

Postoperative fever

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Abstract

Postoperative fever is one of the most common problems seen in the postoperative ward. Most cases of fever immediately following surgery are self-limiting. The appearance of postoperative fever is not limited to specific types of surgery. Fever can occur immediately after surgery and seen to be related directly to the operation or may occur sometime after the surgery as a result of an infection at the surgical site or infections that involve organs distant from the surgery. Therefore, during 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.

Key words: Postoperative, fever

Fever

Fever is a rise of the normal core temperature of an individual that exceeds the normal daily variation and occurs in connection with an increase in the hypothalamic set point.

According to studies of healthy individuals 18 to 40 years of age, the mean oral temperature is $36.8^{\circ} \pm 0.4^{\circ}\text{C}$ ($98.2^{\circ} \pm 0.7^{\circ}\text{F}$) with low levels at 6 am and higher levels between 4 to 6 pm. The maximum oral temperature is 37.2°C (98.9°F) at 6am and 37.7°C (99.9°F) at 4 pm; these values define the 99th percentile for healthy individuals. In light of these studies, an am temperature of greater than 37.2°C (98.9°F) or a pm temperature of greater than 37.7°C (99.9°F) would define a fever. However, there is no coding definition or uniform clinical definition of a significant fever. Temperatures exceeding 38°C (100.4°F) and persisting for more than two postoperative days are generally considered to be

clinically significant.^[1]

Measurement of body temperature

Temperature taken orally is about 0.5°C higher than that taken in the axilla or is about 0.5°C below than that taken rectally. Rectal temperature is considered core. The lower oral readings are probably attributable to mouth breathing, which is a particularly important factor in patients with respiratory infections and rapid breathing. Lower oesophageal temperature closely reflects core temperature.^[2]

Incidence

The incidence of postoperative fever is remarkably high. However, published incidence rates range widely (from 14% to 91%)^[3] depending on how fever was defined and the patient population of the study. Though fever is common, infection is found as the cause in less than one-half of febrile patients. Studies have determined that the incidence of postoperative fever in patients undergoing various surgical procedures is not a specific marker of infection in those settings [Table 1].

The overall sense from Table 1 is that, postoperative fever is more likely to be due to the inflammatory

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Table 1: Studies of causes and incidence of postoperative fever

Patient groups studied	Cause of fever	Total %
Major gynaecologic surgery ^[4]	Without infection	180
	With infection	
Open versus laparoscopic cholecystectomy ^[5]	Without infection (open)	55
	Without infection (lap. chole.)	20
	With infection	0
Orthopedic surgery ^[6]	Without infection	100
	With infection	0
Tonsillectomy ^[7]	Without infection	54
	With infection	0
Major abdominal surgery ^[8]	With infection	43
	With focus of infection (pulmonary, wound, urinary)	36

response to the trauma of surgery and not a response to the infection. The greater surgical trauma, (e.g., open cholecystectomy versus laparoscopic cholecystectomy) the more likely is postoperative fever to occur without the occurrence of infection. The general consensus of workers in this field is that postoperative infection as a cause of fever after surgery is diagnosed best by specific symptoms and signs attributable to the infection.

Although the trauma of surgery and infections are the two most common causes of fever, there are other less common but important causes, including medications, blood transfusion, deep venous thrombosis and pulmonary embolism, myocardial infarction and pancreatitis. Medications are a frequent cause of fever. Probably the most common medications causing fever are antibiotics, which can cause great confusion. Another uncommon but important cause of fever in the postoperative period is alcohol withdrawal. Patients who present with a fever and delirium postoperatively must have alcohol withdrawal in differential diagnosis because appropriate treatment can reduce the significant morbidity and mortality of this clinical problem.

It has been classical teaching that pulmonary atelectasis after abdominal surgery is a common cause of postoperative fever. A study conducted to determine the relation of postoperative fever and atelectasis found, however, no relation between atelectasis and fever postoperatively.^[9] The daily incidence of atelectasis increased after surgery, whereas the incidence of fever decreased.

Pathophysiology

Fever may be a transient and trivial sign, which resolves

rapidly with no treatment (e.g., the immediate mild fever seen in many postoperative patients). It may, however, be a sign of serious significance presaging the onset of systemic inflammatory response syndrome (SIRS) and multiorgan dysfunction syndrome. Clearly, it is important to be able to identify which patients fall into the former category and which into the later.

Infection may cause fever, as part of the inflammatory response of the host to invasion by microorganisms and the production of toxins by these organisms. Gram-negative bacilli have lipopolysaccharides (endotoxins) as structures in the cell wall that act as pyrogens (the term pyrogen is used to describe any substance that causes fever). Gram-positive cocci produce exotoxins, which are excreted from the bacteria and which are pyrogens. The pyrogens produced from either gram-negative or gram-positive bacteria are considered as exogenous pyrogens (i.e., coming from sources other than the host). Exogenous pyrogens stimulate monocytes and macrophages of the infected host to produce substances called pyrogens or pyrogenic cytokines. Pyrogenic cytokines have various effects on stimulating or controlling the inflammatory response and fever. Cytokines act as intercellular mediators and messengers controlling the host response to injury and infection.^[10] The pyrogenic or proinflammatory cytokines, interleukin 1 (IL-1), is a primary activator of the febrile response to tissue injury and the local inflammatory response to infection.^[11]

Trauma, including the trauma associated with surgery, elicits the production of pyrogenic cytokines in the absence of infection. Fever may occur. The production of host endogenous pyrogens or pyrogenic cytokines, is the final common pathway through which fever occurs from such diverse causes as infection and trauma in the absence of infection [Figure 1].

Normal thermoregulation

The control of body temperature depends upon the following components:

1. Temperature receptors
 - A. Peripheral (Ad and C fibers)
 - B. Central (hypothalamus)
 - C. Other (great veins, spinal cord, abdominal viscera)
2. Integration and control

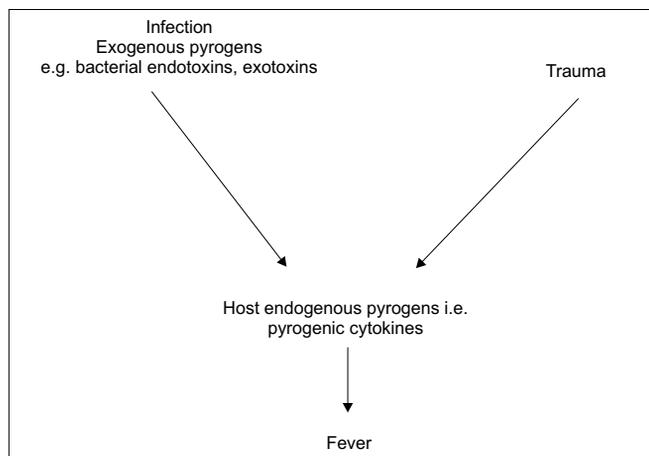


Figure 1: Pathways to the production of fever

Setting of body temperature and detection of core temperature in the preoptic nucleus is done by hypothalamus. Moreover, posterior hypothalamus compares the core and peripheral temperatures with the set temperature. Furthermore, it induces appropriate actions to restore the body temperature to the set temperature. When the body temperature is higher than the set temperature then, the mechanism of heat loss will be controlled by the anterior hypothalamus. However, the posterior hypothalamus controls the mechanisms for heat gain.

Elevation of the hypothalamic set point by cytokines^[2]

During fever, levels of prostaglandin E₂ (PGE₂) are elevated in hypothalamic tissue and the third cerebral ventricle. The concentrations of PGE₂ are highest near the circumventricular vascular organs (organum vasculosum of lamina terminalis) – networks of enlarged capillaries surrounding the hypothalamic regulatory centers. Destruction of these organs reduces the ability of pyrogens to produce fever.

From the results of the animal studies, it appeared that both exogenous and endogenous pyrogens interact with the endothelium of these capillaries and that this interaction is the first step in initiating fever, i.e. in raising the set point to febrile levels.

SIRS and sepsis

SIRS is a term applied to the febrile inflammatory process that occurs after surgery. *SIRS* can have either infectious or noninfectious causes.^[12]

Sepsis is the term used to describe the systemic

inflammatory response resulting from infection.^[12]

These two terms are used frequently to describe fever occurring after surgery, which may be due solely to cytokine activation from surgery itself or due to an infection complicating surgery.

Defense mechanisms of the host, alteration by surgery and increased morbidity caused by infection.

Increased incidence of infection after surgery may depend upon the increased production of pro-inflammatory cytokines and other anti-inflammatory cytokines. The greater the trauma associated with the surgical procedure (e.g., open cholecystectomy versus laparoscopic cholecystectomy) it is more likely to activate the cytokine response with subsequent fever and also greater effect is found on the type 1 and type 2 (Th-1, Th-2) helper T lymphocytes. Th-1 cells are involved with cell-mediated immunity and produce IL-2, whereas Th-2 cells are involved with antibody-mediated immunity and produce IL-10.^[13]

Immune systems and local defense mechanisms are also affected in addition to these systemic effects due to anaesthesia and surgery.

Evaluating postoperative infection

Infection is more likely to be present in a patient with a fever that develops after the first two days following surgery.^[14]

Most common infections occurring after surgery:

1. Wound infections
2. Urinary tract infections
3. Postoperative pneumonias
4. Intravenous catheter-related infections
5. Intra-abdominal infection
6. Sinusitis
7. Prosthesis infection

Wound infections

The surgical incision interrupts the integrity of the defense mechanism of skin. Surgical wound infection depends on:

- a) The type of surgery performed (e.g. cholecystectomy versus colon resection)
- b) The length of operative procedure
- c) Whether appropriate prophylactic antibiotics are given

and given at the correct time.

Furthermore, condition of the patient and coexisting diseases of the patient have an effect on the likelihood of postoperative wound infection. Factors increasing the risk of infection include: diabetes, obesity, length of preoperative stay, prolonged postoperative ventilation, underlying chronic bronchitis.

Urinary tract infection

More likely to occur in women and in patients who are in need of prolonged catheterization.

Postoperative pneumonia

A. Mechanically ventilated patients are at high risks because:

- 1) tracheal intubation bypasses normal defense mechanisms, such as cough and the patient may be more likely to aspirate bacteria from the oropharynx.
- 2) effect of anaesthesia on the ciliary action of the tracheobronchial tree with decreased ability of the cilia to move material to the oropharynx.

B. Age

C. Presence of chronic lung disease

D. Chest surgery

Intravenous catheter- related infections

Can be caused either by peripheral catheters (usually leading to thrombophlebitis or cellulitis) or by central catheters (usually causing bloodstream infection).

Intra-abdominal infection

Especially seen following abdominal or pelvic surgery.

Sinusitis

Typically observed in patients who undergo nasogastric intubation for long periods.

Prosthesis infection

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

Clinical correlation

The timing of fever relative to the postoperative day (POD) will indicate the most likely cause. The *five W's of postoperative fever* – *Wind, Water, Walking, Wound and Wonder drugs*- as a useful memory tool could help a physician when he is following patients after surgery.^[15,16]

POD 1-2: *Wind: Atelectasis (without air) often cause*

fever. Reasons include being on a ventilator, inadequate sighs during surgery and (in the general surgery patient) incisional pain on deep breathing. This is treated with incentive spirometry because there is evidence that deep inspiration prevents atelectasis better than just coughing.

POD 3-5: *Water: Urinary tract infections (UTIs) are common here. Foley catheters are sometimes still in place.*

POD 4-6: *Walking: Deep venous thrombosis can occur. This is more of a problem in patients undergoing pelvic orthopedic or general surgery than in head and neck surgery. Subcutaneous low dose heparin and venous compression devices reduce the incidence of thromboembolization. Walking the patient on POD1 is the best way to prevent this complication.*

POD 5-7: *Wound: Most wound infections occur during this period. Preoperative antibiotics are important to prevent or reduce the risk of infection in head and neck surgery that crosses mucosal linings.*

POD 7+: *Wonder drugs: Drugs can cause fevers. (Note that in obstetrics and gynaecology, this W is "womb" and it precedes "Wonder drugs").*

Noninfectious causes must be considered with infectious causes in the postoperative patient because fever resulting from infection and trauma (i.e., surgery) are produced through the release of similar cytokines. However, fever in patients without evidence of infection occurred closer to the surgical procedure and lasted for a shorter time than did fever resulting from infection. Therefore, empiric antibiotic therapy may not be necessary in these cases, when the fevers are not associated with infections.

Assessment of The Pyrexial Patient^[2,17]

Fever should never be ignored. Appropriate evaluation of early postoperative fever includes a careful history, a targeted physical examination and additional studies if indicated.

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.

Nursing information

Often important, such as if the patient has diarrhea or is coughing.

History

- A previous history of pyrexial illness is important especially for urinary tract infections and also for thoracic infections, e.g. empyema.
- A history of pyrexia related to operation and especially a family history of malignant hyperpyrexia is vital.^[18]
- Pyrexial symptoms alone with no other symptoms may be feature of an endocrine anomaly, e.g. hyperthyroidism.
- The exact nature of the prosthetic materials and/or implanted devices should be ascertained.
- Attention should be directed to the
 - use of tobacco, intravenous drugs or alcohol
 - prior transfusions
 - drug allergies or hypersensitivities.

Physical examination

A meticulous physical examination should be done on a regular basis. All the vital signs are relevant. The temperature may be taken orally or rectally, but the site used should be consistent.

A careful search for the infective cause should be made:

- Skin and subcutaneous tissues for abscess, necrotising fasciitis and gas gangrene
- Abdomen, for the features of peritonitis, localized infection and subphrenic or pelvic abscess
- Chest to be ausculted for pneumonia, effusions and empyema
- Urinary tract: Tenderness over the kidneys, bladder and prostate may be present
- Pelvic organs: Lower abdominal tenderness, tenderness on rectal and vaginal examination and vaginal discharge may be present
- Bone: In the early stages there may be tenderness only over the infected area but with progression there will be swelling, empyema and ultimately discharge of pus
- Central nervous system: Neck stiffness, photophobia

and altered consciousness are important clinical features

Investigation

The tempo and complexity of the workup will depend on the pace of the illness, diagnostic considerations and the immune status of the host. Infective causes of pyrexia should be differentiated from non-infective causes by the history and clinical examinations. However, presence of a noninfective cause does not necessarily exclude an infective cause, e.g. patients with alcohol withdrawal may also have pneumonia. Identification of a causative organism and its antibiotic sensitivities should always be attempted. It is important to sample if possible before starting antibiotics to prevent interference with the culture.

Bacteriological assessment

Includes blood culture, sputum, pleural or peritoneal aspirate, urine, skin and wound swab of discharge or needle aspiration, stool, cerebrospinal fluid (by lumbar puncture), intravascular catheters, aspiration of tissue fluid from spreading edge of cellulitis, should be cultured on removal.

Hematological tests

In the presence of infection, polymorphonuclear leucocyte count is usually raised. However, in severe infections or in the immunosuppressed or malnourished patient, the leucocyte count may be normal or reduced.

Platelet count is usually elevated as part of the normal response to stress. However, it may be markedly reduced if disseminated intravascular coagulation has developed.

In the later stages of infection or when the patient is resuscitated with a large volume of colloid, there will be reduced hemoglobin concentration.

Coagulation screen is essential for patients with severe sepsis and immunological tests are required in the patients with transfusion reactions.

Serum biochemistry

1. Urea, electrolytes and creatinine to detect renal failure as a common complication of severe sepsis
2. Liver function tests may be severely deranged in severe sepsis

3. Glucose- presence of hyperglycemia may complicate sepsis
4. Arterial blood gases give an indication of acid/base balance. Metabolic acidosis is the earliest change in developing septic shock
5. Myocardial enzymes
6. Serum amylase

Imaging

1. Chest X-ray- indicated for identification of areas of occult infections, e.g. infected arterial or cardiac prosthesis
2. Ultrasound-Indicated for identification of venous thrombosis
3. CT and MRI scanning required for:
 - a) identification of intra-abdominal and pleural abscess;
 - b) assessment of infected joints;
 - c) assessment of kidneys.
4. Bone scan-defining intrathoracic infection and respiratory complications of systemic infection.

ECG and Echo cardiography

For the assessments of myocardial ischaemia, mechanical anomalies of cardiac function and the presence of intracardiac thrombosis.

Outcome of diagnostic efforts

In most cases of fever, either the patient recovers spontaneously or the history, physical examination and initial screening laboratory studies lead to a diagnosis. When fever continues for two to three weeks, during which time, repeat physical examinations and laboratory tests are unrevealing, the patient is provisionally diagnosed as having fever of unknown origin.

Usefulness and cost-effectiveness of routine work-up^[19]

Majority of fever work-ups were of low clinical yield and added moderate cost. Significant infection is associated with surgery for malignancy, bowel resection, number of febrile days, higher fever and moderately increased white blood cell count. Only patients with these characteristics are most likely to benefit from laboratory and/or radiographic workup of fever.

Treatment

Treatment of the noninfective cause of pyrexia

The routine use of antipyretics given automatically as

“standing”, “routine” or “prn” orders to treat low-grade fevers in adult patients is entirely unacceptable. This practice masks not only fever but also other important clinical indicators of a patient’s course.

The objectives in treating fever are:

1. To reduce the elevated hypothalamic set point
2. To facilitate heat loss
3. To reduce the demand for oxygen (i.e., for every increase of 1°C over 37°C, there is a 13% increase in oxygen consumption)
4. Prevent to aggravate preexisting cardiac, cerebrovascular or pulmonary insufficiency
5. To prevent seizures in children with a history of febrile or non-febrile seizure

Antipyretics

Aspirin and paracetamol interfere with the production of prostaglandins via the inhibition of cyclo-oxygenase. Prostaglandin is the central messenger in the production of pyrexia, which help to lower the hypothalamic set point. However, antipyretics are indicated if the patient’s temperature approaches more than 39°C. Reducing fever with antipyretics also reduces systemic symptoms of headache, myalgias and arthralgias.^[2]

Oral aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) effectively reduce fever but can adversely affect platelets and gastrointestinal tract.^[20] Therefore, paracetamol is preferred to all of these agents as an antipyretic. In children, paracetamol must be used because aspirin increases the risk of Reye’s syndrome. If the patient cannot take oral antipyretics, parenteral preparations of NSAIDs and rectal suppository preparations of various antipyretics can be used.^[2]

Approach to the treatment of infection as the cause of postoperative fever

The treatment of infection in surgical patients can be described as under:

1. Resuscitation and control of systemic infection
2. Identification of the source of infection
3. Elimination of the source

Antibiotics

The appropriate antibiotic for the sensitives of the cultured organisms should be used. However, in the absence of bacteriological information therapy should

be given on a 'best guess' basis.

The dose of antibiotic depends on age, weight, renal function, allergies and severity of infection as well as toxicity of the antibiotic. Life-threatening infections require intravenous therapy. The duration of therapy should be long enough to cure the infection but should not be unduly prolonged to prevent the risk of developments of resistant organisms.

Fluid resuscitation^[21]

Hypovolaemia is an early feature of developing septic shock and SIRS bacteraemia. Vigorous fluid replacement may abort the progress to the 'cold' shock. Therefore, expansion of plasma volume is required with the usage of gelatine solutions or starch solutions in addition to crystalloid.

Inotropes and vasoactive agents

Systemic infections may have a myocardial depressant effect. Thus, inotropic support may be required with adrenaline, dobutamine or dopexamine. Dopamine may be indicated to produce renal vasodilatation in cases of diminished renal function.

Respiratory support

Seriously ill, infected patients have deranged gas exchange and require oxygen therapy.

Surgical therapy

Elimination of a source of infection is one of the main principles of the management of surgical infections.

- Drainage of pus
- Excision of diseased organ
- Correction of lesions causing obstruction of hollow organs, elimination of spaces in which infection may develop.

Summary

Postoperative fever should alert the caregiver to the possibility of an infection complicating the recovery of the patient, but the presence of fever is not a reliable indicator of the presence of infection and the absence of fever does not guarantee that the postoperative patient is infection-free. The outcome for a patient with postoperative fever is dependent on the cause. Therefore, postoperative fever should be evaluated with a focused approach rather than in "shotgun" fashion. Noninfective

causes generally have a better outlook than infective causes. The outcome for the infected patient is dependent on the rapid identification of the cause, appropriate resuscitation, antibiotic treatment and appropriate surgery to eliminate the source.

For pediatric oncology patients who are often immunocompromized, a postoperative fever may indicate an infection, which can lead to significant complications if not treated promptly. Although a full septic work-up may be unnecessary, additional investigations such as blood cultures may be warranted and an antibiotic therapy should be considered for some or all febrile postoperative cancer patients.^[22]

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