Antibiotic Overview

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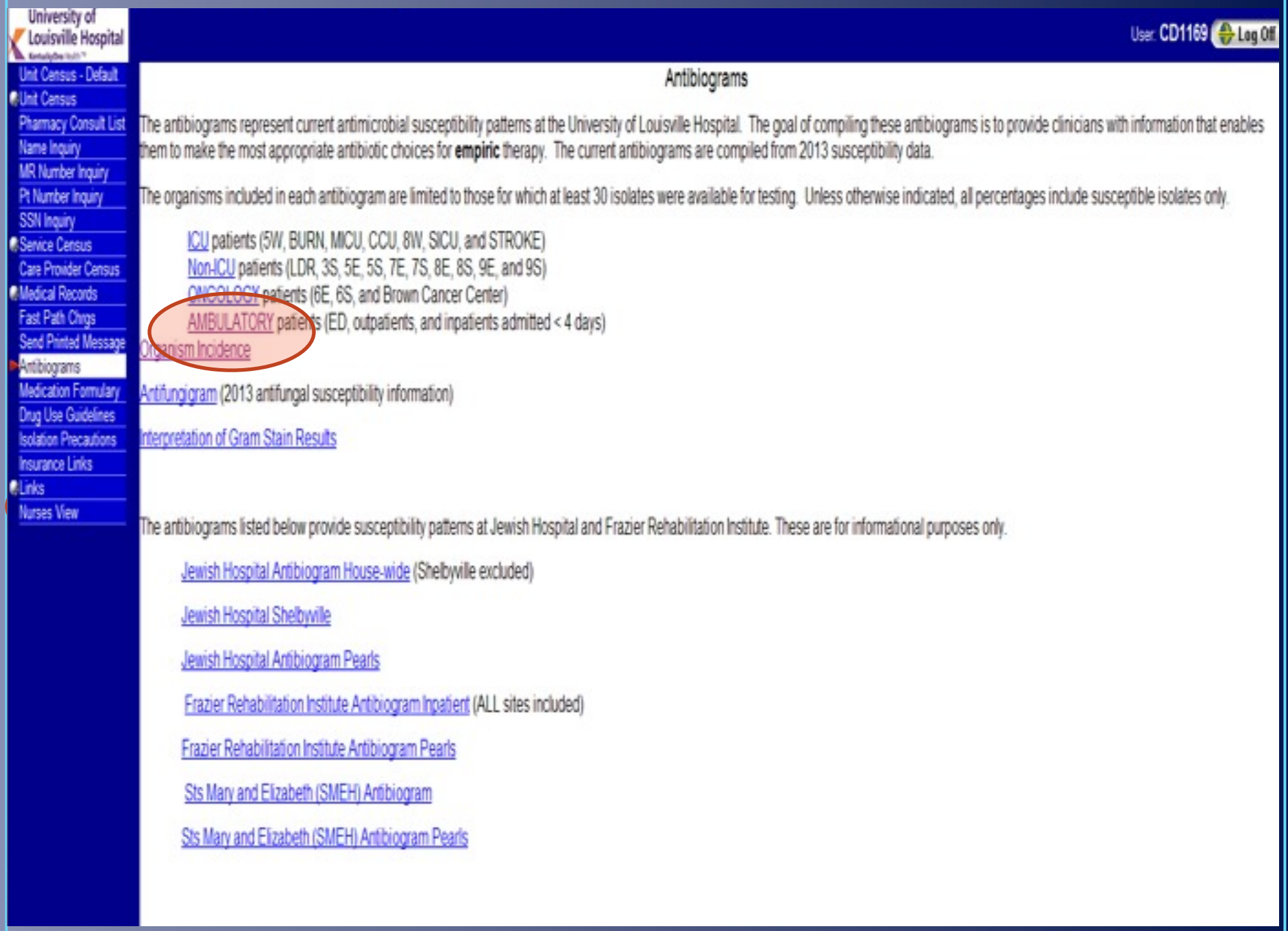
Overview

- Review 2013 antibiogram
- Briefly review EAST guidelines
- Discuss commonly seen infections in the ER

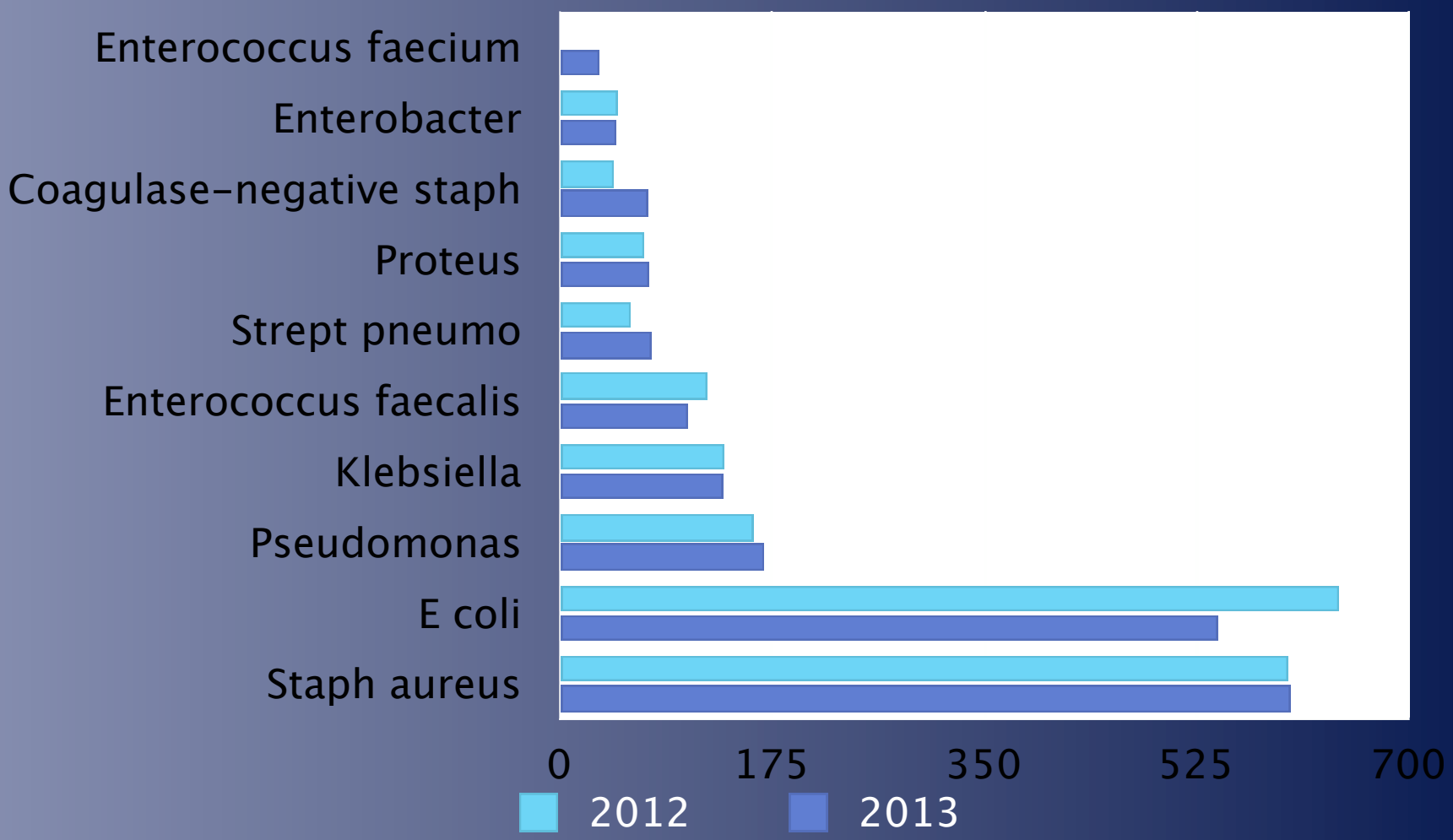
AMBULATORY CARE/ED PATIENTS

Includes isolates obtained from: outpatients and inpatients admitted for < 4 days

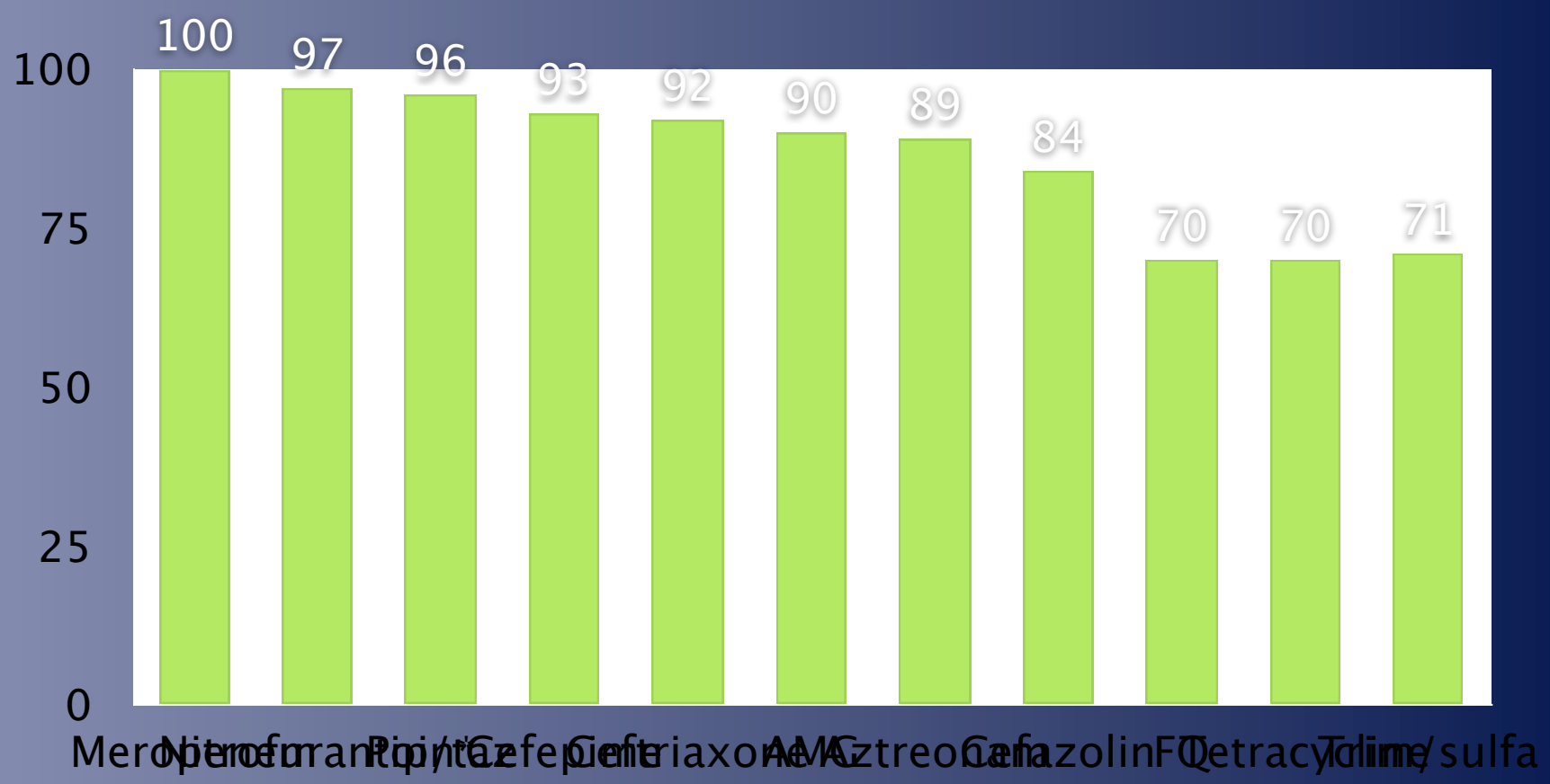
		Total # isolates	Ampicillin	Ampicillin/Sulbactam	Nafcillin	Penicillin	Piperacillin/Tazo	Cefazolin	Ceftriaxone	Cefepime	Imipenem	Meropenem	Aztreonam	Gentamicin	Tobramycin	Amikacin	Ciprofloxacin	Levofloxacin	Clindamycin	Tetracycline	Trimeth/Sulfa	Vancomycin	Daptomycin	Linezolid	Azithromycin	Erythromycin
Gram Negative	*Enterobacter cloacae*	46		11			89		72	91	100	100	89	89	89	98	89	93		83	80					
	E. coli	542	48	52			96	84	92	93	100	100	89	90	90	100	70	70		71	71		29%			
	Klebsiella pneumoniae	134		85			95	92	96	96	100	100	91	95	94	100	91	96		80	94					
	Pseudomonas aeruginosa	168					84			80	75	86	69	72	87	79	61	60	9%							
	Proteus mirabilis	73	89	87			100	92	100	100	99	100	92	92	93	93	73	78		5	75					
	Enterococcus faecalis	105	99											66[1]								99	100	100		6%
	Enterococcus faecium	32	19											66[1]								31	97	91		
Gram Positive	*Staphylococcus aureus*																									
	Methicillin Sensitive (MSSA)	288			100			100											82[2]	94	100	100	100	100	33%	
	Methicillin Resistant (MRSA)	314			0			0	52%										66[2]	94	98	100	100	100		
	Coagulase-negative Staphylococci	72			51																58	100	100	99		
	Streptococcus pneumoniae	75																								
	non-meningeal breakpoints					96			99									99			69	100			54	53
	meningeal breakpoints					47			93									99			69	100			54	53


University of Louisville Hospital
User: CD1169
Log Off
Unit Census - Default
Unit Census
Pharmacy Consult List
Name Inquiry
MR Number Inquiry
Pt Number Inquiry
SSN Inquiry
Service Census
Care Provider Census
Medical Records
Fast Path Chrgs
Send Printed Message
Antibiograms
Medication Formulary
Drug Use Guidelines
Isolation Precautions
Insurance Links
Links
Nurses View
Antibiograms
The antibiograms represent current antimicrobial susceptibility patterns at the University of Louisville Hospital. The goal of compiling these antibiograms is to provide clinicians with information that enables them to make the most appropriate antibiotic choices for empiric therapy. The current antibiograms are compiled from 2013 susceptibility data.
The organisms included in each antibiogram are limited to those for which at least 30 isolates were available for testing. Unless otherwise indicated, all percentages include susceptible isolates only.
ICU patients (5W, BURN, MICU, CCU, 8W, SICU, and STROKE)
Non-ICU patients (LDR, 3S, 5E, 5S, 7E, 7S, 8E, 8S, 9E, and 9S)
ONCOLOGY patients (6E, 6S, and Brown Cancer Center)
AMBULATORY patients (ED, outpatients, and inpatients admitted < 4 days)
Organism Incidence
Antifungigram (2013 antifungal susceptibility information)
Interpretation of Gram Stain Results
The antibiograms listed below provide susceptibility patterns at Jewish Hospital and Frazier Rehabilitation Institute. These are for informational purposes only.
Jewish Hospital Antibiogram House-wide (Shelbyville excluded)
Jewish Hospital Shelbyville
Jewish Hospital Antibiogram Pearls
Frazier Rehabilitation Institute Antibiogram Inpatient (ALL sites included)
Frazier Rehabilitation Institute Antibiogram Pearls
Sts Mary and Elizabeth (SMEH) Antibiogram
Sts Mary and Elizabeth (SMEH) Antibiogram Pearls

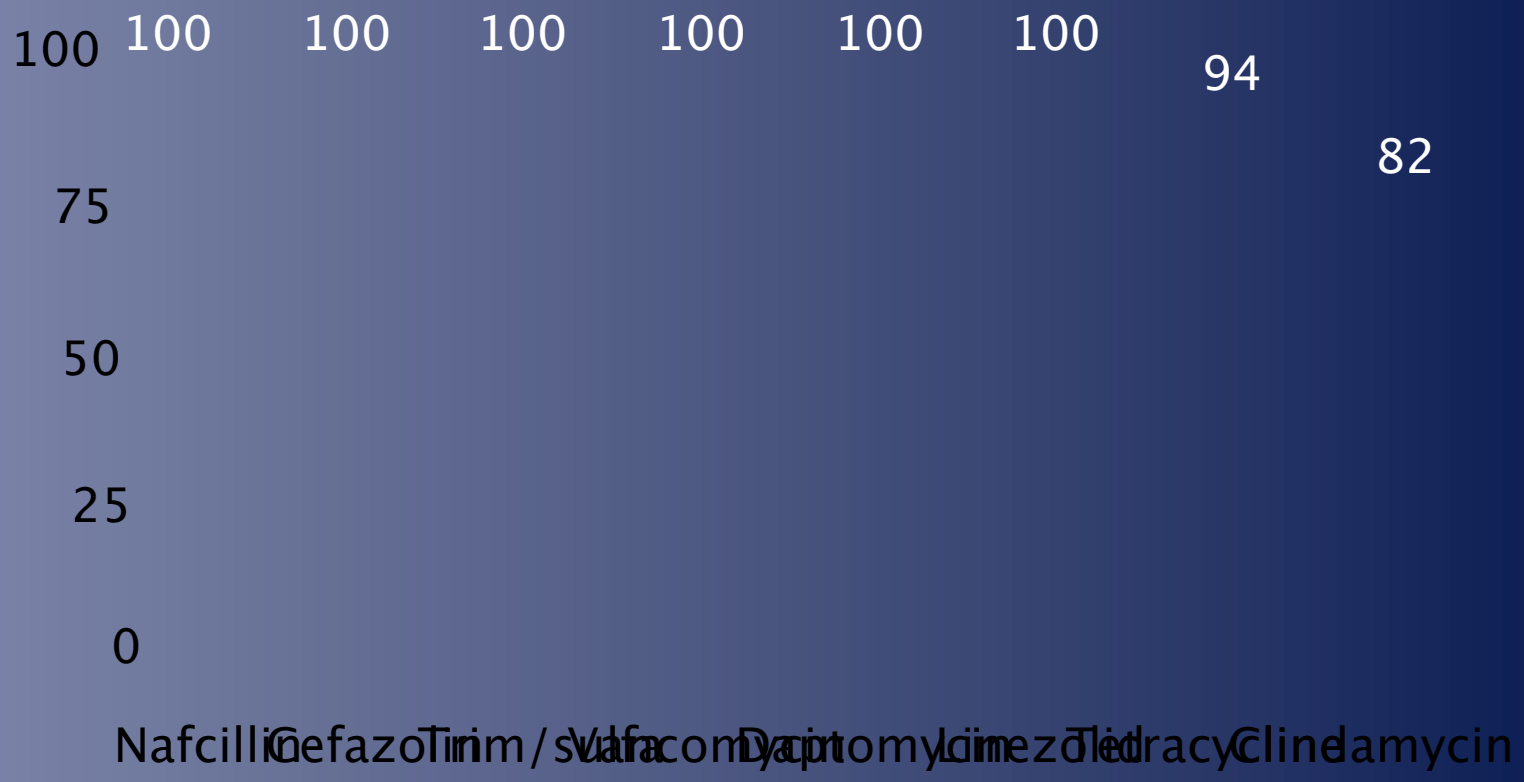
Organism Incidence 2013



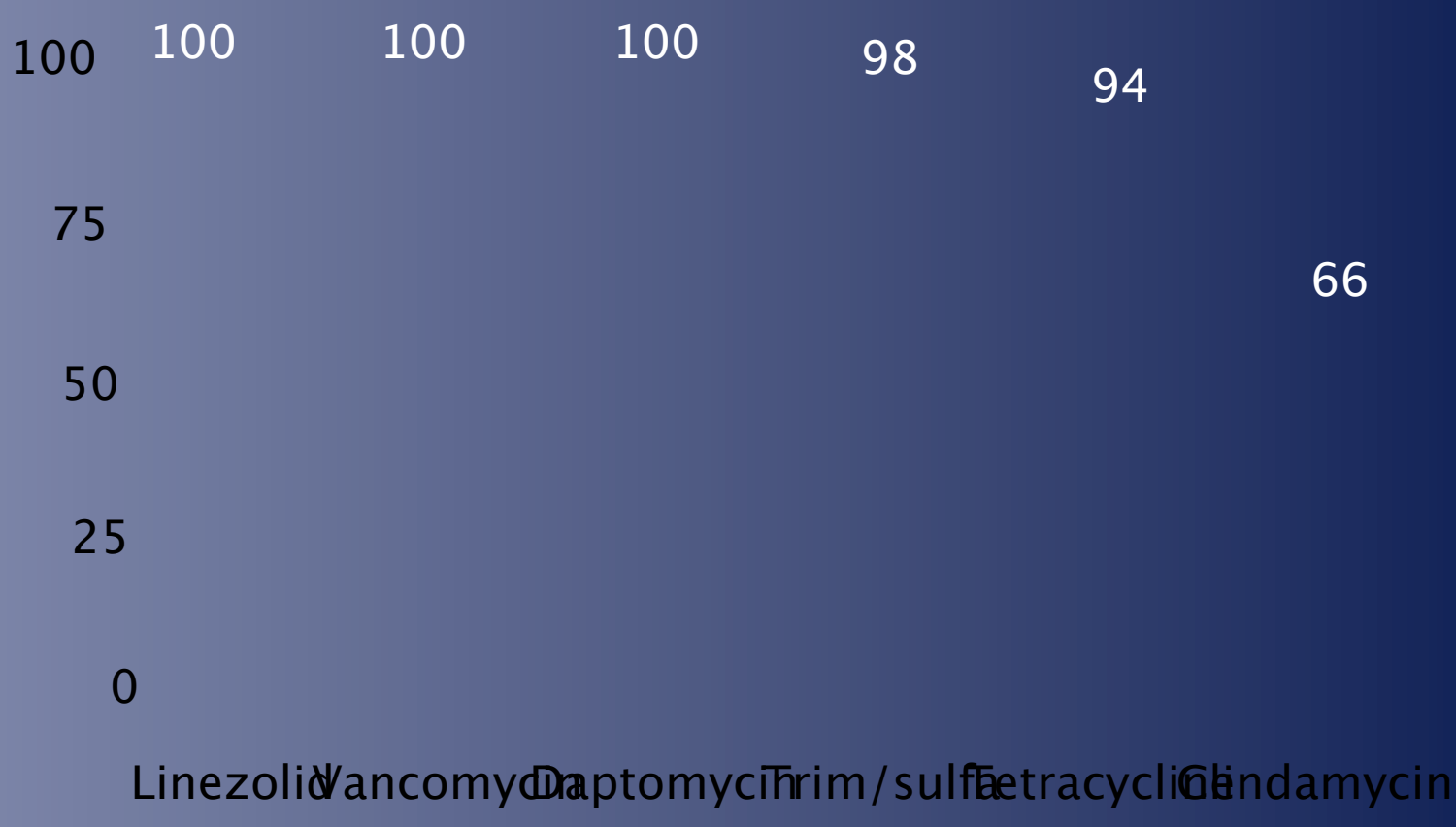
E coli


100
97
96
93
92
90
89
84
70
70
71
100
75
50
25
0
Meropenem
Piperacillin/Tazo
Ceftriaxone
AMG
Aztreonam
Cefazolin
FQ
Tetracycline
Trim/sulfa

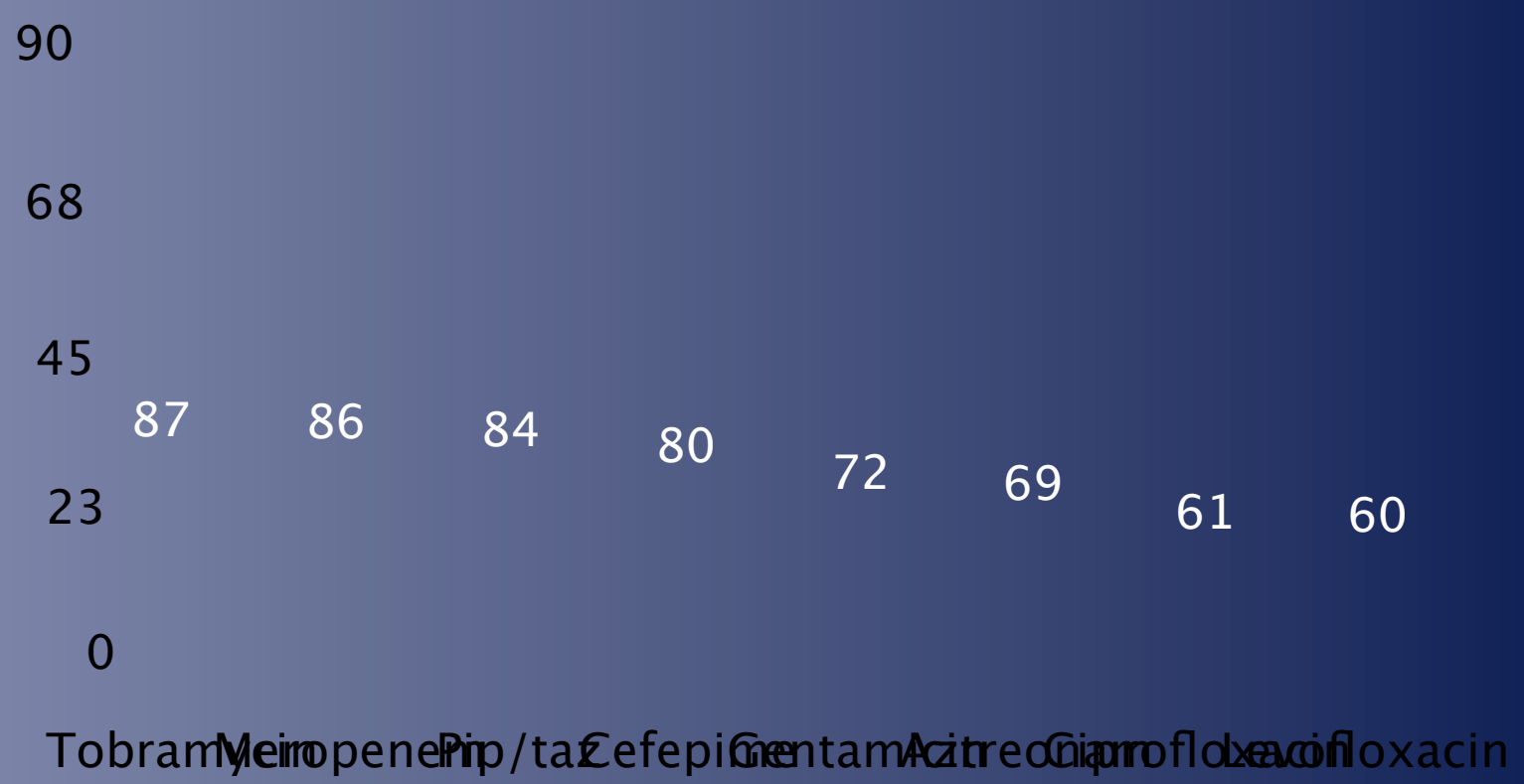
Staph aureus (Methicillin Sensitive)



Staph aureus (Methicillin Resistant)

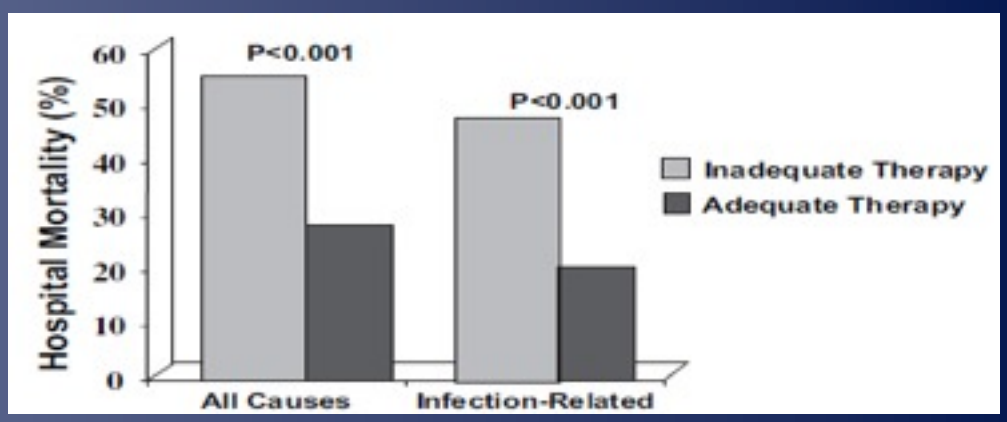


Pseudomonas



Appropriate Antibiotic Therapy

- In sepsis, failure to initiate appropriate therapy correlates with increased morbidity and mortality
- Appropriate regimen inhibits microbial isolate(s) in vitro
- 5-fold reduction in survival in sepsis
  - From 52% to 10%
- Empiric regimens should err on the side of over inclusiveness
- **Abx within 3 hours!**



Crit Care Clin. 2009; 25:733-751
CHEST 2009;136:1237-48

Medication Selection

Diagnosis of Infection	Community vs hospital infections Acute vs chronic infection
Patient Factors	Age, Sex, Weight Drug intolerances Renal/hepatic fx Recent abx use Susceptibility patterns in the community Previously documented pathogens
Medication Factors	Broad-spectrum abx for empiric therapy Narrow- psectrum abx for selective treatment -Cidal vs -static Pharmacokinetics Adverse effects Drug interactions

Risk for MDRO

Immunosuppresive dz and/or Therapy

Family Member with MDRO

Chronic Dialysis

Hospitalization ≥2 days within 90 Days

Nursing Home Resident

Antibiotics within 90 Days

Home Wound Care

Home Infusion Therapy

MRSA Activity

Doxycycline

Clindamycin

Vancomycin

Ceftaroline

Linezolid
Tedizolid

Trime/
Sulfa

Daptomycin

Pseudomonas Activity

Pip/Taz

Aztreonam

Cefepime

AMG

Ceftazadime

Carbapenems

Levofloxacin

Ciprofloxacin

Penicillin Allergies

- 1 in 10 report “allergy”
- People may become less allergic as time passes
- Determine the nature of the allergy
- Non-anaphylactic reactions
  - Drug fevers and drug rashes, hypersensitivity
- Anaphylactic reactions (~10%)
  - Laryngospasm, bronchospasm, hypotension, and hives

Crit Care Clin 2008; 24:313-334
Ann Emerg Med 2009;54:72-7
J Adv Pharm Technol Res
2010;1(1):11-7

Penicillin Allergies

- Patients with a known history of non-anaphylactic penicillin reactions may be given cephalosporins without concern
  - Cross-reactivity is <5%, 3rd/4th generation <1%
  - Typically manifested as a drug fever or rash
- Patients known to have had an anaphylactic reaction to penicillin should not be treated with penicillins, cephalosporins or carbapenems
- Cross-reactivity with carbapenems ~10%
- Aztreonam 2g
  - No cross sensitivity with penicillin
  - Only provides gram negative coverage

Crit Care Clin 2008; 24:313-334
Ann Emerg Med 2009;54:72-7
J Adv Pharm Technol Res
2010;1(1):11-7

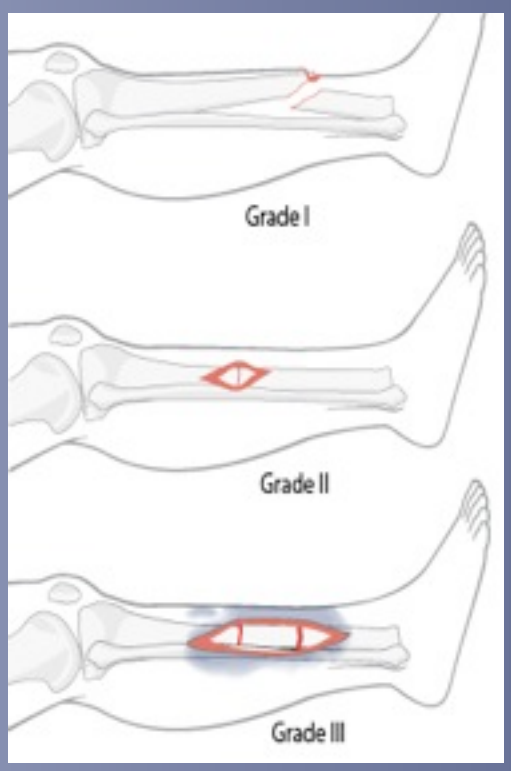
Open Fractures/ EAST Guidelines

- Antibiotics administered before incision reduces risk of infection
- Bacterial contamination is present preoperatively in 55% of all wounds and in 100% of severe wounds
- Start abx as soon as possible
  - Initiated <3 hours → 4.7% infection rate
  - Initiated >3 hours → 7.4% infection rate

J Trauma 2011;70(3):751-3
Clin Orthop Relat Res 1989;243:36-40

Open Fracture Classification (Gustilo and Anderson)

- Add high-dose PCN for fecal or potential clostridial contamination

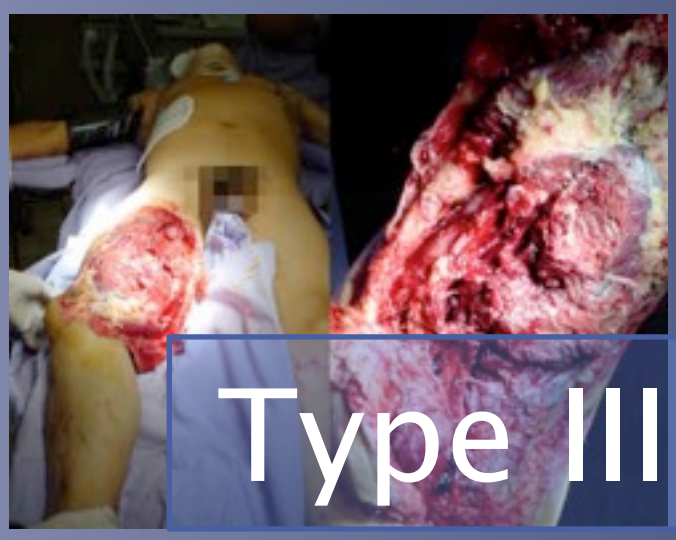


Grade I	Skin wound <1cm long and clean	Cefazolin
Grade II	Laceration >1cm without extensive soft tissue damage, flaps or avulsions	Cefazolin
Grade III	Open segmental fracture >10cm Extensive soft tissue damage Traumatic amputation	Cefazolin + Tobramycin

J Trauma 2011;70(3): 751-3


Type II

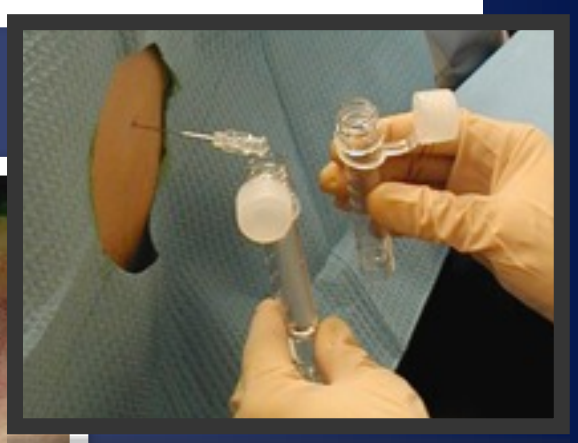

Type III


Type III

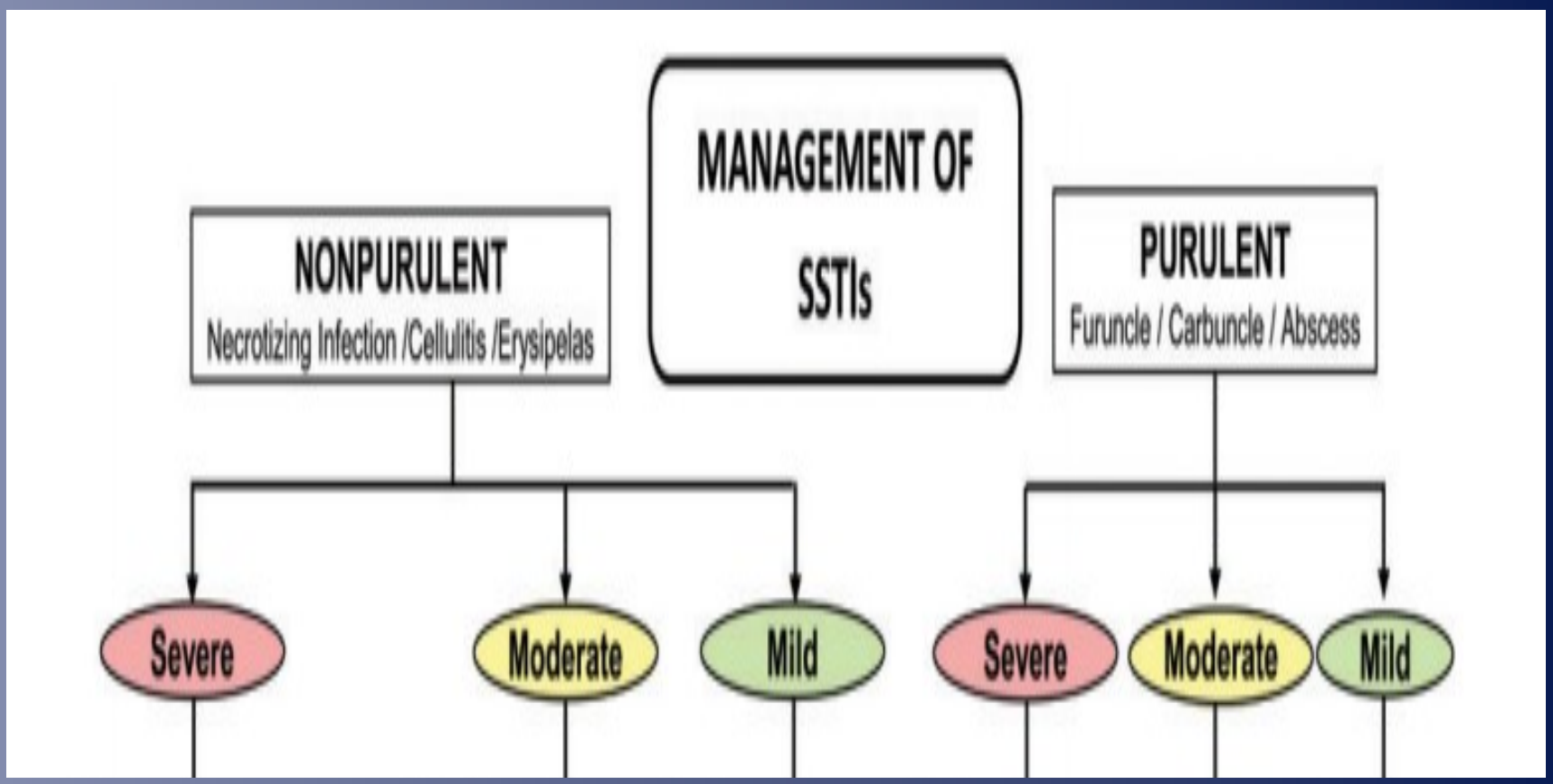

Type I

Suspected Source of Infection

- SSTI
- Urosepsis
- CAP
- HCAP/VAP
- Intraabdominal
- Meningitis



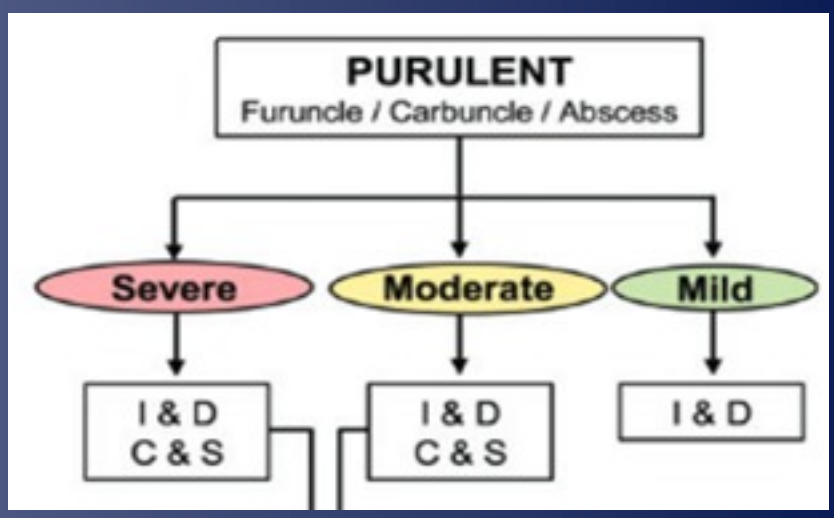
SSTI Treatment Points



Clin Infect Dis 2014;1-46
J Emerg Med 2013;44(5):910-8
Am J Health-Syst Pharm 2009;66:82-98

Abscess Management

- I & D is definitive tx
  - ALWAYS
  - NO ANTIBIOTICS



- To treat with abx
  - Temp >38 or <36
  - Tachypnea >24
  - Tachycardia >90
  - WBC >12,000 or <400

Clin Infect Dis 2014;1-46
J Emerg Med 2013;44(5):910-8
Am J Health-Syst Pharm 2009;66:82-98

NCT00729937NCT00730028 NCT00729937

Infectious Diseases Society of America Centers for Disease Control

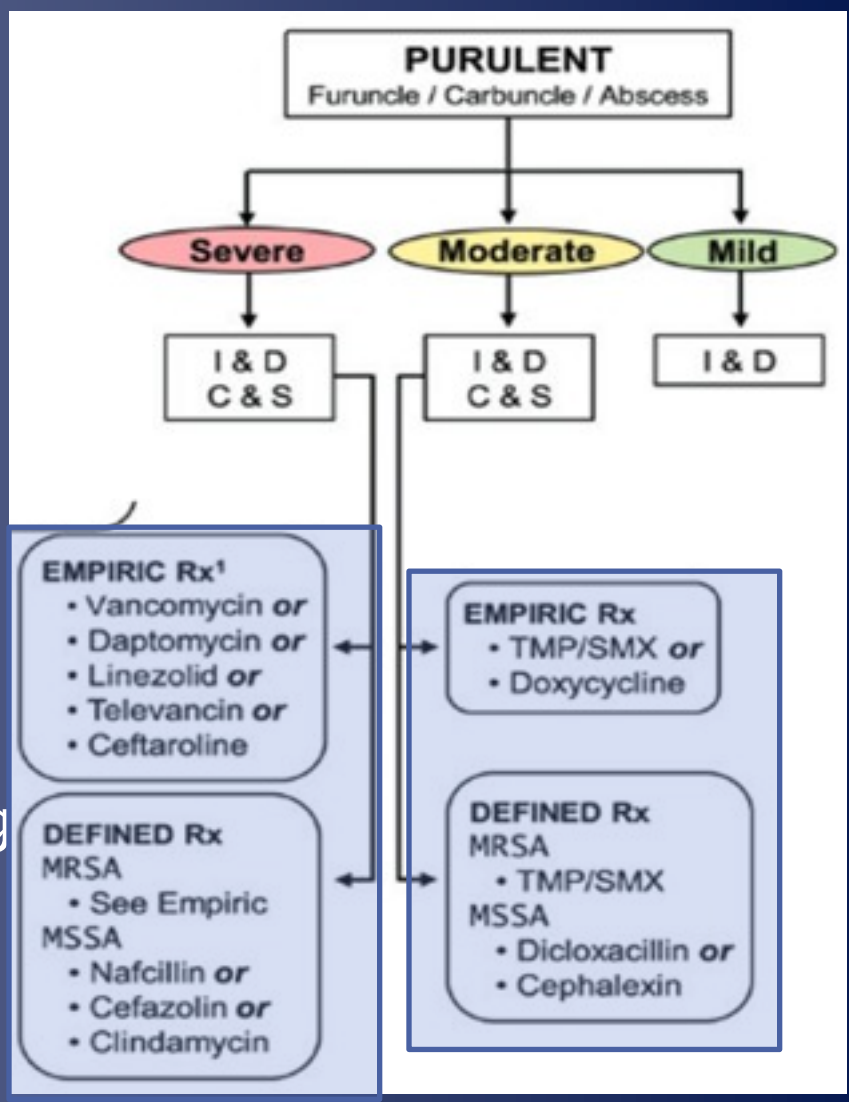
Abscess- When to Add Antibiotics

Severe or extensive disease	Lack of response to I&D
Extremes of age	Associated septic phlebitis
Immunosuppression	Undrainable
Multiple sites of infection	S/s of systemic illness
Abscess in area difficult to drain completely	

Clin Infect Dis 2011;52:e18-55
Clin Infect Dis 2014;1-46

MRSA or MSSA?

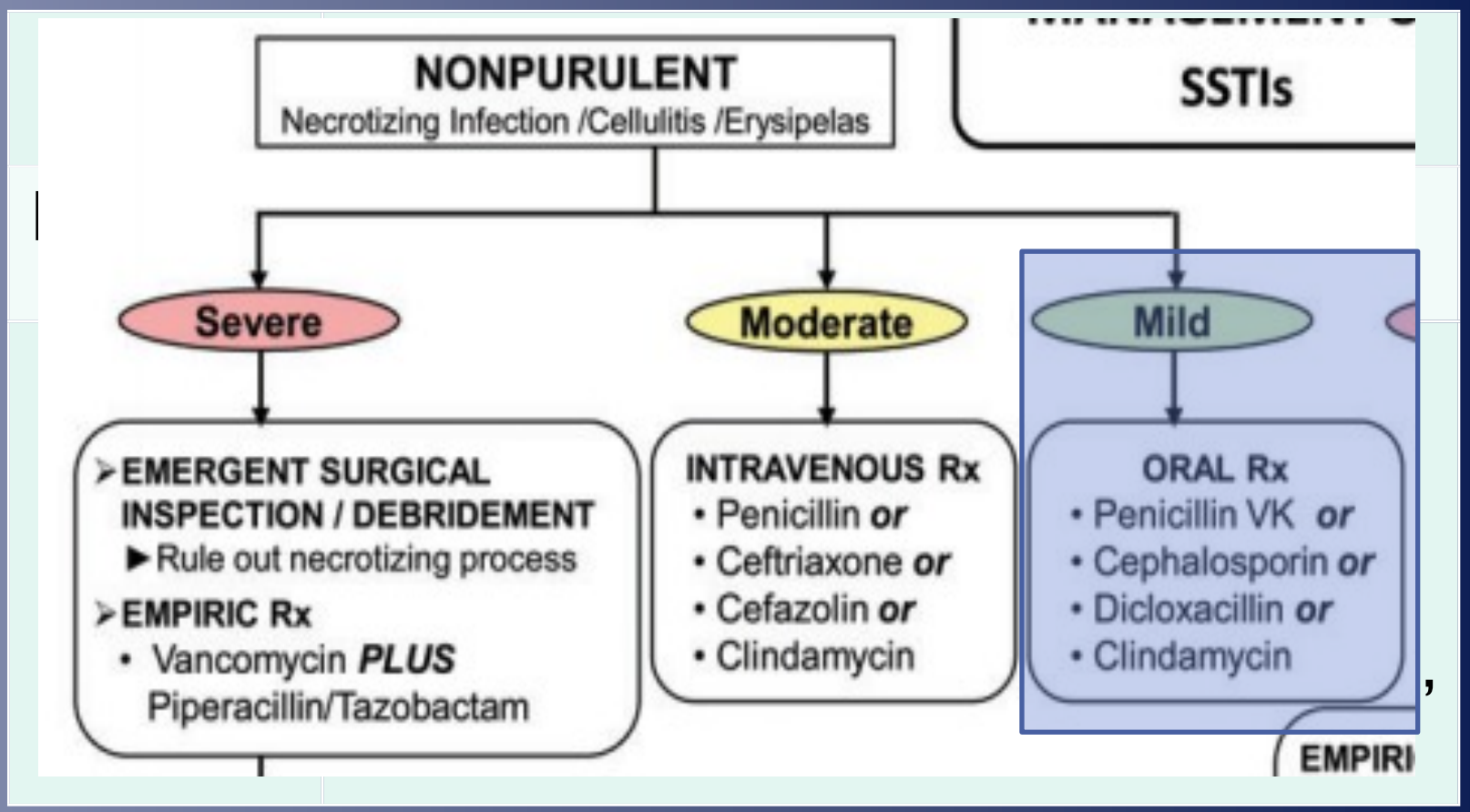
- Era of MRSA
- Consider MRSA
  - H/o MRSA infection
  - Comorbidities
  - Recent abx use
  - Recent hospitalization
- Correctly dose vancomycin
  - Forget that 1g is "default dose"
  - Utilize weight-based dosing strategy 15-20mg/kg (max 2g)



Clin Infect Dis 2014;1-46
J Emerg Med 2013;44(5):910-8
Am J Health-Syst Pharm 2009;66:82-98

increasing MIC with vancomycin

Nonpurulent



Moderate-Severe Cellulitis

- Antibiotic coverage for primarily cellulitic soft-tissue infections ideally includes both MRSA and streptococcal coverage
- Staph aureus
  - Usually associated with furuncles, carbuncles or abscesses
  - High prevalence of resistance, assume MRSA in at risk population
- Strep

Vancomycin 15mg/kg OR **Cefazolin 1g** OR **Nafcillin 2g**

Clin Infect Dis 2005; 41:1373–406
N Engl J Med 2015;372(12): 1093–103

That dose may not be sufficient for all patients

Necrotizing Fasciitis

- High mortality 50%–70% in patients with hypotension and organ failure
- S. pyogenes, S. aureus, V. vulnificus, and anaerobic strep sp.
- Staph and hemolytic strep can occur simultaneously
- Necrotizing = SURGERY (source control)
- Empirically add clindamycin to suspected necrotizing fasciitis and/or strep TSS
  - To promote toxin production inhibition and modulation of cytokine production

Pip/taz 3.375g + **Vancomycin 15mg/kg** + **Clindamycin 600mg**

Clin Infect Dis. 2005; 41:1373–406

Group A Streptococcus spherical Gram-positive bacterium
antigen cell wall beta-hemolysis
Red Blood Cells hemoglobin agar plates
Streptococci catalase incubation
period skin flora
diagnostic failure sepsis

UTI/Urosepsis

- Occurs in pre-existing renal disease, abnormal urinary tract anatomy, foreign bodies (stents), renal or bladder stones, or genitourinary instrumentation with infected urine
- Common pathogens
  - E coli, Proteus, Enterococcus, Klebsiella sp, Pseudomonas

Levofloxacin 500mg OR **Pip/taz 3.375g**

Infect Dis Clin N Am. 2008; 22:1-31
Crit Care Med. 2013; 41(2):

Suspected Source: CAP

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	*Streptococcus pneumoniae*
	Mycoplasma pneumoniae
	Haemophilus influenzae
	Chlamydophila pneumoniae
	Respiratory viruses[a]
Inpatient (non-ICU)	*S. pneumoniae*
	M. pneumoniae
	C. pneumoniae
	H. influenzae
	Legionella species
	Aspiration
	Respiratory viruses[a]
Inpatient (ICU)	*S. pneumoniae*
	Staphylococcus aureus
	Legionella species
	Gram-negative bacilli
	H. influenzae

Atypicals

Clin Infect Dis 2007; 44:S27–72

Atypical Coverage

Doxycycline

FQ

Azithromycin

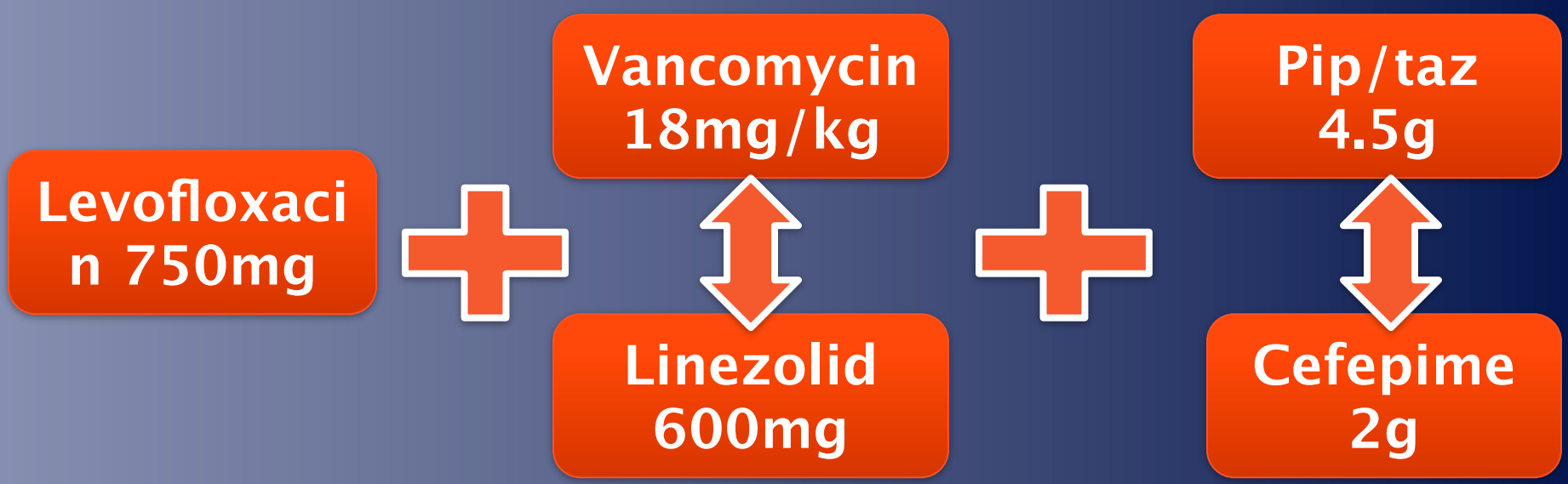
CAP Treatment

ICU Treatment (strong recommendation; level I evidence)	Non-ICU (strong recommendation; level I evidence)
Ceftriaxone or Amp/ sulbactam + Azithromycin or FQ	FQ
	Ceftriaxone or Amp/ sulbactam + Azithromycin

Clin Infect Dis 2007; 44:S27-72

HCAP

- Community pathogens, plus MDRO
- Pseudomonas, Klebsiella, Acinetobacter, MRSA



Infect Dis Clin N Am. 2008; 22:1-31
Crit Care Med. 2013; 41(2):

Intraaabdominal Infections

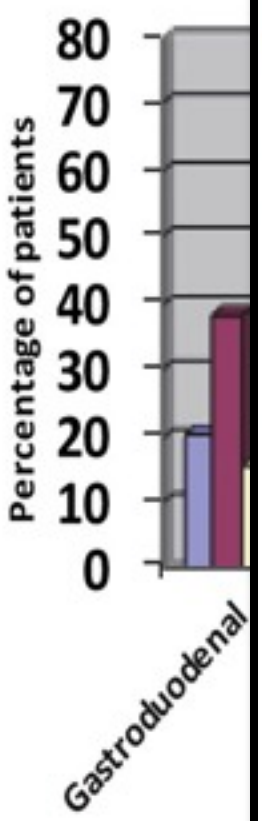


Table 8. Organisms Identified in 3 Randomized Prospective Trials of Investigational Antibiotics for Complicated Intra-abdominal Infection, including 1237 Microbiologically Confirmed Infections

Organism	Patients, % (*n* = 1237)
Facultative and aerobic gram-negative	
Escherichia coli	71
Klebsiella species	14
Pseudomonas aeruginosa	14
Proteus mirabilis	5
Enterobacter species	5
Anaerobic	
Bacteroides fragilis	35
Other *Bacteroides* species	71
Clostridium species	29
Prevotella species	12
Peptostreptococcus species	17
Fusobacterium species	9
Eubacterium species	17
Gram-positive aerobic cocci	
Streptococcus species	38
Enterococcus faecalis	12
Enterococcus faecium	3
Enterococcus species	8
Staphylococcus aureus	4

tive aerobes

tive aerobes

t Dis. 2010; 50:133–64

Infection 2009;37:522–7

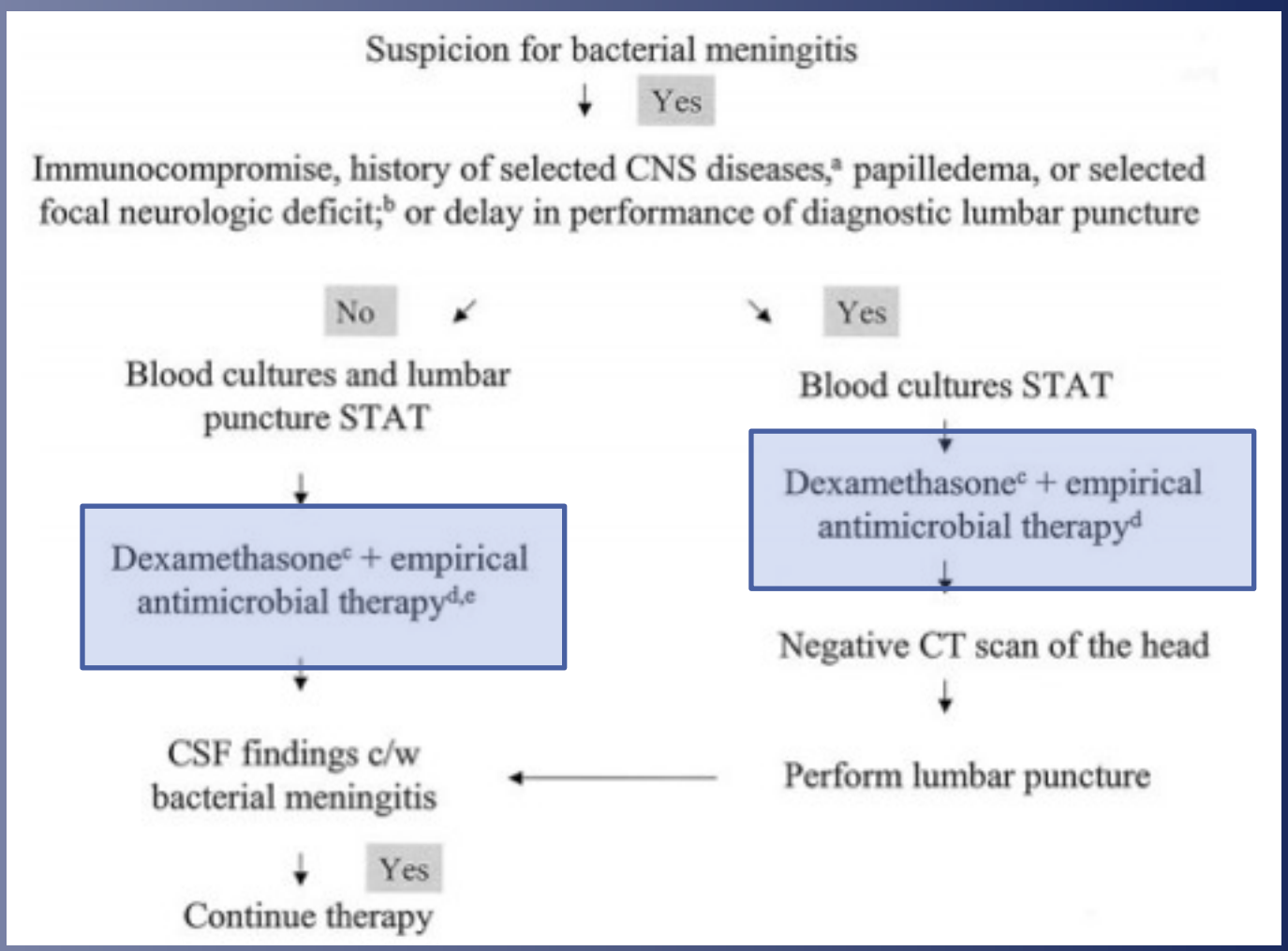
Intraabdominal Infections

- Due to ULH E coli susceptibility rates being <90%, FQ regimen not recommended

Pip/taz 3.375g OR **Cefepime 1g** + **Metronidazole 500mg** OR **Meropenem 500mg**

Infect Dis Clin N Am. 2008; 22:1-31
Crit Care Med. 2013; 41(2): 580-637

Meningitis



Clin Infect Dis 2004; 39:1267–84

Meningitis

Table 3. Recommendations for antimicrobial therapy in ad patients with presumptive pathogen identification by positive Gram stain.

Microorganism		Alternative therapies
Streptococcus pneumoniae	Van	penem (C-III), fluoroquinolone[c] (B-II)
Neisseria meningitidis		, ampicillin, chloramphenicol, fluoro- lone, aztreonam
Listeria monocytogenes	A	m-sulfamethoxazole, meropenem (B-III)
Streptococcus agalactiae		ephalosporin[a] (B-III)
Haemophilus influenza	Third-ge	amphenicol, cefepime (A-I), meropenem (A-I), roquinolone
Escherichia coli	Third-g ratio losp -II)	Ce me, meropenem, aztreonam, fluoroquino- lone, trimethoprim-sulfamethoxazole

Dexamethasone 10mg IV 10 minutes before/with abx!

Ceftriaxone 2g + **Vancomycin 18mg/kg** ± **Ampicillin 2g**

Infect Dis Clin N Am. 2008; 22:1-31

Crit Care Med. 2013; 41(2):

MICU Septic Shock Protocol

CAP	HCAP/VAP	Intra-abdominal
CEFTRIAXONE 1G q24 hours PLUS **AZITHROMYCIN** 500mg q24 hours	**LEVOFLOXACIN** 750mg q24 hours PLUS **VANCOMYCIN** 18mg/kg -OR - **LINEZOLID** 600mg q12 hours PLUS **PIP/TAZ** 4.5g q6 hours - OR -	**CEFEPIME** 1g q12 hours PLUS **METRONIDAZOLE** 500mg q8 hours
LEVOFLOXACIN 750mg q24 hours		**PIP/TAZ** 3.375g q6 hours

MICU Septic Shock Protocol

Meningitis	UTI	SSTI/Nec fasc
CEFTRIAXONE 2g q12 hours PLUS **VANCOMYCIN** 18mg/kg	**LEVOFLOXACIN** 500mg q24 hours	**VANCOMYCIN** 15mg/kg PLUS **PIP/TAZ** 3.375g q6 hours PLUS **CLINDAMYCIN** 600mg q8 hours
AMPICILLIN 2g q4 hours **ACYCLOVIR** 10mg/	**PIP/TAZ** 3.375g q6 hours	

- If penicillin allergic
  - Replace pip/taz or cephalosporin with AZTREONAM 2g q6 hours

"Ed's in a VERY contrary mood today. I'm buying probiotics and he's over there buying antibiotics."

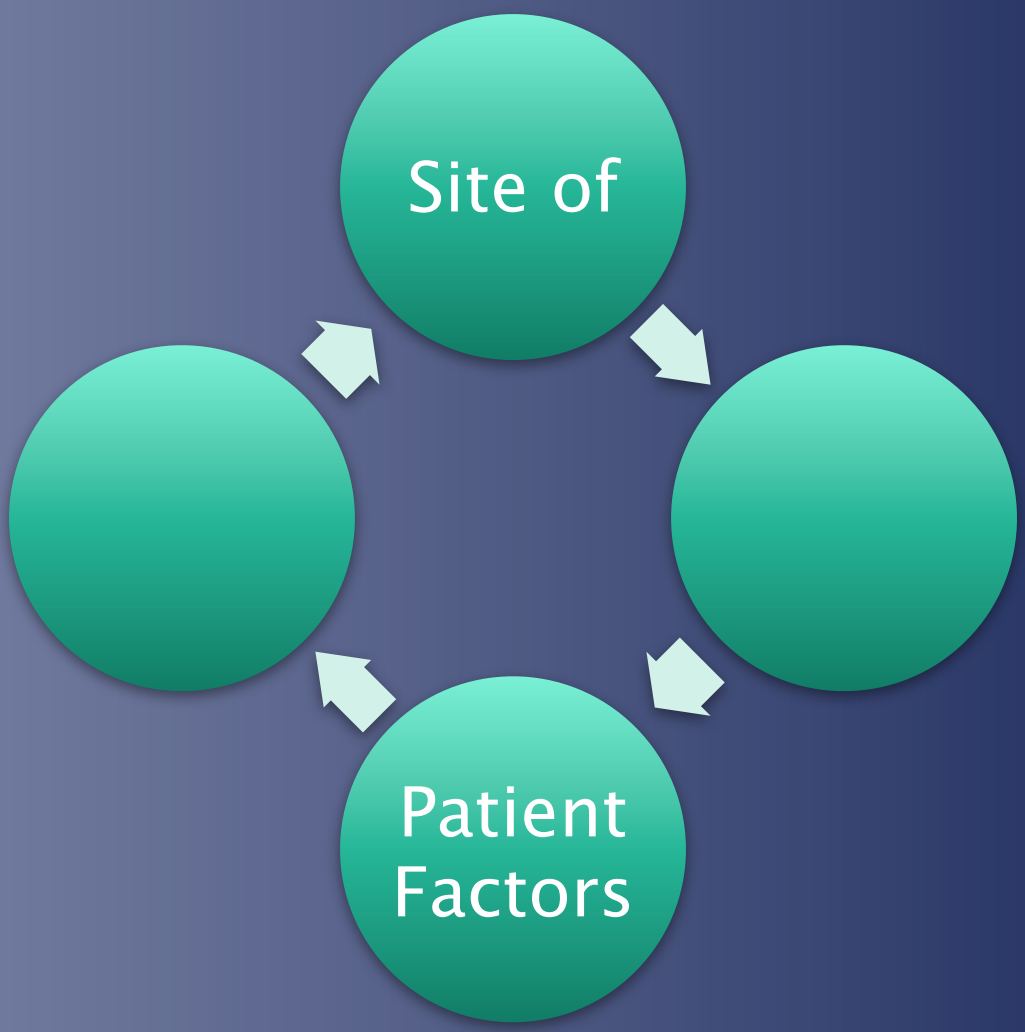
Conclusion

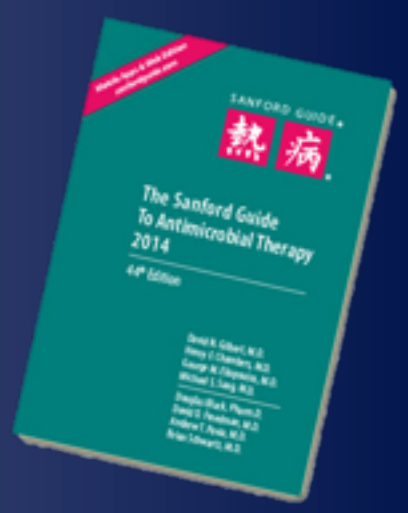
IV Abx Before Discharge: Please NO

- No evidence supports its benefit
- Prolongs ED length of stay
- Increases cost of ED visit
- Pharmacokinetics
  - Vancomycin is a time-dependent killer
- Under-dosing is common
- Risk of MDRO

Am J Emerg Med 2014;32(10): 1195-9
J Emerg Med 2015;49:50-7

Infectious Diseases 101





Diagnosis of infection:

Patients factors:

Drug factors:

Complicated SSTI

- Toxic shock syndrome (TSS)
  - Group A streptococci or S aureus
  - Characterized by multiorgan dysfunction and may be fatal
  - TSS is primarily a toxin-mediated disorder
- Necrotizing fasciitis
  - May be complicated

Clinical Features Suggestive of Necrotizing Infection
Severe, constant pain
Bullae, related to occlusion of deep blood vessels
Skin necrosis or ecchymosis that precedes skin necrosis
Gas in the soft tissues
Edema that extends beyond the margin of erythema
Cutaneous anesthesia
Systemic toxicity
Rapid spread, especially with appropriate antibiotic therapy

Infect Dis Clin N Am. 2008; 22:1-31
Crit Care Med. 2013; 41(2): 580-637

Uncomplicated Cystitis and Pyelonephritis

- Avoid FX, tetracyclines, AMG in pregnancy
  - Avoid trim/sulfa in late third trimester

Acute Uncomplicated Cystitis	Acute Pyelonephritis
Nitrofurantoin (100mg po BID x5 days)	Ciprofloxacin
Trim/sulfa (1 DS tab po BID x3 days)	Trim/sulfa
Fosfomycin (3gm PO x1)	
FQ x3 days	
Beta-lactams	

Clin Infect Dis 2011;52(5)

Medication Selection Cont

- Empiric Therapy
  - Community infection
    - Narrow spectrum
  - Nosocomial infection
    - Broad spectrum, reserved abx
- Targeted Therapy

Empirical th
community

hospital infections

Targeted th

Considerations for Empiric Antibiotic Therapy

- Drug Intolerances
- Previously Documented Pathogens
- Recent Antibiotic Use (<3 months)
- Underlying Disease
- Susceptibility Patterns in the Community
- Clinical Syndrome
- Renal and Hepatic Function

Treatment Principles

- EARLY GOAL DIRECTED THERAPY
  - Aggressive treatment in the ED
  - Proven to reduce mortality in severe sepsis/shock
  - 16% absolute RR in mortality
- Prompt infection source control
- Culture of pertinent sites
- Early and appropriate empiric antibiotics
- Aggressive circulatory support
- Non-injurious ventilatory support

Zosyn Extended Infusion

- Time dependent killer
  - Pharmacodynamic parameter best associated with treatment efficacy is time over the MIC
- Extended infusion strategy has a higher probability of reaching target attainment in pseudomonas than conventional dosing strategies
- Scheduled/continuous orders for pip/taz will be extended infusion only (infused over 4 hours)
- Initial/ one time, “bolus”, will be infused over 30 minutes
- For pseudomonas, 4.5g x1 dose in the ER
  - Will be followed by recommended extended infusion

Pharm 2007;27(11):1490-1497)

Time dependent killing effect is best predicted by the percentage of time

levels greater than MIC for 60 – 70 %

severe infections are best treated by continuous infusion

Pip/taz Extended Infusion

- Go Live Date: Aug 5th

CrCl	>20ml/min	≤20ml/min, HD, PD
Usual Dose	Bolus: 3.375g over 30 minutes, followed 4 hours by: Maintenance: 3.375g over 4 hours q8hrs	Bolus: 3.375g over 30 minutes, followed 8 hours by: Maintenance: 3.375g over 4 hours q12hrs
Febrile Neutropenia Morbidly Obese Cystic Fibrosis	Bolus: 4.5g over 30 minutes, followed 4 hours by: Maintenance: 4.5g over 4 hours q8hrs	Bolus: 4.5g over 30 minutes, followed 8 hours by: Maintenance: 4.5g over 4

Future Antimicrobial Agents For Gram Positives Organisms

- Glycopeptides
  - Telavancin
  - Oritavancin
  - Dalbavancin
- Tetracyclines
  - Tigecycline (broad spectrum activity)
- Cephalosporins
  - Ceftibiprole (5th generation)
    - Excellent gram positive activity (MRSA & Enterococcus)

AMBULATORY CARE/ED PATIENTS

Includes isolates obtained from: outpatients and inpatients admitted for < 4 days

		Total # Isolates	Ampicillin	Ampicillin/Sulbactam	Nafcillin	Penicillin	Piperacillin/Tazo	Cefazolin	Ceftriaxone	Cefepime	Meropenem	Aztreonam	Gentamicin	Tobramycin	Amikacin	Ciprofloxacin	Levofloxacin	Clindamycin	Tetracycline	Trimeth/Sulfa	Vancomycin	Daptomycin	Linezolid	Azithromycin	Erythromycin
Gram Negative	*Enterobacter cloacae*	47		31			85		66	83	100	74	92	92	98	92	92		83	92					
	E. coli	642	44	49			97	88	95	97	100	95	90	92	99	76	76		74	72	34%				
	Klebsiella pneumoniae	135		88			96	91	92	92	96	89	93	93	99	93	94		88	89					
	Pseudomonas aeruginosa	159					87			76	90	76	59	80	67	64	65	8%							
	Proteus mirabilis	69	90	90			100	90	100	100	100	97	91	93	100	77	81		3	81					
Gram Positive	*Enterococcus faecalis*	121	100										73[1]								100	100	99		6%
	Staphylococcus aureus																								
	Methicillin Sensitive (MSSA)	274			100			100										78[2]	98	98	100	99	100	32%	
	Methicillin Resistant (MRSA)	334			0			0										72[2]	95	98	100	99	100	55%	
	Coagulase-negative Staphylococci	54			28															57	100	100	100		
	Streptococcus pneumoniae	57																							
	non-meningeal breakpoints					95			100								98			74	100			66	67
	meningeal breakpoints					68			93								98			74	100			66	67