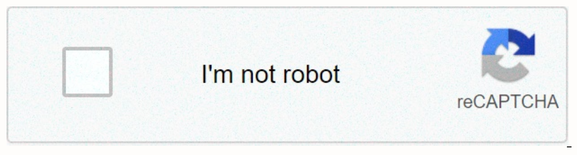

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Idsa neutropenic fever guideline

Fever during chemotherapy-induced neutropenia may be the only indication of a severe underlying infection, as signs and symptoms of inflammation are typically attenuated.10% to 50% of patients with solid tumors and > 80% in those with haematological malignancy will develop fever during one or more cycles of chemotherapy associated with neutropenia. All patients with fever and neutropenia should be treated empirically, quickly and broadly, with antibiotics targeted primarily against severe gram-negative pathogens that can cause life-threatening sepsis. Clinically documented infections occur in 20-30% of febrile episodes. Common sites of tissue-based infection include the intestinal tract, lung, and skin. Bacteremia occurs in 10-25% of all patients, with most episodes occurring in the setting of prolonged or deep neutropenia (absolute neutrophil counts less than 100 neutrophils/mm3). Resistant gram-positive pathogens such as methicillin-resistant staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE) have become more common and are the most prevalent resistant isolates in some centers, accounting for 20% to more than 50% of episodes, respectively. Strains resistant to penicillin of S. pneumoniae and viridan streptococci are less common, but can cause serious infections. Fungi are rarely identified as the cause of the first fever at the onset of the course of neutropenia. Instead, they are found after the first week of prolonged neutropenia and empirical antibiotic therapy. Fever is defined as a single oral temperature measurement of ≥ 38.3°C (101°F) or a temperature ≥ 38.0°C (100.4°F) sustained over 1 hour. Neutropenia is defined as an absolute neutrophil count (NCA) of less than 500 cells/mm3 or one that should fall below 500/mm3 in the next 48 hours. The term deep is sometimes used to describe neutropenia where the ANC is below 100 cells/mm3. The term functional neutropenia refers to patients whose hematological malignancy results in qualitative defects (impaired phagocytosis and death of pathogens) of circulating neutrophils. These patients should be considered at increased risk of infection despite a normal neutrophil count. Risk stratification is a recommended starting point for managing patients with fever and neutropenia. Risk assessment for complications of severe infection should be performed at the presentation of fever (A-II). Risk assessment may determine the type of empirical antibiotic (oral vs. intravenous [IV]), treatment site (hospitalization versus outpatient) and duration of antibiotic therapy (A-II). High-risk patients — those with predicted time (> 7 days) and deep neutropenia (ANC ≤ 100 cells/mm3 after cytotoxic chemotherapy) and/or significant medical conditions, including hypotension, pneumonia, new pain neurological changes. These patients should be in the hospital for empirical therapy (A-II)Low-risk patients — those with early brief (≤ 7 days) days) periods and without or few comorbidities — are candidates for oral empirical therapy (A-II). The formal risk classification can be performed using the validated scoring system of the Multinational Cancer Assistance Association (MASCC). Characteristic WeightBurden of febrile neutropenia without or mild symptoms5No hypotension (systolic blood pressure > 90 mmHg)5No chronic obstructive pulmonary diseaseb4 Tumorsolidos or hematological malignancy without previous fungal infection4 No dehydration requiring parenteral fluids3Solid tumor or hematological malignancy without previous fungal infection4Burden of febrile neutropenia with moderate symptoms3Inon of patient status3Duck < 60 years2NOTE: The maximum score value is 26. Scores below 21 are high risk (B-I).a Burden of febrile neutropenia: Refers to the general clinical status of the patient as influenced by the febrile neutropenic episode. It should be evaluated on the following scale: no mild or mild symptoms (score of 5); moderate symptoms (score of 3); severe or dying symptoms (score 0). Scores of 3 and 5 are not cumulative.b Chronic obstructive pulmonary disease (active chronic bronchitis or emphysema) requiring treatment in the presentation of febrile neutropotic episode: decrease in forced expiratory volumes, need for oxygen therapy and/or steroids and/or bronchodilators.c Previous fungal infection: Demonstrated fungal infection or empirically treated empirical fungal infection. Laboratory tests should include a complete blood count (CBC) with leukocytes and differential platelets, serum creatinine, blood urea nitrogen, electrolytes, hepatic transaminase enzymes, and total bilirubin (A-III). At least 2 sets of blood cultures are recommended:A set collected simultaneously from each lumen of an existing central venous catheter (if present) and a peripheral vein site.2 separate venipuncture sets if no central catheter is present (A-III). Blood culture volumes should be limited to < 1% of total blood volume (usually approximately 70 mL/kg) in patients weighing < 40 kg (C-III). Culture samples from other sites of suspected infection should be obtained as clinically indicated (A-III). A chest x-ray is indicated for patients with respiratory signs or symptoms (A-III). High-risk patients require admission for intravenous empirical antibiotic therapy: monotherapy with an anti-pseudomonal agent β-lactam, such as cefepime, carbapenem (meropenem or imipenem-cylastatin), or piperacilline-tazobactam (A-I). Other antimicrobials (aminoglycosides, fluoroquinolones and/or vancomycin) may be added to the initial regimen for the management of complications (i.e., hypotension, pneumonia) or if antimicrobial resistance is suspected or proven (B-III). Vancomycin (or other active agents against gram-positive aerobic cocci) is NOT recommended as initial antibiotic regimen for fever and neutropenia (A-I). (See table 4 for directions.) Changes in initial empirical therapy may be for patients at risk of infection with MRSA, VRE, extended spectrum beta-lactamase (ESBL) producing gram-negative bacteria and carbapenemase-producing organisms, including klebsiella pneumoniae carbapenemase (KPC) bacteria, particularly if the patient is unstable or has suspected positive blood cultures for resistant bacteria (B-III). Risk factors include infection or prior colonization with the organism or treatment in a hospital with high endemic rates. Most patients allergic to penicillin tolerate cephalosporins, but those with a history of immediate type hypersensitivity reaction (hives, bronchospasmus) should be treated with a combination that prevents β-lactams and carbapenems, such as ciprofloxacin plus clindamycin, or aztreonam plus vancomycin (A-II). Afebrile neutropotic patients who have new signs or symptoms suggesting infection should be evaluated and treated as high-risk patients (B-III). Low-risk patients should receive initial doses of oral or IV empirical antibiotics in a clinical or hospital setting. They can be transitioned to oral or outpatient IV if they meet specific clinical criteria (A-I). Ciprofloxacin plus amoxicilline/clavulanapt in combination is recommended for oral empirical treatment (A-I). Other oral regimens, including levofloxacin or ciprofloxacin monotherapy, or ciprofloxacin plus clindamycin, are less well studied but are commonly used (B-III). Patients receiving fluoroquinolone prophylaxis should not receive oral empirical therapy with fluoroquinolone (A-III). Re-hospitalization or continued hospital stay is necessary for persistent fever, or signs and symptoms of worsening infection (A-III). Changes in the initial antibiotic regimen should be guided by clinical and microbiological data (A-II). Unexplained persistent fever in a stable patient rarely requires an empirical change in the initial antibiotic regimen. If an infection is identified, antibiotics should be adjusted accordingly (A-I). Documented clinical and/or microbiological infections should be treated with appropriate antibiotics for the site and susceptibilities of any isolated organisms (A-I). If vancomycin or other Gram-positive coverage was initiated initially, it may be discontinued after 2 days if there is no evidence of Gram-positive infection (A-II). Hemodynamically instillable patients should have their antimicrobial regimen expanded to include coverage for gram-negative, gram-positive, and anaerobic resistant bacteria and fungi (A-III). Low-risk patients who have been initiated with intravenous or oral antibiotics in the hospital may have their treatment approach simplified if they are clinically stable (A-I). An intra-oral antibiotic exchange can be made if patients are clinically stable and gastrointestinal absorption is considered adequate (A-I). Selected hospitalized patients who meet low-risk criteria may be transitioned to the outpatient setting to receive intravenous or oral antibiotics, provided they are adequate daily (B-III). If the fever persists or is repeated within 48 hours in the outpatient clinic, it is recommended to re-hospitalization, with management for high-risk patients (A-III). Empirical antifungal coverage should be considered in high-risk patients who have persistent fever after 4-7 days of a broad-spectrum antibacterial regimen and no source of fever identified (A-II). In patients with clinically or microbiologically documented infections, the duration of therapy is dictated by the body and location in particular. Appropriate antibiotics should continue at least for the duration of neutropenia (until THE ANC ≥ 500 cells/mm3) or for longer, if clinically necessary (B-III). In patients with unexplained fever, it is recommended that the initial regimen continue until there are clear signs of bone marrow recovery. The traditional endpoint is a rising ANC that exceeds 500 cells/mm3 (B-II). Alternatively, if an appropriate course of treatment has been completed and all signs and symptoms of a documented infection have been resolved, patients who remain neutropotic may resume oral fluoroquinolone prophylaxis until bone marrow recovery (C-III). Fluoroquinolone prophylaxis should be considered for high-risk patients with expected durations of prolonged and deep neutropenia (ANC ≤ 100 cells/mm3 for > 7 days) (B-I). Levofloxacin and ciprofloxacin have been evaluated more comprehensively and are considered approximately equivalent, although levofloxacin is preferred in situations at increased risk for streptococcal infection of the invasive viridans group related to oral mucositis. A systematic strategy for monitoring the development of fluoroquinolone resistance among gram-negative bacilli (A-II) is recommended. The addition of a Gram-positive active agent to fluoroquinolone prophylaxis is generally NOT recommended (A-I). Antibacterial prophylaxis is NOT routinely recommended for low-risk patients who are expected to remain neutropenic for < 7 days (A-III). Empirical antifungal therapy and investigation for invasive fungal infections should be considered for patients with persistent or recurrent fever after 4-7 days of antibiotics and whose overall duration of neutropenia should be > 7 days (A-I). The data are insufficient to recommend a specific empirical antifungal agent for a patient who is already on anti-mold prophylaxis, but switching to a different class of antifungal antimold given intravenously should be considered (B-III). Preventive antifungal management is acceptable as an alternative to empirical antifungal therapy in a subset of high-risk neutropotic patients. Those who remain febrile after 4-7 days of broad-spectrum antibiotics but are clinically stable, have no clinical or chest and sinus signs of fungal infection, have negative serological assays for evidence of fungal, and no recovery of fungi such as Candida or Aspergillus from any site of the body, may have retained antifungal agents (B-II). Antifungal therapy should be instituted if any of these possible indicators are fungal infection was identified. In low-risk patients, the risk of invasive fungal infections is low so that routine use of empirical antifungal therapy is NOT recommended (A-III). Prophylaxis against Candida infections is recommended in groups of patients in whom the risk of invasive candidal infections is substantial, such as allogeneic hematopoietic stem cell transplant recipients (HSCT) or those undergoing intensive remission or salvage induction chemotherapy for acute leukemia (A-I). Fluconazole, itraconazole, posaconazole, voriconazole, caspofungin or micafungin are all acceptable alternatives. Prophylaxis against invasive Aspergillus infections with posaconazole should be considered for selected patients 13 years of age or older who are undergoing intensive chemotherapy for acute myeloid leukemia/myelodysplastic syndrome (AML/MDS) where the risk of invasive aspergillosis without prophylaxis is substantial (B-I). Prophylaxis against Aspergillus infection in allogeneic or autologous transplant recipients was not effective. However, an active molded agent is recommended in patients with previous invasive aspergillosis (A-III), prolonged neutropotic periods of at least 2 weeks (C-III), or a prolonged period of neutropenia immediately prior to HSCT (C-III). Antifungal prophylaxis is NOT recommended for patients in whom the expected duration of neutropenia is < 7 days (A-III). Herpes simplex virus (HSV)-seropositive patients undergoing Allogenetic HSCT therapy or leukaemia induction should receive acycloviral antiviral prophylaxis (A-I). Antiviral treatment for HSV or varicella zoster virus (VZV) is indicated only if there is clinical or laboratory evidence of active viral disease (C-III). Respiratory virus tests (including influenza, parainfluenza, adenovirus, respiratory sincicial virus [RSV], and human metapneumovirus) and chest x-ray are indicated for patients with upper respiratory symptoms (e.g., coryza) and/or cough (B-III). Annual influenza vaccination with inactivated vaccine is recommended for all cancer patients (A-II). The ideal vaccination time is not established, but serological responses may be better between chemotherapy cycles (more than 7 days after the last treatment) or more than 2 weeks before the start of chemotherapy (B-III). Influenza virus infection should be treated with neuraminidase inhibitors if susceptible (A-II). In the scenario of influenza exposure or outbreak, neutropenic patients presenting with flu-like disease should receive treatment empirically (C-III). Routine treatment of RSV in neutropenic patients with upper respiratory disease should NOT be given (B-III). Prophylactic use of myeloid colony stimulating factors (SSCs; also called hematopoietic growth factors) should be considered for patients in whom the risk neutropenia is 20% or more (A-II). CSFs are generally not recommended for the treatment of established established fever neutropenia (B-II). The differentiated time for positivity (DTP) > 120 minutes of qualitative blood cultures simultaneously designed from the central venous catheter and a vein suggests a CLABSI (A-II). For CLABSI caused by S. aureus, P. aeruginosa, fungi or mycobacteria, it is recommended to remove catheters, in addition to systemic antimicrobial therapy for at least 14 days (A-II). Catheter removal is also recommended for tunnel infection or infection at the port pocket site, septic thrombosis, endocarditis, sepsis with hemodynamic instability, or bloodstream infection that persists despite ≥ 72 hours on appropriate antibiotics (A-II). For documented clabsi caused by coagulase-negative staphylococci, the catheter can be retained using systemic therapy with or without antibiotic blocking therapy (B-III). Prolonged treatment (4-6 weeks) is recommended for complicated CLABSI, defined as the presence of deep tissue infection, endocarditis, septic thrombosis (A-II) or persistent bacteremia or fungemia occurring > 72 hours after catheter removal in appropriate antimicrobials (A-II for S. aureus, C-III for other pathogens). Practice hand hygiene, maximum sterile barrier precautions, and skin antisepsis with chlorhexidine for all central venous catheter insertions (A-I). Hand hygiene is the most effective means of preventing transmission of infection in the hospital (A-II). Standard barrier precautions should be followed for all patients and specific isolation of infection for patients with suspected transmissible infections (A-III). HSCT receptors should be placed in private rooms (i.e. from a single patient) (B-III). Aogenetic HSCT receptors should be placed in rooms with > 12 air changes/hour and high-efficiency particulate air filtration (HEPA) (A-III). Dry or fresh plants and flowers should NOT be allowed in the rooms of hospitalized neutropotic patients (B-III). Policies to exclude hospital work should be designed to encourage health professionals to report their diseases or exposures (A-II). Normal gram-positive PathogensCoagulase-negative staphylococciStaphylococcus aureus, including methicillin-resistant isolates Deenterococcus species, including vancomycin-resistant isolatesA streptococciStreptococococcus pneumoniaeStreptococcus pyogenesCommon-negative PathogensEscherichia coliKlebsiella speciesEntoolasSMm