FEVER & NEUTROPENIA

Definition: Single oral temp $\geq 38.3^\circ$ (or $\geq 37.8^\circ$ axillary) or sustained temp $\geq 38^\circ$ for more than 1 hour, and ANC $< 500/mm^3$ (or ANC $\leq 1000$ and predicted decline to $\leq 500$ over next 48 hours)

Important points:
- Only 50% with neutropenic fever have documented infection; of those, only 20% w/ bacteremia
- Site of infection: Pneumonia > bloodstream > urinary tract > skin/soft tissue, GI > other
- Median time to defervescence ~5d in pts with heme malignancy treated with empiric antibiotics; persistent fever in stable patient rarely requires empiric change to initial antibiotic regimen

1) Look for source of infection

<table>
<thead>
<tr>
<th>Review of symptoms</th>
<th>Physical Exam</th>
<th>Laboratory/Radiology</th>
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<tbody>
<tr>
<td>URI sx</td>
<td>Orthostatic BP</td>
<td>CBC</td>
</tr>
<tr>
<td>Sinus tenderness</td>
<td>Sinus</td>
<td>Chemistry (Cr, CO2)</td>
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<td>Odynophagia/nausea/vomiting</td>
<td>Oropharynx (eval for mucositis)</td>
<td>Liver function tests</td>
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<td>Abdominal pain/diarrhea</td>
<td>Lungs, pulse oximetry</td>
<td>Blood cultures x 2 (1 set from each lumen of CVC, 1 set from peripheral vein)</td>
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<td>Cough/SOB</td>
<td>Catheter/IV site</td>
<td>Culture other sites as indicated</td>
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<td>New skin lesions</td>
<td>Abdomen</td>
<td>Chest x-ray</td>
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<tr>
<td>Stiff neck/AMS</td>
<td>Skin (nodules, rash)</td>
<td>Review surveillance cultures</td>
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<tr>
<td>Perirectal tenderness</td>
<td>Perirectal exam (do NOT perform DRE)</td>
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<tr>
<td>Tenderness at catheter site</td>
<td>Lymph nodes</td>
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<tr>
<td></td>
<td>Mental status</td>
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</tbody>
</table>

From Standard Practice Manual

2) Start antibiotics immediately

SCCA Febrile Neutropenia Empiric Treatment Algorithm

\[ T \geq 38.3 \text{ orally, } \geq 37.8 \text{ axillary} \]

**Intra-abdominal or perineal infection?**

- **YES**
  - Clinically stable?
    - NO
      - Carbapenem$^a$ + Gentamicin
    - YES
      - Carbapenem$^a$ or Ceftriaxone$^b$/Flucloxacin
  - YES
    - Ceftazidime$^c$ + Gentamicin
  - NO
    - Ceftazidime$^c$

$^a$ Carbapenem = Meropenem, imipenem

$^b$ Cefepime is equivalent to Ceftazidime for treatment of febrile neutropenia. In patients with severe mucositis, cefepime may be preferable to ceftaz due to increased activity against gram positive organisms
Empiric vancomycin not recommended, but consider in following situations (and discontinue after 48 hours if no evidence of gram-positive infection):
- Hemodynamic instability/sepsis
- Pneumonia
- Blood cultures positive for GP organism, speciation/susceptibility pending
- Suspected CVC infection
- Skin/soft tissue infection
- Severe mucositis (↑ risk S. viridans bacteremia)

What about patients with VRE? Use daptomycin in patients with known VRE colonization when vancomycin would ordinarily be used (SCCA policy)

Empiric anti-fungal coverage
- Consider Voriconazole for patients expected to be neutropenic ≥7 days with fever ≥96 hours despite broad spectrum antibiotics
- Alternative approach: Reasonable to withhold anti-fungal therapy in patients w/ persistent fever who are stable, not colonized with fungi, have no clinical/radiological evidence of fungal infection, and have negative serologies for fungal infection

Duration of antibiotic therapy
- Infectious source identified →
  - Continue antibiotics for standard treatment course based on organism/site of infection AND until ANC ≥500
  - Alternative approach (not well-studied) is to continue antibiotics for standard treatment course and until signs/symptoms resolved, then switch to oral fluoroquinolone for prophylaxis until marrow recovered
- No infectious source identified →
  - Continue antibiotics until patient afebrile and ANC ≥500
  - Alternative approach (not well-studied) is to switch to oral fluoroquinolone for prophylaxis once patient afebrile x 4-5 days, and continue until marrow recovered

Removal of catheter in setting of CVC-related blood stream infection: Recommended for infection due to S. aureus, P. aeruginosa, fungi, mycobacteria (always discuss with attending prior to having catheter removed!)

My patient got the “stat pack” at the SCCA. What is that? “Adult sepsis protocol” implemented at SCCA in attempt to ensure that septic patients receive appropriate antibiotics in timely manner. Includes: 1) Imipenem 500mg IV, 2) Tobramycin 80mg IV, and 3) Linezolid 600mg IV

References
2. SCCA Standard Practice Manual
3. Fellows lecture series: “Infections in oncology patients: Febrile neutropenia and beyond;” Dr. Corey Casper
4. Up To Date