in more than five percent of patients [80]. Pneumonia is correlated with reintubation, hypotension, neurologic dysfunction, and transfusion of more than three units of blood components [80]. Pleural effusions are the rule in patients following cardiac surgery; thoracentesis is rarely required during the evaluation of fever in such patients.

**Sternal wound infection and mediastinitis** — Sternal wound infection occurs in 1 to 5 percent of patients after median sternotomy. It is detected at a median of seven postoperative days; however, the range in one series was 3 to 417 days [81]. Sternal wound infection more than one month after surgery is unusual (only nine percent in another study [82]). Mediastinitis is associated with significant mortality (14 to 47 percent in contemporary series [81,83,84]) and causes protracted hospitalization and an increased need for reoperation and rehospitalization. (See "Postoperative mediastinitis after cardiac surgery" and "Surgical management of sternal wound complications").

A positive blood culture in a persistently febrile patient can be the first manifestation of a sternal wound infection, occurring before apparent wound inflammation [85]. Risk factors for sternal wound infection include surgeries that are emergent, longer, more complex, or include internal mammary artery grafting; and patients who are older, diabetic, dialysis-dependent, obese, or smoke [27,86-89]. Endocarditis should be considered in
patients who develop positive blood cultures after undergoing valve replacement. (See "Epidemiology, clinical manifestations, and diagnosis of prosthetic valve endocarditis").

Culture of Staphylococcus aureus from the blood raises the possibility of mediastinitis, even if the wound appears uninfected [90,91]. (See "Postoperative mediastinitis after cardiac surgery"). Recovery of organisms other than S. aureus from blood cultures, however, does not appear to be associated with mediastinitis. One study found that among patients who had undergone coronary artery bypass graft surgery and had blood cultures that grew an organism other than S. aureus, only 12 percent developed mediastinitis [91]. Coagulase-negative staphylococci are another common cause of sternal wound infections; sternal wound infections due to these organisms are often clinically less apparent than those due to S. aureus [85,86,92]. Sternal wound dehiscence without apparent infection is a clue for infection due to coagulase-negative staphylococci [92].

Candida species account for most postoperative fungal infections, but Aspergillus infections also occur [93]. Aspergillus infections usually present months to years after surgery with persistent fever and negative blood cultures and a mortality rate greater than 80 percent. To minimize the risk of postoperative Aspergillus infection and its associated morbidity and mortality, it is critical to maintain hospital surveillance and to investigate and address any apparent outbreaks [94].

An important noninfectious cause of fever after cardiothoracic surgery is the postpericardiectomy syndrome, which can present days to weeks after surgery with fatigue and chest pain, with or without pericardial effusion [62,95]. (See "Post-cardiac injury syndromes").

**Neurosurgery** — Meningitis is a frequent and serious cause of fever after neurosurgery [96]. Classic symptoms and signs of meningal inflammation, such as headache, photophobia, and nuchal rigidity, are usually not helpful because they can be caused either by infection or by hemolyzed blood from the surgery irritating the meninges. Microscopic and analytical examination of the cerebrospinal fluid (CSF) is indicated in patients with fever, because, combined with specific clinical findings, characteristics of the CSF can help to distinguish patients with infections from those with chemical meningitis. Patients with any of the following criteria can probably be safely observed without administration of antimicrobials: fever less than 39.4°C (102.9°F); CSF WBC less than 7,500/µL; CSF glucose above 10 mg/dL; no delirium, seizure, or surgical site inflammation [97].

Neurosurgical procedures that impact the hypothalamus can lead to disorders of thermoregulation and cause postoperative fever [98].

DVT occurs more frequently after neurosurgery than after many other types of surgery. Not only is the patient likely to have limited mobility before and after surgery, but prophylactic anticoagulation is often less aggressive for neurosurgery because of concern for central nervous system hemorrhage.

**Vascular surgery** — Graft infections after vascular surgery may occur by direct inoculation of the surgical site or, less frequently, by hematogenous spread. Infection is more common in grafts at inguinal and upper leg surgical sites. Vascular graft infections most commonly present soon after surgery, but can occur months to years later.

Determining that a graft is infected can be difficult. In addition to systemic symptoms such as fatigue, and anorexia, and signs such as fever, imaging with CT scanning, MRI, or scintigraphy can be helpful. Negative findings on imaging studies do not rule out a graft infection, but positive findings help to confirm infection and to guide aspiration for microbiologic analysis.

In patients who undergo endovascular repair of aortic aneurysms with endoluminal stent-grafts, a syndrome has been described that can include fever, leukocytosis, elevated C-reactive protein levels, and perigraft gas seen radiographically. Fever above 101.4°F (38.6°C) has been reported in up to two-thirds of patients in some series. Blood cultures are negative, and the fevers resolve without antimicrobial therapy [99,100]. (See "Complications of endovascular abdominal aortic repair", section on 'Postimplantation syndrome'). This is sometimes referred to as "postimplantation syndrome"; its cause is uncertain [101,102].

Another noninfectious cause of fever after vascular surgery is arterial embolization, or "blue toe" syndrome. A similar syndrome can be caused by emboli from an infected graft.

**Abdominal surgery** — The primary cause of postoperative fever that is unique to abdominal surgery is deep abdominal abscess. Distinguishing between abscess, hematoma, and a benign peritoneal fluid collection can
be difficult. Imaging studies and needle aspiration may be helpful, but exploration is sometimes necessary. Empiric antimicrobial treatment should be directed at the combination of aerobic Gram negative enteric bacilli and anaerobes.

Splenoportal thrombosis may cause fever following splenectomy, and is recognized with increased frequency since the availability of CT scanning [103]. Risk factors include massive splenomegaly, and myeloproliferative and hemolytic disorders.

Pancreatitis more frequently causes postoperative fever after upper abdominal surgeries than after other surgeries. Diagnosis can be made by elevated serum amylase and lipase concentrations with the considerations that salivary glands also produce amylase, and macro variants of amylase can produce elevated serum concentrations. (See "Clinical manifestations and diagnosis of acute pancreatitis").

**Obstetric and gynecologic surgery** — Postpartum endometritis, manifested by fever, pelvic pain and purulent vaginal discharge, is more common in patients with preexisting medical problems, after premature rupture of membranes, difficult deliveries, and after the use of internal fetal monitoring. (See "Postpartum endometritis".)

The differential diagnosis of fever after gynecologic surgery includes urinary tract infection (UTI), cellulitis, necrotizing fasciitis, superficial abscess, deep abscess, and pelvic thrombophlebitis. As with other major surgeries, fever in the first day or two after gynecologic surgery usually resolves spontaneously. Extensive laboratory testing is not beneficial; fever evaluation should be targeted to the individual patient, based on repeated assessment of symptoms and signs [104,105].

Deep abscess and pelvic thrombophlebitis are possible causes in patients with an unrevealing evaluation and persistent fever. Similar to abdominal surgery, identifying a fluid collection and distinguishing between abscess, hematoma, and a benign fluid collection, though difficult, can be critically important.

**Urologic surgery** — Infection of the urinary tract at any level is the major consideration in evaluating patients with fever after urologic surgery. Although bacteriuria due to a urethral catheter is common, culture alone is not as revealing as the combination of urine culture findings and urine analysis for pyuria and bacteriuria. (See "Catheter-associated urinary tract infection in adults"). Deep infections, such as prostatic and perinephric abscess, may present with fever and pain, but relatively benign urine findings. Infection can also spread from the lower urinary tract through Batson's venous plexus to the lumbar spine and present after the UTI is resolved.

**Orthopedic surgery** — As with other major surgeries, self-limited fever is the rule after major orthopedic surgery [8]. The dominant special considerations in the differential diagnosis of persistent fever are surgical site infection (SSI), infected prosthesis, hematoma, and DVT. Repeat clinical assessment, imaging, and sometimes needle aspiration may be required to adequately assess the surgical site.

**Transplantation** — Evaluating fever after transplantation surgery requires special considerations due to immunosuppression [106,107]. In addition to usual bacterial infections, medication reactions, and DVT, immunosuppression can enable reactivation of viral and protozoan infections from the patient or the donor [108]. In addition, organ rejection and immunosuppression related lymphoma are both associated with delayed fever. Finally, immunosuppressive medications such as corticosteroids can mask fever.

**APPROACH TO THE PATIENT WITH FEVER AFTER SURGERY** — Chest radiography, urinalysis, and blood and urine cultures are not indicated for all postoperative patients with fever. The need for laboratory testing should be determined by the findings of a careful history and physical examination. The febrile postoperative patient should be evaluated systematically (table 3), taking into account the timing of the onset of fever and the many possible causes (table 1) [7,104,109].

A useful initial screen for the more common causes of postoperative fever is represented by the four-part mnemonic "Wind, Water, Wound, What did we do?". "Wind" refers to pulmonary causes of fever including pneumonia, aspiration, and pulmonary embolism (but not atelectasis). "Water" refers to UTI, and "Wound" refers to SSI. "What did we do?" is a reminder to consider treatments as a cause of fever and includes medications, blood product transfusions, and intravascular, urethral, nasal, and abdominal catheters.
**Procalcitonin** — The value of serum procalcitonin (PCT) concentration for differentiating bacterial infection from other causes of postoperative fever has been explored in a few studies [110-112]. PCT is produced in C cells of the thyroid and is a more specific marker of bacterial infection than CRP. However, postoperative PCT concentrations vary substantially following different types of surgery [112], and from patient to patient following the same type of surgery [113]. Furthermore, PCT has not been found to be a reliable marker for infection in other settings (see "Fever in the intensive care unit" and "Evaluation and management of suspected sepsis and septic shock in adults"). We do not suggest the use of PCT in the evaluation of postoperative fever, pending additional clinical evidence.

**TREATMENT** — Any unnecessary treatments, including medications and catheters, should be discontinued in patients with postoperative fever. It is probably appropriate to suppress the fever in most patients with one or two days of scheduled acetaminophen to minimize patient discomfort and the physiologic stress and metabolic demands of fever and shivering [114]. This approach is unlikely to mask a significant pathologic condition. Additional treatment depends upon the cause of the fever.

The decision to administer antibiotics to a patient with postoperative fever depends upon careful clinical assessment including an appraisal of the patient's stability. Patients who have undergone major surgery and are receiving intensive care and patients with hemodynamic instability generally should be treated empirically with broad-spectrum antibiotics after cultures have been obtained. For example, a patient with a suspected intraabdominal or pelvic infection should be treated with a regimen effective against aerobic Gram negative enteric bacilli and anaerobes. (See "Antimicrobial approach to intra-abdominal infections in adults", section on 'Introduction' and "Antimicrobial approach to intra-abdominal infections in adults", section on 'Empiric antimicrobial therapy'.) Empiric antifungal therapy should not be included unless the patient is at high risk for fungal infection.

Nosocomial pathogens are often resistant to many antimicrobials; hospital antibiograms can be useful for selecting an appropriate broad-spectrum regimen. If a source of fever is not apparent and blood cultures show no growth after 48 hours, then discontinuation of antimicrobials should be seriously considered.

If a site of infection is identified and/or cultures are positive, the broad-spectrum regimen should be focused to cover the probable or known causative organism(s). Antimicrobial treatment beyond the empiric period of 48 hours should be reserved for patients in whom an infection has been identified. Gram stain findings and hospital antibiograms can be used to guide empiric antimicrobial selection, but definitive treatment should be based upon antimicrobial susceptibility results from cultured organisms. Carefully selecting antimicrobial treatment can help to avoid adverse medication reactions and can help to minimize the prevalence of resistant organisms in the hospital.

**SUMMARY AND RECOMMENDATIONS**

- Postoperative fever (>38°C, 100.4°F) is common in the first few days after surgery and usually resolves spontaneously. This febrile response may be due to tissue trauma with cytokine release, circulating bacterial endotoxins from endogenous gut flora, or other causes. (See 'Pathophysiology of postoperative fever' above.)

- In establishing a differential diagnosis for postoperative fever, it is helpful to take into account the timing of fever onset following surgery: immediate, acute, subacute, or delayed. The differential diagnosis of postoperative fever includes infectious and noninfectious etiologies. (See 'Timing of fever' above.)

- Surgical site infection, pneumonia, urinary tract infection, and intravascular catheter infection are the predominant infectious causes of postoperative fever, and are often due to nosocomial multi-drug-resistant organisms (See 'Infectious' above.)

- The most common noninfectious cause of postoperative fever is a medication reaction; antimicrobial agents or heparin are the drugs most frequently implicated (see 'Medication' above)

- Atelectasis and fever can both occur after surgery; however they do not correlate well with each other. Although atelectasis is often cited as a cause of postoperative fever, the association is probably coincidental and not causal. (see 'Atelectasis (not causal)' above)
Fever occurring in a patient who is otherwise doing well clinically within two days following cardiovascular surgery probably does not need further evaluation. A more delayed fever can be due to a variety of causes. Pneumonia occurs in more than 5 percent of sternotomy patients, and sternal complications in 1 to 5 percent. Mediastinitis is a serious complication and is usually due to Staphylococcus species. The postpericardiotomy fever syndrome may occur weeks after surgery. (See ‘Cardiothoracic surgery’ above.)

- Meningitis may be difficult to diagnose following neurosurgery, because neurosurgery can cause meningeal irritation without infection. Cerebrospinal fluid should be obtained for glucose concentration and microbiologic studies (gram stain and bacterial culture) to help determine the need for empiric antimicrobial therapy. (See ‘Neurosurgery’ above.)

- Vascular graft infections are more common after revascularization involving the groin or lower extremities. In patients undergoing endovascular aortic aneurysm repair, a postimplantation syndrome with fever but no infection is uncommon but has been described. (See ‘Vascular surgery’ above.)

- Fever following abdominal surgery may be due to intraabdominal abscess and exploration may be necessary if needle aspiration and imaging studies are inconclusive. Pancreatitis more frequently complicates upper abdominal surgery than other surgeries. (See ‘Abdominal surgery’ above.)

- Endometritis is more common following complicated deliveries. Fever soon after pelvic surgery is most often transient, but may be due to urinary tract infection, cellulitis, abscess, or pelvic thrombophlebitis. (See ‘Obstetric and gynecologic surgery’ above.)

- Fever evaluation in the post-transplant patient is complicated by the increased likelihood of opportunistic infections due to concomitant immunosuppression. (See ‘Transplantation’ above.)

- Chest X-ray, urinalysis, and blood cultures are not indicated for most febrile postoperative patients. Evaluation should be tailored to the individual patient based on history, symptoms and physical findings. (See ‘Approach to the patient with fever after surgery’ above.)

- All unnecessary treatments, including medications, nasogastric tubes and intravascular and urinary catheters should be discontinued in the febrile patient. Treating the fever with acetaminophen is often appropriate. Antibiotics are not routinely indicated for most patients with fever in the early postoperative period, but hemodynamically unstable patients should be treated empirically with broad spectrum antibiotics, which should be discontinued after 48 hours if no source of infection has been identified. (See ‘Treatment’ above.)

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REFERENCES


Topic 2886 Version 11.0
## Causes of postoperative fever

### Infectious

- Surgical site infection
- Pneumonia (ventilator-associated and aspiration)
- Urinary tract infection (usually with an indwelling bladder catheter)
- Intravascular catheter-associated infection
- Antibiotic-associated diarrhea
- Sinusitis
- Otitis media
- Parotitis
- Intraabdominal abscess
- Meningitis
- Acalculous cholecystitis
- Transfusion-associated viral infections
- Foreign body infection (orthopedic hardware, endovascular devices eg, prosthetic heart valves, grafts, and stents)
- Osteomyelitis
- Endocarditis

### Noninfectious

- **Surgical site inflammation without infection**
  - Hematoma/seroma
  - Suture reaction

- **Thrombosis**
  - Deep vein thrombosis
  - Pulmonary embolism (thrombotic or fat embolism)

- **Inflammatory**
  - Gout/pseudogout
  - Pancreatitis

- **Vascular**
  - Cerebral infarction/hemorrhage
  - Subarachnoid hemorrhage
  - Myocardial infarction
  - Bowel ischemia/infarction

- **Other**
  - Medications
  - Drug/alcohol withdrawal
  - Transfusion reactions
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant rejection</td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism (including thyroid storm)</td>
<td></td>
</tr>
<tr>
<td>Hypoadrenalism</td>
<td></td>
</tr>
<tr>
<td>Cancer/neoplastic fever</td>
<td></td>
</tr>
</tbody>
</table>

Graphic 69959 Version 2.0
Pathways of fever production

Starting from the top left, infectious agents and/or microbial products, as well as cytokines and other inflammatory processes, induce macrophages, endothelial cells, and the reticuloendothelial system to produce and secrete pyrogenic cytokines into the circulation. These pyrogenic cytokines induce the synthesis of prostaglandin E2 (PGE2) in the hypothalamus. In addition, microbial toxins, acting as ligands to the toll-like receptors in the hypothalamus, stimulate the synthesis of PGE2 by the hypothalamus. PGE2 raises the thermostatic set point in the hypothalamus to febrile levels. The vasomotor center sends signals for heat conservation (vasoconstriction) and heat production (shivering). Corticosteroids reduce the peripheral synthesis of pyrogenic cytokines, whereas antipyretics reduce PGE2 levels in the brain.

TLR: toll-like receptor; IL-1: interleukin-1; IL-6: interleukin-6; TNF: tumor necrosis factor; IFN: interferon; PGE2: prostaglandin E2.

Courtesy of Reuven Porat, MD and Charles A Dinarello, MD.

Graphic 80455 Version 3.0
Timing of onset of postoperative infection and fever

The timing of fever after surgery is one of the most important characteristics in ordering the differential diagnosis of fever in postoperative patients.


Graphic S1666 Version 5.0
## Medications associated with fever

### Antimicrobials
- Penicillins
- Cephalosporins
- Fluoroquinolones
- Vancomycin
- Sulfonamides
- Nitrofurantoin
- Rifampin
- Amphotericin B

### Cardiovascular medications
- Thiazide diuretics
- Furosemide
- Spironolactone
- Hydralazine
- Quinidine
- Procanamide
- Alpha methylidopa

### Anticonvulsants
- Phenytoin

### Other
- Heparin (especially unfractionated)
- Salicylates
- Nonsteroidal antiinflammatory drugs
- Allopurinol
- Immunoglobulins
- Iodides
- Propylthiouracil
- Hydroxyurea
- Mycophenolate mofetil

Graphic 82602 Version 2.0
# Evaluation of the patient with postoperative fever

<table>
<thead>
<tr>
<th>History</th>
<th>Physical examination</th>
<th>Laboratory*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Review record for:</strong></td>
<td>Review record for vital signs. Determine range in the past day and peak daily values during hospital stay. Check nurses' notes for fevers not recorded in the vital signs chart.</td>
<td>Urinalysis and culture</td>
</tr>
<tr>
<td>Preoperative course and presentation</td>
<td>Temperature</td>
<td>Sputum gram stain and culture</td>
</tr>
<tr>
<td>Operation (emergent or elective, intraoperative complications)</td>
<td>Heart rate</td>
<td>Blood culture (from catheters and peripherally - minimum of two)</td>
</tr>
<tr>
<td>Postoperative course</td>
<td>Respiratory rate</td>
<td>Wound culture</td>
</tr>
<tr>
<td>Past medical history and underlying medical problems</td>
<td><strong>Examine:</strong></td>
<td>Complete blood count with differential</td>
</tr>
<tr>
<td>Allergies</td>
<td>Skin for rash, ecchymoses, injection site erythema, and hematoma</td>
<td>Chest radiograph</td>
</tr>
<tr>
<td>Medications</td>
<td>Lungs</td>
<td>Additional blood or radiographic studies might be indicated by specific findings. As examples, abdominal pain might indicate the need for blood tests for hepatic and pancreatic enzymes or abdominal CT scanning; unilateral leg edema might indicate the need for ultrasound to rule out DVT.</td>
</tr>
<tr>
<td>Location of catheters and time of placement</td>
<td>Heart for tachycardia or new murmur</td>
<td></td>
</tr>
<tr>
<td><strong>Ask nursing staff about:</strong></td>
<td>Abdomen for tenderness, bloating, bowel sounds</td>
<td></td>
</tr>
<tr>
<td>Sputum amount and quality</td>
<td>Operative site and lymphatic drainage</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Catheter entry sites</td>
<td></td>
</tr>
<tr>
<td>Any areas of skin breakdown or rashes</td>
<td>Lower legs for evidence of deep vein thrombosis</td>
<td></td>
</tr>
<tr>
<td><strong>Ask patient about:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Studies should be ordered based upon the patient evaluation; no test is mandatory to obtain.

Graphic 79357 Version 2.0

## Contributor Disclosures

**Harrison G Weed, MS, MD, FACP** Nothing to disclose. **Larry M Baddour, MD, FIDSA** Nothing to disclose. **Hilary Sanfey, MD** Nothing to disclose. **Kathryn A Collins, MD, PhD, FACS** Nothing to disclose.

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