

Decision Making for Empirical Antimicrobial Therapy

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Considerations in Empirical Antimicrobial Therapy

- Pt demographics
- Recent antimicrobial exposure
- Recent surgical intervention/instrumentation
- Recent/current hospitalization
- History of recent/recurrent infection(s)
- Underlying disorders and co-morbidities
- Recent history of travel/unusual exposures
- Knowledge of antimicrobial resistance patterns in your community/hospital

Empirical vs Prophylaxis vs. Pre-emptive Antimicrobial Therapy

- Empirical: Intervention for suspected disease, signs and symptoms, but no firm biologic markers of infection
- Pre-emptive: Intervention before clinical signs and symptoms, but with identifiable risk factors and a biologic marker of infection
- Prophylaxis: Intervention before clinical signs and symptoms, +/- risk, no markers

Case #1

A 60 yo white male presents with 4 week h/o low grade fever, night sweats and progressive dyspnea with mild exertion. He has no other associated sx, routinely takes no meds. He smokes, but does not drink or use illicit drugs. PMH significant for a 'murmur' since childhood, but no other related hx.

PE reveals a healthy appearing man; T 99.5, HR 105, BP 165/90. CV reveals harsh crescendo systolic murmur (4/6) with no diastolic component. No skin, palatal or conjunctival lesions. No organomegaly.

Routine labs remarkable for HCT 34, WBC 6.7 (nl diff), PLT 99K. UA reveals 2+ WBCs, 2+ RBCs, no bacteria.

A routine CXR is unremarkable

Case #1

You make a clinical diagnosis of aortic valve endocarditis. Following admission, you obtain routine blood cultures, and order a TTE.

Questions:

Do you prescribe antibacterials?

If so, which agents do you select?

Case #1

4/4 blood cultures are yield *Enterococcus fecalis*, susceptible to ampicillin and gentamicin.

Question:

Would you modify therapy? If so, how?

Treatment of Native Valve IE

- Initial therapy with vancomycin and gentamicin (some also add ampicillin) is generally advised until cultures are available to guide therapy
- For culture-negative IE, vanco plus gent or ampicillin/sulbactam+ gent is advised
- For enterococcal IE susceptible to pen G and gent, ampicillin or pen G plus gent is advised

Case #2

A 24 yo previously healthy woman presents to the ED with 48 hour history of fever, headache and progressive AMS. She has no h/o recent illness. She works full time; she has two preschool children, both attend day care. She takes no meds routinely.

PE: Lethargic. T 103, HR 125, RR 24, BP 100/60. Arouseable but confused. Meningismus. No other focal neuro findings. There is no rash. An LP is performed revealing cloudy fluid. OP is 320 mm CSF

Routine lab: WBC 18K (90% PMNs); Hct 32%, Plt 90K. CSF: 2200 WBCs (100% PMNs); prot 317, glu <5. Gram stain is negative for bacteria.

Case #2

You make a diagnosis of presumed acute bacterial meningitis.

Question:

What antibacterial therapy do you select?

Are there other interventions you'd initiate?

Case #2

Blood and CSF cultures yield *S. pneumoniae*, susceptible to Pen G and ceftriaxone

Question:

Would you alter therapy? If so, how?

Treatment of ABM

- Initial therapy with vancomycin and ceftriaxone advised (some add ampicillin if *Listeria* is a consideration)
- Generally drop vanco if not Penicillin-resistant *S. pneumoniae*
- Conversion to Pen G not necessary in most cases
- Glucocorticosteroids should be given before or simultaneously with first dose of antibacterials

Case #3

A 40 year old man who has been quadraplegic for 12 years living in a local nursing home presents to the ED with undifferentiated fever for 2 days. He has a long h/o complicated UTIs, including several episodes of bacteremia over the last 3 years. He has a chronic Foley catheter. Among his other meds, he receives TMP/SMX daily for 'prophylaxis' for recurrent UTIs. He has a h/o ciprofloxacin intolerance

PE: Does not appear ill. T 102 HR 120 RR16 BP 90/60 (baseline). He has no skin lesions, no decubiti. Chest/CV clear.

Initial lab: WBC 15.2K (85% PMNs); UA with 3+ bact, 3+WBCs
Cr 1.5, BUN 32, other lab OK.

Case #3

You make a diagnosis of complicated UTI. Blood and urine cultures are obtained and the patient is admitted.

Question:

What is your initial empiric antibacterial choice?

Case #3

Blood and urine cultures yield *Enterobacter cloacae*, susceptible to amikacin, imipenem, and ciprofloxacin.

Question:

Would you alter therapy, and if so how?

How long would you treat for this infection?

Is there anything else you would do diagnostically?

Treatment of Complicated UTIs

- Selection of an agent with predictable activity vs. presumed pathogen (select broad, step down as dictated by cultures)
- Selection of agents with urinary route of elimination; transition to po
- Duration of therapy is important.... abbreviated for pts with frequently recurring infx.
- Imaging studies for pts with persistent fever despite appropriate abx to exclude renal/perirenal abscess
- There are no data that provide guidance in this clinical scenario

Case #4

You are asked to assess a 68 yo woman in the ICU who is febrile for 3 days despite empiric antimicrobial therapy. She is post-op day 7 for subtotal colectomy, but has done poorly. Presently she is intubated and on the ventilator. She is not on vasopressors. Current antimicrobials include imipenem, vancomycin, metronidazole, and fluconazole. Cultures of blood, urine and sputum are negative.

PE: Ill-appearing elderly woman. T 101 HR 120 BP 110/90
Chest/CV clear. Abd distended, poor bowel sounds, midline wound looks good.

Case #4

Lab: WBC 25K, HCT 28, Plt 350K. Cr 1.9, BUN 22. LFTs OK. UA- few yeast, 2+ WBCs, otherwise WNL

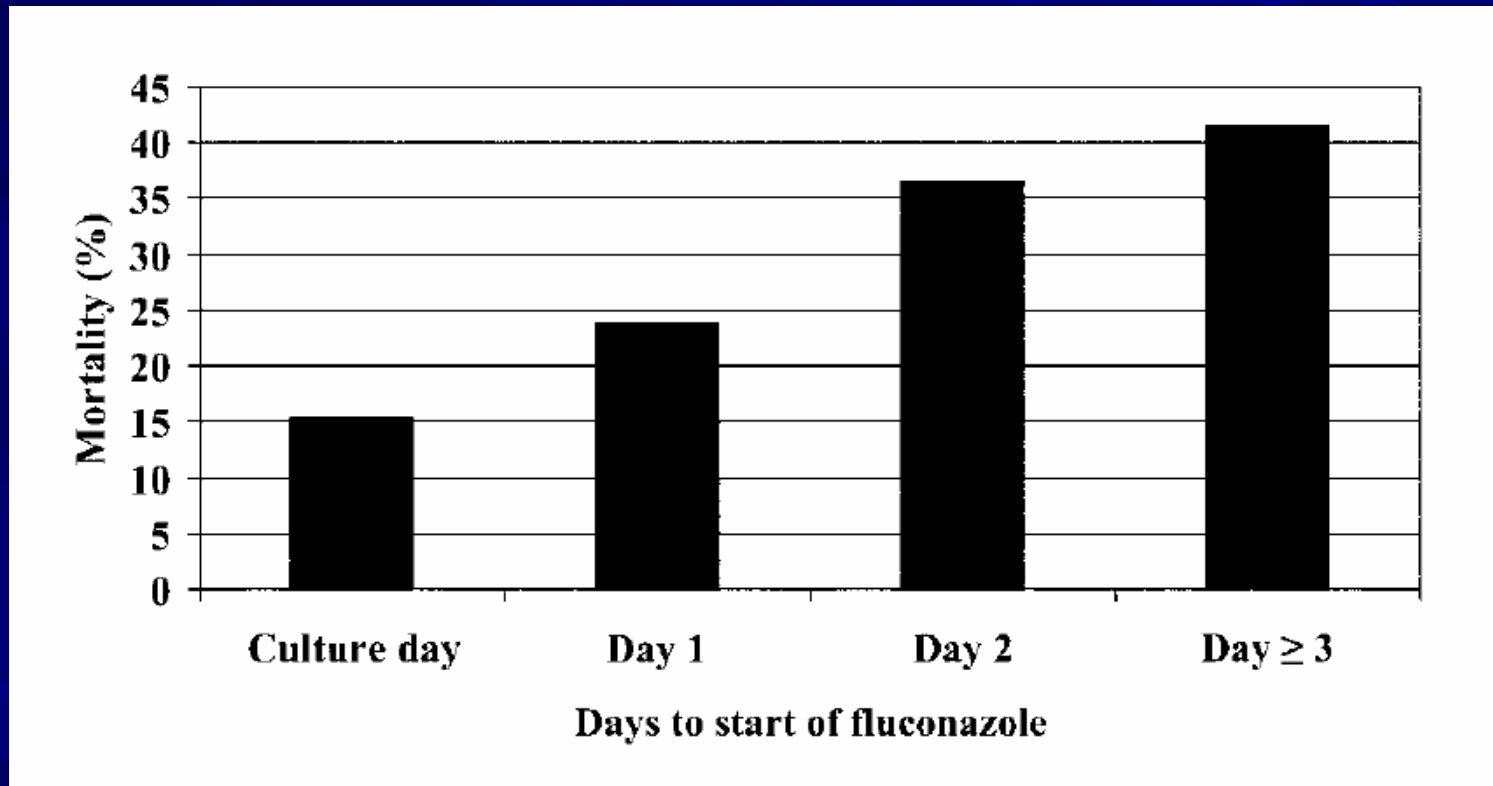
CXR reveals bilateral lower lobe streaky infiltrates c/w atelectasis

Questions:

Would you initiate additional/alternative antimicrobial therapy? If so, what?

Are there additional diagnostic tests you'd order?

Mortality Related to Timing of Empirical Antifungal Therapy



Garey, et al. CID 2006.

Empiric Antimicrobial Therapy in the ICU

- There are no good guidelines that help direct decision making
- Antibacterial coverage is most often based on culture data with limited positive-predictive value (sputum, urine, wound, drain cultures)
- Antifungal coverage often based on colonization data, clinical risk factors.
- No approach is validated

Empiric Antibiotics in the ICU

‘Empiric antibiotics are initiated 4X more often than NI was confirmed, and frequently continued in the absence of infection. We found no evidence that prolonged use of empiric antibiotics improved outcome for ICU patients, but rather a suggestion that the practice may be harmful.’

Empirical Antimicrobial Therapy

- For syndromes that are well characterized (IE, ABM, CAP, febrile neutropenia), initial therapy is relatively straightforward
- However, the vast majority of empirical antimicrobial therapy is driven by uncertainty, fear of bad outcomes, and the perception of the relative safety of antibiotics
- While we need to emphasize the need for early intervention, also need to emphasize stopping therapy early when an alternative dx is established or when it becomes clear that the intervention (ie, abx) is not effective.