

Neutropenic Fever Practice Guidelines (Adults)

Drug Information Center

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The Pharmacy and Therapeutics Committee has approved guidelines for the prevention and management of neutropenic fever. Created in concert with Infectious Diseases and Bone Marrow Transplant, the guidelines include evaluation and diagnosis, antibiotic therapy, and subsequent monitoring for patients with or at risk for neutropenic fever. A flow chart summarizing empiric drug selection can be found on page 2.

UK Hospital Neutropenic Fever Practice Guidelines

Definitions:

- Fever - A single oral temperature $>38.3^{\circ}\text{C}$ (101.0°F) or a 38.0°C or 100.4°F temperature over 1 hour
- Neutropenia - Absolute neutrophil count (e.g., ANC; bands + segs) $\leq 0.5 \times 10^9/\text{L}$
- High-risk patient – Defined as the presence of any of the following:
 - Pulmonary infiltrates;
 - Mental status changes;
 - New onset renal failure;
 - Hypoxia (a 20 point drop from baseline);
 - Patients with a history of VRE, multi-drug resistant *Pseudomonas* or MRSA

MONITORING

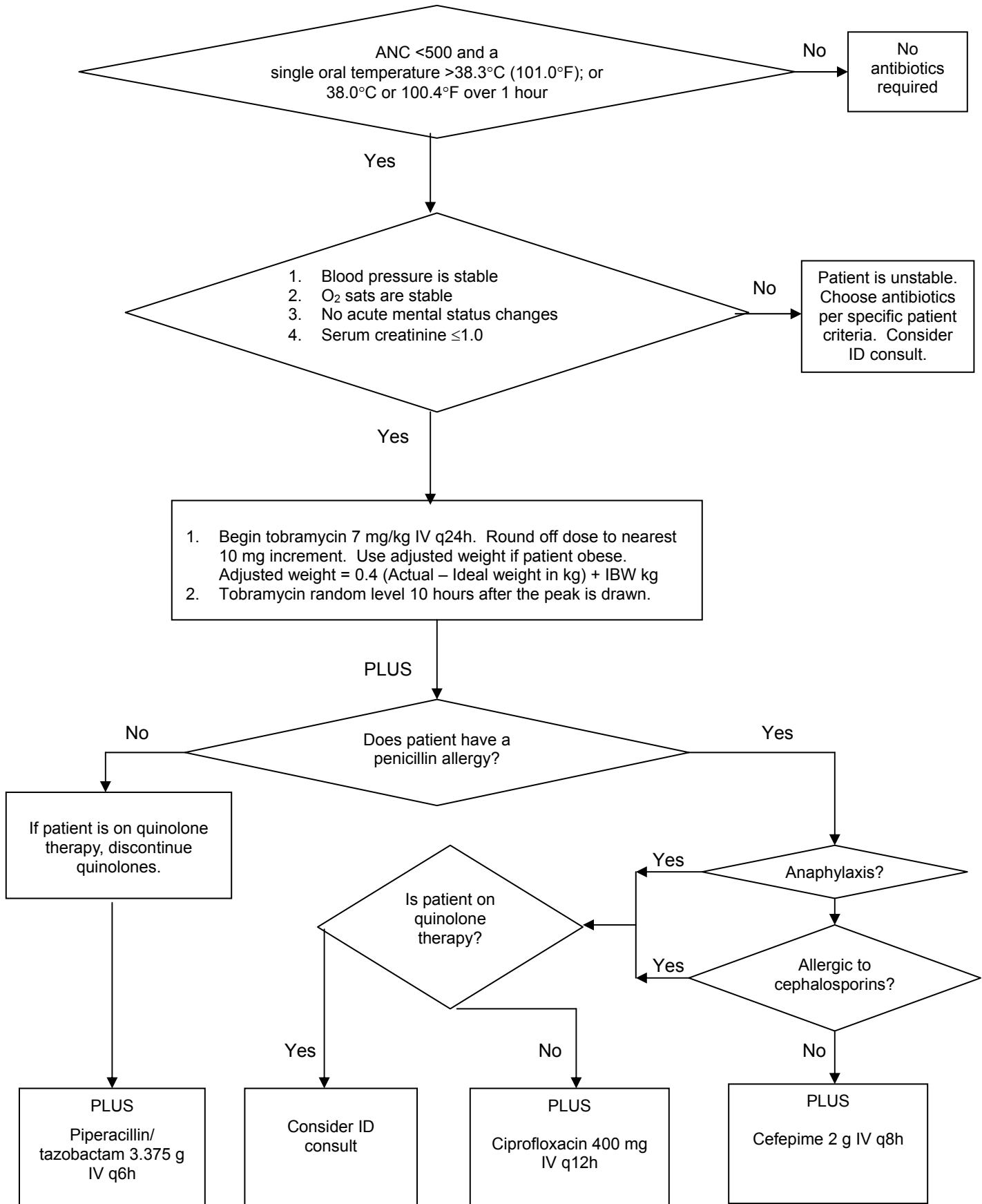
Initial Evaluation:

1. Blood cultures from all ports of indwelling catheters and at least 1 peripheral culture; if no indwelling catheters, then 2 peripheral cultures drawn 30 minutes apart
2. Urinalysis and urine culture
3. Sputum culture if productive cough present, chest x-ray when indicated by symptoms
4. If watery diarrhea present, stool culture for routine pathogens (x1), ova and parasites (x1) and *C. difficile* (x 1)
5. Electrolytes and CBC with differential

Subsequent Evaluation:

1. No more than 2 sets of blood cultures per 24 hour period
2. If initial urine/sputum/stool cultures negative, and no new symptoms present, do not repeat these cultures
3. Twice weekly electrolytes and CBC with differential, unless on amphotericin B (then daily electrolytes with magnesium level)

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TREATMENT

Initiate antibiotic therapy when ANC < 0.5 x 10⁹/L **and** fever is present

Initial Antibiotic Therapy

- If indwelling catheter is not present, or catheter present without obvious infection:
 1. Tobramycin (Nebcin) 7 mg/kg IV q24h. Alter dosing for renal dysfunction per established guidelines. Dose tobramycin on corrected weight if the patient is obese.
Corrected weight in kg = 0.4 (Actual – Ideal weight in kg) + Ideal Body Weight in kg
 2. **Plus** one of the following:
 - a. If patient is **not** allergic to penicillin: piperacillin/tazobactam (Zosyn®) 3.375 gm IV Q6
 - b. If patient is allergic to penicillin and is not on quinolone prophylaxis: ciprofloxacin (Cipro®) 400 mg IV Q12
 - c. If patient has non-anaphylactic allergy to penicillin and is on quinolone prophylaxis: cefipime (Maxipime®) 2 gm IV q8h
 - d. If patient has anaphylactic reaction to penicillin and is on quinolone prophylaxis: obtain ID consult
- If indwelling catheter is present and appears infected:
 1. Add Clindamycin (Cleocin®) 900 mg IV Q8 to antibiotics above
 2. Unless patient has documented MRSA or MRSE colonization or past infection, in which case vancomycin is indicated

Afebrile within 3 days, clinically *stable* and cultures positive:

- If cultures reveal a source of infection, alter antibiotics based on cultures and treat for a standard length of time (minimum: 5 days for UTI, 10 days for bacteremia)
- Caution should be used in prescribing antibiotics for a single blood culture positive for *Staph epidermidis* without clinical signs of infection
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Afebrile within 3 days, clinically *stable* and cultures negative:

1. Continue antibiotics until ANC > 500 (or a maximum of 3 weeks)
2. Consider switching to ciprofloxacin 500 PO BID + TMP/SMX DS PO BID

Persistent fever during first 5 days and clinically *stable* without localizing signs of infection:

- Continue initial antibiotics until ANC > 500 (or a maximum of 3 weeks)

Persistent fever during first 5 days and clinically *unstable* without localizing signs of infection:

- Consult Infectious Disease

Persistent fever after the first 7 days, and clinically *stable* without localizing signs of infection:

- Add antifungal therapy. Notify PharmD to evaluate for availability of anti-fungal study. If no study protocol available:
 1. Creatinine < 2.0:
 - Amphotericin B 0.6 mg/kg IV over 4 hours
 - Prehydrate with 500 cc NS IV over 2 hours
 - Premedicate with:
 - Acetaminophen 650 mg PO
 - Diphenhydramine 25 mg PO or IV
 - Meperidine 25 mg IV q1 hr prn rigors not to exceed 4 doses in a 24 hour period
 - Continue until ANC>500
 2. Creatinine ≥ 2.0:
 - Formulary amphotericin lipid complex at 3-5 mg/kg IV over 2-4 hours (requires ID consult)
 - Continue until
 - ANC>500

General Caveats

- If cultures are positive, empiric antibiotics must be re-evaluated by the physician, and antibiotic regimen tailored to the cultured organism.
- If the patient becomes clinically unstable (see definition of high risk patients), an ID consult is recommended.
- Routine use of growth factors in the treatment of febrile neutropenia is not indicated and is discouraged. Patients on growth factors for other indications should continue therapy per standard of care.

Prophylaxis/Outpatient (post-febrile) Management:

Neutropenic (or anticipated), but afebrile:

- If BMT patient—ciprofloxacin 500 mg PO BID + fluconazole 400 mg PO QD + acyclovir 400 mg PO 5 times per day
- If not BMT patient, None vs Other _____ (MD discretion)

Neutropenic, previously febrile, but now afebrile (maintenance):

- If no amphotericin has been given:
 1. TMP/SMX DS PO BID (until ANC > 500)
 2. If sulfa allergy, ciprofloxacin 500 PO mg BID + amoxicillin/clavulanate 875 mg PO BID (until ANC > 500)
- If amphotericin has been given:
 1. TMP/SMX DS PO BID + fluconazole 400 mg PO QD (until ANC > 500)
 2. Ciprofloxacin 500 PO mg BID + clindamycin 300–450 mg PO TID + fluconazole 400 mg PO QD (until ANC > 500)
 - Consider withholding clindamycin if significant diarrhea present