Fever in Acute and Critical Care
A Diagnostic Approach

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ABSTRACT
Determining the underlying cause of a fever can be a daunting task. Multiple reasons have been found for a patient to have a fever, but the use of an organized approach will assist clinicians in reaching a correct diagnosis. The first step in this process is a complete assessment, including a thorough physical assessment and an evaluation of the history of present illness as well as a detailed review of all the patient’s medications. Infection should always be a primary consideration for the cause of a fever. Evaluating each body system can match symptoms with a possible cause for fever, and proper testing and imaging can be pursued. Noninfectious causes of fever need to be included in the differential diagnostic process. This article provides an analytic approach to fever in adult patients in the acute and critical care environment.

Key words: cytokines, fever, inflammation, intensive care unit, temperature

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The thermal set point is thought to be controlled within a very narrow range. Endogenous and exogenous pyrogens can alter this set point. Endogenous pyrogens are cytokines released by phagocytic leukocytes into the blood as a result of various stimuli. They either cross the blood-brain barrier or cause release of other mediators, in particular prostaglandin E₂, which interact with neuron receptors in the preoptic area. This interaction causes a change in firing rate and leads to an elevation of the thermal set point. Exogenous pyrogens are substances that are released by microbes and are thought to trigger macrophages to produce endogenous pyrogens, resulting in the same end point of increasing the set point. The signaling system with these pyrogens is complex because of the large number and types of cells involved. The most common pyrogenic cytokines include interleukin 1 (IL-1), tumor necrosis factor α, IL-6, and interferon γ. These cytokines are thought to interact with the receptors on the preoptic area neurons, liberating arachidonic acid and ultimately releasing prostaglandin E₂. Thus, the neuron firing rate is changed and the set point is increased.

Experts theorize that the febrile response is an adaptive mechanism that has allowed humans to survive. The acute phase response is considered part of the febrile response. The same cytokines that reset the thermal set point will cause other physiological reactions, including somnolence, anorexia, change in plasma protein synthesis, and altered synthesis of multiple hormones (eg, corticotropin-releasing hormone, glucagon, insulin, hydrocortisone, aldosterone, and many others). Many positive and negative acute phase proteins (APPs) are considered a major part of the acute phase response. Some of these proteins play an active role in the inflammatory process and tissue repair. C-reactive protein is a positive APP that increases in the acute phase response to bind with phospholipid components of pathogenic bacteria as well as necrotic host cells, activating the complement system to eliminate these cells. Albumin is a negative APP that decreases with inflammation and is thought to allow for greater production of positive APPs. Some endogenous cryogens also are cytokines that have antipyretic activity to help maintain the upper limit for temperature resetting. Examples of these cryogens are arginine vasopressin and α-melanocyte-stimulating hormone, whose cytokine activity assists in maintaining the upper temperature limit of 41.0°C (105.8°F).

The acute phase response is a complex series of reactions and counteractions in the maintenance of homeostasis.

**Definition of Fever**

Variation exists in the literature about quantitative values to define fever. Temperature values

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**Figure 1. Causes of fever.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>Head/neck, chest, abdomen/pelvis, postoperative (&gt; 96 hours)</td>
</tr>
<tr>
<td>Noninfectious</td>
<td>Drug, transfusion reaction, endocrine, DVT, postoperative (&lt; 96 hours)</td>
</tr>
<tr>
<td>Other inflammatory</td>
<td>Other inflammatory/system, neuro (CVA, TBI, seizure), cardiac (MI, pericarditis), pulmonary (PE, ARDS), GI (pancreatitis, acaulculus cholecystitis, ischemic colitis)</td>
</tr>
</tbody>
</table>

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**Abbreviations:** ARDS, acute respiratory distress syndrome; CVA, cerebral vascular accident; DVT, deep vein thrombosis; GI, gastrointestinal; MI, myocardial infarction; PE, pulmonary embolism; TBI, traumatic brain injury.
range from a single measurement of 38.0°C (100.4°F) to 2 consecutive elevations of greater than 38.3°C (101.0°F), with other qualifiers in the description including route of measurement, immunological state, and rate of temperature elevation. These variations are justified when considering the complexity of the concept of fever. Variables that must be accounted for include age, sex, immunological status, circadian rhythms, and environmental factors as well as pharmacological and external interventions, that is, extracorporeal membrane oxygenation and continuous renal replacement therapy. To provide a general standard for clinical practice, the American College of Critical Care Medicine and the Infectious Diseases Society of America (IDSA) have published and updated guidelines for evaluation of new fever in critically ill adult patients. Patients who have a temperature of 38.3°C (100.9°F) or higher are considered febrile, and an investigation for the cause of the temperature elevation should be pursued.

Patients who are immunocompromised deserve special consideration, because their immunological system is abnormal and is unable to manifest a normal febrile response. Hughes et al recommend that patients with neutropenia are febrile when a temperature elevation higher than 38°C (100.4°F) is present for more than 1 hour. Although patients with neutropenia are obviously immunologically compromised, a high prevalence of unrecognized immune dysfunction is present in critically ill patients.

Patients who have recently received or are currently being treated with steroids or those with Cushing syndrome with high levels of cortisol are examples of patients with atypical immune suppression. The elderly are another population that can be included in this category. A temperature of less than 36.0°C (96.8°F) without a known cause for the decrease also should be a trigger to investigate the cause.

Hypothermia occurs in more severe cases of sepsis and septic shock. The mechanism for hypothermia with sepsis is not clear but thought to be induced by bacterial lipopolysaccharide in rat models. This research has led to the discovery of new lipid-derived mediators, referred to as endocannabinoids, that interact with cannabinoid-1 and other receptors. The cannabinoid-1 receptors are thought to be expressed by leukocytes, microglialocytes, and neurons. Temperature can, therefore, be another indicator of immunosuppression that can alert practitioners caring for acute and critically ill patients.

Measurement of Temperature

Multiple methods are available to measure temperature, but clinicians should understand the accuracy and limitations of each method and device. The criterion standard remains the measurement of core temperature using a pulmonary artery catheter. Core temperature is the best evaluation of body temperature because it is the least influenced by environmental and other factors and maintains a stable temperature. The issues with using the pulmonary artery catheter are that it is invasive and its use has decreased significantly over the years. The distal esophagus, bladder, posterior nasopharynx, and tympanic membrane are other sites of core temperature measurement. The alternative methods are noninvasive and measure peripheral temperature, which can be influenced by extreme environmental and physiological conditions. The site and instrument used for noninvasive measurement are the most important factors when considering accuracy. Accuracy is affected by common sources of error, including operator technique, anatomic site, and calibration and inherent instrument error.

Research evaluating methods and accuracy for temperature measurement compared with core temperature consider the end result accurate if the mean difference in temperature obtained was ±0.3°C and the instrument to be accurate if the standard deviation was from 0.3°C to 0.5°C. Table 1 compares the different temperature modes, variations from core temperature, and the advantages and disadvantages of each method.

Oral thermometry was thought to be influenced by oxygen therapy, warmed and cooled inspired gases, and respiratory rates, but multiple analyses demonstrate that these factors have no statistical influence if the oral temperature is taken in the left or right posterior (buccal) pocket. Even oral intubation has been tested as to its effect on temperature accuracy and does not influence the value. Tympanic thermometry is commonly used, most likely because of ease, despite studies that were poorly designed and did not address proper technique and instrument testing. Esophageal temperature monitoring, which is a good measurement of core temperature, is used primarily in the operating room, but could be
<table>
<thead>
<tr>
<th>Site of Temperature Measurement</th>
<th>Variation From Core Temperature</th>
<th>Best Practice: Advantages (+) and Disadvantages (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery Reference standard</td>
<td>+ True core temperature  − Highly invasive</td>
<td></td>
</tr>
<tr>
<td>Oral &lt;0.4°C</td>
<td>+ Ease of use  + Oxygen up to 6 L and endotracheal tube do not influence accuracy  + Research has shown that administration of warmed gases and oxygen through an endotracheal tube does not cause significantly different oral temperature compared with core temperature  − Accurate placement of probe in the mouth (posterior sublingual pocket) is necessary for correct temperature reading  − May be influenced by fluids and tachypnea</td>
<td></td>
</tr>
<tr>
<td>Esophagus &lt;0.1°C</td>
<td>+ Correlates closely with pulmonary artery temperature  + Optimal placement requires the esophageal temperature probe to be positioned at the point of maximal heart tones (left atrium) in the distal part of the esophagus and at an insertion depth between 32 and 38 cm  + Minimal lag time for temperature measurement  − Temperature fluctuates according to depth of probe; accurate placement is key</td>
<td></td>
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<tr>
<td>Bladder &lt;0.2°C</td>
<td>+ Easy to perform with urinary catheterization; low risk of dislocation  + Temperature is accurate during dates of increased diuresis  − Accuracy of temperature influenced by low urine flow  − Lag time estimated up to 20 min during therapeutic hypothermia interventions</td>
<td></td>
</tr>
<tr>
<td>Rectum &lt;0.3°C</td>
<td>+ Easy to perform  − Invasive; placed in rectal vault; may be expelled with intestinal motility  − Lag time estimated up to 15 min  − Accuracy of readings influenced by stool in the rectum</td>
<td></td>
</tr>
<tr>
<td>Temporal artery &lt;0.4°C</td>
<td>+ Minimally invasive temperature closely correlated with core temperature  + Temporal artery is not significantly affected by thermoregulatory changes; therefore, perfusion should be stable in most conditions and closely reflect core temperature  − Current research has provided mixed results as to accuracy of this device in different practice settings, patient populations, and physiological conditions  − Diaphoresis may influence accuracy of temperature readings  − Accuracy of temperature measurement procedure required for correct temperature reading from the forehead and behind the ear</td>
<td></td>
</tr>
<tr>
<td>Tympanic membrane Not recommended for temperature monitoring</td>
<td>− Tested in multiple populations of patients; however, user error and patient’s anatomy reduce accuracy of temperature obtained</td>
<td></td>
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The modality used in the ICU once postoperative patients are transferred to that setting. Advanced practice practitioners must be knowledgeable about the methods of thermometry used in their practice setting to make informed treatment decisions.

**Infectious Causes of Fever**

Assessment of fever begins with a thorough history of the patient’s illness, including exposure to people who are or have been sick, travel history both inside (with attention to areas that are sources of specific infections) and outside the United States, and environmental exposures, such as construction where mold and other microbe exposures are common. Animals are also sources of infection and the inquiry should not be limited to domestic pets but also should include farm animals and more exotic animals, including monkeys, reptiles, and others. A thorough physical examination is an integral part of the diagnostic process and should include inspection of all devices, the sites of insertion, and all skin areas, especially the back and sacrum. Laboratory testing should include serial complete blood cell count with a differential to evaluate for leukocytosis or leucopenia as well as a review of the percentage of various types of white blood cells (WBCs), especially neutrophils, lymphocytes, and eosinophils. Leukocytosis is a common finding with infection, but it could also indicate a hematologic disorder such as leukemia or lymphoma. A high eosinophil count could indicate an allergic reaction. The patient’s medication list should be reviewed; a clinical pharmacist is a great resource for any questions about medications. All these data should be considered in this diagnostic process.

The Centers for Disease Control and Prevention (CDC) has recently published a 10-state point-prevalence survey on hospital-acquired infections performed in 2011 that revealed that 1 in every 25 patients in the acute care setting has a hospital-acquired infection. The most common infections are pneumonia (not ventilator associated; 21.8%) and surgical site infections (21.8%) followed by gastrointestinal tract infections (17.1%), with the most common pathogen being *Clostridium difficile*. Urinary tract infections (UTIs; 12.9%) and primary bloodstream infections (9.9%) completed the top 5 infections discovered in this prevalence survey. Data from national surveys and data banks can inform clinicians about patterns of infections.

**Bacteremia and Central Line-Associated Bloodstream Infections**

Bacteremia is the presence of bacteria or pathogens in the blood. Bacteria remain a major concern in the development of bloodstream infections, but the presence of fungi in blood is becoming more prevalent. The most common pathogens involving bloodstream infections reported in the CDC multistate prevalence survey were (1) *Candida* species (11%) including *C. albicans*, *C. parapsilosis*, and *C. glabrata*; (2) coagulase-negative *Staphylococcus* species (9%); and (3) *Staphylococcus aureus* (7%) as well as other pathogens. Central line–associated bloodstream infections can be a cause of fever. If the patient has an abrupt onset of signs and symptoms and has no other local site of infection, an intravascular catheter infection should be a primary consideration as the fever source. The types of catheters associated with the highest risk of infection are short-term, noncuffed central venous catheters, with short-term hemodialysis catheters having an even higher risk. The site of insertion should be examined for inflammation and purulent drainage, but these findings may not always be present. At least 2 sets of blood cultures (1 culture set from the suspected central catheter and 1 set from a peripheral blood draw if able) should be collected, and at least 20 mL of blood should be added to each bottle. The volume of blood is important to optimize possible pathogen growth. If the catheter is thought to be the source of infection, it should be removed, and the tip can be cultured. However, culturing the tip of the catheter is controversial because up to 20% of removed central venous catheters are colonized at removal and can lead to unnecessary therapies as well as extra cost for laboratory testing if the tip culture data are not interpreted appropriately. If the suspected central catheter is a long-term central catheter, removal of the catheter has other ramifications. When virulent pathogens such as *S. aureus* are detected, the catheter should be removed. Other pathogens found in multiple blood cultures such as *Corynebacterium jeikeium*, *Bacillus* species, atypical mycobacteria, or *Malassezia* species suggest an intravascular catheter device infection.
Central Nervous System Infections
Once artificial devices are addressed as a source of infection, using a body system approach is useful for organizing the diagnostic process. Central nervous system infections should be a consideration when a change occurs in level of consciousness or new focal deficits appear in patients with fever in the acute and critical care setting. Diagnostic tests that are most useful with central nervous infections are the lumbar puncture and imaging studies. Noncontrast head computed tomography (CT) is usually the first imaging to be performed because it will give adequate information about mass lesions or obstructive hydrocephalus.

It also will help assess for increased intracranial pressure and whether clinicians can safely perform a lumbar puncture and not risk herniation. The brain parenchyma can be further assessed using magnetic resonance imaging.

Cerebral spinal fluid obtained from a lumbar puncture should be sent for cell counts and differential, glucose and protein concentrations, gram-negative stains, and bacterial cultures. Protein content of cerebral spinal fluid can vary depending on where the fluid is obtained. Further testing for fungi or viruses with polymerase chain reaction tests also can be performed. Lumbar punctures have a low yield for positive results unless the patient is immunocompromised or has instrumentation such as a ventriculostomy, ventriculoperitoneal shunt, or Ommaya reservoir. If spinal cord involvement is suspected, neurosurgery should be consulted before sampling cerebral spinal fluid. Meningitis is the primary diagnosis when infection is suspected. Empiric antimicrobial coverage can be started for virulent microorganisms such as Streptococcus pneumonia, Neisseria meningitidis, and Listeria monocytogenes (especially in older adults) while the diagnostic process proceeds.

A thorough physical examination should be performed to include not only the neurological examination but also the site of any devices.

Pulmonary Infections
Pulmonary infection in acute and critical care patients has been a focus in the literature with the advent of the ventilator-associated pneumonia (VAP) bundle introduced by the Institute for Healthcare Improvement in 2005. Much controversy has arisen about the validity of the VAP bundle in the literature, which has resulted in the CDC convening a board of experts and organizations to help address some of the issues with the bundle. This controversy has demonstrated the difficulty with standardizing a definition for VAP. Radiological confirmation of an infiltrate in pneumonia is required, and other clinical findings have similar appearance on a chest radiograph, including atelectasis, effusion, heart failure, and acute respiratory distress syndrome, which can confound the diagnosis. Overdiagnosis of VAP is now becoming a concern. Although the sample size was small in the CDC point prevalence study, pneumonia rather than VAP may be the more prominent issue currently. Consideration must be given as to whether the infection was acquired in the hospital setting, that is, hospital-acquired pneumonia, or whether infection developed in the community setting, that is, community-acquired pneumonia. Different organisms are primary pathogens in these different settings, so making this determination is an important step. Multiple drug-resistant organisms, especially methicillin-resistant Staphylococcus aureus, are now automatically included in this decision-making process. Carbapenem-resistant Enterobacteriaceae is another group of virulent bacteria that are an increasing infection threat, especially in hospital settings. The CDC provides an epidemiology perspective on multidrug-resistant organisms and has many resources available to assist with prevention. The IDSA has developed guidelines for both hospital-acquired pneumonia and community-acquired pneumonia that are excellent resources for practice.

The 3 components of an initial evaluation for a pulmonary infection include physical examination, chest radiograph, and examination of pulmonary secretions. Physical assessment is a valuable tool but can be misleading, even for experienced clinicians. To optimize the chest radiograph’s information, clinicians must use the best technique in performing the test. The best inspiratory effort of the patient must be captured as well as optimal exposure and patient position. The posterior-anterior technique in the radiology department will usually produce a better image than the portable chest radiograph if the patient is stable. The other important concept is that changes on the image should be seen on serial chest radiographs; 1 image is not sufficient. Chest CT scans provide more specific information about the lung parenchyma, but patient acuity may limit the ability to perform this type of imaging.
Sputum characteristics should be assessed for change in color and volume. If feasible, a sputum sample should be sent before starting any antimicrobial medications. The sample should be sent to the laboratory within 2 hours of collection for optimal microbiological assessment. The method of sputum collection will vary depending on the status of the patient. Bronchoalveolar lavage (BAL) is considered the better method to sample sputum, because it is performed under direct visualization using fiberoptic technology and allows sampling of a larger number of alveolar units. Clinicians should understand that the sensitivity of quantitative BAL fluid cultures ranges from 42% to 93%, implying that BAL fluid is not diagnostic for VAP in approximately 25% of cases. The specificity of quantitative BAL fluid cultures ranges from 45% to 100%, which implies that an incorrect diagnosis may be present, especially in postoperative patients who can present with ileus or toxic megacolon.

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Interpretation of sputum cultures can be challenging, especially when determining whether the microbe is a pathogen or colonizer. Many organisms are usually pathogens if found in the pulmonary system, such as Legionella, Chlamydia, Mycobacterium tuberculosis, influenza and parainfluenza virus, respiratory syncytial virus, and others. Enterococcus, Streptococcus viridians or coagulase-negative staphylococci, and Candida species are rarely the cause of respiratory dysfunction. Normal flora of the upper respiratory tract, such as Pseudomonas aeruginosa, S pneumoniae, S aureus, and Haemophilus influenzae, may be found in sputum culture results. For clinicians to determine whether these flora are true pathogens versus colonizers, gram-negative organisms should be the main organism on the direct gram-negative stain or the culture should report moderate to heavy growth of gram-negative organisms. Drawing blood cultures or polymerase chain reaction tests may assist with determining the cause of pneumonia.

Pleural effusions are hidden sources of infection. An infiltrate can cause an inflammatory process that irritates the adjacent pleura, and an exudative effusion could result. Aspiration of the fluid under ultrasound guidance can be performed, and the sample should be sent for gram-negative stain and routine culture. Glucose, protein, lactate dehydrogenase, amylase, pH, and cell count with differential can also help determine whether the effusion is exudative or transudative in nature, especially if fluid overload is present.

Sinusitis can be an underestimated cause of fever in ICU patients. The most common reason for a sinus infection is obstruction of the ostia, especially of the maxillary sinuses. Obstruction is most commonly caused by nasal intubation or insertion of gastric tubes and can develop after 7 days of intubation. Maxillary sinus trauma is another cause of sinusitis. Clinicians should have a high index of suspicion for sinusitis in patients who have a history of sinus issues and no other source of infection is apparent. The best imaging study for diagnosing sinusitis is a CT of the facial sinuses. Opacification of the sinuses will be present on the CT, and sampling of the fluid by needle puncture may be indicated. Flora of the nasopharynx, especially gram-negative bacilli, are primarily responsible for 60% of bacterial infections, particularly Pseudomonas aeruginosa, whereas gram-positive cocci (S aureus and coagulase-negative staphylococci) are found in approximately 33% of cultures. The IDSA has developed a clinical practice guideline that provides a comprehensive approach for treating acute bacterial rhinosinusitis.

Abdomen and Pelvis Infections
Diarrhea is a common problem in acute and critically ill patients. In the ICU, the cause is usually related to either enteral feedings or drug therapy, especially clindamycin, cephalosporins, and fluoroquinolones. Infection is an important part of the differential diagnostic process for diarrhea and has become more prominent in recent years. Definitions for diarrhea can vary, but the 2008 guideline by O’Grady et al defines diarrhea as more than 2 stools per day that conform to the container in which they are placed. The most common cause of enteric fever in the ICU is C difficile. If leukocytosis without an associated cause is present, C difficile should be considered and diagnosis pursued. Diarrhea may not always be present, especially in postoperative patients who can present with ileus or toxic megacolon.
Testing for the *C. difficile* toxin in stool is quickly evolving. The initial test used was the tissue culture assay, which takes 24 to 48 hours to produce results, but more recent testing uses the enzyme immunoassay because 2 toxins are produced by the microbe, toxin A and B, and 2% to 3% of *C. difficile* strains produce toxin B, which the enzyme immunoassay can detect. A polymerase chain reaction test for *C. difficile* has been developed, which is fast and very sensitive but also expensive. The test can be too sensitive and may find genetic remnants of the microbe when a true infection is no longer present. Research continues in this area to try to perfect the best test to detect *C. difficile* and help prevent outbreaks. The NAP1 strain is causing epidemics in the United States, Canada, and Europe, with serious consequences. Treatment includes metronidazole and/or vancomycin (preferably oral), depending on the clinical situation. The situation has become so serious that fecal microbiota transplantation is an intervention for recurrent *C. difficile* infection and should be prescribed by specialists (usually infectious disease) who have a special investigational new drug permit. The IDSA guidelines for *C. difficile* are helpful in making clinical decisions.

Other intra-abdominal infections can be challenging to diagnose and treat. A basic approach to the diagnostic process should be followed and a surgery consult should be one of the first interventions if the clinician suspects an intra-abdominal process. A physical examination revealing diffuse peritonitis is a presentation that will probably require surgical intervention. Patients with altered level of consciousness, spinal cord injury, or immunocompromised state deserve a higher index of suspicion. The preferred imaging is a CT of the abdomen, and the need and type of contrast will be a decision dependent on the presentation of the patient and the possibility of perforation. Fluid resuscitation should be initiated as soon as possible, and empiric antimicrobial coverage should be initiated. As with pneumonia, community- versus hospital-acquired infection is an important consideration, as different pathogens may need to be treated depending on the presenting situation. Community-acquired intra-abdominal infections should be covered empirically for enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci. With hospital-acquired infections, more virulent organisms may be present, and coverage for multidrug-resistant organisms, as well as for *Candida*, should be included. The IDSA guidelines for the diagnosis and management of the complicated intra-abdominal infection provide extensive guidance on this clinical situation.

Surgical wounds and their care can be costly and represent the third most common infection cited in the CDC point prevalence survey. Many factors influence a diagnosis of a surgical infection, including the medical comorbidity of the patient, whether surgery was prolonged or emergent, and the degree of contamination of the incision. The incision should be examined daily, and if an infection is suspected, the wound should be opened and gram-negative stain and cultures should be sent. The most common pathogen is *S. aureus*, but gram-negative bacilli also can cause surgical site infections, depending on the location. No evidence supports the use of antibiotic therapy in these cases, but the incision/wound should be drained, irrigated, and treated with local care. Additional information on skin and soft tissue infections is available in the IDSA practice guidelines.

**Urinary Tract Infections**

In the acute and critical care setting, UTIs are common but can present a clinical dilemma. Urinary tract infections can be asymptomatic, are discovered incidentally, and usually are not treated except in certain circumstances such as future transurethral resection of prostate. Guidelines for managing asymptomatic UTIs have been developed by the IDSA to try to provide guidance and avoid unnecessary treatment. Cystitis or lower UTIs can be uncomplicated when symptoms are present, including dysuria and vaginal discharge. Assessment for infection should start with a urinalysis. The presence of WBCs, leukocyte esterase, and nitrate (substances released by WBCs) can indicate a UTI and should prompt obtaining a urine culture and Gram stain. Bacteriuria is defined as 2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of 10^5 colony-forming units/mL. The quantitative count is important to help determine whether the bacteria is a colonizer or a pathogen. A degree of contamination from the gastrointestinal tract will be present, especially in women as a result of the proximity of the anus. *Escherichia coli* is...
the single most common organism leading to UTIs. If the integrity of the urinary tract is disrupted, that is, from surgery, injury, or instrumentation, the infection is considered complicated.

A Foley catheter is the most frequent device used that can lead to infection. The best intervention is to use catheters only when needed and remove them as soon as possible. In patients with short-term indwelling urethral catheterization, use of antimicrobial (silver alloy or antibiotic) coated urinary catheters may be considered to reduce or delay the onset of catheter-associated bacteriuria. When collecting a urine sample from a catheter system, the urine should be collected from the sampling port and sent to the laboratory within 1 hour of collection. The IDSA guidelines for catheter-associated urinary tract infections are helpful in dealing with this infection, which is one of the most common hospital-acquired infections. The CDC also has guidelines to help in operationalizing a process improvement program. Patient presentation does not help in operationalizing a process improvement program. When collecting a urine sample from a catheter system, the urine should be collected from the sampling port and sent to the laboratory within 1 hour of collection. The IDSA guidelines for catheter-associated urinary tract infections are helpful in dealing with this infection, which is one of the most common hospital-acquired infections. The CDC also has guidelines to help in operationalizing a process improvement program. Patient presentation does not help in operationalizing a process improvement program.

Fever is common in the first 48 hours postoperatively and is usually inflammatory in nature, unless improper sterile technique or pulmonary aspiration is suspected. Atelectasis has been a common explanation for acute postoperative fever, but little evidence supports this theory. Multiple studies have been conducted to attempt to demonstrate a relationship between postoperative fever and atelectasis by various methods, including measuring cytokine levels, but no relationship can be established. Marvos et al state that little evidence supports any connection between atelectasis and fever. However, postoperative fever that occurs after 96 hours should be evaluated with infection as the cause. Another consideration for the cause of postoperative fever is deep vein thrombosis, superficial thrombophlebitis, or pulmonary embolism. Patients who preoperatively were sedentary, had a history of cancer, or were taking oral contraceptives also may generate a fever.

Noninfectious Causes of Fever
Noninfectious causes of fever are inflammatory conditions that will activate the cytokine system and trigger a systemic inflammatory response syndrome. The cytokines involved in systemic inflammatory response syndrome are the same or similar to those involved in developing a fever. These conditions can be obvious, such as a blood component transfusion reaction, or more subtle when fever is generated with a deep vein thrombosis. Infection should always be the first consideration when clinicians evaluate fever, but inflammation should not be ignored (see Figure 1). These conditions are challenging because treatment can be complicated.

Drug fever is an example of a noninfectious source and can occur for different reasons. One cause for drug fever is a hypersensitivity reaction that is influenced by the severity of the reaction. Other causes are drugs that stimulate heat production (thyroxine), drugs that limit heat dissipation (vasoconstrictors), and drugs that alter thermoregulation (phenothiazines). Drugs that produce a cytokine storm will logically produce a fever. Monoclonal antibodies are being used more frequently for treating malignancies as well as other diseases, and clinicians should expect fever with these drugs. Suspicion of index should begin when examining the list of medications and establishing a temporal relationship between fever and drug introduced. Drug fever can vary in length from 1 day to more than 7 days. Table 2 provides a list of drug categories that commonly produce drug fever, but it is not exhaustive.

A distinction should be made between fever and hyperthermia. Hyperthermia is the unregulated rise in body temperature and a failure of the thermoregulatory homeostasis, whereas fever is an adaptive mechanism to reset the thermostat. Malignant hyperthermia, neuroleptic malignant syndrome, and serotonin syndrome are conditions that produce a high temperature. Malignant hyperthermia is associated with anesthetic agents, including halothane and succinylcholine, and is thought to be a genetic disorder that causes a dysregulation of cytoplasmic calcium control of the skeletal
muscle and results in a severe increase in muscle activity, thereby producing a high fever. This syndrome occurs most frequently in the operating room but can be exhibited up to 24 hours after anesthesia if steroids were administered preoperatively. Dantrolene is the muscle relaxant used to treat malignant hypothermia.

Neuroleptic malignant syndrome is most commonly associated with antipsychotic drugs, especially haloperidol, which is commonly used in the ICU setting. This drug reaction also produces abnormal increased muscle activity, resulting in fever. Serotonin syndrome is related to excessive stimulation of the 5-hydroxytryptamine 1A receptor and is commonly confused with neuroleptic malignant syndrome. It is associated with serotonin reuptake inhibitors and produces increased muscle activity, which is more twitching in nature. Supportive care is given when these syndromes occur, and patients usually require ICU care.

### Updates for Fever Treatment and Diagnosis

The debate about treating a fever remains unanswered. The theory that fever is an adaptive evolutionary process and is an important host defense is a core tenet in this debate. Proponents for treating fever argue that prolonged fever may cause increased oxygen consumption and could possibly lead to organ failure. Some researchers have suggested that fever may affect the mortality rate in the ICU population, but a meta-analysis and systematic review by Niven et al found no evidence that fever treatment influences the mortality rate in critically ill adults without acute neurological injury. A few randomized controlled trials have been conducted; however, studies with small sample sizes, differences in interventions, and variable follow-up duration make it difficult to draw appropriate clinical practice conclusions from the current data.

Interventions to treat fever include antipyretic therapy (nonsteroidal anti-inflammatory drugs and/or acetaminophen as well as physical cooling mechanisms), but they are not without adverse effects. Nonsteroidal anti-inflammatory drugs can be very effective but can contribute to renal dysfunction, especially if the renal dysfunction is not recognized. Acetaminophen dosing of 4 g in a 24-hour period has been associated with transaminitis. Caution also must be taken when giving acetaminophen that all sources of the drug be included in the daily total dose calculation. Pain medications that are narcotic and acetaminophen combinations often are forgotten in the calculation. The advent of intravenous acetaminophen has been helpful in providing another route of administration, but it is expensive. Therapeutic physical cooling methods are available and can be efficient but cause discomfort for patients.

The use of biomarkers along with fever assessment to detect microbiological infection is becoming more accepted in clinical practice, although the supportive evidence is variable. Various markers have been studied including C-reactive protein, tumor necrosis factor α, and IL-6, but their use has not been validated. Another biomarker, procalcitonin, is a precursor to calcitonin, which plays a role in calcium homeostasis. The procalcitonin level is thought to increase with a proinflammatory stimulus, especially those that are bacterial in origin. A procalcitonin level greater than 0.65 ng/mL is associated with high risk of microbial infection, whereas a level less than 0.65 ng/mL may indicate a low risk of infection. However, patient safety and efficacy are not clear in the current evidence.
Summary
Fever is common in acute and critical care settings. A disciplined approach to patient evaluation will increase the chances of arriving at an accurate diagnosis. The process should start with a thorough physical examination as well as a review of the patient’s history and medication list. The method of measuring temperature as well as the strengths and weaknesses of the method must be understood. Each body system should be reviewed, and proper testing and imaging should be ordered. A balance needs to be maintained in today’s health care environment, so that clinicians can assess the patient’s condition properly and can order the appropriate tests using the best evidence available while maintaining a cost-conscious approach.

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REFERENCES
32. Institute for Healthcare Improvement. http://www.ihi.org/knowledge/Pages/Changes/ImplementTheVent
33. Klompas M. Complications of mechanical ventilation—

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