Chapter 99
Approach to Fever in the ICU

99.1 Introduction

Fever in the intensive care unit (ICU) is a prevalent clinical challenge that necessitates prompt identification and management. It is crucial to distinguish between fever (an elevation in body temperature due to a regulated increase in the hypothalamic set point), pyrexia (often used interchangeably with fever but can imply sustained elevated temperature), and hyperthermia (an unregulated rise in body temperature due to excessive heat production or impaired heat dissipation). Each condition has specific clinical implications and requires different management strategies.

Fever can result from both infectious and noninfectious causes, with infections being a primary concern in critically ill patients. Mismanagement can lead to delayed diagnoses, unnecessary testing, and inappropriate treatments. Importantly, immunocompromised patients—such as those who are neutropenic or have undergone organ transplantation—may not mount robust febrile responses. Therefore, lower temperature thresholds are used to define fever in these populations [1–3] [Ref: Algorithm 99.1].

99.2 Initial Assessment and Temperature Confirmation

Accurate temperature measurement is critical to avoid over- or underestimating fever. The hierarchy of accuracy in temperature measurement methods is especially important in the ICU setting.

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Preferred Methods

- Central Thermistors: Pulmonary artery, bladder, or esophageal thermistors provide the most accurate core temperature measurements.
- Oral and Rectal Thermometers: Acceptable alternatives if central monitoring is unavailable.

Less Accurate Methods to Avoid

- Tympanic and Axillary Thermometers: These peripheral methods are less reliable, particularly in critically ill patients with altered hemodynamics.

Limitations in Certain ICU Scenarios

- Extracorporeal Therapies: Patients undergoing extracorporeal membrane oxygenation (ECMO) or continuous renal replacement therapy (CRRT) may have altered peripheral temperatures, affecting the accuracy of peripheral measurements.

Thresholds for Fever

- General ICU Population: A temperature of ≥38.3 °C (100.9 °F) sustained for at least 1 hour defines significant fever.
- Immunocompromised Patients: A lower threshold of ≥38.0 °C (100.4 °F) is often used due to their blunted febrile response.

If the threshold is not met, hourly monitoring for the next 6 hours is recommended [4].

99.3 Etiological Approach

A systematic clinical evaluation is essential to differentiate between infectious and noninfectious causes of fever. Creating a differential diagnostic framework can guide clinicians through potential etiologies specific to the ICU.

Clinical Evaluation

- History: Document recent surgeries, invasive procedures, catheter placements, medication changes, and known comorbidities.
- Physical Examination: Focus on signs of infection or inflammation, such as redness, swelling, discharge, or pain at catheter sites.

Infectious Causes

- Catheter-Related Infections
- Ventilator-Associated Pneumonia (VAP)
- Urinary Tract Infections (UTIs)
- Abdominal Abscesses

Noninfectious Causes (See Table 99.1 for Diagnostic Clues)

- Drug-Induced Fever
- Thromboembolic Events (acute myocardial infarction, fat embolism, venous thrombosis, lung infarction, stroke)
- Autoimmune Responses
- Transfusion Reactions
- Pancreatitis
- Adrenal Insufficiency
- Malignant Hyperthermia
- Neuroleptic Malignant Syndrome
- Nonconvulsive Status Epilepticus
- Serotonin Syndrome
- Thyroid Storm

99.4 Role of Biomarkers

Biomarkers can aid in differentiating between infectious and noninfectious causes of fever, guiding diagnosis and rationalizing antibiotic use.

- Procalcitonin (PCT): Elevated levels suggest bacterial infections and help distinguish bacterial sepsis from other causes of systemic inflammation.
- C-Reactive Protein (CRP): A nonspecific marker of inflammation; trends can help assess response to therapy.

Recommendations

- Use PCT levels to guide initiation and discontinuation of antibiotics in suspected bacterial infections.
- Monitor CRP trends in conjunction with clinical findings to evaluate treatment efficacy.

Table 99.1 Diagnostic clues for noninfectious causes

Noninfectious cause	Diagnostic clues
Drug-induced fever	Recent initiation of new medications; lack of infection signs
Thromboembolism	Unilateral leg swelling, dyspnea, hypoxia
Autoimmune responses	Joint pain, rash, elevated inflammatory markers
Transfusion reactions	Fever shortly after blood product administration

The use of PCT and CRP is done only when there is low to intermediate probability of bacterial infection in a critically ill patient with a new onset fever, but no clear focus of infection.

99.5 Microbiological Evaluation

Microbiological investigations are critical for identifying pathogens.

Blood Cultures

- Collect samples from two different sites sequentially. Ideal volume to be collected—60 mL in total. There should not be any time interval between the two collections.
- For patients with central venous catheters (CVC), collect paired samples from the catheter and peripheral vein to calculate the differential time to positivity. It is better to sample at least two lumens of CVC while sending cultures.
- Utilize rapid molecular diagnostics when available. This should be used only with blood cultures and not as isolated tests to confirm bacterial infections.

Specific Infections

- Urinary Tract Infections: Replace the urinary catheter before obtaining a culture sample to reduce contamination (i.e., culture to be obtained from new catheter).
- Ventilator-Associated Conditions: Consider bronchoalveolar lavage (BAL) for culture and nucleic acid amplification tests (NAATs). BAL is particularly valuable in ventilator-associated conditions.
- SARS-CoV-2 Testing: Include in workup during periods of high community transmission [5].

99.6 Imaging and Diagnostic Pathways

Imaging is pivotal when initial evaluations are inconclusive.

Chest Radiographs

- Routinely assess for pulmonary infections.

Ultrasonography

- Abdominal Ultrasound: Useful for detecting biliary sources of infection or abscesses.
- Doppler Ultrasound: Evaluate for deep vein thrombosis (DVT) in cases where thromboembolism is suspected.

Computed Tomography (CT)

- Abdominal CT: For suspected intra-abdominal infections or abscesses.
- CT Pulmonary Angiography: If pulmonary embolism is suspected.

Positron Emission Tomography/Computed Tomography (PET/CT)

- Considered when the fever source remains elusive after standard workup.

99.7 Therapeutic Recommendations

Antipyretic Use

- Nuanced Approach: Recognize that fever is a natural immune response. Over-suppression may impair host defenses.
- Indications for Antipyretics:
- Patient discomfort.
- Exacerbation of comorbid conditions (e.g., increased intracranial pressure, cardiac ischemia).
- Physical Cooling Methods: Can be used as complementary therapies, including cooling blankets or ice packs. This should be adopted only with antipyretics and not as the first line of management of raised temperature.

Aggressive Temperature Management

- Risks vs. Benefits: Recent studies suggest that aggressive temperature reduction may not improve outcomes and may be associated with adverse effects.
- Best Practices: Individualize temperature management based on patient condition and clinical context [6]

99.8 Economic and Practical Considerations

- Cost-Conscious Approach: Avoid reflexive ordering of tests without a guiding hypothesis.
- Patient-Centric Diagnostics: Prioritize tests that directly impact patient management.
- Stewardship Programs: Engage in antimicrobial stewardship to reduce unnecessary antibiotic use.

99.9 Special Populations

Immunocompromised Patients

- Neutropenic Patients: Use a lower fever threshold (≥38.0 °C or 100.4 °F).
- Organ Transplant Recipients: May have atypical presentations; maintain a high index of suspicion for opportunistic infections.

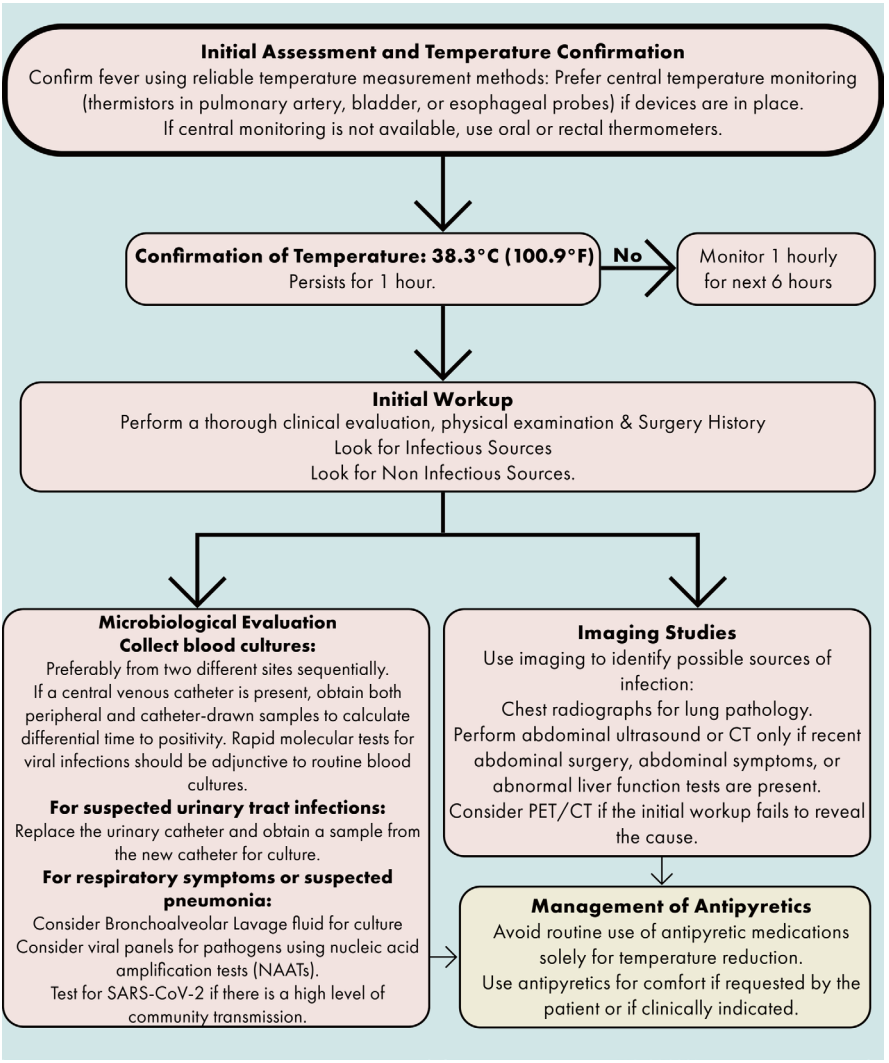
Diagnostic Protocols

- Early Broad-Spectrum Antibiotics: Consider in neutropenic fever after appropriate cultures are obtained.
- Customized Workup: May include fungal cultures, cytomegalovirus PCR, or other specialized tests.

99.10 Conclusion

Managing fever in the ICU requires a comprehensive and systematic approach. Accurate temperature measurement, utilizing the most reliable methods, is the first critical step. Differentiating between infectious and noninfectious causes through a structured framework ensures targeted diagnostics and treatments. The integration of biomarkers like procalcitonin and CRP can refine diagnostic accuracy and guide antibiotic stewardship. Advanced imaging modalities and procedures, such as PET/CT and bronchoalveolar lavage, play significant roles in identifying elusive sources of fever. Therapeutic interventions should balance the benefits of fever reduction with potential risks, avoiding unnecessary suppression of the immune response. Emphasizing a cost-conscious, patient-centric approach minimizes unnecessary testing and interventions. Special populations, including immunocompromised patients, require adjusted thresholds and tailored diagnostic protocols. By adhering to these comprehensive guidelines, clinicians can optimize care for febrile ICU patients, improving outcomes while efficiently utilizing resources.

Algorithm 99.1: Approach to fever in the ICU



Bibliography

1. O'Grady NP, Barie PS, Bartlett JG, Bleck T, Carroll K, Kalil AC, et al. Guidelines for evaluation of new fever in critically ill adult patients: 2008 update from the American College of critical care medicine and the infectious diseases society of America. Crit Care Med. 2008;36(4):1330–49.
2. O'Grady NP, Alexander E, Alhazzani W, Alshamsi F, Cuellar-Rodriguez J, Jefferson BK, et al. Society of critical care medicine and the infectious diseases society of America guidelines for evaluating new fever in adult patients in the ICU. Crit Care Med. 2023;51(11):1570–86.
3. O'Grady NP, Alexander E, Alhazzani W, Alshamsi F, Cuellar-Rodriguez J, Jefferson BK, et al. Executive summary: guidelines for evaluating new fever in adult patients in the ICU. Crit Care Med. 2023;51(11):1566–9.
4. Marik PE. Fever in the ICU. Chest. 2000;117(3):855–69.
5. Niven DJ, Laupland KB. Pyrexia: aetiology in the ICU. Crit Care. 2016;20(1):247.
6. Egi M, Makino S, Mizobuchi S. Management of fever in critically ill patients with infection. J Emer Critical Care Med. 2018;2:10.