CHEST Postgraduate Education Corner
CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

Persistent Fever in the ICU

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Disorders of elevated body temperature may be classified as either fever or hyperthermia. Fever is caused by a pyrogen-mediated upward adjustment of the hypothalamic thermostat; hyperthermia results from a loss of physiologic control of temperature regulation. Fever in the ICU can be due to infectious or noninfectious causes. The initial approach to a febrile, critically ill patient should involve a thoughtful review of the clinical data to elicit the likely source of fever prior to the ordering of cultures, imaging studies, and broad-spectrum antibiotics. Both high fever and prolonged fever have been associated with increased mortality; however, a causal role for fever as a mediator of adverse outcomes during non-neurologic critical illness has not been established. Outside the realm of acute brain injury, the practice of treating fever remains controversial. To generate high-quality, evidence-based guidelines for the management of fever, large, prospective, multicenter trials are needed. ***CHEST 2014; 145(1):158–165***

Abbreviations: CDI = *Clostridium difficile* infection; CFU = colony-forming units; CLABSI = central line-associated blood stream infection; CVC = central venous catheter; CXR = chest radiograph; NMS = neuroleptic malignant syndrome; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; UTI = urinary tract infection; VAP = ventilator-associated pneumonia

Fever is a ubiquitous finding among patients admitted to the ICU. The clinical significance of fever varies with its context. On one hand, fever may represent a response to a serious perturbation in the steady state, such as when an infection is present. On the other, fever may occur as a nonspecific physical sign accompanying critical illness, as is often the case in postoperative patients. Single temperature elevations that resolve without treatment are seldom of significance; however, persistently elevated temperature has major implications for the care of critically ill patients.[1] Not infrequently, the finding of fever in the ICU triggers an unfocused, multimodal diagnostic workup and empirical dispensation of antimicrobial agents. Such an approach contributes to disruption of care, patient discomfort, antimicrobial resistance, and increased cost.[2] This article recapitulates the salient aspects of febrile critical illness; discusses recent advances in its epidemiology, evaluation, and treatment; and advocates for a rational approach to its management.

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Pathophysiology of Thermoregulation

As homeothermic organisms, humans must tightly regulate their core body temperature to maintain optimal conditions for fundamental biologic processes.[3] The target temperature that the thermoregulatory system aims to achieve (ie, the set point) is determined in the preoptic region of the hypothalamus. To minimize variation from the set point, the hypothalamus integrates processes that generate, conserve, or dissipate heat to the environment.

Abnormally elevated body temperature can result from two pathophysiologically distinct disorders of thermoregulation:

1. Fever results from an upward adjustment in the thermoregulatory set point. Pyrogens (eg, bacterial lipopolysaccharide, tumor necrosis factor-α, IL-1) induce the synthesis of prostaglandin E_2, which raises the set point in the anterior hypothalamus. The hypothalamus, in turn, activates heat generation (through shivering and increased

metabolism) and heat conservation (through peripheral vasoconstriction) to bring up the body temperature.[4]
2. Hyperthermia is a pathophysiologic state of uncontrolled heat production (eg, malignant hyperthermia) and/or impaired heat dissipation (eg, heat stroke). There is no adjustment of the hypothalamic set point during hyperthermic syndromes.[5]

Definition of Fever

Normal oral temperature is approximately 36.8°C (98.2°F) with an amplitude of variability of 0.5°C between the morning and the evening.[6] During critical illness, the variability can be even greater due to disruption of circadian rhythm, autonomic disturbances, drugs, the ICU environment, and artifacts. Selecting a single threshold to identify fever in the ICU involves a tradeoff between sensitivity and specificity, with significant implications for care. In the interest of standardization, a joint task force of the American College of Critical Care Medicine (ACCM) and the Infectious Diseases Society of America (IDSA) defined ICU fever as a core body temperature ≥38.3°C (101°F).[7] Importantly, the task force emphasized that any threshold is arbitrary unless informed by the clinical context.

Temperature Measurement

Historically, the pulmonary artery catheter thermistor has constituted the gold standard for the measurement of the core body temperature.[8] Rectal probe, bladder thermistor, and infrared tympanic thermometer have been shown to closely approximate core temperature measurements.[9] In contrast, the oral and the axillary sites are unreliable in critically ill patients and should be avoided. Serial temperature measurements should be performed using the same site, the same instrument, and the same technique, and these specifics should be clearly documented in the patient's medical record.

Epidemiology

The prevalence of ICU fever ranges from 26% to 70% depending on the population studied and the definition of fever used.[10-13] Infectious and noninfectious causes are equally represented.[10,11] Young age, male sex, septic shock, trauma, emergent surgery, and neurocritical illness are associated with the development of fever.[11-13] Prolonged fever (lasting >5 days) and high fever (≥39.3°C) are more likely to be infectious.[10,13] In surgical ICUs, fever occurs most commonly on postoperative day 1.[11]

Both fever and admission hypothermia are associated with an increased ICU length of stay.[12] Prolonged fever[10] and high fever[13,14] are also associated with a significantly increased risk of death. Whether fever plays a causal role in mediating adverse outcomes in nonneurologic critical illness remains to be elucidated.

Differential Diagnosis

The approach to fever in the ICU is at times reflexive, equating fever with infection. The finding of elevated body temperature triggers an order set that includes culturing of several body sites (eg, blood, urine, sputum), imaging of the chest and/or abdomen and the initiation of broad-spectrum antibiotics. To promote a more rational approach, a joint American College of Critical Care Medicine and Infectious Diseases Society of America guideline was issued in 2008.[7] Recognizing that the sources of fever may be either infectious or noninfectious, the guideline panel recommended that "any unexplained temperature elevation merits a clinical assessment by a healthcare professional that includes a review of the patient's history and a focused physical examination before any laboratory tests or imaging procedures are ordered."[7] The goal is to promote individualized management based on consideration of factors unique to each patient. A head-to-toe approach, such as the one suggested in Table 1, can provide a framework for the formulation of a probable differential diagnosis and cost-effective workup.

Selected Infectious Causes of Fever

Approximately 50% of fevers in the ICU are due to infections.[10] Nearly all patients in the ICU undergo placement of devices (eg, central venous catheters [CVCs], arterial lines, urinary catheters, endotracheal tubes, and nasogastric tubes) that bypass natural host defenses and provide easy portals of entry to microorganisms. The use of a "daily goals" checklist to assess ongoing need of these devices is an effective strategy to reduce the rates of ICU-acquired infections.

When clinical evidence makes infection the likely source of fever, culturing of the blood should be performed, preferably prior to initiating antibiotics.[15] Three blood cultures achieve a 99% detection rate of true bacteremia.[16,17] All blood cultures can be drawn simultaneously, as the yield is not increased by serial draws.[18] However, a separate venipuncture site should be used for each blood culture.[17] A blood volume of ≥20 mL per culture is required for optimal yield.[17]

Central Line-Associated Blood Stream Infection

For surveillance purposes, a blood stream infection in a patient with a CVC of ≥48 h duration is considered as a central line-associated blood stream

Table 1—*Common Causes of Persistent Fever in the ICU: A Head-to-Toe Approach to Differential Diagnosis*

Site	Infectious	Noninfectious
Head and neck	Meningitis	Cerebrovascular accident
	Otitis media	Seizure disorder
	Sinusitis	Traumatic brain injury
	CVC-related blood stream infection	
Chest	Infective endocarditis	Myocardial infarction
	Ventilator-associated tracheobronchitis	Pericarditis
	Ventilator-associated pneumonia	Pulmonary embolism
	Empyema	ARDS
Abdomen and pelvis	Intraabdominal infections (eg, SBP, abscesses)	Pancreatitis
	Clostridium difficile infection	Acalculous cholecystitis
	Pyelonephritis	Ischemic colitis
	Catheter-related UTI	
	Perineal or perianal abscess	
Extremities	Femoral line/PICC-related blood stream infection	Gout
	Septic arthritis	DVT
Skin and back	Cellulitis	Drug eruptions
	Infected pressure ulcer	
	Surgical site infection	
Miscellaneous	…	Drugs
		Transfusion reactions
		Endocrine disorders (eg, thyrotoxicosis, adrenal insufficiency)
		Malignancy
		Inflammatory disorders (eg, SLE)

CVC = central venous catheter; PICC = peripherally inserted central catheter; SBP = spontaneous bacterial peritonitis; SLE = systemic lupus erythematosus; UTI = urinary tract infection.

infection (CLABSI) provided that it is not related to an infection at another site (eg, pneumonia, pyelonephritis).[19] Using this definition, the rate of CLABSI in the ICU is estimated to vary from 1.4 to 5.5 per 1,000 catheter-days.[20]

In evaluating a patient in the ICU with fever, a detailed examination of the CVC insertion site should be performed, looking for signs of local inflammation or purulence. Any exudate should be swabbed and sent for Gram staining and culture. In hemodynamically stable patients, a CVC without local signs of infection can be left in place awaiting culture results. However, in unstable patients, it is best to remove the suspicious catheter without waiting for microbiologic confirmation.[21] Vascular access in these cases should be secured using a fresh catheter insertion site prior to the removal of the old line.

Paired blood cultures, from the catheter and from a peripheral venipuncture, should be drawn simultaneously. If the blood culture from the catheter becomes positive $\geq$2 h before the one obtained from the peripheral site and both cultures show growth of the same organism (differential time to positivity method), the diagnosis of CLABSI is established.[22] Alternatively, a quantitative blood culture showing a greater than fivefold higher colony count from the catheter also suggests CLABSI.[21] Finally, semiquantitative culturing of 5 cm of the catheter tip (roll-plate method) should be performed on all CVCs removed from patients with suspected CLABSI. Isolation of $<$15 colony-forming units (CFU) is consistent with contamination, while $\geq$15 CFU per catheter tip represents catheter colonization.[23] A diagnosis of CLABSI is confirmed only if catheter colonization is accompanied by a positive peripheral blood culture with an identical organism.[24] Though not widely available, quantitative culturing of catheter segments (sonication method) provides more accurate results, especially for catheters that have been in place for a longer time.[24,25]

Ventilator-Associated Respiratory Infection

Mechanical ventilation with an endotracheal tube increases the risk of pneumonia sixfold to 20-fold.[26,27] The attributable mortality from ventilator-associated pneumonia (VAP) is estimated around 10%.[28] Importantly, VAP is preventable, and appropriate and timely therapy can improve outcomes.[27]

More recent data suggest that on-demand chest radiography is as safe as routine daily chest radiography for patients undergoing mechanical ventilation.[29,30] In the presence of fever, leukocytosis, purulent secretions, and declining Pa_{O_2}/F_{IO_2}, a chest radiograph (CXR) is indicated. There is no radiographic pattern diagnostic of VAP, but the finding of a new or progressive pulmonary infiltrate is supportive. When symptoms and signs of lower respiratory tract infection are present but the CXR does not demonstrate an infiltrate,

the preferred diagnostic label is ventilator-associated tracheobronchitis. Ventilator-associated tracheobronchitis is increasingly viewed as a precursor to VAP.[31]

Evaluation of lower respiratory secretions is central to the diagnostic workup of VAP. The precise sampling approach (noninvasive vs invasive) remains controversial. Noninvasive approaches include tracheobronchial aspiration and blind mini-BAL. Invasive approaches use bronchoscopy to perform sampling via BAL or protected specimen brushing. A large multicenter trial demonstrated the equivalency of endotracheal aspiration to bronchoscopic BAL sampling.[32] However, the study excluded patients infected or colonized with *Pseudomonas* species and methicillin-resistant *Staphylococcus aureus*, somewhat limiting its external validity.[33] A 2012 meta-analysis concluded that invasive strategies do not result in reduced mortality, reduced time in the ICU or on mechanical ventilation, or higher rates of antibiotic change when compared with noninvasive strategies.[34]

Urinary Tract Infection

An overwhelming majority of urinary tract infections (UTIs) in the ICU are catheter related, with an estimated incidence of nine to 11 per 1,000 catheter-days. Secondary bacteremia occurs in only 1% to 5% of these cases.[35] Although ICU-acquired UTI is associated with increased length of stay, cost, and crude mortality, it is not an independent risk factor for death.[36]

Typical symptoms of UTI (ie, dysuria, urgency, pelvic discomfort, or flank pain) are infrequently reported by patients with catheters in the ICU and have little predictive value.[37] Moreover, neither fever nor leukocytosis is associated with a positive urine culture during the first 14 days of ICU stay.[38] Results of routine urinalysis are insensitive but relatively specific for UTI in critically ill patients who are catheterized.[39,40]

In the evaluation of ICU fever, it is recommended to restrict urine cultures to patients with catheters and no other obvious source of fever. The urine sample should be obtained from the catheter port, not from the urine bag.[41] Any growth $\geq 10^2$ CFU/mL of urine in a patient with a catheter is abnormal and indicates at least colonization of the urinary tract.[41] The traditionally used criterion of $\geq 10^5$ CFU/mL is too insensitive for patients with catheters. As a general guideline, we recommend empirical antibiotics for presumed UTI in febrile patients with catheters when the results of urinalysis are positive and no other source of fever or infection is obvious. The results of the urine culture should be used to guide rapid antibiotic de-escalation.

Clostridium difficile *Infection*

By definition, patients with well-formed stools do not have *Clostridium difficile* infection (CDI). However, a patient in the ICU who has fever, leukocytosis, and diarrhea should be assessed for CDI. Fever is noted in 30% and leukocytosis in 50% of documented CDI cases.[42] Severe CDI may also present with abdominal pain, ileus, and a systemic inflammatory response.[42]

Laboratory assessment of suspected CDI includes enzyme immunoassay for toxin A and toxin B (rapid and widely available but insensitive), cell cytotoxicity assay (highly specific, but of limited availability with a turnaround time of ≥ 48 h), and stool culture (costly and time consuming, with frequent false-positive results).[43,44] Real-time polymerase chain reaction testing for toxin A or toxin B genes is both rapid and accurate and has become the preferred option in the ICU setting.[45] In severe cases, endoscopic finding of pseudomembranes and CT scan evidence of colonic wall thickening, pericolonic stranding, and megacolon are also supportive of the diagnosis.[46]

Oral vancomycin, either alone or in combination with metronidazole, is recommended for critically ill patients with severe CDI. When ileus is present, vancomycin retention enemas should be added. Colectomy should be considered for patients with fulminant CDI characterized by one or more of the following: septic shock, toxic megacolon, acute abdomen, serum lactate > 5 mM, and peripheral blood WBC $> 50{,}000/\mu$L.[43]

Nosocomial Sinusitis

The paranasal sinuses can become colonized and infected if there is anatomic obstruction of ostial drainage. Nasogastric tubes, nasotracheal tubes, and nasal packs are major risk factors for nosocomial sinusitis.[47] While oral placement of gastric and endotracheal tubes can reduce the incidence of nosocomial sinusitis, the risk remains elevated compared with patients without such devices.[47] In a prospective study of orotracheally intubated patients with a new-onset fever > 48 h after ICU admission, sinusitis was found to be the sole cause of fever in 16% of patients and a contributory cause in 30% of patients.[48]

In the presence of risk factors for nosocomial sinusitis, purulent nasal drainage, and no other explanation of fever, a CT scan of the sinuses should be performed. The finding of an air-fluid level or complete opacification of a sinus constitutes radiographic sinusitis. The diagnostic accuracy of CT scan is $> 90\%$ when accompanied by the finding of purulence in the middle meatus.[49] Ultrasonography is not as accurate as CT scanning but has the advantage of point-of-care testing with real-time interpretation of results and is the preferred imaging modality in patients who cannot be safely transported outside the ICU. However, ultrasonography is highly operator dependent and does not

provide adequate assessment of the frontal, ethmoid, and sphenoidal sinuses.[50,51]

Febrile, critically ill patients with radiographic sinusitis should undergo diagnostic sampling of the sinus fluid prior to the initiation of antibiotics. Endoscopic-guided middle meatus aspiration is the modality of choice for this purpose and is recommended in preference to the conventional sinus puncture and aspiration.[52]

Selected Noninfectious Causes of Fever

About one-half of all fevers in the ICU are due to noninfectious etiologies.[2,10] A major goal of the evaluation of persistent fever is to search for clinical clues of noninfectious sources of fever. Infectious and noninfectious fever may occur together in the same patient.

Hyperthermic Syndromes

While pathophysiologically distinct, hyperthermic syndromes can clinically mimic fever. Commonly encountered examples include environmental heat-related illness, malignant hyperthermia, serotonin syndrome and neuroleptic malignant syndrome (NMS). In addition, recreational drug use (eg, cocaine, methamphetamines, mephedrone [bath salts]), and agitated withdrawal from alcohol, opiates, or benzodiazepines can also cause significant elevations of the core body temperature.[2]

Environmental heat-related illness results from a failure of heat dissipation. The spectrum of illness ranges from minor heat cramps, heat syncope, or heat exhaustion to the potentially life-threatening heat stroke (core body temperature $>40°C$ with significant CNS dysfunction).[5] During climatic heat waves, the elderly with limited mobility and chronic medical conditions constitute a cohort at particularly high risk.

Malignant hyperthermia is a pharmacogenetic syndrome associated with the administration of succinylcholine or inhalational anesthetics.[53] In susceptible individuals, these drugs induce dysregulation of calcium homeostasis in the skeletal muscles, resulting in intense tonic contraction and uncontrolled thermogenesis. The syndrome is clinically obvious within 30 min of drug administration, although presentations delayed up to 24 h have been reported. Treatment includes prompt discontinuation of the offending agent, external cooling, IV fluids, and dantrolene.

Serotonin syndrome is caused by the overactivation of 5-HT1a and 5-HT2a receptors. It commonly occurs in patients taking selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs) who then receive either another drug that possesses serotonergic activity or that interferes with the cytochrome P450 metabolism of SSRIs or TCAs.[54] Clinically, the syndrome manifests as a triad of altered mental status, autonomic hyperactivity, and neuromuscular abnormalities. Discontinuation of the offending agent can lead to rapid resolution of symptoms. Benzodiazepines and the serotonin antagonist, cyproheptadine, are used to treat severe cases.

NMS is precipitated by the antidopaminergic activity of neuroleptic agents.[54] The clinical presentation of NMS resembles that of serotonin syndrome (Table 2). NMS can develop at any time during treatment, while serotonin syndrome usually develops within minutes to hours after exposure to the offending drug. In addition to stopping neuroleptic medications, bromocriptine, a central dopamine agonist, is used for treatment.

Drug Fever

Almost any drug can cause fever, but the ones most commonly implicated in the ICU include antibiotics (especially β-lactams), anticonvulsants (diphenylhydantoins), and antiarrhythmics (quinidine and

Table 2—*Neuroleptic Malignant Syndrome vs Serotonin Syndrome*

Feature	Neuroleptic Malignant Syndrome	Serotonin Syndrome
Mechanism	Dopamine receptor antagonism	5-HT1a and 5-HT2a receptor activation
Causative drugs	Neuroleptic agents (eg, haloperidol, phenothiazines, clozapine)	Serotonin agonists (eg, SSRI, TCA)
Type of ADR	Idiosyncratic	Predictable
Onset	Over days to weeks	Within 24 h of drug use
Clinical manifestations		
Altered mental status	Agitation, disorientation, delirium	Anxiety, agitation, disorientation
Dysautonomia	Tachycardia, labile blood pressure	Tachycardia, hypertension, flushing, diarrhea
Neuromuscular hyperactivity	Rigidity, bradyreflexia, tremor	Tremor, hyperreflexia, clonus (particularly lower extremities)
Hyperthermia	92% of cases	34% of cases
Treatment	Discontinuation of all antidopaminergic agents Bromocriptine Dantrolene (for severe rigidity and hyperthermia)	Discontinuation of all serotonergic agents Benzodiazepines Cyproheptadine (in severe cases)
Time to recovery	Over days (average 9 d)	<24 h

ADR = adverse drug reaction; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

procainamide).[55] No fever pattern is characteristic of drug fever. Relative bradycardia, rash, and eosinophilia are seen in a minority of cases.[56] The temporal association between the initiation of a drug and the onset of fever or discontinuation of a suspected drug and resolution of fever provides helpful clues. Drug fever remains a diagnosis of exclusion.

Postoperative Fever

Fever is common in the first 72 h after surgery and is predominantly noninfectious. A rational approach to postoperative fever is to clinically assess for infectious sources, but initiate a workup only if clues other than fever or leukocytosis point toward an infection. The yield of a nonfocused approach is low and adds significantly to cost of care. Routine chest radiography and sputum analysis in the early postoperative period are not indicated, as they fail to prompt a change in management.[57] In a retrospective review of 537 patients undergoing major gynecologic surgery, the prevalence of early postoperative fever was 39%.[58] Of the 77 patients evaluated with blood cultures, none had a positive result. In a separate cohort of 1,100 patients who had undergone orthopedic surgery, the diagnostic yield of CXRs, blood cultures, and urine cultures was 2%, 6%, and 22%, respectively; however, the yield increased substantially for fever occurring after postoperative day 3 (OR, 23.3), for high fever ≥ 39°C (OR, 2.4), and for persistent or recurrent fever (OR, 8.6).[59] The average cost of a fever evaluation was $960, while the cost associated with a change in treatment was $8,208.[59] More recent studies have found no association between fever and postoperative atelectasis.[60]

VTE

In the PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) study, fever ≥ 37.8°C without an alternative cause was noted in 14% of patients with pulmonary embolism.[61] VTE-related fever is usually low grade, short-lived, and resolves with anticoagulation therapy.[62] VTE-related fever is associated with an increased 30-day mortality.[63]

Acalculous Cholecystitis

Spontaneous ischemic or inflammatory injury of the gall bladder may develop during critical illness. Occlusion of the cystic duct, bile stasis, distension, and secondary infection can lead to gangrene and perforation of the gall bladder.[64] The diagnosis should be suspected in any patient with fever, leukocytosis, and a right upper quadrant pain. Bedside ultrasonography has a sensitivity and specificity of > 80%.[65] CT scanning performs slightly better but is limited by the need to transport critically ill patients to the radiology suite.[65] In patients at high surgical risk, percutaneous cholecystostomy can prove a life-saving intervention.[66]

Treatment of Fever

To lower the core body temperature, two approaches can be used: pharmacologic agents, such as acetaminophen and nonsteroidal antiinflammatory drugs; and physical measures, such as ice packs, cooling blankets, and endovascular cooling devices.

The choice of antipyretic agent should be informed by the presence or absence of hepatic and renal injury, and the risk of GI bleeding.[67] Acetaminophen should be avoided in patients with liver failure, but may be preferred over ibuprofen in the setting of coagulopathy, GI bleeding, and kidney injury. Physical measures offer more reliable temperature control[68] and can successfully lower temperature even when pharmacologic antipyretic therapy has failed.[69] External cooling can provoke shivering, which may necessitate the use of sedatives, and even paralytics.

While a standard practice in patients with acute brain injury,[70] the value of treatment of fever in patients with nonneurologic critical illness remains obscure. In a randomized, controlled trial, 82 trauma patients with fever (≥ 38.5°C) but without brain injury were treated with either an "aggressive" or a "permissive" fever control strategy.[71] Patients in the "aggressive" arm received acetaminophen 650 mg q6h for temperature ≥ 38.5°C, with the addition of a cooling blanket for temperature ≥ 39.5°C. Patients in the "permissive" arm were not treated unless the core temperature was ≥ 40°C, at which point they received acetaminophen and cooling blankets to lower their temperature below 40°C. The study was stopped after an interim analysis revealed a trend toward higher mortality and higher rates of infection in the "aggressive" arm (seven deaths vs one death; $P = .06$).

In a multicenter trial, 200 febrile (≥ 38.3°C) patients with respiratory failure and vasopressor-dependent septic shock were randomized to either external cooling targeting normothermia (36.5°C-37°C) or to usual care without cooling.[72] The primary end point, a 50% reduction in the baseline vasopressor dose at 48 h, was not significantly different between the two groups. However, a few secondary end points favored the external cooling strategy, including a lower vasopressor dose at 12 h and greater shock reversal. Importantly, the mortality was not significantly different either at ICU or at hospital discharge. Similarly, a 2013 meta-analysis including 399 patients from five randomized trials found no survival benefit for antipyretic therapy in febrile critical illness (acute neurologic injury excluded).[73]

Conclusions

Fever in the ICU is a common clinical entity. High fever and prolonged fever are associated with an increased risk of death, although a causal relationship has not been established. The reflexive practice of equating fever with infection should be replaced with one that begins with a thoughtful clinical assessment and takes into account both infectious and noninfectious etiologies of elevated body temperature. With the exception of acute brain injury and hyperthermic syndromes, the practice of temperature control in the ICU remains controversial. To develop an evidence-based approach to the management of ICU fever, multicenter, randomized controlled trials are needed.

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