Stanford MEDICINE Health Care

BCPS: Infectious Diseases

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Speaker Disclosures

Nothing to Disclose, No Presence or Conflict of Interest

No Commercial Support

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Learning Objectives

- Identify signs/symptoms, etiology, and risk factors and recommend appropriate treatment and prophylaxis (if applicable) for the following:

    1. Pneumonia
    2. Urinary Tract Infection
    3. Skin and Soft Tissue Infection
    4. Diabetic Foot Infection
    5. Osteomyelitis
    6. Meningitis
    7. Endocarditis
    8. Intra-abdominal Infection
    9. Clostridioides difficile Infection
    10. Human Immunodeficiency Virus
    11. Tuberculosis Infection

Pneumonia

Pneumonia – Background

<table>
<tr><th></th><th>Community-Acquired Pneumonia (CAP)</th><th>Hospital-Acquired Pneumonia (HAP)
Ventilator-Associated Pneumonia (VAP)</th></tr>
<tr><td>Onset</td><td colspan="2">< 48 hours after hospital admission</td><td>HAP: ≥ 48 hours after hospital admission
VAP: ≥ 48 hours after mechanical intubation</td></tr>
<tr><td>Signs and Symptoms</td><td colspan="3"><table><tr><th>Local</th><th>Systemic</th></tr><tr><td>• Cough/dyspnea
• Tachypnea
• Rales/crackles
• VAP: Increased FiO_2, PEEP</td><td>• Fever (T > 38 C)
• Leukocytosis (WBC > 12k cells/mm^3)
• Tachycardia (HR > 90 bpm)</td></tr></table></td></tr>
<tr><td>Diagnostics</td><td colspan="3"><table><tr><th>Imaging</th><th>Cultures</th></tr><tr><td>• Chest x-ray (CXR) and/or computed tomography (CT)
  ○ Infiltrates
  ○ Opacities or consolidations</td><td>• Sputum
• Endotracheal
• Bronchoalveolar lavage (BAL)</td></tr></table></td></tr>
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Pneumonia – Scoring Tools

- Pneumonia Severity Index (PSI)

Risk	Class	Score	Mortality (%)	Recommendation
Low	I	< 51	0.1	Outpatient
Low	II	51-70	0.6	Outpatient
Low	III	71-90	0.9	Outpatient
Medium	IV	91-130	9.5	Inpatient
High	V	> 130	26.7	Inpatient

Minor Criteria
Respiratory rate > 30 breaths/min
PaO2 ratio <= 250
Multilobar infiltrates
Confusion/disorientation
Uremia (BUN >= 20 mg/dL)
Leukopenia WBC < 4.0 x 103 cells/mm3
Thrombocytopenia (Plt < 100,000/mm3)
Hypothermia (Temperature < 36 C)
Hypotension requiring aggressive fluid resuscitation

Major Criteria
Septic shock with need for vasopressors
Respiratory failure requiring mechanical ventilation

Pneumonia – Incidence by Organism

CAP		HAP/VAP	
Organism	Incidence (%)	Organism	Incidence (%)
Unidentified	40-60	Unidentified	50
Mycoplasma pneumoniae	13-37	*Staphylococcus aureus*	10
Streptococcus pneumoniae	9-20	*Pseudomonas aeruginosa*	8
Haemophilus influenzae	3-10	*Enterobacter* species	5
Chlamydophila pneumoniae	1-17	*Klebsiella pneumoniae*	4
Legionella pneumophila	0.7-13	*Acinetobacter* spp.	2
Viruses	Common	*Serratia marcescens*	2
Staphylococcus aureus *Moraxella catarrhalis* Anaerobes Gram-negative bacilli (e.g., *Klebsiella pneumoniae*)	Uncommon	*Escherichia coli*	2
		S. pneumoniae	1

Risk Factors for MDROs

MRSA/*Pseudomonas aeruginosa*

- Prior respiratory isolation within the past one year
- Hospitalization and parenteral antibiotics within the last 90 days
- Locally validated risk factors

MDROs

- Parenteral antibiotics within the last 90 days
- MRSA only: MRSA incidence > 10-20%
- VAP only: Hospitalized ≥ 5 days, septic shock, acute respiratory distress syndrome, acute renal replacement therapy

Empiric CAP Treatment – Outpatient

	Treatment	Duration
No Comorbidities	• Amoxicillin† • Doxycycline • Azithromycin#	5 days

Comorbidities‡	• Beta-lactam + (Azithromycin or Doxycycline)
	  ○ Amoxicillin/clavulanate
	  ○ Cefpodoxime
	  ○ Cefuroxime
	• Respiratory fluoroquinolone¶ (FQ)
	  ○ Levofloxacin
	  ○ Moxifloxacin
		5 days

†High dose amoxicillin dose of 1 g PO TID

‡Comorbidities: Chronic obstructive pulmonary disease, diabetes mellitus, alcoholism, chronic renal/liver failure, congestive heart failure, malignancy, asplenia, immunosuppression

¶Respiratory FQs do not include Ciprofloxacin due to variable coverage of *Streptococcus pneumoniae*

#ATS/IDSA 2019 guidance states to only use macrolides if local pneumococcal resistance is < 25%

Empiric CAP Treatment – Inpatient

- Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe CAP
  - Must meet **≥ 1 major** criteria or **≥ 3 minor** criteria

Major Criteria	Minor Criteria		
• Septic shock requiring vasopressors • Respiratory failure requiring mechanical ventilation	• RR > 30 bpm • PaO2/FiO2 < 250 • Multi-lobar infiltrates	• Confusion/disorientation • Uremia (BUN ≥ 20 mg/dL) • Leukopenia (WBC < 4k cells/mm^3)	• Thrombocytopenia (Plt < 100k/mm^3) • Hypothermia (T < 36 C) • Hypotension requiring aggressive fluid resuscitation

- Based on severity and risk factors

	Treatment	MDRO Risk Factors	Duration
Non-Severe	• Beta-lactam + Macrolide • Respiratory FQ • Beta-lactam + Doxycycline	• Prior respiratory isolation: add empiric coverage • Recent parenteral antibiotics: add empiric coverage if positive cultures	5 days
Severe	• Beta-lactam + Macrolide • Beta-lactam + Respiratory FQ	• Prior respiratory isolation **or** recent parenteral antibiotics: add empiric coverage	5 days

SHC 3 Day Treatment Criteria
Floor Status
Immunocompetent
Uncomplicated pneumonia
Responding quickly to therapy
Normal renal function
No concern for *Legionella* or aspiration pneumonia

Empiric HAP/VAP Treatment

- Empiric therapy

Treatment	MRSA Risk Factors	Duration
• Cover against MSSA† + GNR‡: ○ Cefepime ○ Piperacillin/Tazobactam ○ Levofloxacin ○ Meropenem or Imipenem	• If MRSA¶ risk factors are present, add MRSA coverage: ○ Vancomycin ○ Linezolid	7 days

- Dual Pseudomonal coverage

	Indications	Beta-Lactams	Non Beta-Lactams
HAP	• Parenteral antibiotics within the last 90 days • High risk of mortality (septic shock or mechanical ventilation)	• Cefepime • Ceftazidime • Piperacillin/ Tazobactam • Meropenem or Imipenem • Aztreonam	• Ciprofloxacin or Levofloxacin • Aminoglycoside • Colistin
VAP	• > 10% resistance to monotherapy • Structural lung disease (cystic fibrosis or bronchiectasis)		

†MSSA: Methicillin-sensitive *Staphylococcus aureus*
‡GNR: Gram negative rods
¶MRSA: Methicillin-resistant *Staphylococcus aureus*

SHC Preferred Agent

- GNR coverage: Piperacillin/Tazobactam or Cefepime
- MRSA: Linezolid (Restricted to proven MRSA pneumonia) or Vancomycin

SHC Anaerobic Coverage

- Do not cover UNLESS:
  - Evidence of empyema
  - Necrotizing pneumonia
  - Lung abscess
- Preferred Agent:
  - Piperacillin/Tazobactam monotherapy or add Metronidazole

Patient Case 1

B.P. is a 66 y/o F with CAD, MI 2 years ago, COPD, and HTN and was placed on a ventilator 8 days ago. Her temperature is now rising and CXR shows a new infiltrate. Which is the best empiric therapy for B.P.?

A. Ceftriaxone 2 g IV Q24H + Gentamicin 7 mg/kg IV Q24H + Linezolid 600 mg IV Q12H
B. Piperacillin/Tazobactam 4.5 g IV Q6H
C. Levofloxacin 750 mg IV Q24H + Linezolid 600 mg IV Q12H
D. Cefepime 2 g IV Q8H + Tobramycin 7 mg/kg IV Q24H + Vancomycin 15 mg/kg IV Q12H

Answer: D

Urinary Tract Infections (UTI)

UTI – Background

	Cystitis	Pyelonephritis
Definition	Lower → bladder	Upper → kidney
Signs and Symptoms	• Dysuria • Urinary urgency/frequency • Hematuria	• Dysuria • Urinary urgency/frequency • Hematuria • Fever/chills • Leukocytosis • Costovertebral angle tenderness

Factors Associated with Complicated UTIs

- Male sex
- Hospital-acquired
- Pregnancy
- Anatomic abnormality of urinary tract
- Poorly controlled diabetes mellitus
- Recent antimicrobial use
- Indwelling urinary catheter
- Recent urinary instrumentation
- Immunosuppression

UTI – Laboratory Findings

- Urinalysis findings

Finding	Criteria
Pyuria	WBC > 10 cells/mm^3
Bacteriuria	> 100,000 CFU/mL
Nitrite	Positive (*E. coli*, *Proteus*, *Klebsiella*)
Leukocyte esterase	Positive
Casts	Positive (if pyelonephritis)

Asymptomatic bacteriuria should **NOT** be treated unless in pregnant women or patients undergoing urologic procedures

- Consider incidence by organism when empirically treating

Community-Acquired	
Organism	Incidence (%)
Escherichia coli	73
Staphylococcus saprophyticus	13
Proteus mirabilis	5
Klebsiella pneumoniae	4
Enterococcus	2

Nosocomial	
Organism	Incidence (%)
Escherichia coli	31
Pseudomonas aeruginosa	10
Other GNR	10
Klebsiella pneumoniae	9
Staphylococcus aureus	6
P. mirabilis	5
Enterococcus	2

UTI – Empiric Treatment

Uncomplicated Cystitis		Complicated Cystitis or Pyelonephritis	
Regimen	Duration	Regimen	Duration
Primary Regimens		**Outpatient**	
Nitrofurantoin 100 mg PO BID†	5 days	Trimethoprim/Sulfamethoxazole DS 1 tab PO BID	7-14 days
Fosfomycin 3 g PO x1	1 day	Levofloxacin 750 mg PO daily	5 days
Trimethoprim/Sulfamethoxazole DS 1 tab PO BID‡	3 days	Ciprofloxacin 500 mg PO BID	7 days
Alternative Regimens		Beta-lactams	7-14 days
Ciprofloxacin 250 mg PO BID	3 days	**Inpatient**	
Levofloxacin 250 mg PO daily	3 days	Ceftriaxone	5-14 days
Beta-lactams¶	5-7 days	Ciprofloxacin/Levofloxacin^	
		Aminoglycoside*	

†Avoid nitrofurantoin if CrCl < 30 mL/min (CrCl < 60 mL/min per manufacturer)
‡Avoid Bactrim if resistance > 20% or if used for UTI in previous 3 months
¶Beta-lactams: Augmentin, cefdinir, cephalexin, cefaclor, cefpodoxime
^Moxifloxacin should not be used due to minimal urine concentration
*Gentamicin is no longer recommended to be used for pseudomonal infections

SHC Preferred Agent

- Uncomplicated UTI: Nitrofurantoin x5 days
- Complicated UTI: Ceftriaxone 1 g IV daily (2 g if bacteremia) x7 days

Can use Ceftriaxone susceptibilities to predict Cefpodoxime coverage

Patient Case 2

G.N. is a 62 y/o F with poorly controlled T2D, HTN, h/o DVT who presents to the ED with urinary frequency/dysuria, nausea/vomiting, flank pain x3 days. Which is the best empiric therapy for G.N.?

Vitals	
Temperature	102.8°F (39°C),
Heart rate	120 beats/minute
Respiratory rate	16 breaths/minute
Supine blood pressure	140/75 mm Hg
Standing blood pressure	110/60 mm Hg.

Labs	
INR	2.7
BUN	26 mg/dL
SCr	1.88 mg/dL
WBC	12,000 cells/mm3

Urinalysis	
Turbidity	Cloudy
Glucose	2+
pH	7.0
Protein	100 mg/dL
WBCs	50 – 100
Nitrites	+
RBCs	3-5
Bacteria	Many

A. Trimethoprim/Sulfamethoxazole DS PO BID x7 days. Monitor INR carefully.
B. Ciprofloxacin 400 mg IV BID and then 500 mg PO BID x total of 7 days. Monitor INR carefully.
C. Gentamicin 140 mg IV Q24H x3 days
D. Tigecycline 100 mg once, then 50 mg IV Q12H and then Doxycycline 100 mg PO BID x total of 10 days

Answer: B

Skin and Soft Tissue Infections

Cellulitis

- Clinical Findings

Etiology	Signs and Symptoms
• *Streptococcus pyogenes* • *Staphylococcus aureus*	• Warmth/erythema • Edema • Pain • Fevers/chills

- Empiric Treatment

	Treatment	Duration
No MRSA Risk Factors	• Penicillin G • Cefazolin/Cephalexin • Ceftriaxone	5-10 days (extend if no clinical improvement)
MRSA Risk Factors	• Trimethoprim/ Sulfamethoxazole • Doxycycline • Clindamycin • Vancomycin • Lipoglycopeptides	

MRSA Risk Factors: **Purulent** drainage, penetrating trauma, intravenous drug use, concomitant MRSA infection elsewhere, and/or severe disease

SHC Purulent Cellulitis Protocol

- Duration: 5 days
- Preferred Agent
  - Mild: Trimethoprim/Sulfamethoxazole DS 1-2 PO BID or Doxycycline 100 mg PO BID
  - Moderate
    - Empiric: Trimethoprim/Sulfamethoxazole DS 1-2 PO BID or Doxycycline 100 mg PO BID
    - Definitive MRSA: Trimethoprim/Sulfamethoxazole DS 1-2 PO BID
    - Definitive MSSA: Cephalexin 500 mg PO Q6H or 1g PO Q8H
  - Severe
    - Empiric: Vancomycin
    - Definitive MRSA: Vancomycin
    - Definitive MSSA: Cefazolin 2g IV Q8H

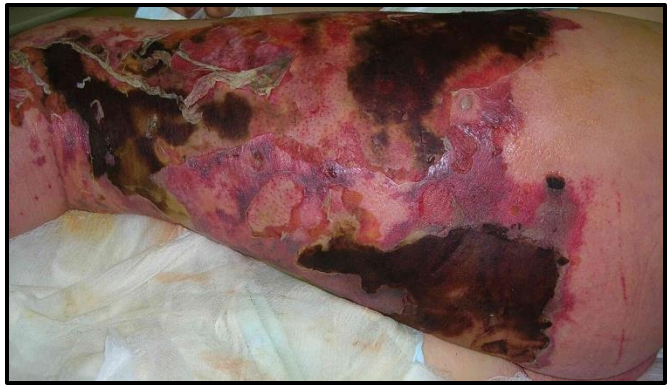
SHC Non-Purulent Cellulitis Protocol

- Duration 5-10 days
- Preferred Agent
  - Mild: Cephalexin 500 mg PO Q6H or 1 g PO Q8H
  - Moderate: Cefazolin 1 g Q8H or Cephalexin 500 mg PO Q6H
  - Severe: Vancomycin + Cefazolin 2 g IV Q8H

Necrotizing Fasciitis

- Clinical Findings

Etiology	Signs and Symptoms
<u>Polymicrobial</u> • Anaerobes: *Bacteroides, Clostridium* • Enterobacteriaceae: *E. coli, Klebsiella Enterobacter* <u>Monomicrobial</u> • *Streptococcus* • *Staphylococcus*	• Erythema/edema • Severe pain • Crepitus • Skin necrosis • Fevers/chills



- Empiric Management

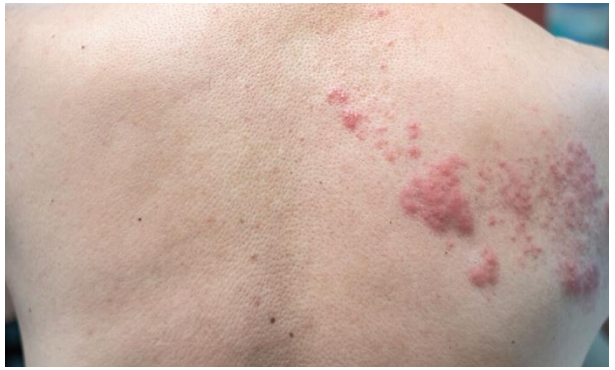
Surgery	Antibiotic Therapy
• Surgical emergency • Most important intervention • Often requires serial debridement	• MRSA: Vancomycin, Linezolid • GNO†: Cefepime, Piperacillin/Tazobactam, Carbapenem • + Anaerobes: Piperacillin/Tazobactam, Metronidazole, Carbapenem • + Anti-toxins: Clindamycin

†GNO: Gram negative organisms

Varicella

- Clinical Findings and Treatment

Microorganism	Presentation	Recommended Treatment
Varicella-Zoster Virus	Maculopapules, vesicles, scabs	Acyclovir 800 mg PO 4-5x daily x5 days
	Lesions initially with clear vesicular fluid before pustulating and scabbing	
	Appear on trunk and face before spreading	Valacyclovir 1 g PO TID x5-7 days



Surgical Site Infection Prophylaxis

- Administer antibiotic(s) within 60 minutes prior to incision
  - Exception: vancomycin and FQs should be administered 60-120 minutes prior
  - Re-dose if surgery lasts > 4 hours, > 2 half-lives of the antibiotic, or considerable blood loss

- Post-operative antibiotics are **ineffective** and **not necessary**
  - Recommended for < 24 hours only if used
  - Exception: solid organ transplantation

- Dependent on type of surgery

Surgery	Recommended Prophylaxis
Most surgeries†	Cefazolin‡
Colorectal	Cefazolin + Metronidazole
Solid organ transplantation	Generally broader coverage Organ and institution specific

†Most surgeries: Upper gastrointestinal, plastic surgery, orthopedic surgery, neurosurgery
‡In patients with beta-lactam allergies, may consider vancomycin, clindamycin, or FQs

Patient Case 3

G.N. returns to the clinic in 6 months with no urinary symptoms, but now presenting with an ulcer on her right foot. Her foot is red and swollen around the deep ulcer. All vitals and labs are WNL. Which is the best empiric therapy for G.N.?

A. Nafcillin 2 g IV Q6H x6–12 weeks
B. Tobramycin 120 mg IV Q12H + Levofloxacin 750 mg IV Q24H x1–2 weeks
C. Piperacillin/Tazobactam 3.375 g IV Q6H x1–2 weeks
D. Below-the-knee amputation followed by Ceftriaxone 1 g IV Q24H x1 week

Answer: C

Diabetic Foot Infection

Diabetic Foot Infection

- Etiology and Treatment

Etiology	Disease Progression	Treatment		Duration
S. aureus Group A and B *Streptococcus* *Enterococcus* *Proteus* *E. coli* *Klebsiella* *Enterobacter* *P. aeruginosa* *Bacteroides fragilis* *Peptostreptococcus*	Mild	No MRSA Risk Factors	Dicloxacillin/Nafcillin/Oxacillin Cephalexin/Cefazolin Levofloxacin/Moxifloxacin Doxycycline Trimethoprim/Sulfamethoxazole Clindamycin	1-2 weeks
		High Risk for MRSA	Linezolid Clindamycin Doxycycline Trimethoprim/Sulfamethoxazole	
	Moderate/Severe	Use most narrow spectrum: Ampicillin/Sulbactam, second/third generation Cephalosporin If at risk for other pathogens, add coverage.		2-4 weeks

Osteomyelitis

Osteomyelitis – Background

- Clinical Findings

Signs and Symptoms	Diagnostics

• Pain/swelling
• Tenderness
• Fever/chills
• Leukocytosis
• Elevated CRP and ESR
	• Imaging
	  ○ Computed tomography (CT)
	  ○ Magnetic resonance imaging (MRI)
	• Microbiology
	  ○ Blood cultures
	  ○ Bone biopsies

- Characteristics

	Hematogenous	Contiguous	Vascular Insufficiency
Etiology	Bloodstream	Adjacent tissue or direct inoculation	Insufficient blood supply
Population	Children: femur, tibia, humerus Adults: vertebrae	Adults (25-50 years)	Adults (> 50 years)
Risk Factors	• Bacteremia • Intravenous drug use	• Open fractures • Soft tissue infections	• Diabetes mellitus • Peripheral vascular disease
Microbiology	<u>Monomicrobial</u> • *Staphylococcus* • *Streptococcus* • GNR	<u>Polymicrobial</u> • GPO: *Staphylococcus, Streptococcus* • GNO: *Pseudomonas, Proteus, Klebsiella, E. coli* • Anaerobes	

Osteomyelitis – Empiric Treatment

- Management
  - Obtain cultures prior to empiric antibiotics for definitive therapy
  - Surgery: debridement, amputation, and/or prosthetic replacement (if applicable)

- Pathogen-Directed Empiric Treatment

	Directed Antibiotics	Considerations for Oral Antibiotics
MSSA	Cefazolin, Oxacillin, Nafcillin	• High bioavailability • Patient adherence • Identified organism • CRP < 2 mg/dL • Source control • Resolving clinical course
MRSA	Vancomycin, Linezolid, Clindamycin, Doxycycline, Daptomycin	
GNR	Parenteral Beta-lactams	

- Antibiotic Duration
  - Highly dependent on ability to obtain source control
  - Acute: 3-6 weeks
  - Chronic: 6-8 weeks of parenteral therapy and 3-12 months of oral therapy

Patient Case 4

W.A. is a 55 y/o M with HTN and h/o diverticulitis who is admitted with weight loss, malaise, and severe back pain and spasms that have progressed during the past 2 months. Four months before this admission, he had surgery for a fractured tibia, followed by an infection treated with unknown antibiotics. Magnetic resonance imaging reveals bony destruction of lumbar vertebrae 1 and 2, which is confirmed by a bone scan. Cultures from biopsy reveal gram-positive cocci in clusters. Which is the best therapy for W.A.?

A. Vancomycin 15 mg/kg intravenously every 12 hours for 6 weeks.
B. Nafcillin 2 g intravenously every 6 hours for 2 weeks.
C. Levofloxacin 750 mg orally every 24 hours for 6 weeks.
D. Ampicillin/Sulbactam 3 g intravenously every 6 hours for 2 weeks.

Answer: A

Meningitis

Meningitis – Background

- Clinical Findings

Signs and Symptoms	Diagnostics

• Headache
• Classic triad
  ○ Fever
  ○ Altered mental status
  ○ Nuchal rigidity
	• Blood cultures
	  ○ Obtain prior to antibiotic administration
	• Lumbar puncture
	  ○ Elevated opening pressure

- Cerebrospinal Fluid (CSF) Characteristics

	Normal	Bacterial	Viral
Glucose (mg/dL)	30-70	< 50	Normal
Protein (mg/dL)	< 50	**> 150**	Normal
WBC (cells/mm^3)	< 5	**> 1000-5000** (neutrophil predominant)	5-300 (lymphocyte predominant)
pH	7.3	**7.1**	Normal
Lactic acid (md/dL)	< 14	**> 35**	Normal

Meningitis – Bacterial Etiology

- Causative pathogens are highly dependent on age

Age	More Common Organisms	Less Common Organisms
< 1 month	• *Listeria monocytogenes* • *Streptococcus agalactiae* • *Streptococcus pneumoniae* • *Neisseria meningitidis*	• *Escherichia coli* • *Klebsiella* spp. • Herpes simplex virus
1-23 months	• *Streptococcus pneumoniae* • *Neisseria meningitidis* • *Haemophilus influenzae* • *Streptococcus agalactiae*	• *Escherichia coli* • Viruses
2-50 years	• *Streptococcus pneumoniae* • *Neisseria meningitidis*	• *Haemophilus influenzae* • Viruses
> 50 years	• *Listeria monocytogenes* • *Streptococcus pneumoniae* • *Neisseria meningitidis*	• *Streptococcus agalactiae* • *Haemophilus influenzae* • Viruses • Aerobic gram-negative bacilli

Meningitis – Empiric Treatment

- Empiric antibacterial treatment is highly dependent on age

Age	More Common Organisms	Empiric Treatment
< 1 month	• *Listeria monocytogenes* • *Streptococcus agalactiae* • *Streptococcus pneumoniae* • *Neisseria meningitidis*	Ampicillin + ceftazidime Ampicillin + aminoglycoside
1-23 months	• *Streptococcus pneumoniae* • *Neisseria meningitidis* • *Haemophilus influenzae* • *Streptococcus agalactiae*	Vancomycin + ceftriaxone
2-50 years	• *Streptococcus pneumoniae* • *Neisseria meningitidis*	Vancomycin + ceftriaxone
> 50 years	• *Listeria monocytogenes* • *Streptococcus pneumoniae* • *Neisseria meningitidis*	Vancomycin + ceftriaxone + ampicillin

- If concerned for Herpes Simplex Virus infection, treat with Acyclovir 10 mg/kg/dose IV Q8H infused over 1 hour

Meningitis – Dosing and Duration

- **High** and **frequent** dosing regimens of antibiotics are necessary to ensure adequate central nervous system penetration

	Dosing Regimen
Ampicillin	2 g IV Q4H
Cefepime	2 g IV Q8H
Ceftriaxone	2 g IV Q12H
Penicillin G	4 MU IV Q4H
Vancomycin	Trough 15-20 mg/L

	Duration (days)
N. meningitidis	7
H. influenzae	7
S. pneumoniae	10-14
S. agalactiae	14-21
L. monocytogenes	**21**

- Duration of antibiotics are dependent on the identified pathogen

Meningitis – Additional Considerations

- Evidence demonstrates benefit with adjunctive steroids

Adjunctive Steroids

- Given to attenuate inflammatory response to reduce pathophysiologic consequences
  - Reduction in hearing loss and other neurologic sequelae in children caused by ***H. influenzae***
  - Reduction in mortality in adults caused by ***S. pneumoniae***
- Dexamethasone 0.15 mg/kg Q6H or 10 mg Q6H x2-4 days
  - Administer 10-20 minutes **before** or **with the first antibiotic dose**

- Chemoprophylaxis for high-risk contact

Chemoprophylaxis

- Given for close contacts of patients with meningitis due to specific organisms (**not** for post-surgical patients)

	N. meningitidis	*H. influenzae*
Children/Infants	• Rifampin • Ceftriaxone	• Rifampin
Adults	• Rifampin • Ceftriaxone • Ciprofloxacin	• Rifampin

Patient Case 5

D.M. is a 21 y/o M with no PMH who presents to the emergency department with the worst headache of his life. He cannot remember the last time he received a vaccination. Which is the best empiric therapy for D.M.?

Vitals	
Temperature	102.4°F (39.1°C)
Heart rate	110 beats/minute
Respiratory rate	18 breaths/minute
Blood pressure	130/75 mm Hg.

Labs	
WBC	22,500 cells/mm3
CSF Glucose	44 mg/dL (peripheral, 110)
CSF Protein	220 mg/dL
CSF WBC	800 cells/mm3

A. Penicillin G 4 million units IV Q4H
B. Ceftriaxone 2 g IV Q12H
C. Ceftriaxone 2 g IV Q12H + Dexamethasone 10 mg IV Q6H
D. Ceftriaxone 2 g IV Q12H + Vancomycin 1000 mg IV Q8hours + Dexamethasone 10 mg IV Q6H

Answer: D

Endocarditis

Endocarditis – Background

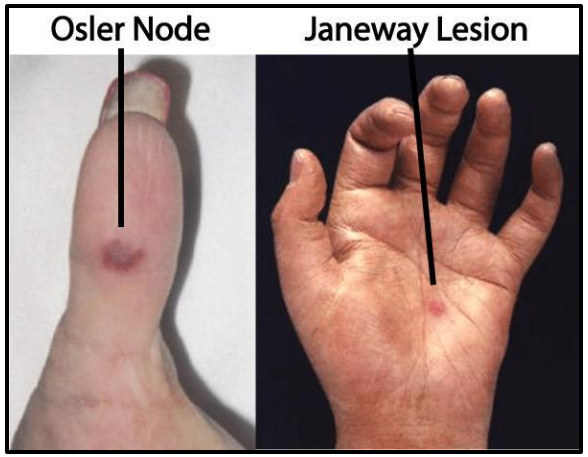
- Clinical Findings

Signs and Symptoms	Diagnostics

• Fever/chills
• Fatigue/anorexia
• Cardiac murmur
• Skin manifestations
  • Splinter hemorrhages
  • Osler's nodes/Janeway lesions
	• Imaging
	  ○ Echocardiography (TTE/TEE) with vegetations
	• Laboratory findings
	  ○ Persistent bacteremia
	  ○ Leukocytosis
	  ○ Anemia

- Microbiology

Organism	Incidence (%)
Streptococcus	50
Staphylococcus aureus	25
Enterococcus	8
Coagulase (-) *Staphylococcus*	7
GNR	6
Candida albicans	2



Endocarditis – Treatment

Organism	Length of Therapy (weeks)	
	Native Valve	Prosthetic Valve
Viridans Group *Streptococci*		
Penicillin G	4	6
↳ plus **Gentamicin**	**2**	
Ceftriaxone	4	
↳ plus **Gentamicin**	**2**	
Vancomycin	4	
Staphylococcus aureus		
Oxacillin or Nafcillin	6	≥ 6 weeks (with Gentamicin and Rifampin)
Cefazolin		
Vancomycin		
Daptomycin		Do not use

Endocarditis – Treatment

Organism	Length of Therapy (weeks)	
	Native Valve	Prosthetic Valve
Enterococcus		
Ampicillin + Gentamicin	4-6	6
Vancomycin + Gentamicin	6	
Ampicillin + Ceftriaxone	6	
Daptomycin + Ampicillin	> 6	> 6
HACEK† Organisms		
Ceftriaxone	4	6
Ampicillin + Gentamicin		
Ciprofloxacin/Levofloxacin/ Moxifloxacin		

†HACEK: *Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*

Intra-Abdominal Infections

Spontaneous Bacterial Peritonitis (Primary)

- Clinical Findings

Signs and Symptoms	Diagnostics

• Fever/chills
• Abdominal pain
• Tenderness to palpation
• Ascites
	• Paracentesis
	  • Ascitic fluid PMNs > 250 cells/mm^3
	• Microbiology
	  ○ Typically monomicrobial
	  ○ *E. coli*, *S. pneumoniae*, *Klebsiella* spp.

- Empiric Management

	Treatment	Duration
SBP Treatment	• Ceftriaxone 2 g Q24H • Ciprofloxacin	5-7 days
SBP Prophylaxis for patients with liver cirrhosis and GI bleed	• Ceftriaxone 1 g Q24H • Ciprofloxacin	5-7 days
Long-term SBP prophylaxis for patients with prior episode of SBP	• Ciprofloxacin • Trimethoprim/ Sulfamethoxazole DS	Indefinite

SHC SBP Protocol	
Prophylaxis	Ceftriaxone 1 g IV Q24H x5 days
Treatment	Ceftriaxone 2 g IV Q24H x5-7 days
Oral Step Down	Ciprofloxacin 500 mg PO BID

Secondary Peritonitis

- Empiric Treatment
  - Coverage is based on source and anatomic locations

Mild/Moderate Disease	Severe Disease
• Ceftriaxone + Metronidazole • Ciprofloxacin + Metronidazole • Piperacillin/Tazobactam <u>Beta-lactam allergy</u>: • Moxifloxacin • Ciprofloxacin/Levofloxacin + Metronidazole	• Piperacillin/Tazobactam • Cefepime + Metronidazole • Ceftazidime + Metronidazole • Imipenem/Cilastatin or Meropenem <u>Beta-lactam allergy</u>: • Aztreonam + Metronidazole + Vancomycin

SHC Secondary Peritonitis Preferred Agents	
Community-acquired without sepsis/shock	Ceftriaxone 2 g IV Q24H + Metronidazole 500 mg PO/IV Q8H
Community-acquired with sepsis/shock or MDRO risk factor	Piperacillin/Tazobactam 4.5 g IV Q8H extended infusion

- Continue therapy for **4 days** following adequate source control
  - May require longer duration if inadequate source control or lack of clinical improvement

Clostridioides difficile Infections

C. difficile – Background

- Clinical Findings

Signs and Symptoms	Diagnostics

• Watery diarrhea (≥ 3 loose stools within 24 hours)
• Abdominal pain
• Leukocytosis
	• Nucleic acid amplification tests (NAAT)
	• Enzyme immunoassays
	  ○ *C. difficile* GDH
	  ○ *C. difficile* toxins

- Classification

	Non-Severe	Severe	Fulminant
WBC (cells/mm^3)	≤ 15k	> 15k	• Hypotension or shock • Ileus or megacolon
SCr (mg/dL)	< 1.5	≥ 1.5	

C. difficile – Management

- Initial Episode Treatment

Non-Severe	Severe	Fulminant
• Fidaxomicin • Vancomycin PO • Metronidazole	• Fidaxomicin • Vancomycin PO	• Vancomycin PO + Metronidazole IV • Vancomycin PR (if ileus present)

- Recurrent Episode Treatment

First Recurrence	Second and Subsequent Recurrences
• Fidaxomicin • Vancomycin PO • Vancomycin PO pulse taper	• Fidaxomicin • Vancomycin PO pulse taper • Vancomycin PO followed by rifaximin • Fecal microbiota transplantation
Bezlotoxumab • MOA: Binds and neutralizes *C. difficile* toxin B • Recommended as adjunct therapy for recurrent disease ○ 10 mg/kg IV x1 during administration of standard antibiotic regimen	

Patient Case 6

R.K. is a 72 y/o M with GERD, HTN, HLD, and OA who presents to the ED a 2-day history of redness and swelling of his upper right extremity. He scraped his arm while clearing some brush in his yard. R.K. is sent home with PO clindamycin for his cellulitis. Two weeks after completing therapy for his cellulitis, R.K. has watery diarrhea, represents to the ED. Which is the best therapeutic regimen for R.K.?

Labs	
C. difficile toxin	Positive
WBC	24,500 cells/mm3
Albumin	2.8 g/dL
SCr	is 1.74 mg/dL (baseline ~ 0.90 mg/dL)

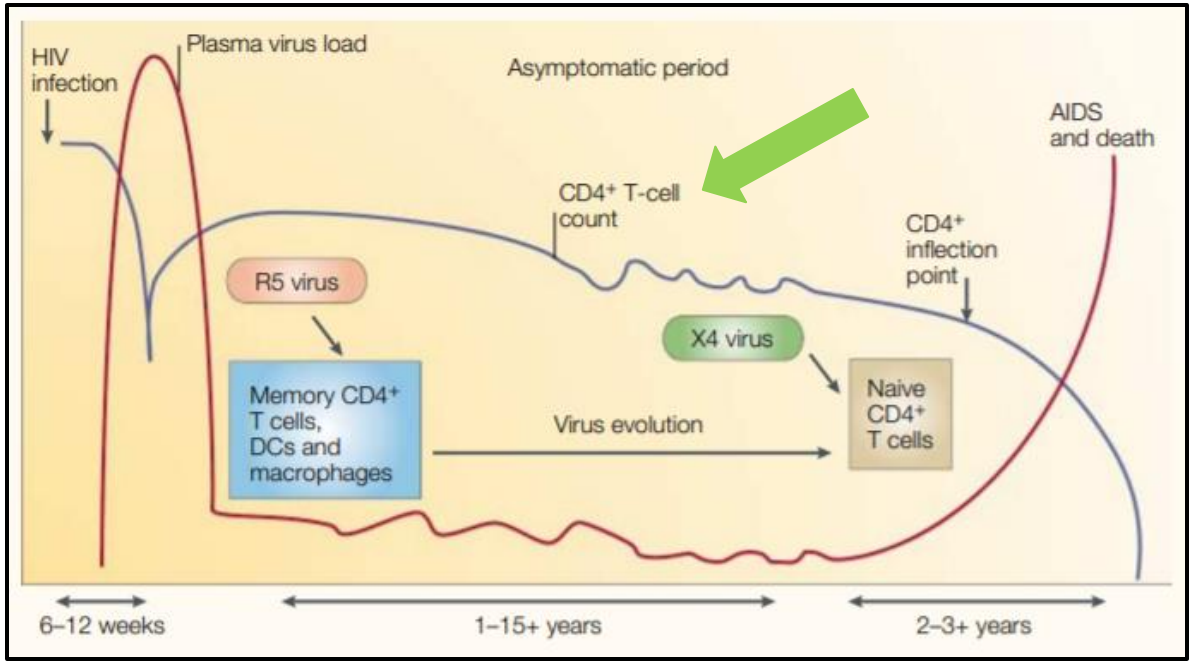
A. Metronidazole 500 mg PO TID x7 days
B. Vancomycin 125 mg PO QID x10 days
C. Fidaxomicin 200 mg PO BID x14 days
D. Rifaximin 400 mg PO BID x7 days

Answer: B

Human Immunodeficiency Virus

HIV – Background

- Single-stranded, positive-sense retrovirus
  - Chronic infection can lead to significant depletion of CD4 cells
- Acquired Immunodeficiency Syndrome (AIDS)
  - **CD4 < 200 cells/mm^3**
  - AIDS defining conditions (i.e., Pneumocystis jiroveci pneumonia, Kaposi sarcoma, etc.)
- Diagnostics
  - Immunoassay tests for antigen and antibody
- Transmission
  - Sexual
  - Parenteral exposure to blood +/- products
  - Perinatal during delivery or breastfeeding



HIV – Antiretroviral Therapy

	Mechanism	Adverse Effects	Common Agents
Nucleoside Reverse Transcriptase Inhibitors (NRTI)	Competitively inhibits reverse transcriptase	• Nausea • Diarrhea	• Abacavir • Emtricitabine, • Lamivudine • Tenofovir (TDF, TAF)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)	Non-competitively inhibits reverse transcriptase	• Severe rash • Hepatotoxicity	• Efavirenz • Rilpivirine
Integrase Inhibitors (INSTI)	Prevents viral DNA integration	• Weight gain • Insomnia • CK elevation • DDI: PV cations	• Bictegravir • Elvitegravir • Dolutegravir • Raltegravir
Protease Inhibitors (PI)	Inhibits virion assembly	• GI upset • Metabolic effects • Hepatotoxicity • DDI: CYP3A4 substrates and inhibitors	• Atazanavir • Darunavir

HIV – Antiretroviral Therapy Regimens

- Regimens for treatment-naïve patients
  - **2 NRTIs + 1 INSTI**

Brand Name	Generic
Biktarvy	Bictegravir/Emtricitabine/TAF
Triumeq	Dolutegravir/Abacavir/Lamivudine
Dovato	Dolutegravir/Lamivudine
Tivicay + Truvada	Dolutegravir + Emtricitabine/TDF
Tivicay + Descovy	Dolutegravir + Emtricitabine/TAF

HIV – Pre-Exposure and Post-Exposure Prophylaxis

- Pre-Exposure Prophylaxis (PrEP)

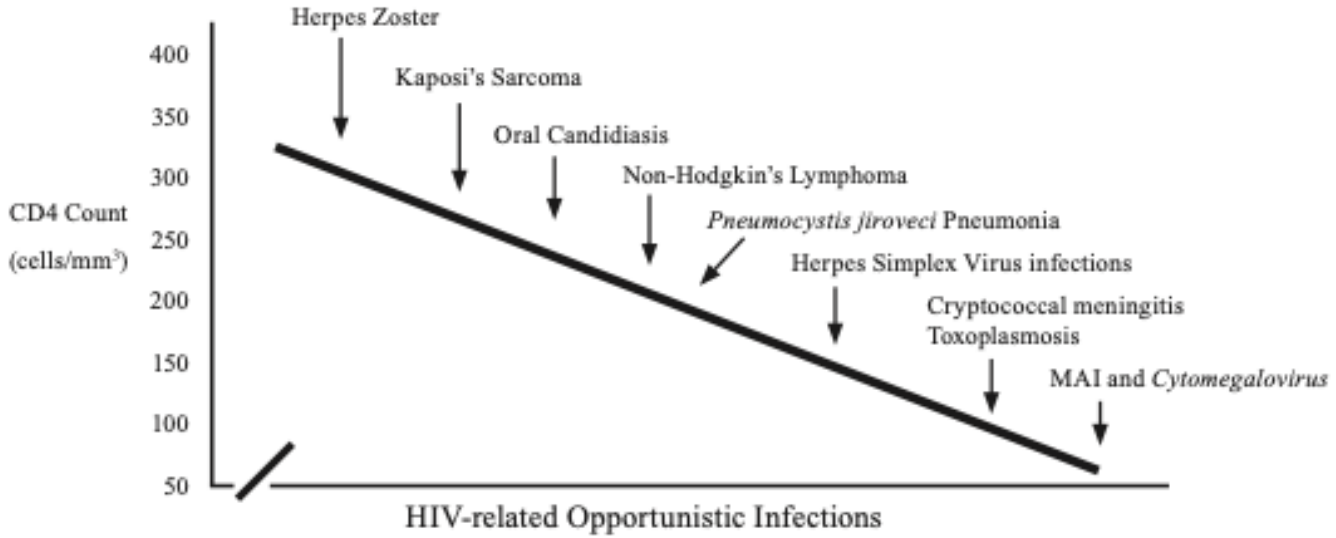
Indications	Preferred Regimens

• Anal or vaginal sex in the past 6 months and one of:
  ○ HIV-positive sexual partner
  ○ Recent bacterial STI
  ○ History of inconsistent/no condom use
• Persons who inject drugs and one of:
  ○ HIV-positive injecting partner
  ○ Shares drug preparation or injection equipment
	• Truvada (TDF + Emtricitabine) daily
	• Descovy (TAF + Emtricitabine) daily

- Post-Exposure Prophylaxis (PEP)

Indications	Preferred Regimens
• Occupational exposure (i.e., needlestick) • Non-occupational exposure (i.e., bodily fluid contact with person with known HIV infection)	• (Raltegravir or dolutegravir) + TDF/Emtricitabine • Start **within 72 hours** and treat for **28 days**

HIV – Opportunistic Infection Prophylaxis



Infection	CD4 Count (cells/mm^3)	Primary Regimens	Alternative Regimens
Pneumocystis jiroveci Pneumonia (PJP)	< 200	• Trimethoprim/ Sulfamethoxazole	• Dapsone • Atovaquone • Aerosolized pentamidine
Toxoplasmosis	< 100 with Toxoplasma-seropositive	• Trimethoprim/ Sulfamethoxazole	• Dapsone + Pyrimethamine + Leucovorin • Atovaquone
Mycobacterium avium complex (MAC)	< 50 without initiation of ART	• Azithromycin • Clarithromycin	• Rifabutin

Patient Case 7

F.G. is a 27 y/o M who is HIV positive but asymptomatic. His CD4 count is 550 cells/mm3, and his viral load is 5000 copies/mL by reverse transcriptase polymerase chain reaction. Which is the best treatment for F.G.?

A. ART should not be given because his CD4 count is still above 500 cells/mm3
B. Initiate Emtricitabine/Tenofovir only because his CD4 count is still above 500 cells/mm3
C. Initiate combination therapy of Abacavir, Lamivudine, and Atazanavir/Ritonavir
D. Initiate combination therapy of Tenofovir, Emtricitabine, and Dolutegravir

Answer: D

Tuberculosis Infections

Tuberculosis – Background

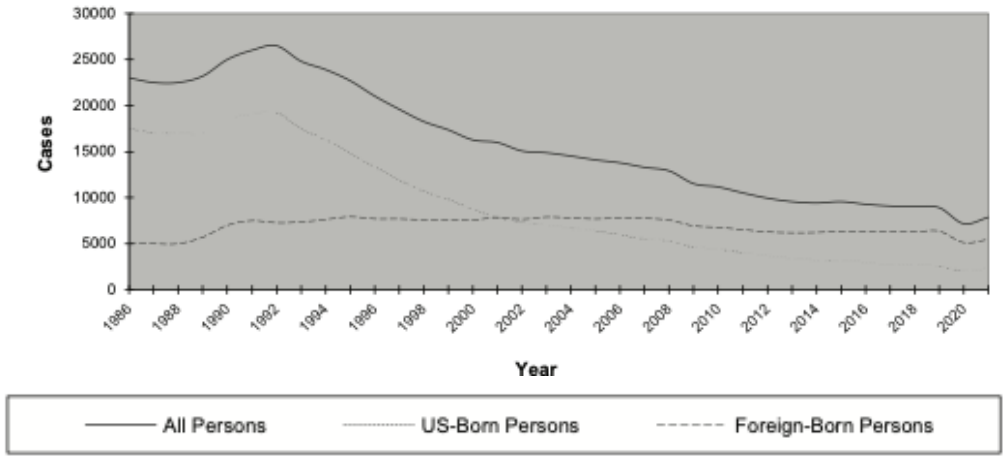
- Clinical Findings

Signs and Symptoms	Diagnostics

• Cough +/- blood
• Fevers/chills
• Malaise
• Night sweats
• Weight loss
	• Imaging
	  • Patchy/nodular infiltrates
	  • Cavitary lesions
	• Microbiology
	  • AFB sputum smear
	  • Sputum culture
	  • PCR

- Latent TB
  - Asymptomatic with potential to develop into symptomatic disease
  - Must rule out active TB and assess immune response to TB antigens

Population	TB Skin Test Positive Result
Close TB contact or immunosuppression	≥ 5 mm induration
IV drug use or high-risk setting	≥ 10 mm induration
No risk factors	≥ 15 mm induration



Tuberculosis – Management

	Treatment	Duration
Latent TB	Rifapentine + Isoniazid Rifampin Rifampin + Isoniazid	3 months 4 months 3 months
Active TB	<u>Intensive Phase</u> Rifampin + Isoniazid + Pyrazinamide + Ethambutol <u>Continuation Phase</u> Rifampin + Isoniazid (based on susceptibility)	 2 months 4 months
MDR TB†	Amikacin Bedaquiline Carbapenem + Clavulanate Levofloxacin Linezolid Moxifloxacin Para-amino salicylate	Varies

†4 months of Rifapentin/moxi/INH/PZA as effective as standard RIPE 6 month regimen per CDC 2022 MMWR.

Drug	Monitoring
Rifampin	• Hepatotoxicity • Orange bodily fluids • Significant DDIs
Isoniazid	• Hepatotoxicity • Peripheral neuropathy (Pyridoxine)
Pyrazinamide	• Hepatotoxicity • Hyperuricemia
Ethambutol	• Hepatotoxicity • Hallucinations • Optic neuropathy

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Thank You

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