



Evaluating postoperative fever:

A focused approach

JAMES C. PILE, MD

Postoperative fever is one of the most common problems seen by both surgeons and medical consultants. Most cases of fever immediately following surgery are self-limiting, but it is critical not to miss more serious etiologies. When evaluating postoperative fever, it is important to recognize when a wait-and-see approach is appropriate, when further work-up is needed, and when immediate action is indicated.

Using case studies, this article discusses typical scenarios involving postoperative fever, and provides a framework for evaluating and managing them.

■ CASE 1: FEVER IMMEDIATELY AFTER SURGERY

A 58-year-old man is referred to your clinic for a preoperative evaluation before bilateral total knee arthroplasty. He has well-controlled hypertension, hyperlipidemia, and osteoarthritis, and you determine that he is medically optimized for surgery.

The day after surgery, the patient is feeling well except for moderate knee pain controlled by pain medication.

- New medications: cefazolin for prophylaxis of surgical site infection.
- Physical examination: normal except for a small amount of serosanguineous drainage from the right knee.
- Vital signs: temperature 38.7°C (101.6°F), blood pressure 130/72 mm Hg.
- Laboratory results: white blood cell count 11,000/mm³.

From the Division of Hospital Medicine, MetroHealth Medical Center, Cleveland, OH.

Address: James C. Pile, MD, MetroHealth Medical Center, Division of Hospital Medicine, 2500 MetroHealth Drive, Cleveland, OH 44109; jpile@metrohealth.org.

Disclosure: Dr. Pile reported that he has no financial relationships that pose a potential conflict of interest with this article.

Which of the following diagnostic studies and treatment options do you recommend?

- A. Blood and urine cultures
- B. Choice A plus chest radiography
- C. Choice B and begin vancomycin
- D. Observation only

The correct answer is D. Most early postoperative fevers (within the first 48 hours after surgery) have no clearly defined infectious cause and resolve without therapy.

Is the fever caused by infection?

Postoperative fever is very common. However, published incidence rates range widely (from 14% to 91%)¹ depending on how fever was defined and the patient population of the study. The more important issue is whether infection is the underlying cause. In the vast majority of studies, the incidence of infection in patients with postoperative fever is less than 10%, indicating that fever is not a specific marker of infection in this setting.

Fanning et al,² in a retrospective review of 537 patients who underwent gynecologic surgery, found that 211 (39%) developed fever postoperatively, but no infectious etiology was found in 92% of these cases.

Shaw and Chung,³ in a retrospective review of 200 patients undergoing total hip or knee arthroplasty, reported that “virtually all” had elevated temperatures postoperatively but none had documented infection. Most patients had a maximum temperature on the first postoperative day and had normal temperatures by the fourth postoperative day. Nearly one fifth of the patients had a maximum temperature of 39.0°C (102.2°F) or greater, indicating that the magnitude of fever is also not a reliable marker of infection.

Garibaldi et al,⁴ in a prospective study of 81 patients who developed unexplained postoperative fever, found that 80% of those with fever on the first postoperative day had no infection. However, the sit-

uation was quite different for patients who developed a fever on or after the fifth day following surgery, as approximately 90% of these patients had an identifiable infection, in most cases wound infection (42%), urinary tract infection (29%), or pneumonia (12%).

Fever as a response to injury

A variety of conditions—including trauma and infection—lead to the release of pyrogenic cytokines, primarily interleukin 1 (IL-1), IL-6, tumor necrosis factor, and interferon- γ . These cytokines act directly on the anterior hypothalamus and its surrounding structures, causing the release of prostaglandins, which appear to mediate the febrile response.

Wortel et al⁵ measured IL-6 levels in 16 patients who developed postoperative fever in the first 24 hours after undergoing a Whipple procedure. Levels of IL-6 directly correlated with the magnitude of fever (average maximum temperature, 38.8°C [101.8°F]).

Other investigators have found that the more traumatic the surgery, the higher the risk of postoperative fever, and that IL-6 is an important driver of this response. Frank et al⁶ prospectively studied 271 patients in the first 24 hours following various vascular, abdominal, and thoracic surgeries. Patients who underwent peripheral vascular procedures involving the lower extremities were the most likely to develop a fever, followed by patients who underwent thoracic procedures, abdominal procedures, and carotid endarterectomies. The mean time to maximum temperature elevation was 11 hours after surgery. Blood concentrations of IL-6 correlated with fever elevation.

■ CASE 2: FEVER 4 DAYS AFTER SURGERY

A 61-year-old woman with rheumatoid arthritis (medications: methotrexate and hydroxychloroquine) who is otherwise in generally good health undergoes a left total hip replacement. A Foley catheter is placed during surgery. Following surgery, she is sent to the regular orthopedic unit, where she begins to ambulate the day following surgery. A fever of 38.1°C (100.6°F) is noted on the first postoperative day. Her Foley catheter is removed on postoperative day 2. Her temperature is normal on postoperative days 2 and 3, but on postoperative day 4, her temperature is 38.5°C (101.3°F).

What is the most likely cause of her fever now?

- A. Joint hemarthrosis
- B. Urinary tract infection
- C. Superficial wound infection
- D. Prosthesis infection

B is correct. Although all choices are possible, urinary tract infection is the most common cause of fever appearing 4 days after surgery.

The patient's urine is cultured, and grows *Proteus mirabilis* ($>10^5$ colonies). Oral ciprofloxacin therapy is started, and the patient's fever subsides.

Evaluating postoperative infection

Infection is much more likely to be present in a patient with a fever that develops after the first 2 days following surgery. The most common causes are:

Urinary tract infection, especially in a patient who has had urinary catheterization.

Surgical site infection, typically seen on postoperative day 4 or 5 or later.

Pneumonia, especially in patients with preexisting chronic obstructive pulmonary disease or who have been mechanically ventilated.

Intravenous catheter-related infections, which can be caused either by peripheral catheters (usually leading to thrombophlebitis or cellulitis) or by central catheters (usually causing bloodstream infection).

***Clostridium difficile*-associated diarrhea**. Appropriate prophylactic antibiotics can help prevent surgical site infections. However, even a few doses of perioperative antibiotics can make a patient susceptible to *C difficile*, the frequency and virulence of which are increasing.

Less common causes of postoperative infection include:

Intra-abdominal infection, especially following abdominal or pelvic surgery.

Sinusitis, typically in patients who undergo nasogastric intubation for long periods.

Acalculous cholecystitis, particularly in very sick and debilitated patients who are not receiving enteral nutrition.

Prosthesis infection, which may manifest within a few days of surgery, especially if it is caused by *Staphylococcus aureus*.

■ CASE 3: FEVER AND ATELECTASIS

A 48-year-old woman in generally good health undergoes an abdominal hysterectomy. On the first day following surgery, she develops a maximum temperature of 38.7°C (101.7°F), and she remains febrile on postoperative day 2. She has some pain at the incision. She looks comfortable and is hemodynamically stable.

- Physical examination: normal except for mild bibasilar crackles heard in the lung fields.
- Chest radiography: atelectasis in both lung bases.

- Laboratory results: white blood cell count 10,500/mm³.

What is the most likely cause of her fever?

- A. Urinary tract infection
- B. Atelectasis
- C. Deep venous thrombosis
- D. Other

The answer is D. Considering that it is still only 2 days after surgery, and that the patient generally looks and feels well, the fever is more likely to be caused by cytokine release from the surgical trauma than from infection.

Atelectasis does not cause fever, despite widespread misconception to the contrary. Engoren⁷ monitored 100 patients for 2 days following cardiac surgery with daily portable chest radiography and continuous bladder thermometry. During this period, the incidence of fever progressively declined while that of atelectasis increased, demonstrating a negative correlation between them. Roberts et al⁸ similarly reported poor correlation between fever and atelectasis in a study of 270 patients following abdominal surgery.

How to target the evaluation of postoperative fever Fever should never be ignored. Appropriate evaluation of early postoperative fever includes a careful history, a targeted physical examination, and additional studies if indicated. Special attention should be paid to the following:

Preoperative course. Details of the period before hospitalization can be critical. For example, a patient with a hip fracture may have fallen because of an occult urinary tract infection, pneumonia, or cardiac arrhythmia.

Details of the procedure. Duration of surgery, blood products administered, and any complications may be important. The operative note can be helpful if present; if questions remain, directly speaking to the surgeon can fill in the gaps.

Nursing information is often important, such as if the patient has diarrhea or is coughing.

Physical examination should target vital signs and the heart and lungs, as well as the surgical and catheter sites for infection, the skin for rash, and the joints for inflammation.

Laboratory and imaging studies should be used sparingly and only as directed by the history and physical examination. Blood cultures for fever within the first 48 hours following surgery are usually unnecessary, as the chance of an abnormal result is very low in most patients.^{2,9-11} In general, blood cultures should be reserved for high-risk patients, such as those who

appear septic, are immunocompromised, have a central venous catheter, or have an obvious wound infection.

■ CASE 4: OTHER NONINFECTIOUS ETIOLOGIES OF POSTOPERATIVE FEVER

A 49-year-old man is admitted to the vascular surgery service with dry gangrene of the left foot. He has a history of lower extremity arteriosclerosis obliterans, hyperlipidemia, gout, and hypertension, as well as a 60-pack-year smoking history.

- Medications: hydrochlorothiazide, lisinopril, atorvastatin, aspirin.
- Magnetic resonance imaging: evidence of osteomyelitis in the left foot.

The patient undergoes a left transmetatarsal amputation. He is given combined piperacillin and tazobactam postoperatively, as well as his previous medications and opiates for pain. He does well over the first 2 days. On day 3, however, he develops a temperature of 38.5°C (101.3°F) and right knee pain. The knee is warm and tender.

What is the next step?

- A. Aspirate the knee
- B. Change his antibiotics to imipenem
- C. Begin indomethacin
- D. "Pan-culture" and obtain a chest radiograph

There is no good reason to change his antibiotics or to obtain blood, urine, or sputum cultures at this time. Knee aspiration would be a reasonable option for determining whether gout or infection is the cause of this episode. Since the patient is known to have a history of gout, the physician opts to empirically begin indomethacin. One study found a 15% incidence of gouty attacks in the early postoperative period among patients with a history of gout. The knee appears to be the most commonly affected joint in this setting, and this study found that fever accompanied the gout flare in virtually all cases.¹²

The symptoms resolve rapidly and the patient does well. He is moved to a skilled nursing facility, where he develops a fever of 38.8°C (101.8°F) on postoperative day 7. At this time, the physical examination is normal, with no apparent infection at the site of the peripherally inserted central catheter or at the amputation site. Laboratory findings are notable only for a white blood cell count showing 18% eosinophils.

What is the most appropriate next step?

- A. Discontinue indomethacin
- B. Change the combined piperacillin and tazobactam to another antibiotic

- C. Add vancomycin to cover resistant gram-positive organisms in the wound
D. Both A and B

The best answer is D. Both indomethacin and particularly piperacillin/tazobactam are reasonably likely causes of drug fever. Based on available information, there is no reason to implicate a resistant gram-positive organism causing infection at the operative site.

The most common noninfectious causes of postoperative fever include:

Drug fever, which may present with skin rash or eosinophilia, but often provides no clue. It is an especially important diagnosis to consider with phenytoin, beta-lactam antibiotics, and sulfonamide antibiotics.

Hematoma, which can cause both fever and leukocytosis.

Gout (see above).

Transfusion reactions are usually obvious because they occur at the time of transfusion, although the temporal relationship is sometimes less clear.

Venous thromboembolic disease must always be suspected postoperatively. Although fever is not clearly linked with deep venous thromboembolism, low-grade fever is not uncommon in patients with pulmonary embolism, and high fever, though rare, may also occur.¹³

Pancreatitis may complicate intra-abdominal procedures, particularly those involving the upper abdomen, and often manifests with fever.

Alcohol withdrawal is frequently accompanied by low-grade fever, along with mental status changes and adrenergic hyperactivity.

■ CASE 5: FEVER AND ACUTE ILLNESS 1 DAY AFTER SURGERY

A previously healthy 58-year-old man has a right nephrectomy for asymptomatic renal cell carcinoma. On the first postoperative day, the patient appears ill and is anxious. His temperature is 38.7°C (101.7°F), his blood pressure 88/40 mm Hg, and his heart rate 122 beats per minute. The surgical site is dressed.

Which of the following is *unlikely* to be the cause of the patient's condition?

- A. Malignant hyperthermia
B. Clostridial wound infection
C. Pulmonary embolism
D. Acute adrenal insufficiency

The correct answer is A. Malignant hyperthermia generally becomes apparent intraoperatively, although rarely it may present as long as several hours after surgery. Fever beginning on postoperative day 1 may be

safely assumed *not* to be due to malignant hyperthermia. The other three answers are all plausible in an individual who develops fever and becomes hemodynamically unstable in the early postoperative period.

The patient's wound is undressed, and the surrounding tissue is pale and tender, with copious foul-smelling, seropurulent drainage from the wound. Gram staining of the drainage shows many gram-positive bacilli and few neutrophils. Antibiotic therapy is initiated, and the patient is taken urgently to the operating room for wound debridement.

Emergent causes of early postoperative fever

Early postoperative fever, while usually self-limiting, can be caused by life-threatening conditions. If these conditions are present, it is critical to recognize them immediately. The following are important possibilities to consider:

Myonecrosis, due to either *Clostridium* species (as in the case above) or group A streptococci, is a surgical emergency. Antibiotics, although important, play an adjunctive role to debridement, which may need to be extensive.

Pulmonary embolism may present with fever, although most commonly it does not. The possibility of pulmonary embolism should always be considered in the postoperative patient with unexplained hemodynamic instability.

Alcohol withdrawal, as already noted, frequently presents with fever. Prompt recognition and treatment will reduce morbidity and even prevent mortality.

Bowel leak should be considered in a patient who has undergone abdominal or pelvic surgery and develops evidence of sepsis in the early postoperative period. Intraperitoneal contamination may occur from an inadvertent bowel enterotomy during surgery or from leakage from a bowel anastomosis.

Adrenal insufficiency may cause fever and refractory hypotension postoperatively, typically in the setting of a patient whose hypothalamic-pituitary-adrenal axis is iatrogenically suppressed due to prolonged corticosteroid administration. Timely steroid supplementation may be lifesaving in this situation.

Malignant hyperthermia may present up to 10 hours after induction of general anesthesia.¹⁴ The disorder is characterized by muscle rigidity, tachycardia, and life-threatening hyperthermia. Prompt administration of dantrolene is critical.

■ SUMMARY

Postoperative fever should be evaluated with a focused approach rather than in "shotgun" fashion. Most fevers

that develop within the first 48 hours after surgery are benign and self-limiting. However, it is critical that physicians who provide postoperative care be able to recognize the minority of fevers that demand immediate attention, based on the patient's history, a targeted physical examination, and further studies if appropriate.

Fever that develops after the first 2 days following surgery is more likely to have an infectious cause, but noninfectious causes that require further evaluation and treatment must also be considered. When evalu-

ating postoperative fever, a helpful mnemonic is the "four Ws":

- Wind (pulmonary causes: pneumonia, aspiration, and pulmonary embolism, but *not* atelectasis)
- Water (urinary tract infection)
- Wound (surgical site infection)
- "What did we do?" (iatrogenic causes: drug fever, blood product reaction, infections related to intravenous lines).

REFERENCES

1. **Dellinger EP.** Approach to the patient with postoperative fever. In: Gorbach SL, Bartlett JG, Blacklow NR, eds. *Infectious Diseases*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2004:817.
2. **Fanning J, Neuheff RA, Brewer JE, Castaneda T, Marcotte MP, Jacobson RL.** Frequency and yield of postoperative fever evaluation. *Infect Dis Obstet Gynecol* 1998; 6:252-255.
3. **Shaw JA, Chung R.** Febrile response after knee and hip arthroplasty. *Clin Orthop Relat Res* 1999; 367:181-189.
4. **Garibaldi RA, Brodine S, Matsumiya S, Coleman M.** Evidence for the non-infectious etiology of early postoperative fever. *Infect Control* 1985; 6:273-277.
5. **Wortel CH, van Deventer SJ, Aarden LA, et al.** Interleukin-6 mediates host defense responses induced by abdominal surgery. *Surgery* 1993; 114:564-570.
6. **Frank SM, Kluger MJ, Kunkel SL.** Elevated thermostatic setpoint in postoperative patients. *Anesthesiology* 2000; 93:1426-1431.
7. **Engoren M.** Lack of association between atelectasis and fever. *Chest* 1995; 107:81-84.
8. **Roberts J, Barnes W, Pennock M, Browne G.** Diagnostic accuracy of fever as a measure of postoperative pulmonary complications. *Heart Lung* 1988; 17:166-170.
9. **Freischlag J, Busuttil RW.** The value of postoperative fever evaluation. *Surgery* 1983; 94:358-363.
10. **Theuer CP, Bongard FS, Klein SR.** Are blood cultures effective in the evaluation of fever in perioperative patients? *Am J Surg* 1991; 162:615-618; discussion 618-619.
11. **Swisher ED, Kahlefeh B, Pohl JF.** Blood cultures in febrile patients after hysterectomy. Cost-effectiveness. *J Reprod Med* 1997; 42:547-550.
12. **Craig MH, Poole GV, Hauser CJ.** Postsurgical gout. *Am Surg* 1995; 61:56-59.
13. **Stein PD, Afzal A, Henry JW, Villareal CG.** Fever in acute pulmonary embolism. *Chest* 2000; 117:39-42.
14. **Mechem CC.** Severe hyperthermia: heat stroke and malignant hyperthermia. In: Rose BD, ed. *UpToDate*. Waltham, MA: UpToDate; 2005.