CLINICAL USE OF BETA-LACTAMS

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WHY IS INFECTIOUS DISEASE PHARMACOTHERAPY SO CONFUSING?

- Microbial taxonomy constantly changes
- New antimicrobials are continually being developed, although maybe not at the rate we would like
- Treatment is straightforward when the pathogen is known, but empiric therapy is difficult
- Antibiotic resistance must always be taken into account
- There are often many possible treatment choices but usually only one **best** choice

MASTERING TREATMENT OF AN INFECTIOUS DISEASE

- Know the most common pathogens in rank order of likelihood or importance
- Know the resistance patterns of the pathogens in question
- Know the drug(s) of choice in a patient with a classic case
- Know the best alternative for a patient unable to receive the drug of choice for whatever reason (e.g. allergy, pregnancy)

CASE 1. A 5-year-old boy presents with fever, purulent tonsillar exudate, and cervical lymphadenopathy. No rash is evident.

Diagnosis: Tonsillopharyngitis

CASE 1: TONSILLOPHARYNGITIS

- Most likely pathogens:
  - Virus
  - *Streptococcus pyogenes* (also known as Group A ß-hemolytic *Streptococcus* or GABS)
  - *Arcanobacterium haemolyticum* (rare)
- Drug of choice
  - Penicillin VK (won't cover *A. haemolyticum*)
- **PEARL: Penicillin-resistant *S. pyogenes* has never been reported**

CASE 2. A 20-month-old girl comes to the clinic with a cough and runny nose. She is very fussy and continually tugs at her left ear. Her temperature is 102 F, her left ear drum is red and immobile, and bony landmarks are not visible.

Diagnosis: Acute otitis media

Most likely pathogens: *Streptococcus pneumoniae, Hemophilus influenzae, Moraxella catarrhalis*

CASE 2: ACUTE OTITIS MEDIA

- Most likely pathogens:
  - *Streptococcus pneumoniae*
  - *Hemophilus influenzae*
  - *Moraxella catarrhalis*
- Drug of choice
  - Amoxicillin (90 mg/kg/day, divided bid)
- **PEARL: amoxicillin/clavulanate is not considered a better initial choice**

CASE 3. Same 20-month-old girl, 48 hours later, no improvement.

Diagnosis: Refractory acute otitis media

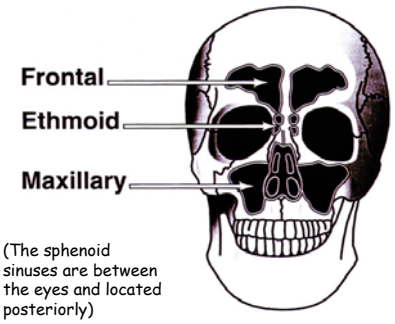
CASE 3: REFRACTORY AOM

- Most likely pathogens:
  - *Hemophilus influenzae*
  - *Moraxella catarrhalis*
  - Could be something unusual
- Drug of choice
  - Amoxicillin/clavulanate (Augmentin)
- **PEARL: cefdinir is the best-tasting liquid cephalosporin**

CASE 4. A 46-year-old male complains of headache and facial pain aggravated by stooping, and continuous nasal discharge. He says he caught a cold ten days ago and has had symptoms ever since. Decongestants provide little relief.

Diagnosis: Acute bacterial sinusitis

THE PARANASAL SINUSES



(The sphenoid sinuses are between the eyes and located posteriorly)

CASE 4: ACUTE BACTERIAL SINUSITIS

- Most likely pathogens:
  - *Streptococcus pneumoniae*
  - *Hemophilus influenzae*
  - *Moraxella catarrhalis*
- Drug of choice
  - Amoxicillin
- **PEARL: Some otolaryngologists prefer amoxicillin/clavulanate for initial therapy**

CASE 5. A 35-year-old construction worker complains of a tender and swollen right arm. The arm is erythematous and warm to the touch.

Diagnosis: Cellulitis

Most likely pathogens: *Staphylococcus aureus, Streptococcus pyogenes*

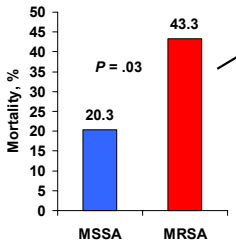
Complicating issue: the possibility of CA-MRSA

IMPORTANT MILESTONES IN THE HISTORY OF RESISTANT *STAPHYLOCOCCUS AUREUS*

EVENT	YEAR	COMMENT
Penicillinase-producing *S. aureus* appears in an Oxfordshire constable	1942	Penicillin introduced into clinical practice in 1942
Emergence of MRSA	1961	Methicillin approved in 1961
Emergence of VISA (GISA)	1996	Vancomycin approved in 1958
"Clinical" emergence of CA-MRSA	1999	TMP/SMX may be the best initial option
Emergence of VRSA	2002	Reported 3 times so far

IMPACT OF MRSA ON BACTEREMIA

***S aureus* bacteremia: mortality**



Methicillin resistance is an independent predictor for shock and risk factor for death in *S aureus* bacteremia†

MRSA is also associated with increased length of stay and higher hospital costs, although data are conflicting (Engemann et al, CID 2003; 36: 592)

Overall risk = 2.97 (95% CI: 1.12 - 7.88)*

*Talon D, et al. *Eur J Intern Med.* 2002; †Soriano A, et al. *Clin Infect Dis.* 2000.

CASE 5: CELLULITIS

- Most likely pathogens:
  - *Staphylococcus aureus*
  - *Streptococcus pyogenes*
- Drug of choice (if using oral therapy)
  - Dicloxacillin or cephalexin?
- Drug of choice (if using IV therapy)
  - Nafcillin or cefazolin?
- **PEARL: the choice depends in part on the patient**

CASE 6. A 67-year-old man is seen by his physician for fever, chills, malaise, and night sweats. A new heart murmur is audible. The man mentions a visit to the dentist a month ago. He has poor dentition.

Diagnosis: Acute bacterial endocarditis

CASE 6: ENDOCARDITIS

- Most likely pathogens:
  - Viridans group *Streptococcus*
  - Fastidious Gram-negative bacillus (part of oral flora)
- Drug of choice
  - Penicillin G (± gentamicin)
  - Ceftriaxone
- **PEARL: oral beta-lactams should never be used for endocarditis**

CASE 7. A 24-year-old woman develops fever, chills, flank pain, abdominal pain, nausea, and vomiting. She is barely able to get out of bed. She is flushed and diaphoretic.

Diagnosis: acute pyelonephritis

Most likely pathogens: *E. coli*, maybe another enteric Gram-negative bacillus

CASE 7: PYELONEPHRITIS

- Most likely pathogens:
  - *E. coli*
  - Maybe another enteric Gram-negative bacillus, e.g. *P. mirabilis*
- Drug of choice
  - Ceftriaxone (used to be, anyway)
  - Levofloxacin is cheaper
- **PEARL: pyelonephritis (upper UTI) is much different than cystitis (lower UTI), despite the pathogens being the same**

CASE 8. A 56-year-old intubated patient in the ICU recovering from heart surgery spikes to 39.9 C. His WBC is 25,900 with a neutrophil predominance and he has impressive infiltrates on chest x-ray. Sputum Gram stain reveals 4+ WBC, 4+ GNR, 2+ GPC.

Diagnosis: Hospital-acquired pneumonia

CASE 8: HOSPITAL-ACQUIRED PNEUMONIA

- Most likely pathogens:
  - Enteric Gram-negative bacilli, especially resistant strains
  - *Pseudomonas aeruginosa*
  - *Staphylococcus aureus,* possibly MRSA
- Drug of choice
  - Imipenem/cilastatin or meropenem
  - Vancomycin might be added
- **PEARL: The offending organism will be conclusively identified <50% of the time**

CASE 9. A 55-year-old diabetic male complains of fevers to 38.3, worsening erythema, and purulent drainage from a chronic foot ulcer. His WBC is 14,800 with 83% neutrophils. ESR (erythrocyte sedimentation rate) is 76 mm/hr.

Diagnosis: Diabetic foot ulcer, possible osteomyelitis

CASE 9: DIABETIC FOOT

- Most likely pathogens:
  - Just about anything: Gram-negative bacilli including *Pseudomonas*, Gram-positive cocci, anaerobes
- Drug of choice
  - Piperacillin/tazobactam
  - Ticarcillin/clavulanate
- **PEARL: not all infections are approached with curative intent**