Infections in Non-HIV Immunocompromised Host

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Special Populations Discussed
- Diabetes mellitus
- Neutropenia
- Solid-organ transplant recipients
- Bone marrow transplant recipients
- Chronic corticosteroid use

Diabetes & Immune System
- Alters several aspects of immune system
- Impairs neutrophil & lymphocyte function
  - Exaggerated with concomitant acidosis
- Control of hyperglycemia:
  - Normalizes neutrophil function
  - Some evidence reduces incidence of infection

Diabetes Mellitus & Risk of Infection

- DM as risk factor for community-acquired infections
  - 7417 DM vs. 18,911 control patients with HTN
  - Increased risk for LRTIs, SSTIs, UTIs
- Infections strongly associated with DM:
  - Emphysematous pyelonephritis
  - Malignant otitis externa
  - Mucormycosis (zygomycosis)
  - Emphysematous cholecystitis


Diabetes & Microorganisms

- Group B *Streptococcus*
  - 37% in 1998 ↔ 44% in 2007
  - Bacteremia without focus, SSTIs, & pneumonia
- *Klebsiella*: Bacteremia, liver abscess
- Tuberculosis
  - 4 x more frequent than in general population
  - Aggressive, lower lobes, with pleural effusion
- Candida species
  - Oropharynx, perineum, cutaneous (intertriginous)

Diabetic Foot Infections

- *Pseudomonas* & MRSA not common culprits
- Specimen collection for culture:
  - Best from debrided base by curettage or biopsy
  - Superficial wound swab not preferred
- Consider osteomyelitis when:
  - Ulcer does not heal after 6 weeks of therapy
  - Bone visible or palpable with a probe
- Treat concomitant fungal infections


Diabetes Mellitus & UTI

- Higher incidence of asymptomatic bacteriuria in ♀
  - Pyuria commonly present
  - Dx based on culture
  - Treatment not recommended
- 7 day Tx recommended for symptomatic cystitis
- Poor response / persistent fever think complications
  - Abscess, necrosis, & emphysematous infections

≥ 48 hrs Tx + no clinical improvement = CT scan

**Emphysematous Pyelonephritis**

- Life-threatening, suppurative, necrotizing infection
- *E. coli* most common cause
- CT scan imaging modality of choice
- Differentiate emphysematous pyelonephritis:
  - Emphysematous pyelitis
  - Emphysematous cystitis
- Broad-spectrum antibiotics (cover *Pseudomonas*)
- Immediate surgical consultation


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**Malignant Otitis Externa**

Involves external auditory canal & temporal bone

*Pseudomonas* most common culprit

Fever commonly absent

Confused with severe perichondritis or otitis externa

Workup includes CT scan / MRI of temporal bone

Initiate antipseudomonal therapy

Consult ENT

- Cultures to determine susceptibility
- Tissue biopsy R/O epidermal carcinoma
- Debridement usually required


Habif TP. Clinical Dermatology. 1996.
Rhinocerebral Mucormycosis

- Infection involves sinuses & surrounding structures
- Clues to Dx:
  - Ulcers, black eschars on palate, nasal mucosa
- Dx: Biopsy & culture of necrotic tissue
- Workup includes CT / MRI of head & neck
- Initiate high-dose IV amphotericin B
  - Major concern nephrotoxicity
  - Newer lipid formulations with less toxicity
- Emergent surgical consultation


Emphysematous Cholecystitis

- Clinically similar to acute cholecystitis
- More common in males
- Gangrene & perforation more frequent
- High rate of mortality
- Gallstones present (50%)
- Dx: Abdominal CT scan
- Microbiology: *E. coli, C. perfringens, B. fragilis*
- Initiate broad-spectrum antibiotic therapy
- Emergent surgical consultation


Neutropenia & Fever

- Neutropenia:
  - ANC < 500 cells/mm$^3$ or an ANC expected to decrease to < 500 during the next 48 hours
- Fever:
  - Single oral temp ≥ 38.3°C (101°F)
  - Temp ≥ 38.0°C (100.4°F) for ≥ 1 hour
- Risk or severity of infection increases with:
  - Profound neutropenia (ANC ≤ 100 cells/mm$^3$)
  - Duration of neutropenia > 7 days

Clinical Presentation
- Fever may be only feature of infection
- Signs & symptoms of infection may be minimal
- Pain despite absence of signs suspect occult infection
- Special attention to:
  - Oral cavity, perineum, toes, bone marrow aspiration site & vascular catheters
  - Look for splenectomy scar
- Higher risk of infection with *S. pneumoniae*, *H. influenzae*, & *N. meningitidis*

Bacterial Microbiology
- Majority: Gram-positive organisms
  - *Staphylococcus & streptococcus* species
  - *Enterococcus faecalis / faecium*
  - *Corynebacterium* species (PICC lines)
- Gram-negative organisms
  - *Escherichia coli*, *Klebsiella species*
  - *Pseudomonas aeruginosa*
- Anaerobes uncommon, unless:
  - Oral mucositis, perirectal, intra-abdominal source

Initial Evaluation
- Initial workup must include blood cultures (x 2)
  - One set from device lumen (if present)
- Gram stain & culture of exudate at catheter entry site (if present)
- Initiate empiric antibiotic therapy:
  - All febrile neutropenic patients
  - Afebrile neutropenic patients with new signs or symptoms suggestive of infection

**Neutropenic Fever: Decision-Making Process**

- **High risk**
  - Inpatient therapy
  - Initiate empiric IV antibiotics (within 2 hrs)
  - Decide if need to add vancomycin & metronidazole
- **Low risk**
  - Outpatient therapy

- Involve Heme/Onc
- Cipro plus amox-clav or Cipro plus clindamycin


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**Empiric IV Antibiotics**

- Piperacillin-tazobactam
- Imipenem / Meropenem
- Cefepime
- Ceftazidime
  - Poor activity against many gram-positives
- Penicillin-allergy:
  - Ciprofloxacin *plus* clindamycin
  - Aztreonam *plus* vancomycin


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**Additional Antibiotics**

- Add vancomycin if:
  - Severe sepsis / septic shock
  - Pneumonia
  - Catheter-related infection
  - Skin & soft-tissue infection
  - Known history of MRSA
- Add metronidazole if using cefepime/ceftazidime:
  - Oral mucositis
  - Perirectal infection
  - Intra-abdominal infection

**Multinational Association for Supportive Care in Cancer Risk Index (MASCC)**

- To identify low-risk for complications in febrile neutropenic cancer patients
- Age > 16 years
- Derivation n=756
- Validation n=383
- Risk-index score ≥ 21
  - PPV 91%; NPV 36%
  - Sensitivity 71%
  - Specificity 68%
  - Misclassification rate 30%

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<td>No or mild symptoms</td>
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<tr>
<td>No hypotension</td>
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<td>No COPD</td>
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<td>Solid tumor or no prior fungal infection</td>
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<td>No dehydration</td>
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**Other Factors Favoring Low-Risk**

- Absolute neutrophil count ≥ 100 cells/mm³
- Neutropenia < 7 days
- Peak temp < 39°C & RR ≤ 24 breaths/min
- Normal chest X-ray
- No IV catheter-site infection

**Disposition**

- Decision **always** made with Heme-Onc
- Patient agreeable to plan ➡ Obtain consent
- Ability to care for self /or presence of a caregiver
- Ability to access medical care

**IV Catheter-Related Infections**

- Most common cause of catheter-related infection:
  - Coag-negative staph (often methicillin-resistant)
  - Vancomycin first line of therapy
- Removal indicated if:
  - Signs of infection (pain, erythema, purulence, induration)
  - Septic shock with no other source of infection
- In general, not emergent to remove lines in ED
- **Always** involve Hem-Onc

Infections in Solid-Organ Transplant Recipients

- Difficult to differentiate infection from rejection
- Broad spectrum of potential pathogens
- Dx often requires invasive diagnostic procedures
- Predictive temporal pattern of infections:
  - < 1 month: Nosocomial & post-op infections
  - 1-6 months: Opportunistic infections
  - > 6 months: Community-acquired infections


Infections in Bone Marrow Transplant Recipients

- Predictive temporal pattern of infections
- 0-30 days
  - Profound neutropenia
  - Bacterial infections common
- 31-100 days
  - Acute graft vs. host dz.
  - CMV infection
- > 100 days
  - *S. pneumoniae, H. influenzae*

- Primarily involves skin, liver, & GI tract
- Alters neutrophil function
- Further adds to immunosuppression
- Increases risk of infections

Infections & Corticosteroid Use

- Interferes with many aspects of immune system
- Chronic use predisposes to a variety of infections
  - Equivalent ≥ 15 mg/day prednisone ≥ 1 month
- Risk of infectious complications multifactorial
  - Underlying medical condition
  - Route of administration
  - Dose: Risk ↑ if > 10 mg/day or cumulative dose of > 700 mg of prednisone
  - Durations of therapy: Risk ↑ if given > 21 days

Infections & Corticosteroid Use

- Broad spectrum of potential pathogens
- Most infections due to pyogenic bacteria
  - *S. aureus* & streptococci
  - Enterobacteriaceae
- Tuberculosis
  - Often miliary or disseminated
  - Chronic use suppresses tuberculin reactivity
  - Induration ≥ 5 mm is considered positive
- Consider fever etiology infectious until proven otherwise

CDC. MMWR. 2000;49(No. RR-6):1-51. [Tuberculin skin testing & steroid use]

Take Home Points

- Diabetic foot infections:
  - Think osteo if persistent ulcer after 6 weeks of effective therapy

- Pyelonephritis & DM:
  - CT if ≥ 48 hrs of Tx & no clinical improvement

- Malignant otitis externa:
  - Needs culture & biopsy

Take Home Points

- Neutropenic febrile patients:
  - Initiate antipseudomonal therapy in all patients

- Solid-organ transplant patients:
  - Difficult to differentiate infection from rejection

- Chronic steroid use & tuberculin reactivity:
  - Induration ≥ 5 mm is considered positive