# **Postoperative Fever**

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### Abstract

Fever is one of the most common and treatable cause of morbidity. Though mostly benign, it can sometimes lead to a fulminant and malignant course. Postoperative fever has greatly perplexed the treating physician due to its varied etiologies. If not timely evaluated, it can lead to waste of health resources and increased health care cost. In the present article, we will be discussing the important causes of fever and their treatment.

Keywords: Postoperative fever, Pyrexia, Management.

### Introduction

Pyrexia is one of the common causes of disability, perplexing to the medical professionals due to its varied etiologies and pathophysiologies.<sup>(1)</sup> Fever following surgery has been equally baffling to the surgeons as well as anaesthesiologists. Besides searching for the overt or hidden source of fever, a big question arises whether to treat the fever or not, and answer to which is likewise puzzling.<sup>(2,3,4)</sup> In-order to further enhance the knowledge regarding postoperative fever, we did the literature search, using such search engines like PubMed, Google Scholar, and Medline, besides exploring books at our disposal. The relevant articles in English language only were selected.

We will be comprehensively enumerating the common causes of postoperative fever, followed by their respective pathophysiology, before embarking on the approach to further work-up such patients.

## Causes

Most postoperative fevers that develop within the first 48 hours after surgery are benign and self-limiting.<sup>(1-3)</sup> Fever that a develops after the 2 days following surgery is more likely to have infectious cause; but noninfectious causes that require further evaluation and treatment must be considered. When evaluating postoperative fever, a helpful pneumonic 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).<sup>(2)</sup>

Classifying further, the causes of fever can be grouped according to the time when it first manifested. Hence they can be divided into intraoperative causes of fever (extending into the postoperative period), fever initiating less than 24 hours postoperative, postoperative day 1-2 (24-48 h), and postoperative day  $3-7.^{(5)}$ 

**Intraoperative:** endocrine disturbances (Addisonian crisis, thyroid storm, or pheochromocytoma),

transfusion reaction, drug hypersensitivity, preexisting infection, intraoperative manipulation of purulent material, or malignant hyperthermia.

**Less than 24 hours:** Fever is mostly due to normal inflammatory response to surgery. Additional causes include atelectasis or necrotizing wound infection. Later though rare, is caused by beta-hemolytic streptococci or clostridia.<sup>(5)</sup> Atelectasis is now a debatable cause of fever.<sup>(2)</sup>

**Postoperative day 1-2 (24-48 h):** Wound infection, thrombophlebitis, and central venous line sepsis or drugs.<sup>(5)</sup>

**Postoperative day 3-7:** Mostly due to infectious causes. Risk factors include diabetes, immune suppression, obesity, catheterization, and prolonged ventilation.<sup>(5)</sup>

Fever is a complex physiologic and behavioral response to infection and injury, the key feature of which is a temporary resetting of body's thermostatic set point that causes increase in core temperature.<sup>(4)</sup> Pyrogenic cytokines (interleukin 1 and 6, tumour necrosis factor, interferon- $\gamma$ ), released due to variety of conditions, especially trauma and infections, act on the anterior hypothalamus, causing the release of prostaglandins, which appear to mediate the febrile response.<sup>(2)</sup>

Skin temperature normally rises and falls with the temperature of patient's surroundings. However the temperature of deep body tissues, that is, the core temperature, remains relatively constant at  $98.0^{\circ}$ F to  $98.6^{\circ}$ F ( $37^{\circ}$ C).<sup>(6)</sup> In fact, core temperature normally remains between  $97^{\circ}$  F and  $100^{\circ}$ F, even when environmental temperatures fluctuates from as low as  $55^{\circ}$ F to as high as  $130^{\circ}$ F. This is due to remarkable thermoregulatory system, which tightly regulates the body temperature.<sup>(6,7)</sup> Hence unlike core temperature which is tightly regulated, skin temperature varies widely as a function of environmental exposure.<sup>(7)</sup>

Postoperative fever is very common. However, published incidence ranges widely (from 14% to 91%). In the vast majority of studies the incidence of infection in patients with postoperative fever is less than 10%, indicating that fever is not the specific marker of infection in this setting.<sup>(2)</sup> The majority of the episodes of postoperative fever occurred early (within 48 hours following surgery). These patients with unexplained fever were young, had less severe underlying disease and underwent less extensive surgeries than patients who subsequently developed infections.<sup>(3)</sup>

Wound infection is a common and serious postoperative complication. In patients undergoing colon surgery, there is a 9% - 27% risk of wound infection.<sup>(8)</sup> It can prolong hospitalization by 5 to 20 days and substantially increase the medical costs. Risk of wound infection depends on several factors such as length of surgery and underlying medical problem. Intraoperative hypothermia increases patient's susceptibility to wound infection by causing vasoconstriction and impaired immunity. Vasoconstriction decreases partial pressure of oxygen in tissues which lowers resistance to infection. Oxygen is also critical substrate for tissue repair and wound healing.(8,9)

Besides the inflammatory and infectious causes, other causes enumerated above can be easily diagnosed. Some are clinically diagnosed by exclusion, especially causes like malignant hyperthermia and thyroid storm.<sup>(5,10,11)</sup> Similarly drug fever is the diagnosis of exclusion. A case of a patient developing fever after an intake of Piperacillin / Tazobactam has been described. Patient developed fever after the intake of these antibiotics for 3 days. Fever lasted for 2 weeks and came down normal 4 days after their cessation. Eosinophil count, erythrocyte sedimentation rate (ESR) and C-reactive proteins were increased. However, history, X-ray chest, blood cultures, physical examination, and urinalysis revealed no evidence of fever.<sup>(12)</sup>

Incorrect blood component transfusion resulting in hemolytic transfusion reactions and transfusion related acute lung injury (TRALI) remain major sources of morbidity and mortality. Febrile transfusion reactions are defined as 1° Celsius increase in temperature during or within 3 hours of transfusion that cannot be explained by sepsis or hemolytic transfusion reaction. Reforms in transfusion medicine has resulted in reductions in infectious complications of transfusion, however awareness and reporting of noninfectious complications of transfusion have increased. The number of febrile reaction is significantly reduced by leukoreduction of erythrocyte units.<sup>(13)</sup>

Bacterial infections after spinal and epidural anaesthesia are rare events; hence they have not been included in the list. It has been estimated that epidural abscesses develop in no more than 1 of 506,000 patients receiving epidural anaesthesia for delivery. Similarly, bacterial meningitis following spinal anaesthesia is rare, with incidence being less than 1 for every 5000 procedures.<sup>(14)</sup> A study showed that although 35% of the continuous epidural catheters were culture positive

after being in place for  $3\pm 1$  days in children, none of the children demonstrated serious systemic infection (meningitis, epidural abscess, or systemic sepsis).<sup>(15)</sup>

Atelectasis following surgery requires special mention. Kane J. M. et.al. (2011) observed that although postoperative fever and atelectasis are common after pediatric cardiac surgery, there was no association between the two.<sup>(16)</sup> Other authors have also found sparse evidence supporting the concept that atelectasis is associated with early postoperative fever. More so, there is no such evidence that atelectasis causes fever at all.<sup>(17)</sup>

## Approach to a patient with Fever

Although fever has been recognized as a component of acute-phase response to infection, risk: benefit relationship of fever in infected host has been an ongoing source of controversy.<sup>(4)</sup>

Early postoperative fever is a common event and rarely caused by infection. A brief bedside evaluation has a highest yield for determining the fever etiology.<sup>(18)</sup> According to Garibaldi et al, patients with early postoperative fever should be evaluated to identify any obvious source of infection. If no focus is identified, empiric antibiotic therapy should not be initiated nor should prophylactic antibiotics be extended for prolonged durations. Unexplained fever will resolve in time without specific therapeutic interventions.<sup>(3)</sup>

It has been observed that fever as a general hallmark of inflammation was frequent with an incidence of 19% in orthopedic patients, despite the fact that all patients were under antipyretic medications. In majority fever was no proof of SSI (surgical site infection) or of remote infection. Moreover, occurrence of postoperative fever does not seem to be linked to a worse outcome in these kinds of patients.<sup>(19)</sup>

However if risk factors for infection are present preoperatively or intra-operatively, then empiric treatment can be timely started, before waiting for the results of urine and blood culture. Yang et al, in their study on patient undergoing percutaneous nephrolithotomy (PCNL), observed that preoperative urine white blood corpuscles count and stone size were risk factors for both fever and systemic inflammatory response syndrome (SIRS).<sup>(20)</sup>

Even though fever may cause diagnostic confusion (central fever vs infectious), maintenance of normothermia appears to be desirable therapeutic goal in managing patients with damaged or at-risk brain tissue.<sup>(21)</sup> Laboratory evidence is quite clear regarding the adverse effects of fever in terms not only of functional outcomes, but also histological and neurochemical injury in these cases.<sup>(21)</sup>

Necrotizing wound infection should be immediately treated. These wounds are especially painful. Treatment includes emergent operative debridement and antibiotics. Treatment of fever in noninfected patient should focus on returning the thermoregulatory set-point to normal with antipyretics.<sup>(5)</sup>

#### Conclusion

Postoperative fever is a common entity. If occurring in the immediate postoperative period, most of the time it is non-infective. However, every fever demands its due evaluation. Overall workup of fevers in postoperative patient should be guided by a thorough history and physical examination. Asymptomatic and low risk individuals should be observed and treated with antipyretics. For high risk patients, urine, blood and sputum cultures should be obtained along with X-ray chest and other laboratory investigations.<sup>(5,18,19)</sup>

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