The Journal of Emergency Medicine, Vol. 57, No. 5, pp. 689–700, 2019
Published by Elsevier Inc.
0736-4679/$ - see front matter

https://doi.org/10.1016/j.jemermed.2019.08.009

Selected Topics: Oncological Emergencies

ONCOLOGIC EMERGENCIES: THE FEVER WITH TOO FEW NEUTROPHILS

Brit Long, MD* and Alex Koyfman, MD†

*Department of Emergency Medicine, Brooke Army Medical Center, Fort Sam Houston, Texas and †Department of Medicine, The University of Texas Southwestern Medical Center, Dallas, Texas

Reprint Address: Brit Long, MD, Department of Emergency Medicine, Brooke Army Medical Center, 3841 Roger Brooke Drive, Fort Sam Houston, TX 78234

☐ **Abstract—Background: Cancer is associated with a variety of complications, including neutropenic fever, which can result in severe morbidity and mortality. This oncologic emergency requires ED management. Objective: This narrative review provides focused updates for emergency clinicians regarding neutropenic fever. Discussion: Neutropenic fever is defined by fever with oral temperature >38.3°C or temperature >38.0°C for 1 hour with an absolute neutrophil count (ANC) < 1000 cells/microL. Patients who have received chemotherapy within 6 weeks of presentation are at high risk for neutropenia. While most patients with neutropenic fever do not have an identifiable bacterial source of fever, clinicians should treat patients for bacterial infection. Rapid assessment and management are vital to improving outcomes in patients with suspected or confirmed neutropenic fever. History and examination should focus on the most common sites of infection: the gastrointestinal tract, blood, skin, lung, and urinary tract. However, physical examination and laboratory or imaging assessment may not display classic signs of infection. Blood cultures should be obtained, and broad-spectrum antibiotics are recommended. Oncology consultation is an integral component in the care of these patients. Several risk scores can assist in stratifying patients who may be appropriate for discharge home and follow-up. Conclusions: Neutropenic fever is an oncologic emergency. Rapid diagnosis and care of patients with neutropenic fever can improve outcomes, along with oncology consultation. Published by Elsevier Inc.**

☐ **Keywords—cancer; malignancy; therapy; infection; neutropenic fever; febrile neutropenia**

CLINICAL SCENARIO 1

A 43-year-old female with history of breast cancer receiving docetaxel for chemotherapy presents to the emergency department (ED) with fever at home. She has felt fatigued, but has no other complaints. Her vital signs include oral temperature 38.2°C, heart rate 101 beats/min, blood pressure 118/71 mm Hg, respiratory rate 17 breaths/min, and oxygen saturation 98% on room air. On examination, she has dry oral mucosa, but no evidence of mucositis. Urinalysis and chest radiograph are negative for acute findings. Her absolute neutrophil count (ANC) returns at 480/μL. She receives acetaminophen, i.v. fluids, and cefepime. She feels improved after 5 h and is afebrile. She asks to be discharged home.

CLINICAL SCENARIO 2

A 62-year-old male presents with cough, fatigue, decreased oral intake, and subjective fever at home. He has a history of chronic lymphocytic leukemia and received chemotherapy 10 days ago. Examination reveals oral temperature 38.2°C, heart rate 119 beats/min, blood pressure 88/49 mm Hg, respiratory rate 23 breaths/min, and oxygen saturation 90% on room air. He appears critically ill. Lung auscultation reveals normal breath sounds bilaterally. Chest radiograph and urinalysis are also normal. Cefepime and azithromycin are administered,

Received: 31 March 2019; Final submission received: 10 June 2019;
Accepted: 2 August 2019

along with i.v. fluids. Chest computed tomography (CT) demonstrates an infiltrate in the right middle lobe, with a small pleural effusion.

INTRODUCTION

More than 15 million people in the United States were alive in 2016 with a history of cancer (1–5). Cancer and its treatment can result in a variety of complications that can be challenging to diagnose and manage. These complications can range from asymptomatic to life-threatening. Due to improved cancer therapies and life expectancy, patients with cancer are increasingly being treated as outpatients, are living longer, and frequently present to the ED.

Why is Neutropenic Fever Important?

Neutropenic fever is a significant complication of cancer therapy and an oncologic emergency. More than 100,000 cases of neutropenic fever occurred in the United States in 2012 (1–3). During treatment, neutropenic fever can occur in up to 50% of patients with solid tumor and up to 80% of patients with hematologic malignancy (3–7). Patients with neutropenic fever may appear non-toxic, with fever the only sign of infection, but their compromised immune system places them at high risk for sepsis and severe morbidity and mortality (2,3,8,9). Unfortunately, the mortality rate for neutropenic fever ranges from 5% to 20%, though mortality can reach up to 50% if septic shock is present (8–12).

METHODS

This narrative review is part of a series evaluating several classes of complications associated with malignancy and therapy. To complete this narrative review on neutropenic fever, authors completed a literature search of PubMed, Google Scholar, and MEDLINE using search terms *neutropenic fever* OR *fever* AND *neutropenia*. Authors included guidelines, randomized controlled trials, cohort/observational studies, narrative reviews, and systematic reviews/meta-analyses. Studies were limited to English and adult patients. Initial literature search revealed 380 resources. Authors excluded studies not focusing on emergency medicine evaluation and management, resulting in inclusion of 68 resources.

DISCUSSION

Neutrophils are an essential component of the immune system, which play key roles in defense against bacterial and fungal pathogens. Neutropenia in cancer patients most commonly occurs due to chemotherapeutic agents, which act on several cellular functions, specifically damaging the bone marrow and the ability of immune cells to proliferate (2,3,8–12). The most common chemotherapies associated with neutropenia include alkylating agents, anthracyclines, antimetabolites, camptothecin, hydroxyurea, mitomycin C, the taxane class, and vinblastine (8–12). Though clinicians typically first assume infection in patients with neutropenia and fever, there are a variety of causes of neutropenia (Table 1). A single session of chemotherapy with one of the previously mentioned chemotherapy agents can result in a decrease in the ANC, typically in 5–14 days (2,3,13). The duration of neutropenia is dependent upon the malignancy and agent utilized for therapy: chemotherapy in solid organ cancer patients is associated with a duration of neutropenia < 5 days, while chemotherapy in hematologic cancers can cause neutropenia that lasts > 14 days (13–16). Other causes of neutropenia and depressed cell lines include hematologic malignancies and myelodysplastic syndromes that result in bone marrow suppression or solid organ tumors that infiltrate and replace bone marrow (13–16).

Table 1. Causes of Neutropenia

Cause	Specifics
Hereditary	Cohen syndrome, cyclic neutropenia, Barth syndrome, Kostmann syndrome, Chediak-Higashi syndrome, Hermansky-Pudlak syndrome Type 2, and many others
Immune	Autoimmune and alloimmune conditions (Crohn's disease, rheumatoid arthritis, Sjögren syndrome, systemic lupus erythematosus, granulomatosis with polyangiitis)
Infectious	Bacteria, virus, fungus, parasite
Medications	Chemotherapeutic agents, psychotropic medications, antidepressants, anticonvulsants, H2 antagonists, antibiotics, diuretics, thionamides, rheumatologic agents, nonsteroidal anti-inflammatory medications, allopurinol
Metals	Gold, arsenic, mercury exposure
Nutritional	B-12, copper, and folate deficiency

How is Neutropenic Fever Defined?

The Infectious Diseases Society of America (IDSA) defines neutropenic fever as a single oral temperature ≥ 38.3°C or temperature ≥ 38.0°C for 1 h in a neutropenic patient (8,10). The definition of neutropenia varies, but it is typically defined by an ANC < 1000 cells/μL, with further classification by severity: severe (<500 cells/μL) and profound (<100 cells/μL) (8–10). The ANC is calculated by the following: ANC = white blood cell

count × ([neutrophils/100] + [bands/100]) (8–10). As the ANC decreases, the risk of infection and poor outcome is increased due to a worsening immune system. For example, an ANC < 100 cells/μL is associated with higher risk of severe infection compared to an ANC < 1000 cells/μL (8–12). Other high-risk features for neutropenic fever and severe infection include a duration of neutropenia > 7 days (2,3,8–12).

What Microbes Can Cause Neutropenic Fever?

Approximately 20–30% of patients with neutropenia and fever have an identifiable source of infection (13,17–20). Although neutropenia can be due to a variety of causes (Table 1), consideration of an infectious source is necessary in the patient with fever and neutropenia in the ED. The most common infectious organisms include endogenous flora, such as *Staphylococci*, *Streptococci*, *Escherichia coli*, Enterobacter, anaerobes, *Klebsiella, Pseudomonas*, and *Corynebacterium* (8,9,19–24). *Staphylococcus epidermidis* is the most common Gram-positive cause. Increasing use of long-term central venous catheters, prophylactic and empiric antibiotics targeting *Pseudomonas*, and newer chemotherapeutic regimens may be potential etiologies of this rise in Gram-positive infections (8,9,19–24). Patients at low-risk with no prophylaxis are more commonly affected by Gram-negative bacteria, while high-risk patients receiving antibacterial prophylaxis are more commonly affected by Gram-positive organisms (8,9). *Candida* may result in mucosal infections, though bloodstream and device infections may also occur. Mold fungal species, including *Aspergillus,* Zygomycetes*, Mucor,* and *Fusarium*, can cause life-threatening invasive infection with > 2 weeks of neutropenia. Patients with acute myeloid leukemia are also susceptible to mold species. Viral infections commonly affect those with hematologic malignances and hematopoietic stem cell transplantation (HSCT), including influenza, respiratory syncytial virus (RSV), and parainfluenza virus (PIV). Influenza and RSV are common in the winter, while PIV is more common in the summer. Upper respiratory symptoms (congestion, rhinorrhea, sinusitis, sore throat) are common initial complaints; however, this may progress to lower respiratory tract infection with hypoxemia, tachypnea, and dyspnea, which increases mortality. Risk factors for upper respiratory tract infection progressing to a lower respiratory tract infection include smoking, neutropenia, lymphocytopenia, allogeneic HSCT, graft-vs-host disease, and older age (8,9,19–24).

How Should You Evaluate the Patient with Neutropenic Fever?

Due to its life-threatening nature, patients with suspected neutropenic fever require rapid diagnosis and management. Patients who have received chemotherapy within the last 6 weeks and present to the ED with fever should be assumed to be neutropenic until proven otherwise. Treatment should not be delayed pending laboratory evaluation. The most common sites of infection listed in decreasing order include the gastrointestinal tract, blood, skin, lung, and urinary tract (2,3,8–12,25). Physician assessment within 15 min of initial triage is recommended (10). History and examination should focus on organ-specific infections. Examination is not always straightforward, as patients may not display typical inflammatory responses of local infections, apart from fever (2,3,10). An oral temperature should be obtained with initial vital signs. Temperature should be obtained via tympanic membrane or axillary thermometry if mucositis is present (8–10). Rectal temperatures should be avoided due to risk of local mucosal trauma and bleeding (8,9,25). Evaluation of the oral cavity for mucositis is important, as breakdown in mucosal barriers increases risk of infection and is a marker for worse outcome (Table 2) (8–12,25).

Recommended ED assessment includes complete blood cell count with differential, two sets of blood cultures (aerobic and anaerobic, including 1 set from each lumen of indwelling devices plus 1 peripheral set or 2 cultures from separate venipuncture sites), liver function tests, electrolytes, lactate, and renal function (2,3,8–10). Chest radiograph for patients with respiratory symptoms is recommended. Other tests, including imaging, should be based upon clinical suspicion of other sources and microbes. Fungal pathogens include *Aspergillus fumigatus* and *Candida* species (8,9,26,27). Fungal blood cultures are usually not indicated acutely in the ED, but the oncologist may request these cultures in those with high risk of candidemia, including patients undergoing active chemotherapy, hematologic malignancy, solid organ or hematopoietic transplantation, central venous catheter, and those receiving total parenteral nutrition (2,3,8,9). Viral

Table 2. National Cancer Institute Oral Mucositis Grading (9,25)

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
No or mild symptoms; no interventions needed	Moderate pain but does not interfere with oral intake; modified diet indicated	Severe pain that interferes with oral intake	Life-threatening, urgent intervention indicated	Death

Table 3. Neutropenic Fever Considerations

Infection	Considerations	Therapy
Oropharyngeal and esophagitis (8,9,46)	Oral mucosa breakdown increases risk of infection. Mucositis presents with erythema, pain, pseudomembranes, ulcers, and xerostomia; fever is also common. *Streptococcus viridans* and HSV can result in oral ulceration and severe mucositis. Oral candidiasis may present with white plaques, which are often otherwise asymptomatic. Oral painful ulcers or vesicles more commonly present with HSV. Dysphagia, odynophagia, and retrosternal burning can be due to *Candida*, HSV, or CMV. Upper endoscopy and biopsy are needed to assist in management.	Fluconazole is the first-line therapy for oral candidiasis and esophagitis. Endoscopy and biopsy guide therapy for HSV and CMV, which require antivirals.
Sinusitis (2,3,47)	Sinuses are a common site of bacterial infection in neutropenia. Patients with prolonged neutropenia, high-dose corticosteroids, or graft-vs.-host disease are at high risk for mold infection (mucormycosis). Periorbital swelling/cellulitis, sinus tenderness/pain, nasal congestion/erosion require further evaluation. CT of the sinuses is recommended, with consideration of ENT/ophthalmology consultation. MRI is recommended if cranial nerve deficits or proptosis is present.	Broad-spectrum coverage, including for anaerobes, is recommended. Periorbital cellulitis also requires vancomycin, due to high risk of *Staphylococcus aureus* Invasive fungal sinusitis requires liposomal amphotericin B.
Skin/soft tissue infection (2,3,8,9)	Minimal erythema, warmth, or induration may be present. These findings are more common in non-neutropenic patients. Abscesses may have limited purulent drainage. Group A streptococcus and *S. aureus* are the most common pathogens, though *Pseudomonas*, *Candida* species, *Escherichia coli*, and HSV may also cause skin infection. Necrotizing fasciitis must always be considered. Evaluation for bullae, crepitus, pain out of proportion, and skin discoloration is needed.	Broad-spectrum coverage with vancomycin, daptomycin, or linezolid is recommended. Consideration of deep space infection, such as necrotizing fasciitis, requires surgical consultation with broad-spectrum antibiotics.
Cardiovascular (2,3,48)	Endocarditis is a concern with new murmur or fever with central venous catheter. Blood cultures are required with echocardiography for diagnosis of endocarditis.	If patient is toxic, broad-spectrum antibiotics are recommended. If not critically ill and endocarditis is suspected, antibiotics can be provided after blood cultures are obtained.
Pulmonary infection (2,3,26–28)	Pneumonia mortality rate approaches > 50% in neutropenic fever. The most common organisms remain *Streptococcus pneumoniae, Mycoplasma pneumoniae*, and *Chlamydia pneumoniae.* Hospital-acquired infections are more common than in other populations, but atypical organisms, such as *Aspergillus* species, *Mycoplasma pneumoniae, C. pneumoniae, Legionella pneumophilia*, *Nocardia* species, and viral species may cause infection. *Pneumocystis jiroveci* is more common in ALL or lymphoma. These patients are at high risk of fulminant respiratory disease. Pneumonia due to bacterial organisms typically presents with lower respiratory tract symptoms. Viral species such as influenza, respiratory syncytial virus, parainfluenza, and CMV can cause severe infection. Viral infections more commonly present with upper respiratory type symptoms, such as congestion, sore throat, and cough. Chest radiography is recommended for pulmonary symptoms, though pulmonary infiltrates may not be present with neutropenia.	Broad-spectrum coverage with a β-lactam or carbapenem plus a fluoroquinolone or aminoglycoside, or other atypical coverage. Severe pneumonia or suspicion of MRSA requires addition of vancomycin or linezolid. *Aspergillus* infection should be considered in patients with hematologic malignancy, graft-vs-host disease, nodular/cavitary pneumonia, segmental consolidation, or ground glass infiltrates on imaging, with antifungal therapy recommended. If influenza is present, antiviral therapy is recommended. *Pneumocystis* pneumonia should be treated with trimethoprim/sulfamethoxazole.

(*Continued*)

Table 3. Continued

Infection	Considerations	Therapy
	Chest CT or US may be better diagnostic evaluations for early infiltrates. Respiratory virus testing (including influenza) and urine *Legionella* testing is recommended. Sputum testing may assist in the inpatient setting.	
Genitourinary infection (2,3,49)	Patients with dysuria, urgency, frequency, suprapubic pain, or hematuria should undergo urinalysis and urine culture. Indwelling urinary catheters increase risk of UTI. Risk of pyelonephritis increases in patients with obstruction (mass). Pyuria may not be present in neutropenic patients with UTI. Ultrasound can be used to assess for hydronephrosis and degree of obstruction. Vulvovaginal candidiasis may present with vaginal discharge, pruritis, soreness, and dyspareunia. Antibiotic use is a risk factor.	No specific addition to therapy is recommended beyond empiric antibiotics for UTI or pyelonephritis. Uncomplicated vulvovaginal candidiasis can be treated with fluconazole.
Catheter-related bloodstream infection (2,3,44,45)	Intravascular access devices can be an entry site for infection. Risks increase with prolonged hospitalization, duration of catheterization, neutropenia, parenteral nutrition, and colonization of the catheter site. Subcutaneous ports have lower risk of infection. Inflammation and erythema at the entry site suggest infection, and culture of any drainage and the lumen of the device should be obtained. Coagulase-negative staphylococci, *E. coli* species, Candida species, and *S. aureus* are the most common species. May result in three types of infection: exit site infection, tunnel infection, or pocket infection. Mucositis increases risk of translocation across mucosal barriers, resulting in bloodstream infection. Evaluate with one blood culture from the furthest distal port of the indwelling line, as well as one from a separate site.	Vancomycin should be added to empiric therapy. Decision on whether to remove an infected device depends on the blood culture obtained from the device. In the ED, consultation with oncology, infectious disease, and the admitting clinician is recommended, as most infected lines can remain in place.
Neutropenic enterocolitis (50–52)	Also known as typhlitis, which is life-threatening. Mucosal damage results in microbial invasion of the intestinal wall and translocation. This leads to inflammation, ulceration, transmural necrosis, and perforation. Invasive fungal infection is the cause of up to 20% of cases, with higher rates if septic shock is also present (30%). Abdominal pain (often right lower quadrant), nausea/vomiting, diarrhea, hemorrhage, and peritonitis can occur. If neutropenic fever and right-sided abdominal pain are present, or in the setting of significant abdominal pain or peritoneal findings, CT of the abdomen/pelvis with surgical consultation is recommended. CT often demonstrates bowel wall thickening, mesenteric stranding, intestinal dilatation, mucosal enhancement, and pneumatosis intestinalis (this finding is specific for typhlitis in neutropenia).	Antibiotic therapy should cover Gram-negative and anaerobic species (piperacillin-tazobactam, carbapenem, or antipseudomonal cephalosporin plus metronidazole). Antifungal coverage is also recommended due to risk of fungal etiology. Surgical consultation is recommended for patients with sepsis, ischemia, peritonitis, perforation, or gastrointestinal bleeding.
Clostridium difficile (53,54)	Patients with new-onset diarrhea, defined by > 3 stools in 24 h, should be tested for *C. difficile*. Risk factors include antibiotics, chemotherapy, and exposure to *C. difficile*. Patients are at high risk whether or not they have taken antibiotics. Severe infection is marked by lactate > 2.2 mmol/L, hypotension, ileus, WBC > 15,000 cells/μL, or creatinine > 1.5 mmol/L.	Oral vancomycin is recommended for mild infection Severe infection should be treated with metronidazole 500 mg i.v. with vancomycin p.o. Fidaxomicin is another option for treatment.

(*Continued*)

Table 3. Continued

Infection	Considerations	Therapy
	Stool PCR is recommended. If diarrhea is not present, no testing is recommended.	
Other gastrointestinal infection (2,3)	Patients with solid tumors are at high risk of bowel obstruction and mechanical complications. Appendicitis, cholecystitis, hepatitis, diverticulitis, and colitis must be considered in these patients. Other causes of diarrhea include ischemia, bacterial colitis, CMV colitis, parasitic infection, and mucositis.	Treat per condition, along with broad-spectrum antibiotics and fluid resuscitation.
Central nervous system infection (2,3,55,56)	Patients with headache, confusion/altered mental status, focal neurologic deficit should undergo central nervous system imaging. Classic symptoms of meningitis/encephalitis may not be present. Patients with CLL, HSCT, and prolonged neutropenia are at risk for *Cryptococcus neoformans* and *Listeria monocytogenes* infection. Asplenic patients and those with antibody deficiency (CLL, multiple myeloma) are at risk of infection with encapsulated bacteria. Encephalitis is most commonly caused by viral infection, especially in the setting of T-cell deficiency. Mass lesions may be caused by bacterial, viral, parasitic, or fungal species. CT head is recommended, with and without i.v. contrast, though if spinal infection, such as epidural abscess, is a consideration, MRI of the whole spine with contrast is recommended. Lumbar puncture is recommended if considering meningitis or encephalitis. CSF cell count, lactate, glucose, protein, gram stain, culture, and HSV PCR are recommended. Neutropenia may result in the absence of pleocytosis and a normal CSF profile in meningitis. If considering meningitis, provide antibiotics that treat for meningitis.	An anti-pseudomonal antibiotic that penetrates the CSF is needed (cefepime, meropenem, ceftazidime), along with vancomycin and ampicillin. Acyclovir should be added for encephalitis. Treatment for *Cryptococcus* includes amphotericin B flucytosine, followed by fluconazole.

ALL = acute lymphocytic leukemia; CLL = chronic lymphocytic leukemia; CMV = cytomegalovirus; CSF = cerebrospinal fluid; CT = computed tomography; ED = emergency department; ENT = otolaryngology; HSCT = hematopoietic stem cell transplantation; HSV = herpes simplex virus; MRI = magnetic resonance imaging; PCR = polymerase chain reaction; p.o. = per os; US = ultrasound; UTI = urinary tract infection; WBC = white blood cell.

testing should be based on clinical suspicion as well, with testing including polymerase chain reaction (PCR) for influenza, RSV, and PIV (8,9,28). Other tests such as *Clostridium difficile* toxin and cultures, including urine, sputum, wound, and cerebrospinal fluid, depend on history and examination (8,9,29,30).

What About Other Biomarkers, Including Procalcitonin?

A variety of biomarkers have been evaluated in neutropenic fever. Procalcitonin (PCT), C-reactive protein (CRP), CD14, human plasma cell-free DNA, cytokines (ie, interleukin [IL]-6, IL-8, and IL-10), serum urokinase plasminogen activation receptor, presepsin, and several others are currently under study as biomarkers for infection and inflammation (31–41). PCT in particular has been studied for determining the presence of bacteremia and prognostication, with IL-6 and CRP also studied in differentiating infection due to bacterial illness vs. fungal or viral infection (37–41). Though PCT is typically elevated in bacteremia, its rate of increase in patients with neutropenic fever may be slower compared to other patient populations (37,38). Levels < 0.2 μg/L are unlikely with bacteremia, while levels > 0.5 μg/L suggest bacterial infection (2,3,37–39). A systematic review and meta-analysis evaluating use of PCT found a sensitivity of 66% and specificity of 78% for the diagnosis of bacteremia with PCT > 0.5 ng/mL in patients with immunocompromise/neutropenia (40). However, due to the high risk of bacterial etiology in these patients, these biomarkers should not be used to determine need for antibiotic therapy alone. PCT can be used in the inpatient setting to determine timing of antibiotic de-escalation, and combination of PCT with other biomarkers such as CRP or IL-6 is promising. However, biomarkers require further study in neutropenic fever patients (31–41).

Table 4. Multinational Association for Supportive Care in Cancer Risk Index Score Breakdown (60–64)

Characteristic	Points
Febrile neutropenia with no or mild symptoms	5
Febrile neutropenia with moderate symptoms	3
Febrile neutropenia with severe symptoms	0
No hypotension (defined by SBP < 90 mm Hg)	5
No COPD	4
Solid tumor or hematologic malignancy with no previous fungal infection	4
No dehydration requiring parenteral fluids	3
Outpatient status	3
Age < 60 years	2

COPD = chronic obstructive pulmonary disease; SBP = systolic blood pressure.
Low risk: ≥21 points; high risk: <21 point.

How Should You Treat the Patient with Neutropenic Fever?

Sepsis and septic shock require early empiric antibiotics, source control, and fluid resuscitation, as well as vasopressors if needed to improve end organ perfusion (2,3,42). Adrenal insufficiency should be considered due to the common use of corticosteroids. If hypotension remains despite fluid resuscitation and vasopressors, hydrocortisone 100 mg i.v. should be administered (2,3,42). Antibiotics should be initiated early in neutropenic fever once cultures are obtained if possible. However, collection of cultures should not result in a delay of administration of antibiotics > 45 min.

Bactericidal antibiotics are recommended, with coverage of *Pseudomonas aeruginosa* (2,3). Admitted patients should initially receive monotherapy with an antipseudomonal carbapenem, β-lactam, or piperacillin-tazobactam if no source is found on evaluation (2,3,8,9,43). Double coverage for *Pseudomonas* or methicillin-resistant *Staphylococcus aureus* (MRSA) is not recommended except for specific indications (2,3,43). Specifically for *Pseudomonas*, monotherapy is as effective as dual therapy (2,3,10,43). If using cefepime or ceftazidime, metronidazole should be added for oral mucositis or perirectal and intra-abdominal infections (8,9). Patients with soft tissue infection, known history of MRSA, bloodstream infection, severe pneumonia, mucositis, line infection, or hemodynamic instability should receive MRSA coverage (8,9,44,45). This may include vancomycin, linezolid, or daptomycin, though daptomycin is not recommended for pneumonia due to inhibition by pulmonary surfactant. Linezolid or daptomycin is needed for vancomycin-resistant enterococci (2,3). A carbapenem is effective against extended spectrum β-lactamase species, but tigecycline or polymyxin-colistin is needed for carbapenemase-producing Gram-negative bacteria. Patients with true penicillin allergy should receive aztreonam plus vancomycin or clindamycin plus ciprofloxacin, while for those on fluoroquinolone prophylaxis, a fluoroquinolone should not be a component of the initial antibiotic regimen (8–10). Expanding coverage for antibiotic-resistant organisms may be required, as neutropenic patients are at risk of infection from these agents due to health care exposure and prior antibiotic use (2,3). Clinicians should base coverage on prior cultures if available and local/institutional antibiotic sensitivities (8–10). Treatment for fungal infection is recommended for those with persistent fever after 4–7 days of antibiotics, or in the setting of mucormycosis or neutropenic enterocolitis (2,3,8–10). Voriconazole, liposomal amphotericin B, or an echinocandin is recommended for fungal infection (2,3,8,9). Table 3 lists dangerous sources of neutropenic fever, including evaluation and management.

Table 5. Clinical Index of Stable Febrile Neutropenia Score (65–67)

Characteristic	Points
Eastern Cooperative Oncology Group Performance Score ≥ 2	2
Stress-induced hyperglycemia (initial blood glucose ≥121 mg/dL or ≥250 mg/dL in diabetics or if on steroids)	2
Chronic obstructive pulmonary disease	1
Chronic cardiovascular disease	1
Mucositis grade ≥2	1
Monocytes <200 cells/μL	1

Low risk: 0 points; intermediate risk: 1–2 points; high risk: ≥ 3 points.
Interpretation: 1.1% risk of complication within 7 days; 6.2% risk of complication within 7 days; 36% risk of complication within 7 days.

Table 6. Infectious Diseases Society of America Risk Criteria for Neutropenic Fever (8).

Low-Risk Criteria	High-Risk Criteria
Anticipated brief neutropenia (<7 days)	Prolonged and profound neutropenia (<100 cells/μL for > 7 days)
Clinically stable	Hemodynamically unstable
No medical comorbidities	Poor functional status
	Chronic obstructive pulmonary disease
	Advanced age
	Pneumonia, pulmonary infiltrate, hypoxia
	Altered mental status
	Gastrointestinal symptoms
	Mucositis interfering with swallowing
	Indwelling catheter infection
	Uncontrolled pain
	Uncontrolled cancer
	Hepatic or renal insufficiency

Special Considerations

Due to the high risk of infection in cancer patients, departments should isolate these patients. Family, visitors,

Table 7. National Comprehensive Cancer Network Risk Criteria for Neutropenic Fever (9).

High Risk	Low Risk	Outpatient
Anticipated prolonged severe neutropenia	Anticipated short duration of severe neutropenia (≤100 cells/microliter for <7 days)	No critical laboratory results on screening tests
Pneumonia or other complex infection	No comorbid illnesses requiring inpatient management	24-h home caregiver available
Clinically unstable	ECOG performance score 0–1	Home telephone
Significant comorbidity	Outpatient status at time of fever onset	< 1 h from appropriate medical care
Mucositis grade 3 or 4	MASCC low risk (≥21)	Access to emergency facilities
Inpatient status at time of fever onset	No hepatic (5× upper limit transaminases) or renal insufficiency (CrCl < 30)	Adequate home environment
MASCC high risk (<21)		Patient consent
Hepatic or renal insufficiency		
Allogenic HSCT		
Alemtuzumab therapy		
Uncontrolled or progressive cancer		

CrCl = creatinine clearance; ECOG = Eastern Cooperative Oncology Group; HSCT = hematopoietic stem cell transplant; MASCC = Multinational Association for Supportive Care in Cancer.

and ED staff should not enter the patient's room if they have a communicable disease. All personnel entering the room should wash their hands with soap and water, and health care providers should utilize standard barrier precautions. Regarding diet, well-cooked foods are recommended, with avoidance of uncooked deli lunch meats, unpasteurized cheeses, and undercooked meats. Clean raw fruits and vegetables are acceptable.

Granulocyte-stimulating factors, such as filgrastim, may be utilized as primary or secondary prophylaxis for febrile neutropenia after chemotherapy, which may reduce episodes of neutropenic fever, documented infection, and hospitalization (57,58). This therapy is not routinely utilized in the ED. These factors typically improve neutrophil counts within 1 day, with a peak ANC by day 3 (59). Leukocytosis approaching 50,000/μL may be found (59). However, if febrile, these patients should be evaluated and managed similar to neutropenic fever.

Does Every Patient Require Admission to the Hospital?

Many patients with neutropenic fever are admitted; however, society recommendations support outpatient management for carefully selected patients after providing initial intravenous antibiotics and observing for ≥4 h (8–10). A variety of risk scores are available that can assist in risk stratification. The Multinational Association for Supportive Care in Cancer (MASCC) risk index is a validated tool used to calculate the risk of medical complications in neutropenic patients (Table 4) (60–64). Patients at low risk must have no hypotension, no chronic obstructive pulmonary disease, age older than 60 years, no dehydration, have a solid tumor or hematologic malignancy, and minimal symptoms. A score ≥ 21 has a sensitivity of 71% and specificity of 68% for identifying patients at low risk for poor outcome who may be appropriate for outpatient therapy (60–64). The MASCC score has been validated in different populations, though several studies have suggested poor sensitivity in its ability to predict complications (60–64). The American Society of Clinical Oncology (ASCO) and IDSA guidelines state that patients categorized as high risk according to the MASCC score should be hospitalized, while patients categorized as low risk may be appropriate for outpatient therapy (8,10).

The Clinical Index of Stable Febrile Neutropenia (CISNE) score is derived to evaluate outpatients with solid tumors who are low risk for serious complications (Table 5) (65,66). These patients may be appropriate for outpatient therapy with a 0% mortality rate and 1.1% rate of complications (65–67). According to the ASCO and IDSA guidelines, patients with scores 0–2 may be candidates for outpatient therapy, while those with scores ≥ 3 should be considered for admission (8,10). Compared to the MASCC score, the CISNE score displays greater specificity (100%) in identifying low-risk patients with neutropenic fever in the ED. The CISNE score was validated for use in patients with solid malignancy, while the MASCC score is used in both hematologic and solid malignancies (60–68). The CISNE score is promising, and the ASCO and IDSA guidelines state the CISNE score may be used as an additional tool to risk stratify patients with neutropenic fever (10).

The IDSA possesses its own low-risk vs. high-risk criteria (Table 6), as does the National Comprehensive Cancer Network (Table 7) (8,9). For the National Comprehensive Cancer Network criteria, patients can be managed as outpatients if they meet all outpatient criteria, most of the low-risk criteria, and none of the high-risk criteria (9). Success rates in outpatient treatment approximate 80% in low-risk patients, with 20% requiring readmission. Those at risk for failing outpatient treatment include age older than 70 years, poor performance status at home, severe mucositis, and neutropenia < 100 cells/μL (9).

In the ED, consultation with the patient's oncologist is needed, as well as antibiotic administration and monitoring for ≥4 h if discharge is possible (2,3,8–10). Patients on prophylactic fluoroquinolones or those with suspected antibiotic-resistant organisms should be admitted. Other patients who should be admitted include those receiving induction chemotherapy or HSCT. Although there are several risk scores that can assist in patient risk stratification, all patients should be discussed with oncology. These scores do not replace physician judgment, as patients who do not seem appropriate for scoring and outpatient management should be admitted. Patients must be reliable, compliant, and able to return promptly to the hospital. Patients who are discharged with oral antibiotics but remain febrile after 2–3 days of outpatient antibiotic therapy, those with positive blood cultures, or those with new evidence of infection require further evaluation and consideration of admission (10). If patients do not require hospitalization and the patient's oncologist agrees with outpatient management, ciprofloxacin plus amoxicillin/clavulanate or clindamycin is recommended as the antibiotic regimen (10). Single-agent moxifloxacin is being used at some centers.

Clinical Bottom Line

1. Neutrophils are essential to a functioning immune system. Neutropenia, defined by absolute neutrophil count < 1000 cells/μL, is common after chemotherapy, with levels decreasing 5–14 days after treatment. The expected nadir is usually 10 days after chemotherapy.
2. Fever in the setting of neutropenia is an emergency. The IDSA defines neutropenic fever as oral temperature ≥38.3°C or temperature ≥38.0°C for 1 h with neutropenia.
3. Although the majority of patients with neutropenic fever do not have an identifiable bacterial source of infection, neutropenic fever requires emergent administration of antibiotics within 1 h of ED arrival.
4. The gastrointestinal tract, blood, skin, lung, and urinary tract are the most common sites of infection.
5. Physical examination and laboratory or imaging assessment often do not display classic signs of infection in patients with neutropenic fever.
6. Evaluation includes blood cultures, hematology and chemistry assessment, lactate, and imaging based on suspected source, with administration of broad-spectrum antibiotics. Laboratory and imaging evaluation should not delay administration of antibiotics.
7. Several risk scores can be used with oncology consultation, including the MASCC and CISNE scores.

Acknowledgments—BL and AK conceived the idea for this manuscript and contributed substantially to the writing and editing of the review. This manuscript did not utilize any grants, and it has not been presented in abstract form. This clinical review has not been published, it is not under consideration for publication elsewhere, its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. This review does not reflect the views or opinions of the US government, Department of Defense, US Army, US Air Force, Brooke Army Medical Center, or San Antonio Uniformed Services Health Education Consortium Emergency Medicine Residency Program.

REFERENCES

1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin 2016;66:271–89.
2. Charshafian S, Liang SY. Rapid fire: infectious disease emergencies in patients with cancer. Emerg Med Clin N Am 2018;36:493–516.
3. Cantwell L, Perkins J. Infectious disease emergencies in oncology patients. Emerg Med Clin N Am 2018;36:795–810.
4. Kuderer NM, Dale DC, Crawford J, et al. Mortality, morbidity, and cost associated with febrile neutropenia in adult cancer patients. Cancer 2006;106:2258–66.
5. Dulisse B, Li X, Gayle JA, et al. A retrospective study of the clinical and economic burden during hospitalizations among cancer patients with febrile neutropenia. J Med Econ 2013;16:720–35.
6. Klastersky J. Management of fever in neutropenic patients with different risks of complications. Clin Infect Dis 2004;39(suppl 1): S32–7.
7. Bryant AL, Deal AM, Walton A, et al. Use of ED and hospital services for patients with acute leukemia after induction therapy: one year follow-up. Leuk Res 2015;39:406–10.
8. Freifeld AG, Bow EJ, Sepkowitz KA, et al., Infectious Diseases Society of America. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2011; 52(4):e56–93.
9. Baden LR, Swaminathan S, Angarone M, et al. Prevention and treatment of cancer-related infections, version 2.2016, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2016; 14:882–913.
10. Taplitz RA, Kennedy EB, Bow EJ, et al. Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America clinical practice guideline update. J Clin Oncol 2018;36: 1443–53.
11. Lyman GH, Kuderer NM, Crawford J, et al. Predicting individual risk of neutropenic complications in patients receiving cancer chemotherapy. Cancer 2010;117:1917–27.
12. Lyman GH, Rolston KV. How we treat febrile neutropenia in patients receiving cancer chemotherapy. J Oncol Pract 2010;6: 149–52.
13. Melendez E, Harper MB. Risk of serious bacterial infection in isolated and unsuspected neutropenia. Acad Emerg Med 2010;17:163–7.
14. Kang CI, Song JH, Chung DR, et al. Korean Network for Study on Infectious Diseases (KONSID). Bloodstream infections in adult patients with cancer: clinical features and pathogenic significance of

Staphylococcus aureus bacteremia. Support Care Cancer 2012;20:2371–8.
15. Anatoliotaki M, Valatas V, Mantadakis E, et al. Bloodstream infections in patients with solid tumors: associated factors, microbial spectrum and outcome. Infection 2004;32:65–71.
16. Nosari A, Barberis M, Landonio G, et al. Infections in haematologic neoplasms: autopsy findings. Haematologica 1991;76:135–40.
17. Wisplinghoff H, Seifert H, Wenzel RP, et al. Current trends in the epidemiology of nosocomial bloodstream infections in patients with hematological malignancies and solid neoplasms in hospitals in the United States. Clin Infect Dis 2003;36:1103–10.
18. Zinner SH. Changing epidemiology of infections in patients with neutropenia and cancer: emphasis on gram-positive and resistant bacteria. Clin Infect Dis 1999;29:490–4.
19. Ramphal R. Changes in the etiology of bacteremia in febrile neutropenic patients and the susceptibilities of the currently isolated pathogens. Clin Infect Dis 2004;39(suppl 1):S25–31.
20. Oliveira AL, de Souza M, Carvalho-Dias VM, et al. Epidemiology of bacteremia and factors associated with multi-drug-resistant gram-negative bacteremia in hematopoietic stem cell transplant recipients. Bone Marrow Transplant 2007;39:775–81.
21. Portugal RD, Garnica M, Nucci M. Index to predict invasive mold infection in high-risk neutropenic patients based on the area over the neutrophil curve. J Clin Oncol 2009;27:3849–54.
22. Yadegarynia D, Fatemi A, Mahdizadeh M, et al. Current spectrum of bacterial infections in patients with nosocomial fever and neutropenia. Caspian J Intern Med 2013;4:698–701.
23. Mandal PK, Maji SK, Dolai TK, et al. Micro-organisms associated with febrile neutropenia in patients with haematological malignancies in a tertiary care hospital in eastern India. Indian J Hematol Blood Transfus 2015;31:46–50.
24. Kanamaru A, Tatsumi Y. Microbiological data for patients with febrile neutropenia. Clin Infect Dis 2004;39(suppl 1):S7–10.
25. de Naurois J, Novitzky-Basso I, Gill MJ, et al. Management of febrile neutropenia: ESMO Clinical Practice Guidelines. Ann Oncol 2010;21(suppl 5):v252–6.
26. Aoun M, Klastersky J. Respiratory infections in the immunocompromised patient. Int J Antimicrob Agents 1993;3(suppl 1):S99–108.
27. Heussel CP, Kauczor HU, Ullmann AJ. Pneumonia in neutropenic patients. Eur Radiol 2004;14:256–71.
28. Chemaly RF, Shah DP, Boeckh MJ. Management of respiratory viral infections in hematopoietic cell transplant recipients and patients with hematologic malignancies. Clin Infect Dis 2014;59(suppl 5):S344–51.
29. Pruitt AA. Nervous system infections in patients with cancer. Neurol Clin 2003;21:193–219.
30. Schuchat A, Swaminathan B, Broome CV. Epidemiology of human listeriosis. Clin Microbiol Rev 1991;4:169–83.
31. Richter ME, Neugebauer S, Engelmann F, et al. Biomarker candidates for the detection of an infectious etiology of febrile neutropenia. Infection 2016;44:175–86.
32. Korpelainen S, Intke C, Hämäläinen S, et al. Soluble CD14 as a diagnostic and prognostic biomarker in hematological patients with febrile neutropenia. Dis Markers 2017;2017:9805609.
33. Purhonen AK, Juutilainen A, Vänskä M, et al. Human plasma cell-free DNA as a predictor of infectious complications of neutropenic fever in hematological patients. Infect Dis (Lond) 2015;47:255–9.
34. Chan SM, Chadwick J, Young DL, et al. Intensive serial biomarker profiling for the prediction of neutropenic fever in patients with hematologic malignancies undergoing chemotherapy: a pilot study. Hematol Rep 2014;6:5466.
35. Kaya S, Köksal I, Menteşe A, et al. The significance of serum urokinase plasminogen activation receptor (suPAR) in the diagnosis and follow-up of febrile neutropenic patients with hematologic malignancies. Int J Infect Dis 2013;17:e1056–9.
36. Stoma I, Karpov I, Uss A, et al. Diagnostic value of sepsis biomarkers in hematopoietic stem cell transplant recipients in a condition of high prevalence of gram-negative pathogens. Hematol Oncol Stem Cell Ther 2017;10:15–21.
37. von Lilienfeld-Toal M, Dietrich MP, Glasmacher A, et al. Markers of bacteremia in febrile neutropenic patients with hematological malignancies: procalcitonin and IL-6 are more reliable than c-reactive protein. Eur J Clin Microbiol Infect Dis 2004;23:539–44.
38. Sakr Y, Sponholz C, Tuche F, et al. The role of procalcitonin in febrile neutropenic patients: review of the literature. Infection 2008;36:396–407.
39. Bruno B, Busca A, Vallero S, et al. Current use and potential role of procalcitonin in the diagnostic work up and follow up of febrile neutropenia in hematological patients. Expert Rev Hematol 2017;10:543–50.
40. Hoeboer SH, van der Geest PJ, Nieboer D, et al. The diagnostic accuracy of procalcitonin for bacteraemia: a systematic review and meta-analysis. Clin Microbiol Infect 2015;21:474–81.
41. Ebihara Y, Kobayashi K, Ishida A, et al. Diagnostic performance of procalcitonin, presepsin, and C-reactive protein in patients with hematological malignancies. J Clin Lab Anal 2017;31(6).
42. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Crit Care Med 2017;45:486–552.
43. Paul M, Dickstein Y, Schlesinger A, et al. Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia. Cochrane Database Syst Rev 2013;6:CD003038.
44. Weber DJ, Rutala WA. Central line-associated bloodstream infections: prevention and management. Infect Dis Clin North Am 2011;25:77–102.
45. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1–45.
46. Epstein JB. Mucositis in the cancer patient and immunosuppressed host. Infect Dis Clin North Am 2007;21:503–22. vii.
47. Long B, Koyfman A. Mucormycosis: what emergency physicians need to know? Am J Emerg Med 2015;33:1823–5.
48. Long B, Koyfman A. Infectious endocarditis: an update for emergency clinicians. Am J Emerg Med 2018;36:1686–92.
49. Schulz L, Hoffman RJ, Pothof J, et al. Top ten myths regarding the diagnosis and treatment of urinary tract infections. J Emerg Med 2016;51:25–30.
50. Nesher L, Rolston KV. Neutropenic enterocolitis, a growing concern in the era of widespread use of aggressive chemotherapy. Clin Infect Dis 2013;56:711–7.
51. Shahani L. Typhlitis: a neutropenic complication. BMJ Case Rep 2012;2012.
52. Duceau B, Picard M, Pirrachio R, et al. Neutropenic enterocolitis in critically ill patients: spectrum of the disease and risk of invasive fungal disease. Crit Care Med 2019;47:668–76.
53. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis 2018;66(7):e1–48.
54. Dupont HL. Diagnosis and management of *Clostridium difficile* infection. Clin Gastroenterol Hepatol 2013;11:1216–23. [quiz: e73].
55. Safdieh JE, Mead PA, Sepkowitz KA, et al. Bacterial and fungal meningitis in patients with cancer. Neurology 2008;70:943–7.
56. Lukes SA, Posner JB, Nielsen S, et al. Bacterial infections of the CNS in neutropenic patients. Neurology 1984;34:269–75.
57. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline update. J Clin Oncol 2015;33:3199–212.
58. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. J Clin Oncol 2006;24:3187–205.
59. Sickles EA, Greene WH, Wiernik PH. Clinical presentation of infection in granulocytopenic patients. Arch Intern Med 1975;135:715–9.
60. Klastersky J, Paesmans M, Rubenstein EB, et al. The Multinational Association for Supportive Care in Cancer risk index: a multinational scoring system for identifying low-risk febrile neutropenic cancer patients. J Clin Oncol 2000;18:3038–51.

61. Klastersky J, Paesmans M. The multinational association for supportive care in cancer (MASCC) risk index score: 10 years of use for identifying low-risk febrile neutropenic cancer patients. Support Care Cancer 2013;21:1487–95.
62. Klastersky J, Paesmans M, Georgala A, et al. Outpatient oral antibiotics for febrile neutropenic cancer patients using a score predictive for complications. J Clin Oncol 2006;24:4129–34.
63. Innes H, Lim SL, Hall A, et al. Management of febrile neutropenia in solid tumours and lymphomas using the Multinational Association for Supportive Care in Cancer (MASCC) risk index: feasibility and safety in routine clinical practice. Support Care Cancer 2008; 16:485–91.
64. Bitar RA. Utility of the Multinational Association for Supportive Care in Cancer (MASCC) risk index score as a criterion for nonadmission in febrile neutropenic patients with solid tumors. Perm J 2015;19:37–47.
65. Carmona-Bayonas A, Gomez J, Gonzalez-Billalabeitia E, et al. Prognostic evaluation of febrile neutropenia in apparently stable adult cancer patients. Br J Cancer 2011;105:612–7.
66. Carmona-Bayonas A, Jimenez-Fonseca P, Virizuela Echaburu J, et al. Prediction of serious complications in patients with seemingly stable febrile neutropenia: validation of the clinical index of stable febrile neutropenia in a prospective cohort of patients from the FINITE study. J Clin Oncol 2015;33:465–71.
67. Coyne CJ, Le V, Brennan JJ, et al. Application of the MASCC and CISNE risk stratification scores to identify low-risk febrile neutropenic patients in the emergency department. Ann Emerg Med 2017; 69:755–64.
68. Cherif H, Johansson E, Bjorkholm M, et al. The feasibility of early hospital discharge with oral antimicrobial therapy in low risk patients with febrile neutropenia following chemotherapy for hematologic malignancies. Haematologica 2006;91:215–22.

ARTICLE SUMMARY

1. Why is this topic important?

Neutrophils are a key component of the immune system, and neutropenia is defined by absolute neutrophil count < 1000 cells/μL. Fever with oral temperature $\geq$38.3°C or temperature $\geq$ 38.0°C for 1 h with neutropenia is a potentially deadly oncologic emergency.

2. What does this review attempt to show?

This review provides focused updates for the emergency clinician concerning neutropenic fever evaluation and management.

3. What are the key findings?

Neutropenic fever is a potentially deadly complication of oncologic therapies, and patients who have received chemotherapy within 6 weeks of presentation are at high risk for neutropenia. Rapid assessment and management are vital to improving outcomes in patients with suspected or confirmed neutropenic fever. History and examination should focus on the most common sites of infection: the gastrointestinal tract, blood, skin, lung, and urinary tract. Unfortunately, physical examination and laboratory or imaging assessment may not display classic signs of infection. Blood cultures should be obtained, and broad-spectrum antibiotics are recommended. Oncology consultation is an integral component in the care of these patients.

4. How is patient care impacted?

Rapid diagnosis and care of patients with neutropenic fever can improve outcomes, along with oncology consultation.