Pharm Module 16: Infectious Diseases Selected Treatment Guideline

Skin and Soft Tissue Infections

Disease State-based approach to Therapy

- Have a working diagnosis
    - We will NOT focus on that in these lectures – diagnosis focus of other courses in curriculum
    - But always remember, we treat infections, not cultures!
- That diagnosis will be associated with certain organisms
- Decide what antibiotics are optimal for that disease state
    - Likely pathogens, penetration to site of infection
    - Cover resistant forms of likely pathogens if frequent enough or patient is unstable
    - De-escalate therapy down the road once you know definitive pathogen
- Decide duration of therapy

SSTI: The Usual Suspects

- Skin and soft tissue infections have two organisms more often than any others
    - *S. aureus, S. pyogenes* (Group A strep)
- Common disease states where this is the case
    - Impetigo
    - Erysipelas (think strep!)
    - Cellulitis
- Always remember these as the skin organisms – will come in handy

Streptococcus pyogenes

- Drug of choice
    - Penicillin
- Nearly universally susceptible to penicillin
- Narrow spectrum therapy (YAY!)
- Penicillin should be your first choice if targeting *S. pyogenes*
    - BUT only if you are treating strep alone
- Most Gram (+) agents will reliably cover this organism
    - PCN allergy
    - Important exception(s) coming soon

Don't forget about Staph!

- Empiric coverage will usually need to cover for *S. aureus* as well
- Historically unless risk factors present for MDR organisms we would expect MSSA
- Increase in community acquired (CA) MRSA
- MRSA should get routine coverage in purulent cellulitis and abscesses
    - Usually not warranted but often covered in systemic infections even without these characteristics (just say no!)

Oral Options for *S. Aureus*

- MSSA
    - Amoxicillin/clavulanic acid
    - Dicloxacillin
    - Cephalexin
    - (+ those listed for MRSA)
- MRSA
    - Doxycycline
    - TMP/SMX
    - Linezolid (and tedizolid)

        - Clindamycin
            - Remember resistance issues
            - Empirically unreliable

Back to Causative Agents

- Which of those would also cover *S. pyogenes*?
    - All of them apart from doxycycline
    - Some aren't comfortable with TMP-SMX, but should work well
    - Remember – clindamycin has resistance issues here too
- Many options for use
    - MSSA – Cephalexin, Amoxicillin/Clavulanic Acid
    - MRSA – TMP/SMX, doxycycline, linezolid
- If MRSA of particular concern – TMP/SMX or linezolid
- Follow up at 24 – 48 hours prudent
    - Assess success of regimen
    - If more deep-seeded infection, we will know

If I Choose Those Agents: What Do I Need to Warn My Patients About?

Agent	Side Effects	Drug Interactions
Doxycycline	Photosensitivity	Chelation
TMP/SMX	Hypersensitivity, Hyperkalemia	Other agents that raise K+, warfarin
Amoxicillin/Clavulanic Acid	Allergic Reaction, GI ADE	
Linezolid	Platelet count	Serotonergic agents (SSRI)
Clindamycin	Diarrhea (and CDI)	

Severe Cellulitis

- Usually defined by
    - Failure of oral antibiotics and debridement
    - Systemic symptoms
- When IV therapy is indicated
    - MSSA/strep only
        - Nafcillin or Cefazolin
    - MRSA
        - Vancomycin
            - Daptomycin
        - Still should only be used if indication for MRSA coverage or critically ill

Cellulitis: Duration of Therapy

- Tailored to clinical scenario
    - Importance of follow up assessment
- 5-day course has been shown effective in uncomplicated cellulitis
- May go up to 14 days of therapy if started IV
    - Can step down to oral
    - Longer if bone/joint involvement
- Guideline push is for 7 days of therapy for most patients

Animal Bites

- Animal bites account for ~1% of all ED visits
- Dog bites more common than cat bites
    - But cat bites are more likely to get infected!
- Pasteurella multocida is a bug that needs to be covered empirically
    - Staph and strep
    - Anaerobes
- Each bite has an average of 5 organisms
- Treatment
    - We treat if infection is present or prophylactically in certain high-risk populations
    - Make sure regimen covers *Pasteurella*
        - Often has a beta-lactamase that hydrolyzes early generation penicillin and cephalosporins
    - DOC: Amoxicillin/clavulanic acid
        - IV options: Ampicillin/Sulbactam or 3G cephalosporin
        - Alternatives (e.g., PCN allergy)
            - Doxycycline, Moxifloxacin
    - Human bites (and fist to mouth) should be treated the same way (minus *Pasteurella*)

Diabetic Foot Ulcers

- Etiologic agents
    - Gram (+) cocci → especially *S. aureus* (including MRSA) predominate
    - However, as ulcer gets deeper over time Gram (-) rods are commonly seen
        - *Enterobacteriaceae*
        - *P. aeruginosa*? Anaerobes?
    - Deep culturing is crucial (as it can be anything)
- **Uninfected ulcers should not be treated!!!**
- Empiric therapy
    - IV therapy used (at least initially) and it depends on how deep the ulcer is
    - Common empiric regimen is Vancomycin +/- Ceftriaxone – but can vary
- Duration of therapy
    - 1-2 weeks for mild; 2-4 weeks for moderate to severe; 4-6 weeks if bone involvement (osteomyelitis)
    - Do not need to treat until the ulcer heals; just until infection resolves!

Urinary Tract Infections and Asymptomatic Bacteriuria

Urinary Tract Infection Lingo

- Cystitis
    - Lower UTI, infection in the bladder
- Pyelonephritis
    - Upper UTI, migrated to the kidney +/- bacteremia
- Complicated urinary tract infection
    - Has a complicating factor that leads to worse outcomes, longer durations of therapy needed
- Catheter-associated urinary tract infection
    - UTI associated with a urinary catheter (foley)
- Asymptomatic bacteriuria
    - Colonization with bacteria in urine, no infection

Cystitis

- E. coli is the organism that empiric therapy is directed towards (local susceptibility data, risk factors for drug-resistance)
    - Other Gram-negatives, S. saprophyticus, and enterococcus as well, but therapy routinely directed (empirically) towards E. coli
- Duration of therapy is antibiotic specific
    - 3 days
        - TMP/SMX
        - Fluoroquinolones (remember, no moxifloxacin here!)
    - 5 days
        - Nitrofurantoin
    - 7-days
        - B-lactams

Fosfomycin

- MOA: inhibits enolpyruvate transferase, an enzyme in the beginning stages of peptidoglycan syntheses
- Spectrum: many urinary Gram (-) (and some Gram (+), including drug resistant isolates
- Can be given as a 3g x 1 dose for cystitis
    - Maybe. Recent evidence that this is inferior to nitrofurantoin
- Safe for pregnancy
- Can be given every 2-3 days for complicated UTI
- There is little to no evidence to do this, but it does happen
- People like this agent because it is easy (x 1) and it covers resistant organisms
    - But if you ask me, consider it second line

What is a complicated UTI (cUTI)

- Depends somewhat on who you ask!
- "Structural or functional abnormality"
    - Obstruction (stones, tumor, narrowing)
    - Foreign body (catheter, stents)
    - Males
    - Pyelonephritis
- Recent guidelines define it as extending beyond the bladder
- Notably, it will extend the necessary duration of therapy to 7+ days

Community Acquired Pyelonephritis

- *E. coli* and other Gram (-)
- Oral options
    - FQ, TMP/SMX
    - 3rd generation cephalosporins (data limited, not first choice)
    - **Nitrofurantoin and Fosfomycin NOT appropriate***
    - 7-14 days of therapy
        - Recent evidence moving towards shorter courses (7 days should be considered standard, even in setting of bacteremia)
        - Clinical response should dictate duration, but do not be afraid of shorter courses
- IV therapy (often when patient is initially hospitalized)
    - FQ
    - Aminoglycosides
    - Ceftriaxone
    - Expended spectrum beta-lactams, carbapenems
        - When suspected or documented drug-resistant organism

- Target therapy against isolated pathogen(s)
    - Can also transition to oral to complete course

Healthcare-associated UTI

- Have to cover for resistant pathogens
    - Can differ based on risk factors
        - Foley catheter, prolonged hospitalization → *P. aeruginosa*
        - Nursing home, recent antibiotics → ESBL
- Empirically cover with broader spectrum depending on risk factors **AND** severity of illness
    - Cefepime
    - Piperacillin/Tazobactam
    - Aminoglycosides
    - Ciprofloxacin/Levofloxacin
    - Carbapenems

Asymptomatic Bacteriuria

- Presence of bacteria in urine culture, with no symptoms of infection
    - Altered mental status doesn't count!
- Even if pyuria present with bacteria, without another symptom this is not an indication for antibiotics
    - Pyuria is a non-specific marker for inflammation
- Asymptomatic bacteriuria should only be treated when it has a benefit for the patient
    - Pregnancy, Undergoing urological procedure (TURP)
- Treatment
    - Has not
        - Led to any improvement in patient outcomes
    - Has been associated with
        - *C. difficile* infection
        - Increase in incidence in multi-drug-resistant organisms
        - Side effects with the medications
        - INCREASES in recurrent UTI's

Be Aware – Asymptomatic Bacteriuria is Common!

Population	Prevalence, %
Healthy, premenopausal women	1.0-5.0
Pregnant women	1.9-9.5
Postmenopausal women aged 50-70	2.8-8.6
Diabetic patients	
Women	9.0-27
Men	0.7-11
Elderly person in the community (≥70 yrs.)	
Women	10.8-16
Men	3.6-19
Elderly person in a long-term care facility	
Women	25-50
Men	15-40
Patients with spinal cord injuries	
Intermittent catheter use	23-89
Sphincterotomy and condom catheter in place	57
Patients undergoing hemodialysis	28
Patients with indwelling catheter use	
Short-term	9-23
Long-term	100

* Also common in sexually active females

- Symptom–Free Pee: let it be

Candiduria

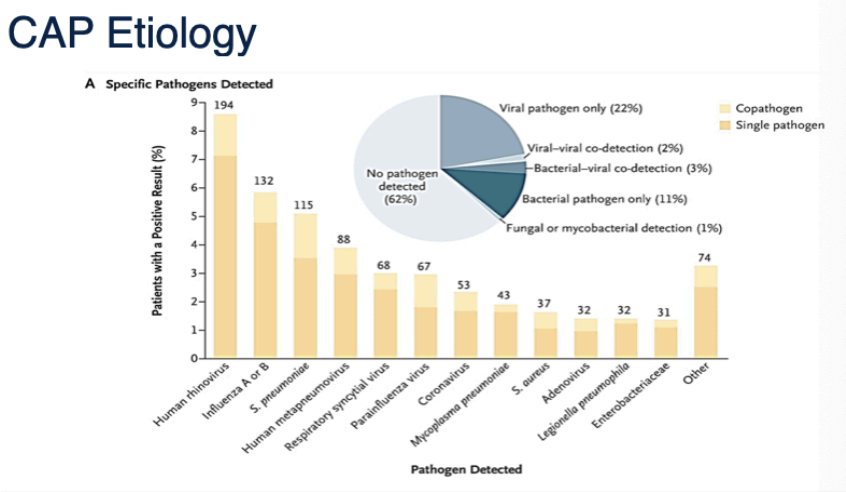
- Almost always represents colonization rather than active infection and thus very rarely warrants therapy
- Discontinue foley and unnecessary antibiotics (if possible)
- If need to treat, options are limited to fluconazole, amphotericin B

Respiratory Tract Infections

RTIs

- Community Acquired Pneumonia (CAP)
- Hospital-acquired/Ventilator-Associated Pneumonia (HAP/VAP)
- COVID-19
- Influenza
- Upper Respiratory Tract Infections (URI)

Community Acquired Pneumonia (CAP)



- Common CAP Bacterial Pathogens
    - "The big 6"
        - *S. pneumoniae, H. influenzae, M. cattarhalis*
        - *M. pneumoniae, C. pneumoniae, L. pneumophilia*
    - Others that may warrant consideration
        - *S. aureus*
            - Increasing incidence of CA- MRSA
            - Post-influenza
            - Severe, necrotizing
        - Anaerobes and aspiration
            - Misconception that they are players here
            - Only need to cover when empyema, lung abscess
    - Scoring systems dictate how/where to treat
        - CURB-65, PSI, PORT
- Outpatient Therapy
    - Otherwise, healthy adults without below comorbidities or risk factors for resistant pathogens
        - Amoxicillin or Doxycycline
        - Macrolides no longer recommended
    - Presence of comorbidities (e.g., CHF; lung, liver, renal disease; DM) or recent antibiotic exposure
        - B-lactam + Doxy or macrolide

                - Amox/clav; 2nd/3rd gen cephalosporin
            - Respiratory fluoroquinolone
- Inpatient Therapy
    - Non-severe (generally think floor patients)
        - B-lactam + Doxy or Macrolide
            - Amp/sulbactam or IV 3rd generation cephalosporin
            - Can transition to oral when stable
        - Respiratory Fluoroquinolone
    - Severe (think ICU)
        - Same as above, but tetracyclines aren't listed as an option
        - Consider addition of vancomycin
            - Not a guideline recommendation
- So Long HCAP…
    - There used to be a category of pneumonia called "HCAP"
        - Health-care associated pneumonia
        - Patients from community, but with risk factor for drug resistant organisms
    - These patients were treated the same as HAP/VAP
        - Lots of broad-spectrum antibiotic use
        - No data to support
    - HCAP went away in 2016
    - Now previous microbiology is the primary driver of when to cover for organisms like MRSA, *P. aeruginosa*
        - Recent hospitalization (or SNF/LTAC residence) + broad-spectrum antibiotic also
        - Detailed history, personalized approach is key
- Duration of Therapy
    - Huge opportunity for antimicrobial stewardship
        - Michigan data show > 90% treated for excess duration of therapy
    - Minimum of 5 days of therapy (currently)
        - Afebrile x 48 – 72 hours
        - No more than 1 CAP-related sign of instability
            - Fever, Leukocytosis, Elevated heart rate or respiratory rate
    - Patients discharged (or sent home from office/ED) almost always already meet these criteria
    - Some recent data suggest 3 days may be sufficient

HAP/VAP

- Treatment Paradigm
    - From a causative microbiology pathway, they are considered one in the same
        - Largely true, although VAP/ICU patients have more resistant microbiology
    - Start broad
        - Appropriate empiric therapy has a mortality benefit for patient
        - Particularly appropriate for VAP/ICU patients
    - Obtain cultures
    - De-escalate therapy
    - Optimize duration of therapy
- Organisms of Concern
    - *S. aureus*
        - MRSA needs covered, but MSSA there too
    - *P. aeruginosa*

- *E. coli* and *K. pneumoniae*
  - Increasing consideration needed for ESBLs
- *Enterobacter spp., Citrobacter spp., Serratia spp.*
- In certain units/hospitals
  - *A. baumannii, S. maltophilia*
- Bottom line – target resistant organisms, but know that individual institution pathway may vary
  - Based on organisms and severity of illness

- Empiric Therapy–General Approach
  - Vancomycin or Linezolid (Covering for MRSA)

    PLUS
  - Anti-pseudomonal B-lactam (e.g., Cefepime)

    PLUS/MINUS
  - Anti-pseudomonal fluoroquinolone (cipro/levo) or aminoglycoside (tobramycin)

Balancing Appropriateness and Overuse

Hospital-Acquired and Ventilator Associated Pneumonia (HAP and VAP)			
	Recommended	Recent Piperacillin-tazobactam or Cefepime Exposure within 90 Days (>/= to 48-72 hours)	Anaphylactic reactions to β-lactam (i.e., hives, angioedema)
HAP in floor patient admitted ≥ 48 hours	Cefepime* 2gm IV every 8 hours plus vancomycin* IV PTD	Meropenem* 1gm IV every 6 hours plus vancomycin* IV PTD	Aztreonam* 2gm IV every 8 hours* plus vancomycin* IV PTD
VAP or HAP in ICU patient admitted ≥ 48 hours	Cefepime* 2gm IV every 8 hours plus vancomycin* IV PTD plus tobramycin* IV PTD	Meropenem* 1gm IV every 6 hours plus vancomycin* IV PTD plus tobramycin* IV PTD	Aztreonam* 2gm IV every 8 hours* plus vancomycin* IV PTD plus tobramycin* IV PTD

- That's a General Rule, but it is not always that simple
  - Patient specific factors need considered
  - What if the patient has drug allergies?
  - What if the patient has a history of resistant organisms?
  - What if the patient just received two weeks of the preferred anti-pseudomonal b-lactam?
- You started Broad, but Reel it in
  - Step 1
    - If not MRSA, ditch the Gram (+) coverage
  - Step 2
    - Do I need to continue both Gram (-) drugs?
    - What if it is P. aeruginosa?
      - In vitro synergy
      - Resistance development
      - Improve empiric therapy
    - Streamline to single, narrowest spectrum agent possible
  - Step 3: Duration of Therapy
    - Historically 14 – 21 days

        - 2003 study showed no difference in outcomes of 8-day course versus a 15-day course in VAP
        - Guidelines recommend 7 days currently
            - Assumes initial clinical response and no complication

Covid-19

- Rapidly evolving treatment paradigm – pay attention to IDSA guidelines for latest
- There are multiple extremely effective vaccines available, and prevention is key
- Treatment strategy and goals of therapy are dependent on where patient is in course of illness
    - Early/Less severe – viral phase of illness
    - Severe disease – hyperinflammatory phase
- Treatment options: Outpatient
    - Goals of therapy – stop progression to hospital/death
    - Oral antivirals
        - Nirmatrelvir/ritonavir (Paxlovid)
            - MOA: protease inhibitor; inhibits viral replication
            - ADE: dysgeusia (bitter, metallic taste disturbances) ≥ 5% of pts
            - DDI: ritonavir CYP3A4 inhibitor- MANY – check DDI databases
        - Remdesivir
            - MOA: RNA polymerase inhibitor
            - Inhibits viral replication
            - IV only – logistically challenging
    - Molnupiravir
        - MOA: RNA polymerase inhibitor
        - Relative contraindication in pregnant/pregnant potential
- Treatment options: Hospitalized
    - Breathing room air
        - Moderate disease
        - No therapy proven to benefit, supportive care
        - High risk of progression- consider outpatient therapies
    - Hypoxia – requiring supplemental oxygen
        - Moderate – severe disease, pulmonary and/or hyperinflammatory phase
            - Goal: Prevent progression and death, decrease time to resolution
            - Therapy: Remdesivir, dexamethasone, +/- tocilizumab or baricitinib
        - Inpatient – invasive mechanical ventilation
            - Critical disease, hyperinflammatory phase
                - Goal: Save life
                - Therapy: Dexamethasone, tocilizumab or baricitinib

Influenza

- Vaccination is key to prevent acquisition/transmission
    - Less efficacious than COVID-19 vaccines
- Treatment is modestly effective
    - Limited agents
    - Must start early in course of disease
    - Decrease the duration and severity of illness
- Oseltamivir mainstay; baloxavir (x 1) recent approval
- Treatment 5 days; but critically ill patients will get longer courses

Acute Bronchitis

- Vast majority of cases are viral and therefore there is no real role of antibiotics for this disease state
- Symptomatic treatment is mainstay of therapy
- Antimicrobial therapy usually not warranted
    - Data shows no clinically meaningful benefit
- Exceptions are if positive diagnostics for…
    - *B. pertussis* → macrolides
    - Influenza → oseltamivir
    - Mycoplasma/Chlamydia → macrolide, doxycycline

COPD Exacerbation

- Who gets antibiotics?
    - Patients with the three cardinal symptoms
        - Increased dyspnea, increased sputum volume, increased sputum purulence
        - Or 2 of these 3 if one is increased purulence
        - Patients requiring mechanical ventilation
- What are the causative organisms?
    - Our old friends the respiratory pathogens!
    - *S. pneumoniae, H. influenzae, M. catarrhalis, C. pneumoniae, M pneumoniae*
- Treatment
    - Oral therapy for mild-moderate infection
        - Amoxicillin/clavulanic acid
        - Doxycycline, Macrolides
        - Respiratory fluoroquinolones
    - IV therapy for patients with risk factors for poor outcomes
        - Co-morbidities, severe COPD, frequent exacerbations
    - Duration driven by clinical improvement
        - Typically, 5 – 7 days

Sinusitis

- Usually, viral
    - If bacterial, microbiology is similar
- Only treat with antibiotics if one of the following
    - Persistence of signs/symptoms for > 10 days with no evidence of improvement
    - Severe symptoms (fever > 39 + purulent nasal discharge or facial pain lasting ≥ 3-4 days)
    - Worsening symptoms
- Therapy
    - Amoxicillin/clavulanic acid, Doxycycline, FQ
- Duration of therapy: 5 – 7 days

Central Nervous System Infections

Bacterial Meningitis

- General treatment considerations
    - IV therapy at maximal doses
        - Can possibly down the road switch to highly bioavailable orals
    - Bactericidal therapy preferred and B-lactams are the mainstay
        - Evidence lacking for need for cidal therapy, but standard
    - Blood brain barrier (BBB) will decrease the amount of drug (to a variable degree) that gets to the site of action
    - Important to know what organisms to cover for different patient populations
    - Fast, appropriate therapy saves lives

Antibiotic Penetration into the CNS

- Probably sufficient
    - Later generation cephalosporins (3rd/4th)
    - Penicillin
    - Ampicillin
    - Vancomycin
    - TMP/SMX
    - Fluoroquinolones
    - Metronidazole
- Probably insufficient
    - Tetracyclines
    - Aminoglycosides
    - Polymyxins

< 1 Month of Age

- *S. agalactiae, E. coli, L. monocytogenes, Klebsiella spp.*
- Children < 1 month do NOT have an intact BBB
- Empiric Therapy
    - Ampicillin + gentamicin
    - Ampicillin + cefotaxime (avoid ceftriaxone!)

1-23 Months of Age

- *S. pneumoniae, N. meningitidis, S. agalactiae, H. influenzae* (maybe?), *E. coli*
- Vancomycin + 3rd generation cephalosporin
    - If small degree of resistance (mildly elevated MICs) are seen to 3rd generation cephalosporins in *S. pneumoniae*, this is generally not a problem
    - However, due to variable penetration through BBB, vancomycin is added to cover for these "resistant" *S. pneumoniae*

2-50 years of age

- *N. meningitidis, S. pneumoniae*
- *H. influenzae*?
- Vancomycin + 3rd generation cephalosporin
- Patients should receive dexamethasone

Dexamethasone

- Dexamethasone 10 mg IV q6h x 4 days
- Rationale: decrease inflammation in subarachnoid space; decrease neurologic sequelae
- Give PRIOR to first antibiotics dose – if received antibiotics already, do not administer
- Inconsistent mortality benefit seen in literature thought to outweigh possible immune suppression

> 50 years of age

- *S. pneumoniae, N. meningitidis, L. monocytogenes*
- Vancomycin + 3rd generation cephalosporin + ampicillin

Listeria monocytogenes

- Remember, this was a HELPS bug
    - Hence, ampicillin is the DOC
- Alternative options
    - TMP/SMX with good efficacy data
    - Meropenem
    - Gentamicin sometimes added as adjunctive therapy, but this is silly

Remembering Bacterial Meningitis Pathogens

- For most patients, the most causative pathogens are *S. pneumoniae* and *N. meningitidis*
    - Third generation cephalosporins (high dose!) would cover the majority of these
    - Vancomycin added (high dose!) to cover for potential pneumococcal issues with ceftriaxone
        - If causative pathogen not *S. pneumoniae* with elevated MIC stop vancomycin!
- Extremes of age need coverage for listeria
- Avoid ceftriaxone in neonates
- DOT varies by bug – most 7 – 21 days

Prophylaxis

- *N. meningitidis*
    - Household contacts and those exposes to oral secretions
    - Ciprofloxacin x 1
    - Alternatives: Rifampin (2 days), Ceftriaxone IM
- *H. influenzae*
    - Everyone in household with unvaccinated children
    - Rifampin

Special Populations: CNS Shunt Infections

- Most commonly skin organisms; in particular coagulase-negative staphylococci
- Others include *S. aureus* (total staph ~75%), GNR, streptococci
- Gram stain for pathogens and start broad spectrum antibiotics
    - Vancomycin + Cefepime common
    - Intraventricular antibiotics may be used as an adjunct
- Remove shunt if possible (failure rate remains high with antibiotics)
- Clear cultures; treat 7 – 21 days; replace shunt

Intra-abdominal Infections and Sexually Transmitted Infections

Outline

- Intra-abdominal infections
    - Spontaneous bacterial peritonitis (SBP)
    - Ruptured bowel
    - Cholangitis
    - Cholecystitis
    - Intra-abdominal abscesses
- *C. difficile* infection

Normal Enteric Flora

- Anaerobes >>> aerobes
    - 99% anaerobes: *Bacteroides, Clostridium, peptostreptococci*
    - 1% aerobes: *E. coli, Proteus, Klebsiella, enterococcus*
- Enterococcus spp. present, but not something we routinely target with our empiric therapy
    - If it is cultured, then we cover it (sometimes)
    - Streptococci also present in GI tract, but all regimens cover well

Enteric Flora: things to know!

- *B. fragilis*
    - Most resistant anaerobe
    - Good: penicillin/BLI, carbapenems, metronidazole
    - Good enough: cefoxitin, moxifloxacin
    - Just say no: clindamycin
- *E. coli*
    - Vary greatly from location to location

    - Important to know local susceptibility
    - 2nd/3rd generation cephalosporins, common empiric, but can differ!

Community Acquired vs Hospital Acquired

- Community acquired
    - Susceptible Gram (-) organisms
    - Anaerobes
    - Enterococcus (not necessary for empiric coverage)
- Hospital acquired
    - Recent antimicrobial exposure (most common) or failing therapy
    - *P. aeruginosa, ESBL, Enterococcus, candida spp.*

Spontaneous (Primary) Bacterial Peritonitis (SBP)

- Common complication seen in patients with impaired liver function
    - Cirrhosis → ascites → bacterial translocation → volia!
- Most common organisms
    - *E. coli, Streptococcus spp., Klebsiella pneumoniae*
- Treatment
    - 3rd generation cephalosporins are the mainstay
    - Duration of therapy 5 – 7 days
- Prophylaxis
    - High risk or history of SBP
    - TMP/SMX 5 days/week or ciprofloxacin once weekly

Intra-Abdominal Infections: Others

- Abscesses, ruptured bowel, cholangitis
- Normal flora (as previously discussed)
    - *B. fragilis, E. coli*
- Community acquired infection
    - 1st/2nd/3rd gen cephalosporin + metronidazole OR cefoxitin
    - FQ + metronidazole commonly alternative for allergy – but suboptimal!
- Nosocomial/critically ill community acquired
    - Expand coverage
        - Cefepime/MTZ, piperacillin/tazobactam, carbapenem

Acute Cholecystitis

- Often an inflammatory, but NOT infectious condition
- Treatment given to most (all) patients; however, in patients lacking systemic inflammatory response the need remains unclear
    - If patient lacks systemic symptoms and gallbladder removed can d/c antibiotics in 24 hours
- Same bugs and drugs

Intra-Abdominal Infections: DOT

- No hard and fast rule for this group of infections
- If removable focus of infection and get source control (this is KEY) RCT data support 4-5 days of therapy
    - And this is the guideline recommendation
- If no source control allow clinical response to dictate
    - Resolution of signs and symptoms
    - Improvement on imaging

C. Difficile Infection

- Treatment should include discontinuing exacerbating causes

    - Broad-spectrum antibiotics (if possible)
    - Acid-suppressive agents
- Historically metronidazole was the drug of choice
    - Almost never recommended anymore – inferior
- Two mainstays of therapy
    - Fidaxomicin (superior, but costly)
    - Oral vancomycin
- Duration of therapy 10 – 14 days (for the first occurrence, but after that it gets complicated)
- Recurrence common, increasing role of fecal microbiota therapy (FMT)

Fidaxomicin

- MOA: inhibits RNA synthesis by inhibiting RNA polymerases
- Spectrum: EXTREMELY narrow therapy, really focusing on Clostridium
- Bactericidal
- Has demonstrated equivalence to oral vancomycin for clinical cure
    - Significantly decreased recurrence
- Targeted use for patients at risk for recurrence
    - Cost

Sexually Transmitted Infections (STI)

- Genital Ulcer conditions
    - Chancroid
    - Genital Herpes
    - Syphilis
- Urethritis and Cervicitis
    - Chlamydia and Gonorrhea
- Vaginosis
    - Trichomoniasis
- Pelvic Inflammatory Disease

Chancroid

- Causative organism *Haemophilus ducreyi*
- Characterized by painful ulcers
    - Possibility for co-infections with HSV, syphilis, and HIV
- Treatment to cure infection, resolve symptoms, and prevent transmission
    - Azithromycin 1 g PO x 1 dose
    - Ceftriaxone IM
    - Ciprofloxacin x 3 days
    - Topical erythromycin x 7 days
- Treat partners regardless of presence/absence of symptoms if they had sexual contact within 10 days of partners symptoms

Genital Herpes (Herpes Simplex Virus)

- Chronic, life-long viral infection
    - Recurrences much more likely in HSV-2
    - “Drugs, neither eradicate latent virus nor affect the risk, frequency, or severity of recurrences after the drug is discontinued”
- Treatment: first clinical episode
    - Acyclovir x 7 – 10 days
    - Valacyclovir
        - Offers twice daily dosing as opposed to 3-5 with others!
- Recurrent infections

        - Suppressive therapy reduces frequency 70 – 80% in patients with frequent (≥ 6) episodes/year
            - Many patients will have no outbreaks with suppressive therapy
            - Can also **decrease** the likelihood of transmission
            - Valacyclovir once daily
        - Episodic regimens
            - 5-day course
- Severe disease
    - Disseminated infection
        - Pneumonitis, hepatitis, meningitis, encephalitis
    - IV acyclovir
        - 5-10 mg/kg q8h
        - Usually start with IV and transition to PO valacyclovir once patient stabilizes to complete a 10-day course
- Management of sexual partners – counseling!

Syphilis

- Caused by *T. pallidum*
- Various manifestations
    - Primary infection
        - Ulcer/chancre at infection site
    - Secondary infection
        - Skin rash, mucocutaneous lesions, lymphadenopathy
    - Tertiary infection
        - Cardiac/ophthalmic manifestations, auditory abnormalities
    - Latent infection
        - Lack clinical symptoms, but positive serology
- Penicillin is the preferred agent for ALL stages of syphilis
    - Different formulation/dosage/durations for different manifestations
- Primary/secondary treatment
    - Benzathine penicillin IM x 1
- Latent syphilis
    - Treatment to prevent late complications
    - Same as above – if late latent 3 doses at 1-week intervals
- Tertiary syphilis
    - Same 3 dose regimen as late-latent
- Neurosyphilis
    - CNS involvement at any stage; high dose IV penicillin

C. trachomatis

- Doxycycline 100 mg PO BID x 7 days
- Azithromycin 1 g orally x 1
- Recent evidence in MSM suggest doxycycline superior for rectal chlamydia
    - Guidelines updated July 2021 – doxycycline first line
- Sex partners should be referred for evaluation if had sexual contact in last 60 days
- Need to abstain until treatment completed
    - 7 days, even if Azithromycin!

N. gonorrhea

- Uncomplicated gonococcal infections
    - Cervicitis, urethritis

        - Ceftriaxone 500 mg x 1 (≥ 150 kg = 1 gram)
            - + doxycycline 500 mg PO x 7 days (unless ruled out chlamydia)
- Disseminated gonococcal infection (DGI)
    - Septic arthritis, endocarditis, meningitis
    - Full dose 3rd generation cephalosporins (IV)
    - DOT depends on the site

Vaginosis

- Vaginal infections fall under 3 main categories
    - Bacterial: Anaerobes like G. vaginalis
    - Trichomoniasis – T. vaginalis
    - Candidiasis – C. albicans
- Treatment
    - Bacterial: Metronidazole x 7 days
    - Trichomoniasis: Metronidazole 2g x 1 dose
    - Fungal: Fluconazole x 1 dose (or a variety of topicals)

Pelvic Inflammatory Disease

- Causative organisms
    - *N. gonorrhea, C. trachomatis*, some gram (-) organisms, anaerobes, and maybe even strep!
- Empiric recommendation
    - Cefoxitin + doxycycline
- If mild to moderate disease OR clinical response seen can transition to oral therapy covering same organisms