CLINICAL REVIEW

Medical Care of the Surgical Patient: Postoperative Fever

Spencer R. Adams, MD and Roger M. Lee, MD

Fever in the immediate postoperative period ('postoperative fever') is common and is only rarely caused by infection. However, costly non-directed tests are often ordered by physicians to exclude infection. In most patients, fever is caused by the release of pyrogenic cytokines as part of the body's normal response to tissue injury from surgery. Fever typically begins within 72 hours of surgery and abates spontaneously in two or three days. It is vital that medical consultants are familiar with postoperative fever recognize when a 'wait and see' approach is appropriate and when more tests or interventions are indicated. A directed approach guided by a basic bedside history and examination dramatically increase yield of testing and saves resources. We review relevant literature regarding postoperative fever with the goal reducing random, unnecessary, and costly workups for this common condition.

Despite limited formal training on the case of rare surgical patients during Internal Medicine residency programs, Hospitalists are co-managing patients who have undergone a wide variety of surgeries. The care of post-surgical patients differs in many ways from that of medical patients. Thus, it is imperative for Hospitalists to gain knowledge and skill in perioperative medicine and surgical co-management to provide high quality and cost-effective care to surgical patients. There is some evidence that Hospitalists with such expertise who work closely with surgical teams may help decrease morbidity and costs.[1] Of all of the events that occur after surgery, fever is one of the most common. Unlike fever seen in medical patients, early postoperative fever is usually non-infectious and self-limiting and does not require further investigation unless signs or symptoms of infection are present.[2-7] It has been said that resources are wasted on the workup of early postoperative fever than any other aspect in postoperative care. Therefore, it is critical for Hospitalists to be familiar with the literature regarding postoperative fever and adopt a focused rather than a shotgun approach when evaluating postoperative fever.

Extensive literature on postoperative fever is available and patients undergoing a variety of surgeries including orthopedic, major gynecologic, abdominal operations, and others have been studied. Regardless of the type of surgery, authors have all come to similar conclusions. Fever is common and occurs in 15-90% of post-surgical patients and infection is a very rare cause of postoperative fever (<10 % in the vast majority of studies).[4-10] In 1968, Roe identified the causes of postsurgical fever as: pneumonia, wound infection, drug reaction, dehydration, blood transfusion reaction, malignancy, atelectasis, phlebitis, abscess, urinary tract infection, and "benign postoperative fever".[11] Beginning in the 1980s, in classic medical school teaching, many of us were taught the pneumonic of the '5 W's of postoperative fever: wind (pneumonia or atelectasis), water (urinary tract infection (UTI)), wound (wound infection), walking (venous thromboembolism), and wonder drugs (drug fever). However, there is no research to establish how this 'Rule of W' was formed and there was no mention that in actuality infection is a rare cause of fever and that the majority of postoperative fevers are benign and self-limited.

The published literature clearly shows that early postoperative fever is not a specific indicator of infection. In a retrospective review of 537 patients who underwent gynecologic surgery, 39% (211) developed postoperative fever, and no infection was found in 92% of these cases.[4] In another retrospective review of 200 patients undergoing hip or knee replacement, 'virtually all' patients had elevated temperatures postoperatively, but none had documented infection.[9] Several other studies showed similar results that fever is not a specific indicator of infection.[6-8, 10] A study by Shaw and others sheds further light on typical fever trends seen after surgery. Most patients had a maximum temperature on postoperative day (POD) 1 and normal temperatures by POD 4. Around 20% of patients had a maximum temperature of 39.0°C (102.2°F) or higher.[9] In another study of 98 consecutive patients undergoing total hip arthroplasty, 39 patients had fever on POD 1 and only 5 patients had fever on POD 5. By far the highest incidence of fever is on POD 1, 2, or 3.[12] In addition, in a prospective study of 81 patients with unexplained postoperative fever, it was found that 80% of those with fever on POD 1 had no infection. In contrast, in patients who developed postoperative fever on or after POD 5, around 90% had an identifiable infection (wound infection 42%, UTI 29%, pneumonia 12%).[13] Thus, the vast majority of early postoperative fevers (those that begin within the first 48-72 hours of surgery) have no infectious etiology and resolve spontaneously. The fever may last several days (typically 2-3 days) but the key is when it begins. It can be concluded that early postoperative fever is common and not a specific indicator of infection although fevers that begin later in the postoperative course (POD 5 or later) are much more likely to be infectious.

Since infection is rare, is atelectasis responsible for postoperative fever? Many physicians believe a widespread misconception, also frequently taught in medical training, that atelectasis causes fever after surgery. To the contrary, there is no evidence that atelectasis causes or is associated with fever. In a study of 100 patients after cardiac surgery, atelectasis increased as the incidence of fever decreased over the first

several postoperative days.[14] In another study of 270 patients following abdominal surgery, there was no correlation between fever and atelectasis.[15] However, the misbelief that atelectasis leads to fever may not be harmful after all as physicians encourage incentive spirometry and mobilization rather than ordering unnecessary diagnostic tests. It should be noted that pulmonary complications are higher the closer the surgery is to the diaphragm, so incentive spirometry is important especially in thoracic and abdominal surgeries for reducing postoperative pulmonary complications, but not for reducing fever per se.

If early postoperative fever is not caused by infection or atelectasis, then what is the etiology? A variety of conditions, including trauma and infection, can trigger the release of pyrogenic cytokines (interleukin 1 (IL-1), IL-6, tumor necrosis factor, and interferon-γ) that cause fever.[16] Trauma, including the trauma associated with tissue injury during surgery, stimulates the production of pyrogenic cytokines in the absence of infection.[3] These cytokines act on the hypothalamus leading to the febrile response. Several investigators have found that postoperative IL-6 levels directly correlate with the magnitude of fever after a variety of surgeries including abdominal, thoracic, and vascular surgery. In a study comparing open versus laparoscopic cholecystectomy, fever was more frequent, and levels of pyrogenic cytokines were higher in patients undergoing open cholecystectomy. The authors concluded that the greater surgical trauma associated with open cholecystectomy was more likely to prompt the cytokine response and subsequent fever.[17] Other studies have shown similar results: the more traumatic the surgery, the higher the blood concentration of IL-6 and the higher the risk of postoperative fever.[16,18-20] Consequently, the major cause of postoperative fever is not infection nor atelectasis, but cytokine release as part of the normal inflammatory response to tissue injury during surgery.

Despite strong evidence that postoperative fever is only rarely infectious, physicians often order a "fever work up" typically consisting of blood culture, urinalysis and culture, and CXR to rule out infection. Ordered indiscriminately, these tests have significant costs and are extremely low-yield. Ward and others performed a large single institution, retrospective study evaluating the clinical relevance and cost associated with postoperative fever evaluations in Orthopedic patients undergoing total joint arthroplasty. All 1,100 patients who underwent total knee or total hip arthroplasty were reviewed with postop fever occurring in 161 patients (14.6%). Of these 161 patients, 69 (43%) had diagnostic tests. Thus, 57% of the febrile patients had no workup. It is unclear why some patients were tested while others were not but suggests that a physician's decision to initiate a fever workup in postoperative patients may be random or indiscriminate. Workup for fever included 236 separate tests with urinalysis, urine culture, blood culture, and CXR being the most frequent. Of these tests, 35/236 (14.8%) had positive results. Most of these positive tests were urinalysis (14) or urine cultures (11), but only two patients had both a positive urinalysis and urine culture raising the distinct possibility that these were not indicative of true urinary infections. The largest predictor of a positive workup was the first fever occurring after POD #3 (odds ratio 22.3). Those fevers starting on POD 1 or 2 were not predictive of infection. Fever evaluation led to a change in management in only 9 patients and the majority (6/9) had a prolonged and complicated hospital course with 4 of them requiring intensive care unit admission. Furthermore, the two patients with positive blood cultures both had sepsis physiology and the only patient diagnosed with pneumonia had both shortness of breath and a productive cough. The costs of these workups were substantial with an estimated cost per change in treatment management of greater than $8200 which did not include potential costs of an increased length of stay. The authors concluded that fever is a part of the body's normal response to the tissue injury of surgery and that ordering diagnostic tests based on fever alone without specific symptoms or signs of infection is wasteful and almost always clinically unnecessary.[5]

In another retrospective study, Yoo and colleagues examined postoperative fever on 25,558 total joint replacement patients over a 12-year period. Per their protocol, no fever evaluation was done if patients developed fever before POD 1, but for those patients that developed fever after POD 1, CXR was obtained on all patients looking for pneumonia or atelectasis, and blood culture, urinalysis, and urine culture was obtained only for those patients having fever greater than 102ºF. They found, 46% of the patients developed postoperative fever and over 90% of these patients had a fever work up performed. The yield of these fever workups were very low with only 2.4% having a positive evaluation: including urinalysis (38.7%), urine culture (9.5%), blood culture (7%), and CXR (0.18%) respectively. They diagnosed pulmonary embolism (1.5%), prosthetic joint infection (1.2%), pneumonia (0.16%), UTI (0.16%), and sepsis (0.08%) on these patients. The estimated cost of the over 11,000 negative workups in this study was $4,652,239 with CXR costs comprising $4,613,182 of the total amount. The authors did find a higher rate of infection in those with higher temperatures, multiple fever spikes, and those undergoing revision joint replacement. Also, as in other studies, infection was more likely for delayed fevers (after POD 3 in this study). The authors concluded that this protocolized approach to postoperative fever was very costly and only rarely positive with CXR in particular being extremely high cost and low yield.[21]

Schey and colleagues studied over 500 patients having surgery for benign gynecologic conditions (90% abdominal hysterectomy). Fever occurred in 30% of patients. Around half of the patients had some sort of testing. The yield of testing was extremely low for blood culture (9.7% positive), CXR (14% positive), urinalysis and urine culture (~18% positive for either). Again, it should be emphasized there was zero correlation between urine culture results and urinalysis positivity raising the possibility that these were not true urine infections. As in other studies, it was found that while an extensive fever workup is frequently ordered, it is rarely positive, and that physicians do not seem to discriminate between patients and order workups randomly.[10] Several other

retrospective studies have come to a similar conclusion that the yield of haphazard postoperative fever evaluations is very low and costly.[4,6-8,20]

However, the time that a fever begins after surgery is key as early fevers (those that begin within 48-72 hours or surgery) are rarely infectious although they may last for several days from onset. When fever does begin after 72 hours from surgery, infection is more likely, and a more aggressive approach should be considered. The most commonly identified infections are UTI, wound infection at the surgical site, pneumonia, intravenous catheter-related infection, or clostridium difficile-associated diarrhea.[2]

Multiple studies have evaluated the role of blood cultures specifically in the assessment of postoperative fever. Vijaysegaran et al, analyzed patients over 24 months who had blood cultures taken for fevers between postoperative days 0 to 5 after arthroplasty procedures. They found 141 blood culture sets taken from 101 patients with 123 total instances of fever. Of the 141 sets of blood cultures, only 2 sets returned positive with both growing coagulase-negative staphylococcus identified as a skin contaminant with neither patient requiring antibiotic therapy. Both patients were followed for 10 months and neither developed any evidence of infection. They concluded that the yield of blood cultures is low and rarely contributes to clinical management in postoperative arthroplasty patients and that fever alone is not an indication to perform blood cultures.[22] Swisher and others looked at blood cultures after hysterectomy and found 97% of the cultures to be negative.[23] Many other studies have come to similar conclusions that blood cultures have almost no utility in the assessment of febrile, otherwise asymptomatic patients, in the early postoperative period and that the liberal use of blood cultures in this setting is associated with significant costs.[4,6-7,24] Blood cultures should be reserved for patients with central venous catheters or clinically unstable patients with other signs of sepsis in addition to fever such as tachycardia or hypotension although other acute conditions such as hemorrhage or pulmonary embolus should be considered as well.

All physicians should elicit a history and perform a brief examination and be guided by clinical signs and symptoms in determining which tests to evaluate a patient with postoperative fever. Unfortunately random and indiscriminate testing is the norm. In perhaps the most informative study on the subject of postoperative fever, Schwandt and others tested the implementation of a diagnostic algorithm for postoperative fever that included a bedside history and brief examination to guide testing. This could dramatically decrease unnecessary testing, increase diagnostic yield and reduce costs.[25] They retrospectively evaluated 537 patients who had undergone major gynecological surgery. Of the 537 patients, 211 (~ 40%) had postoperative fever. Of the 211 patients with fever, 194 (92%) had no infection. However, of the febrile patients, urine cultures were ordered in 50%, blood cultures in 30%, and chest radiograph (CXR) in 25%. Thus, ~50% of patients had some sort of test in the evaluation of their fever. Of these multitude of tests, the yield was very low with none of the blood cultures being positive, only 10% of the urine cultures positive, and only 9% of the CXRs positive (of these 4/5 had obvious symptoms of pneumonia). The costs of these low-yield evaluations were substantial and estimated of a 1-year period to be > $26,000.[4,25]

Subsequently, the same group evaluated a postoperative fever algorithm based on symptoms and physical examination with the explicit goal of decreasing random and indiscriminate testing (mainly urine culture, blood culture, and CXR). The algorithm required a bedside assessment including a history and physical examination and a directed, rather than a shotgun approach for ordering tests. They assessed for productive cough, dysuria, abdominal pain, incisional redness/pain and any other new symptoms. If no signs or symptoms of infections were present, no tests were ordered. Of 105 consecutive patients, 28 (27%) had fever and only 3/28 (11% vs ~50% of patients prior to the algorithm) underwent testing based on the algorithm. In total, 4 febrile patients (14%) had documented infections. All 3 patients evaluated according to the algorithm had UTIs (one also had concurrent pneumonia) and one patient evaluated in violation of the algorithm had a UTI. They followed the patients for 30 days after discharge and 2 additional patients developed uncomplicated UTIs. Using this logical and simple algorithm, the yield of positive tests was dramatically increased from less than 10% in the prospective trial to greater than 80% for UTIs and 100% for CXR using the algorithm. The authors showed that the simple intervention of requiring a history and examination prior to testing was feasible, safe, greatly decreased random testing, and the yield of positive tests was greatly increased. They estimated a savings of more than $20,000 per year at their institution.[25] It is clear from this and other studies that a shotgun approach or 'full-fever workup' is wasteful and inappropriate. Instead, physicians should obtain a clinical history and perform a brief bedside physical examination to guide a focused fever workup for an individual patient only if it is indicated. If no signs or symptoms of infection are present, a watchful waiting approach is appropriate.

Since most early postoperative fevers are benign and self-limited, can patients be discharged from the hospital with fever? Traditionally, many physicians believe that patients who have had a fever within 24 hours should not be discharged from the hospital. In the current era of increased efforts for cost containment and earlier discharge after a variety of surgeries, this practice should be challenged. Fanning and Brewer found 95% of patients discharged with postoperative fever within 12 hours of discharge did not have a documented infection at home. They determined it was safe to discharge patients with fever if no signs or symptoms of infection were identified on history or physical examination.[26] In another study of 300 postoperative patients, 45 patients (15%) had a fever within 24 hours of discharge. The presence of fever had no impact on the rate of readmission within 30 days and the authors also concluded that febrile patients who have no signs or symptoms of infection can safely be discharged with same expected rate of readmission as nonfebrile patients.[27] We agree with these conclusions with the

caveat that all patients should be given appropriate follow up instructions should they develop any new symptoms of infection.

While it is clear that infectious causes are rare, postoperative fever should never be ignored and a focused evaluation is always necessary to identify those patients who require further evaluation and/or treatment. Details of the preoperative course, the surgical procedure, nursing information, and a targeted physical examination are imperative. Physical examination should focus on vital signs, heart and lung exam, as well as the surgical site and catheter sites, and the skin for rash. Allergic reactions to drugs or fever after a blood transfusion can occur. Emergent causes of postoperative fever should be evaluated including: necrotizing soft tissue infections, pulmonary embolism, anastomotic leak or abdominal abscess, alcohol withdrawal, adrenal insufficiency, and malignant hyperthermia.[2] A recent review provides a good summary of these conditions.[28] If one of these conditions exists, one would expect other symptoms and signs to be present in addition to fever. As emphasized previously, laboratory and imaging studies should be reserved for patients with specific symptoms or signs of infection and are not indicated as screening tests. Blood cultures have an extremely low yield and should be reserved for high-risk patients such as patients that appear septic on examination (hypotensive), are immunocompromised, have a central venous catheter, or have an obvious wound infection.[4,22-24]

In conclusion, early postoperative fever is common and typically benign and self-limiting, and caused by cytokine release as a result of tissue injury from surgery. No testing is necessary for most patients, but it is critical to determine who may benefit from further evaluation. An extensive and random fever workup is of extremely low yield and wasteful and not advised. Timing is important as fevers that begin within the first 72 hours of surgery are rarely infectious while those beginning after 72 hours from surgery are more likely to be infectious and likely warrant a more aggressive approach. The magnitude of fever is not a reliable marker of infection. A variety of other noninfectious causes of fever are possible and physicians need to evaluate for emergent causes of fever. Certain high-risk patients such as those with central lines, immunocompromised, or mechanically ventilated are at higher risk for infection and require a more aggressive approach. As this is a very common condition, it is critical that hospitalists and surgeons are well educated regarding postoperative fever. Postoperative fevers should never be ignored, however, based on the literature, we conclude that a bedside history and examination should be performed on all patients with postoperative fever prior to ordering tests and that any further evaluation be focused and guided by signs and symptoms.

REFERENCES

1. **Rohatgi N, Loftus P, Grujic O, Cullen M, Hopkins J, Ahuja N**. Surgical Comanagement by Hospitalists Improves Patient Outcomes: A Propensity Score Analysis. *Ann Surg*. 2016 Aug;264(2):275-82. doi: 10.1097/SLA.0000000000001629. PubMed PMID: 26764873.
2. **Pile JC**. Evaluating postoperative fever: a focused approach. *Cleve Clin J Med*. 2006 Mar;73 Suppl 1:S62-6. PubMed PMID: 16570551.
3. **Perlino CA**. Postoperative fever. *Med Clin North Am*. 2001 Sep;85(5):1141-9. PubMed PMID: 11565491.
4. **Fanning J, Neuhoff RA, Brewer JE, Castaneda T, Marcotte MP, Jacobson RL**. Frequency and yield of postoperative fever evaluation. *Infect Dis Obstet Gynecol*. 1998;6(6):252-5. PubMed PMID: 9972487; PubMed Central PMCID: PMC1784817.
5. **Ward DT, Hansen EN, Takemoto SK, Bozic KJ**. Cost and effectiveness of postoperative fever diagnostic evaluation in total joint arthroplasty patients. *J Arthroplasty*. 2010 Sep;25(6 Suppl):43-8. doi: 10.1016/j.arth.2010.03.016. Epub 2010 May 10. PubMed PMID: 20452174.
6. **de la Torre SH, Mandel L, Goff BA**. Evaluation of postoperative fever: usefulness and cost-effectiveness of routine workup. *Am J Obstet Gynecol*. 2003 Jun;188(6):1642-7. PubMed PMID: 12825005.
7. **Freischlag J, Busuttil RW**. The value of postoperative fever evaluation. *Surgery*. 1983 Aug;94(2):358-63. Pub Med PMID: 6410527.
8. **Lyon DS, Jones JL, Sanchez A**. Postoperative febrile morbidity in the benign gynecologic patient. Identification and management. *J Reprod Med*. 2000 Apr;45(4):305-9. PubMed PMID: 10804486.
9. **Shaw JA, Chung R**. Febrile response after knee and hip arthroplasty. *Clin Orthop Relat Res*. 1999 Oct;(367):181-9. PubMed PMID: 10546613.
10. **Schey D, Salom EM, Papadia A, Penalver M**. Extensive fever workup produces low yield in determining infectious etiology. *Am J Obstet Gynecol*. 2005 May;192(5):1729-34. PubMed PMID: 15902186.
11. **Roe CF**. Surgical aspects of fever. *Curr Probl Surg*. 1968 Nov:1-43. PubMed PMID: 5701961.
12. **Summersell PC, Turnbull A, Long G, Diwan A, Macdessi S, Cooke PJ, Li GS**. Temperature trends in total hip arthroplasty: a retrospective study. *J Arthroplasty*. 2003 Jun;18(4):426-9. PubMed PMID: 12820083.
13. **Garibaldi RA, Brodine S, Matsumiya S, Coleman M**. Evidence for the non-infectious etiology of early postoperative fever. *Infect Control*. 1985 Jul;6(7):273-7. Pub Med PMID: 3847403.
14. **Engoren M**. Lack of association between atelectasis and fever. *Chest*. 1995 Jan;107(1):81-4. PubMed PMID: 7813318.
15. **Roberts J, Barnes W, Pennock M, Browne G**. Diagnostic accuracy of fever as a measure of postoperative pulmonary complications. *Heart Lung*. 1988 Mar;17(2):166-70. PubMed PMID: 3350683.
16. **Wortel CH, van Deventer SJ, Aarden LA, Lygidakis NJ, Büller HR, Hoek FJ, Horikx J, ten Cate JW**. Interleukin-6 mediates host defense responses induced by abdominal surgery. *Surgery*. 1993 Sep;114(3):564-70. PubMed PMID: 7690162.

17. **Dauleh MI, Rahman S, Townell NH**. Open versus laparoscopic cholecystectomy: a comparison of post-operative temperature. *J R Coll Surg Edinb*. 1995 Apr; 40(2):116-8. PubMed PMID: 7776273.
18. **Andres BM, Taub DD, Gurkan I, Wenz JF**. Post-operative fever after total knee arthroplasty: the role of cytokines. *Clin Orthop Relat Res*. 2003 Oct;(415):221-31. PubMed PMID: 14612649.
19. **Frank SM, Kluger MJ, Kunkel SL**. Elevated thermos-static setpoint in postoperative patients. *Anesthesiology*. 2000 Dec;93(6):1426-31. PubMed PMID: 11149437.
20. **Lesperance R, Lehman R, Lesperance K, Cronk D, Martin M**. Early postoperative fever and the "routine" fever work-up: results of a prospective study. *J Surg Res*. 2011 Nov;171(1):245-50. doi: 10.1016/j.jss.2010.03.009. Epub 2010 May 11. PubMed PMID: 20655062.
21. **Yoo JH, Restrepo C, Chen AF, Parvizi J**. Routine Workup of Postoperative Pyrexia Following Total Joint Arthroplasty Is Only Necessary in Select Circumstances. *J Arthroplasty*. 2017 Feb;32(2):520-525. doi: 10.1016/j.arth. 2016.09.025. Epub 2016 Sep 28. PubMed PMID: 27810308.
22. **Vijaysegaran P, Coulter SA, Coulter C, Crawford RW**. Blood cultures for assessment of postoperative fever in arthroplasty patients. *J Arthroplasty*. 2012 Mar;27(3):375-7. doi: 10.1016/j.arth.2011.05.025. Epub 2011 Jul 28. PubMed PMID: 21802251.
23. **Swisher ED, Kahleifeh B, Pohl JF**. Blood cultures in febrile patients after hysterectomy. Cost-effectiveness. *J Reprod Med*. 1997 Sep;42(9):547-50. PubMed PMID: 9336749.
24. **Theuer CP, Bongard FS, Klein SR**. Are blood cultures effective in the evaluation of fever in perioperative patients? *Am J Surg*. 1991 Dec;162(6):615-8; discussion 618-9. PubMed PMID: 1670237.
25. **Schwandt A, Andrews SJ, Fanning J**. Prospective analysis of a fever evaluation algorithm after major gy-necologic surgery. *Am J Obstet Gynecol*. 2001 May; 184(6):1066-7. PubMed PMID: 11349158.
26. **Fanning J, Brewer J**. Delay of hospital discharge sec-ondary to postoperative fever--is it necessary? *J Am Osteopath Assoc*. 2002 Dec;102(12):660-1. PubMed PMID: 12501983.
27. **Barone JE**. Does fever at the time of discharge have any impact on the incidence of readmission? *Am Surg*. 2008 Dec;74(12):1151-3. PubMed PMID: 19097527.
28. **Narayan M, Medinilla SP**. Fever in the postoperative patient. *Emerg Med Clin North Am*. 2013 Nov;31(4):1045-58. doi: 10.1016/j.emc.2013.07.011. Review. PubMed PMID: 24176478.

Submitted October 10, 2018