

## A Note on Febrile Neutropenia

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### COMMENTARY

A single oral temperature greater than or equal to 101°F, or a temperature greater than or equal to 100.4°F for at least an hour, along with an absolute neutrophilic count (ANC) of fewer than 1500 cells/microliter, is considered neutropenic fever. The ANC is less than 500 cells per microliter in severe neutropenia, or it is likely to fall below 500 cells/micro-L in the next two hours. The ANC in deep neutropenia is less than 100 cells per microliter. Multiply the total white blood cell (WBC) count by the percentage of polymorphonuclear cells (PMNs) and band neutrophils to get the anemia count (ANC). Neutropenic fever is the most prevalent condition encountered during the pre-engraftment period, and it is associated with a 10% in-hospital death rate. Bloodstream infections are the most common cause of neutropenic fever, with gram-positive organisms being the most common, followed by gram-negative organisms. Antimicrobial prophylaxis, on the other hand, influences the incidence of positive blood cultures, and only 10%–25% of all patients with neutropenic fevers will be identified bacteremia. These patients are predisposed to bloodstream infections due to mucosal barrier damage. Bacterial pneumonia can develop in HCT recipients with neutropenic fevers, with a reported rate of 20%–50% in the pre-engraftment phase. During this time, neutropenic typhilitis is also seen. Among recent years, multidrug-resistant (MDR) organisms, including as vancomycin-resistant *Enterococcus* (VRE) and carbapenem-resistant Enterobacteriaceae, have grown more common in HCT patients (CRE).

#### Initial FN evaluation should include the following:

- Complete blood count with differential
- Complete metabolic panel
- Blood cultures from each lumen of the CVC or peripheral cultures if without a CVC ( $\geq 1$  ml of blood)
- Clean-catch bacterial urine cultures (urine catheterization should not be done, especially in the neutropenic patient)
- Gram stain and culture from suspicious skin, oropharyngeal, or CVC sites.

Peripheral blood cultures, in addition to central blood cultures, can be used to distinguish bacteremia versus CVC infection based on the differential time to positive, though the significance of this

metric on treatment decision-making in FN is uncertain followed by coagulation tests in patients who are bleeding. Also, chest radiography is not routinely suggested and should only be performed in patients who have respiratory compromise, pulmonary infection symptoms, or auscultatory signs. A Computed Tomography (CT) of the sinuses should be performed on patients who have sinus soreness. Endo gastroduodenoscopy with biopsy and culture should be considered for patients with esophagitis to rule out viral and fungal causes. A stool sample from patients with diarrhea should be sent for culture, rotavirus, and *Clostridium difficile* testing. Although lumbar puncture is rarely necessary, if the patient exhibits CNS symptoms, a head CT should be performed first to rule out mass lesions or hemorrhagic stroke, both of which can result in elevated intracranial pressure. Shunt fluid testing from implanted devices such VP shunts or Ommaya reservoirs is uncommon.

In most cases, the infectious etiology cannot be confirmed, and the patient is diagnosed with a fever of unknown origin (FUO). FUO is defined as neutropenic cases with a fever of more than 38.3 degrees Celsius and no clinically or microbiologically diagnosed illness. Infections that have been documented account for just about 30% of all cases. In patients with cancer who have a fever and neutropenia, infections are the leading cause of morbidity and mortality. Most infections are caused by bacteria, but they can also be caused by viruses or fungi. Gram-positive bacterial infections, such as *Staphylococcus*, *Streptococcus*, and *Enterococcus* species, are common bacterial pathogens. Infectious agents have also been found, including *Pseudomonas aeruginosa*, *Acinetobacter* species, *Stenotrophomonas maltophilia*, *Escherichia coli*, and *Klebsiella* species. Neutropenic fever is the most prevalent and dangerous complication associated with hematological malignancies or individuals undergoing cancer chemotherapy. When a neutropenic patient meets an infectious pathogen, neutropenic fever develops. In this immunocompromised state, patients' immunity to infections is lost or impaired. The host's defenses, such as the mucosal lining of the GI tract or the sinuses, may be compromised, leaving the body vulnerable to an infectious pathogen's invasion. This problem affects about 1% of people undergoing chemotherapy and radiation.

Oral empiric therapy with a fluoroquinolone plus amoxicillin/clavulanate is indicated in the outpatient environment for low-risk individuals. Clindamycin can be used by people who are allergic to

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penicillin. If the patient is still febrile after 48 to 72 hours, he or she will need to be admitted. Intravenous antibiotic therapy should be given within 1 hour of triage for high-risk patients with neutropenic fever, and patients should be observed for at least 4 hours before discharge. Monotherapy with antipseudomonal beta-lactam drugs such as cefepime, carbapenems, or piperacillin and tazobactam

is recommended by the Infectious Disease Society of America (IDSA). Vancomycin is not indicated for first-line treatment, but it should be explored if a catheter-related infection, skin or soft tissue infection, pneumonia, or hemodynamic instability are suspected. If patients do not react to treatment, coverage should be increased to encompass species that are resistant to treatment.