

## Evaluation of the Patient with Fever

Fever = Temp > 38.3°C

1. Is the fever infectious or non-infectious?
  - a. Infectious
    - i. Bacterial
    - ii. Viral
    - iii. Fungal\*
  - b. Non-infectious
    - i. Inflammatory: vasculitis, autoimmune, DVT
    - ii. Malignancies: especially hematologic
    - iii. Drug mediated: serotonin syndrome, neuroleptic malignant syndrome, meds (antibiotics [ $\beta$ -lactams, sulfa], anticonvulsants, allopurinol, others)
  - c. \* Risk factors include steroids, CVN, malignancies, prolonged neutropenia
2. If infectious, what is the likely source?
  - a. Most common nosocomial infections are pneumonia, UTI, bloodstream infections from an IV or central line.
  - b. Hospital acquired pneumonia/ventilator associated pneumonia; MRSA; VRE; Clostridium difficile; line associated bacteremia; urinary tract infection
3. What is the patient's immune status?
  - a. Recognize that some patients with altered immune systems may have difficulty mounting a febrile response to infection.
  - b. Immune suppressed/Increased infection risk populations
    - i. Medications (steroids, TNF- $\alpha$  inhibitors, others)
    - ii. Hematologic malignancies
    - iii. Elderly
    - iv. Chronic liver disease/cirrhosis
    - v. Chronic renal failure
    - vi. Splenectomized patients (encapsulated organisms like pneumococcus, H. flu, meningococcus – ask about vaccinations)
4. What should the initial workup be?
  - a. Rule out infectious causes
    - i. CXR, U/A with micro and culture, blood cultures (including one from any indwelling lines)
    - ii. Target other areas for workup per clinical suspicion based on history and physical exam

### Neutropenic Fever

- Neutropenia = < 500 – 1000 neutrophils (PMNs + bands)
- Neutropenic fever = Temp > 38.0°C for more than one hour or single temp > 38.3°C
  - Indication for admission for IV antibiotics
  - Work-up with CXR/panculture, clinical suspicion as above
  - Always get cultures before starting antibiotics
  - Select/tailor antibiotics to target known infection

- In absence of obvious source need to empirically treat with broad spectrum coverage (IDSA guidelines suggest cefepime, ceftazidime, meropenem, or imipenem ± vancomycin)
- If still febrile after 48 hours of antibiotics, empirically add Vancomycin (if not started already)
- If still febrile after five days, consider adding an anti-fungal agent
- GCSF shown to shorten hospital stays, but does not change mortality

## Fever of Unknown Origin (FUO)

- Definition:
  - Fever of 38.5°C on more than one occasion
  - Duration at least three weeks
  - No diagnosis despite one week of intensive evaluation
- Etiologies
  - 30% Infection (TB, endocarditis, intraabdominal abscess, osteomyelitis, viral/parasitic)
  - 30% Connective Tissue Disease (giant cell arteritis, Polyarteritis nodosa, RA, DLE, sarcoidosis)
  - 20% neoplasm (lymphoma, renal cell, hepatocellular, pancreatic, colon, atrial myxomas, leukemia, myelodysplasia)
  - 20% miscellaneous (drugs, factitious, hematoma, thyroid, adrenal insufficiency)
- Work-Up
  - Thorough Hx and PE
  - D/C unnecessary drugs
  - Labs (CBC, ESR, chem7, LFTs, ANA, RF, cryoglobulin)
  - Blood cultures X3
  - U/A, micro and culture
  - PPD
  - Consider HIV, CMV, heterophile antibody
  - Consider bone marrow
  - Imaging (CXR, CT, ?tagged WBC scan)
- Empiric antibiotics not indicated unless neutropenia

## Antibiotics

1. Coverage
  - a. Drugs that cover MRSA
    - i. Vancomycin (IV)
    - ii. Linezolid (PO)
    - iii. Daptomycin (IV)
    - iv. Bactrim (IV/PO)
    - v. Clindamycin (IV/PO)
  - b. Drugs that cover Pseudomonas
    - i. Piperacillin-tazobactam (Zosyn – IV)
    - ii. Cefepime (IV)
    - iii. Ceftrazidime (IV)

- iv. Ciprofloxacin (PO)
  - v. Gentamicin (IV)
  - vi. Meropenem (IV)
  - vii. Aztreonam (IV)
- c. Drugs that cover anaerobes
  - i. Metronidazole (IV/PO)
  - ii. Clindamycin (IV/PO)
  - iii. Amoxicillin-clavulanic acid (Augmentin – PO)
  - iv. Piperacillin-tazobactam (Zosyn – IV)
  - v. Ampicillin-sulbactam (Unasyn – IV)
- 2. 12% of MRSA infections may be community acquired. Community acquired infections most commonly cause cutaneous infections.
- 3. Dosing Vancomycin
  - a. Standard starting dose: 1g IV q 12h but adjusted according to patient's age, body mass, and renal function (generally 10 – 15 mg/kg)
  - b. Check trough immediately prior to the 4<sup>th</sup> dose
  - c. Goal trough in uncomplicated bacteremia is 10 – 15
  - d. In hardware, bone, endocarditis, CNS goal of trough 15 – 20
  - e. Dialysis patients and patients with chronic kidney disease should get single doses and then re-check levels over next few days to maintain levels > 15
- 4. Other considerations
  - a. Antibacterial cross-reactivity
    - i. Be aware that an allergic response to penicillins carries risk of allergy to other beta lactams like cephalosporins and carbapenems (imipenem and meropenem), but does not to monopenams (aztreonam)
  - b. Bacterial colonization
    - i. Growth on culture without inflammatory response (no WBCs on gram stain) suggests colonization rather than true infection
    - ii. Beware of this type of interpretation in neutropenic patients
  - c. Abscess/Closed Infection
    - i. Treatment is drainage or removal (placement of drain or surgical removal)
    - ii. Antibiotics can slow progression/suppress bacteremia but are NOT curative

#### SIRS: Systemic Inflammatory Response Syndrome

- Defined as patients having two or more of the following
  - Temp > 38.0°C or < 35.0°C
  - RR > 20 or pCO<sub>2</sub> < 32
  - HR > 90
  - WBC > 12,000 or < 4,000 or with > 10% band forms
- Sepsis = SIRS + documented infection as the cause
- Estimated mortality

- SIRS: 7%
- Sepsis (not severe sepsis or septic shock): 16%