Appropriate antibiotics for sepsis

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SEPSIS STEPS

SIRS

T: >100.4 F
< 96.8 F
RR: >20
HR: >90
WBC: >12,000
<4,000
>10% bands
PCO2 < 32 mmHg

SEPSIS

2 SIRS

+

Confirmed **or** suspected infection

SEVERE SEPSIS

Sepsis +

Signs of End Organ Damage

Hypotension (SBP <90)

Lactate >4 mmol

SEPTIC SHOCK

Severe Sepsis with persistent:

Signs of End Organ Damage

Hypotension (SBP <90)

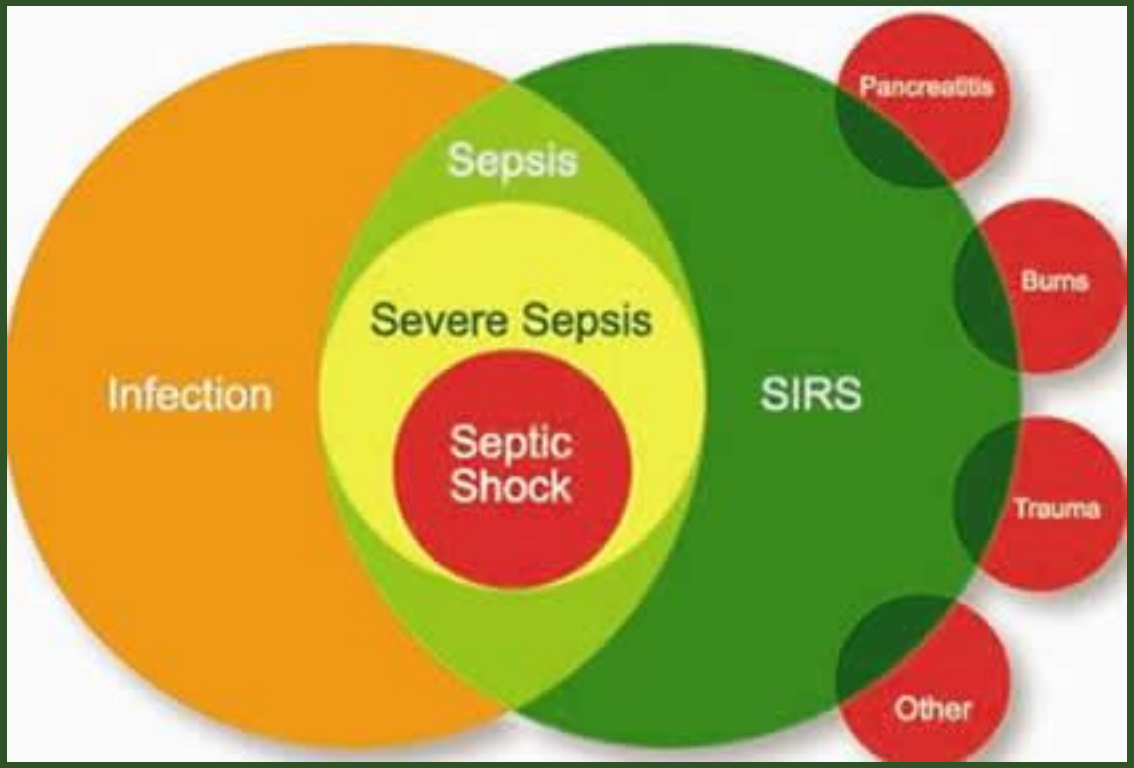
Lactate >4 mmol

Slides Courtesy of Curtis Merritt, D.O.

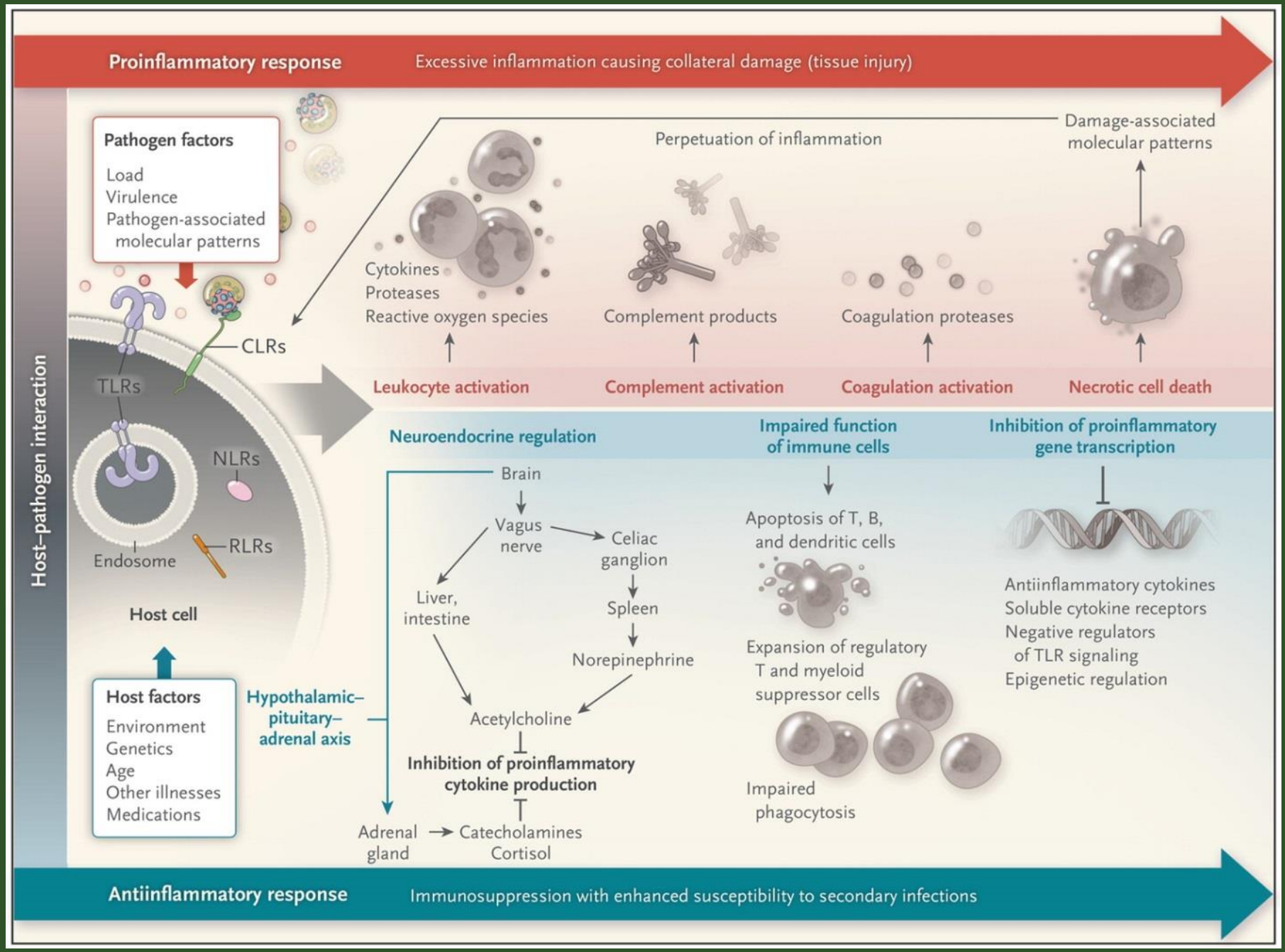
Epidemiology of Sepsis

- 1999-2014 CDC found that a total of 2,470,666 decedents (6% of all deaths) had sepsis listed among the causes of death
  - for 22% of these decedents, sepsis was listed as the underlying cause of death. *
- 750,000 annual cases
  - 2% of all hospital admissions are due to “severe sepsis”
- $23 billion in health care expenditures in 2013
- Most commonly occurs among patients with 1 or more risk factors
- Majority of patients have health care exposure or a chronic comorbidity
- **In many cases, a specific pathogen is not identified**

*https://www.cdc.gov/sepsis/datareports/index.html



http://www.differencebetween.info/difference-between-sepsis-and-infection



Angus DC NEJM 2013

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Protocol-Based EGDT (N=439)	Protocol-Based Standard Therapy (N=446)	Usual Care (N=456)
Age — yr†	60±16.4	61±16.1	62±16.0
Male sex — no. (%)	232 (52.8)	252 (56.5)	264 (57.9)
Residence before admission — no. (%)‡			
Nursing home	64 (14.6)	72 (16.1)	73 (16.0)
Other	373 (85.0)	373 (83.6)	382 (83.8)
Charlson comorbidity score§	2.6±2.6	2.5±2.6	2.9±2.6
Source of sepsis — no. (%)			
Pneumonia	140 (31.9)	152 (34.1)	151 (33.1)
Urinary tract infection	100 (22.8)	90 (20.2)	94 (20.6)
Intraabdominal infection	69 (15.7)	57 (12.8)	51 (11.2)
Infection of unknown source	57 (13.0)	47 (10.5)	66 (14.5)
Skin or soft-tissue infection	25 (5.7)	33 (7.4)	38 (8.3)
Catheter-related infection	11 (2.5)	16 (3.6)	11 (2.4)
Central nervous system infection	3 (0.7)	3 (0.7)	4 (0.9)
Endocarditis	1 (0.2)	3 (0.7)	3 (0.7)
Other	28 (6.4)	31 (7.0)	26 (5.7)
Determined after review not to have infection	5 (1.1)	14 (3.1)	12 (2.6)
Positive blood culture — no. (%)	139 (31.7)	126 (28.3)	131 (28.7)
APACHE II score¶	20.8±8.1	20.6±7.4	20.7±7.5
Entry criterion — no. (%)			
Refractory hypotension	244 (55.6)	240 (53.8)	243 (53.3)
Hyperlactatemia‖	259 (59.0)	264 (59.2)	277 (60.7)
Physiological variables			
Systolic blood pressure — mm Hg	100.2±28.1	102.1±28.7	99.9±29.5

ProCESS study NEJM 2016

Last Updated: Version 5.0a

NQF-ENDORSED VOLUNTARY CONSENSUS STANDARDS FOR HOSPITAL CARE

Measure Information Form
Collected For: CMS Only

Measure Set: Sepsis

Set Measure ID #: SEP-1

Performance Measure Name: Early Management Bundle, Severe Sepsis/Septic Shock

Description: This measure focuses on adults 18 years and older with a diagnosis of severe sepsis or septic shock. Consistent with Surviving Sepsis Campaign guidelines, it assesses measurement of lactate, obtaining blood cultures, administering broad spectrum antibiotics, fluid resuscitation, vasopressor administration, reassessment of volume status and tissue perfusion, and repeat lactate measurement. As reflected in the data elements and their definitions, the first three interventions should occur within 3 hours of presentation of severe sepsis, while the remaining interventions are expected to occur within 6 hours of presentation of septic shock.

SEP-1

- Goal: improve patient care and reduce variability in care
- SEP-1 is currently an IQR clinical process measure-not an outcome claims-based measure.
  - In FY 2017, there is a **potential** HVBP cumulative penalty of 2%. In addition, process of care measures will be reassigned to a new domain-clinical care-and decrease to 5% of the HVBP composite.
  - Display of public outcomes data in media, non-compliant providers may face the repercussions of a tarnished reputation.

Severe Sepsis	Septic Shock
All three must be met within 6 hours: 1. Documentation of a **suspected source** of infection 2. Two or more manifestations of **SIRS** criteria: a. Temperature >38.3 C/101 F or <36 C/96.8 F b. Heart rate >90 c. Respiratory rate >20 d. WBC >12 or <4 or >10% bands 3. **Organ Dysfunction**, evidenced by any one of the following: a. SBP < 90 or MAP <65, or a SBP decrease of more than 40 pts b. Cr >2.0 or urine output < 0.5 cc/kg/hour for 2 hours c. Bilirubin >2 mg/dL (32.4 mol/L) d. Platelet count < 100 e. INR >1.5 or PTT > 60 f. Lactate >2 mmol/L 4. Or if a provider documents severe sepsis, r/o sepsis, possible sepsis, or septic shock	1. There must be documentation of septic shock present and 2. **Tissue hypoperfusion** persisting in the hour after crystalloid fluid administration, evidenced by: a. SBP < 90 b. MAP < 65 c. Decrease in SBP by >40 points from the patient's baseline d. Lactate ≥4 3. Or if the criteria are not met, but there is provider documentation of septic shock or suspected septic shock

SEP-1: Early Management Bundle, Severe Sepsis/Septic Shock

Numerator: Patients who received ALL of the following:

Received within three hours of presentation of severe sepsis:

- Initial lactate level measurement
- Broad spectrum or other antibiotics administered
- Blood cultures drawn prior to antibiotics

AND received within six hours of presentation of severe sepsis:

- Repeat lactate level measurement only if initial lactate level is elevated

AND ONLY if Septic Shock present:

Received within three hours of presentation of septic shock:

- Resuscitation with 30 ml/kg crystalloid fluids

AND ONLY if hypotension persists after fluid administration, received within six hours of presentation of septic shock:

- Vasopressors

AND ONLY if hypotension persists after fluid administration or initial lactate >= 4 mmol/L, received within six hours of presentation of septic shock:

- Repeat volume status and tissue perfusion assessment consisting of either:
  - A focused exam including:
    - Vital signs, AND
    - Cardiopulmonary exam, AND
    - Capillary refill evaluation, AND
    - Peripheral pulse evaluation, AND
    - Skin examination

      OR
  - Any two of the following four:
    - Central venous pressure measurement
    - Central venous oxygen measurement
    - Bedside cardiovascular ultrasound
    - Passive leg raise or fluid challenge

Denominator: Inpatients age 18 and over with an ICD-10-CM Principal or Other Diagnosis Code of Sepsis, Severe Sepsis or Septic Shock as defined in Appendix A, Table 4.01

Variable Ke

Sepsis Discharge Tir
Shock Discharge Tir
Shock Three Hour Count
Shock Six Hour Count
Shock Physical Assessment Six Hour Count

Table 5.0 Antibiotic Monotherapy, Sepsis

Antibiotic Selection Options (includes trade & generic name)	Generic Name Crosswalk
Doribax	Doripenem
Doripenem	Doripenem
Eratepenem	Eratepenem
Invanz	Eratepenem
Imipenem/Cilastatin	Imipenem/Cilastatin
Meropenem	Meropenem
Merrem	Meropenem
Primaxin	Imipenem/Cilastatin
Cefotaxime	Cefotaxime
Claforan	Cefotaxime
Ceftazidime	Ceftazidime
Ceftriaxone	Ceftriaxone
Fortaz	Ceftazidime
Rocephin	Ceftriaxone
Cefepime	Cefepime
Maxipime	Cefepime
Ceftaroline fosamil	Ceftaroline fosamil

Antibiotic Selection Options (includes trade & generic name)	Generic Name Crosswalk
Teflaro	Ceftaroline fosamil
Avelox	Moxifloxacin
Gatifloxacin	Gatifloxacin
Levaquin	Levofloxacin
Levofloxacin	Levofloxacin
Moxifloxacin	Moxifloxacin
Tequin	Gatifloxacin
Amoxicillin/clavulanate	Amoxicillin/clavulanate
Ampicillin/sulbactam	Ampicillin/sulbactam
Augmentin	Amoxicillin/clavulanate
Piperacillin/tazobactam	Piperacillin/tazobactam
Ticarcillin/clavulanate	Ticarcillin/clavulanate
Timentin	Ticarcillin/clavulanate
Unasyn	Ampicillin/sulbactam
Zosyn	Piperacillin/tazobactam

Combination Antibiotic Therapy Table

Column A		Column B
Aminoglycosides OR Aztreonam OR Ciprofloxacin	+	Cephalosporins (1st and 2nd Generation) OR Clindamycin IV OR Daptomycin OR Glycopeptides OR Linezolid OR Macrolides OR Penicillins

NOTE: Metronidazole (Flagyl) is not represented on any table because it is not approved for monotherapy and if given, must be given with 2 other combination antibiotic therapy drugs. Since giving those 2 antibiotic therapy drugs will allow Value "1" to be chosen, the metronidazole is not required to be administered or abstracted.

My critiques of the antibiotics

- Do NOT allow for individualization of care
- Do NOT allow for optimal treatment of streptococcal toxic shock
- Encourage broad spectrum antibiotic use
- Augmentin for sepsis? Really?
- Ticarcillin-clavulonic acid has not been available for years!
- Gatifloxacin is LONG gone
- Ceftaroline monotherapy for sepsis?
  - Who here would use vanco and cefazolin for a early sepsis?
- Cannot even spell the antibiotics correctly
  - Eratapenem

So what do we do about antibiotic therapy?

Disclaimer

- Antibiotic selection in 2016 is site specific
  - Your antibiogram should determine your antibiotic selection
  - What works in Dayton may not work in Cleveland

Core concepts in Antibiotic Selection

- Cook book medicine has to end!!!
- Routine use of triple antibiotics have to stop (outside of septic shock/select patient)!!!
- Optimize PK/PD (aka push the doses)
- Key concepts when selecting antibiotics:
  - What antibiotics have they been exposed to (90 days)
  - Prior health-care exposure
  - Comorbidities
  - Prior culture results / colonization
  - Patient allergies

Treatment: The balancing act

- Weighing the risks/benefits of antibiotics
  - Risks of overuse:
    - Antimicrobial resistance
    - C difficile infection
    - Renal failure
    - Systemic toxicities
  - Benefits of correct and appropriate antibiotics:
    - Improved outcomes
      - Chest 2000: 118:146
      - Mortality rate was associated with inadequate initial antimicrobial therapy
      - Prior antibiotics, Candida, low albumin, central lines days all associated with inadequate therapy
    - Reduced deaths

Penicillin and Cephalosporin allergy

Michael E. Pichichero, MD; and Robert Zagursky, PhD

Rochester General Hospital Research Institute, Rochester, New York

Ann Allergy Asthma Immunol 112 (2014) 404–412

- Penicillin cross reaction to cephalosporin is maximum with class I and II
- Percentage of cross reaction is variable based on studies (0.001 – 3%).
- Not as high as (8-10%) as thought previously.
- Risk of anaphylaxis is 0.015% maximum to PCN and 0.1% to cephalosporin
- Monobactams have no cross reaction with PCN and most cephalosporin
  - Aztreonam has cross reaction with Ceftazidime
  - Both drug shares identical side chains
- Less cross reactions to Carbapenems

Pneumonia – the alphabet soup of ID

HAP, VAP, CAP, HCAP

2005 HAP/VAP/HCAP Guidelines

American Thoracic Society Documents

TABLE 2. RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS CAUSING HOSPITAL-ACQUIRED PNEUMONIA, HEALTHCARE-ASSOCIATED PNEUMONIA, AND VENTILATOR-ASSOCIATED PNEUMONIA

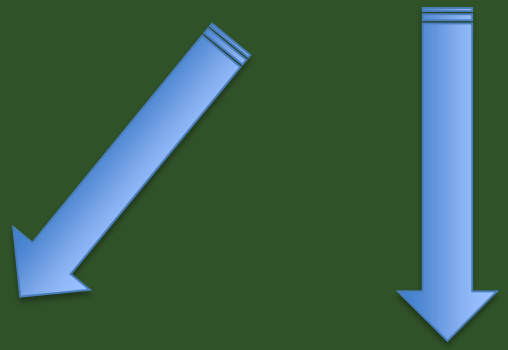
- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP:
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic dialysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy

Pneumonia

Hospital-Acquired Pneumonia

Ventilator Associated Pneumonia

Community-acquired Pneumonia



MDR Risk Factors Present

No MDR Risk Factors Present

Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

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It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

These guidelines are intended for use by healthcare professionals who care for patients at risk for hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), including specialists in infectious diseases, pulmonary diseases, critical care, and surgeons, anesthesiologists, hospitalists, and any clinicians and healthcare providers caring for hospitalized patients with nosocomial pneumonia. The panel's recommendations for the diagnosis and treatment of HAP and VAP are based upon evidence derived from topic-specific systematic literature reviews.

Table 4. Recommended Initial Empiric Antibiotic Therapy for Hospital-Acquired Pneumonia (Non-Ventilator-Associated Pneumonia)

Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c]	Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c]	High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[a,c]
One of the following:	One of the following:	Two of the following, avoid 2 β-lactams:
Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h
OR	OR	OR
Cefepime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR	OR	OR
Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily
	Ciprofloxacin 400 mg IV q8h	Ciprofloxacin 400 mg IV q8h
	OR	OR
Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h
	OR	OR
	Aztreonam 2 g IV q8h	Amikacin 15–20 mg/kg IV daily
		Gentamicin 5–7 mg/kg IV daily
		Tobramycin 5–7 mg/kg IV daily
		OR
		Aztreonam[e] 2 g IV q8h
	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness)
	OR	OR
	Linezolid 600 mg IV q12h	Linezolid 600 mg IV q12h
		If MRSA coverage is not going to be used, include coverage for MSSA. Options include: Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP.
If patient has severe penicillin allergy and aztreonam is going to be used instead of any β-lactam–based antibiotic, include coverage for MSSA.		

Abbreviations: HAP, hospital-acquired pneumonia; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

[a] Risk factors for mortality include need for ventilatory support due to pneumonia and septic shock.

[b] Indications for MRSA coverage include intravenous antibiotic treatment during the prior 90 days, and treatment in a unit where the prevalence of MRSA among *S. aureus* isolates is not known or is >20%. Prior detection of MRSA by culture or non-culture screening may also increase the risk of MRSA. The 20% threshold was chosen to balance the need for effective initial antibiotic therapy against the risks of excessive antibiotic use; hence, individual units can elect to adjust the threshold in accordance with local values and preferences. If MRSA coverage is omitted, the antibiotic regimen should include coverage for MSSA.

[c] If patient has factors increasing the likelihood of gram-negative infection, 2 antipseudomonal agents are recommended. If patient has structural lung disease increasing the risk of gram-negative infection (ie, bronchiectasis or cystic fibrosis), 2 antipseudomonal agents are recommended. A high-quality Gram stain from a respiratory specimen with numerous and predominant gram-negative bacilli provides further support for the diagnosis of a gram-negative pneumonia, including fermenting and non-glucose-fermenting microorganisms.

[d] Extended infusions may be appropriate.

[e] In the absence of other options, it is acceptable to use aztreonam as an adjunctive agent with another β-lactam–based agent because it has different targets within the bacterial cell wall [137].

Who gets triple antibiotics for HAP/VAP in 2016?

- High risk for mortality (septic shock)

AND

- Patient exposed to IV antibiotics in the last 90 days**

Indications for MRSA therapy: HAP

- Prior IV antibiotics within 90 days
- Hospitalization in units with >20% MRSA
- High risk for mortality (septic shock, acute need for ventilatory support)
- Prevalence of MRSA is unknown
- Prior MRSA colonization or infection

S. aureus at a local facility

	N	MSSA	MRSA
All S aureus	105	61%	39%
CAP	21	66.7%	33.3%
HCAP	17	35.3%	64.7%
HAP	67	65.7%	34.3%

Indications for dual gram negatives for HAP

- High risk for mortality (septic)
- Prior IV antibiotics last 90 days
  - "heavily antibiotic exposed”
  - Cefazolin does NOT = piperacillin/tazobactam as a risk factor
- History of MDR gram negative pathogen
- Structural lung disease (bronchiectasis, CF)

Pseudomonas aeruginosa

% susceptible n=36

		Add Levoflox	Add tobramycin
Pip Tazo	78%	80.5%	88.9%
Cefepime Add intermediate	66.7% 88.9%	66.7% 88.9%	72.2% 94.4%
Meropenem	94.4%	94.4%	97.2%
Aztreonam Add intermediate	61.1% 77.8%	69.4% 83.3%	77.8% 94.4%

All gram negative HCAP and HAP isolates

	N=135	Add levoflox	Add tobramycin
Pip tazo	87.7%	91.4%	90.8%
Cefepime	86.6%	88.8%	89.6%
Meropenem	95.5%	96.3%	97%

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

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d'Investigacions Biomèdiques August Pi i Sunyer, CIBER CB06/06/0028, Barcelona, Spain.

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

Condition	Commonly encountered pathogen(s)
Alcoholism	*Streptococcus pneumoniae,* oral anaerobes, *Klebsiella pneumoniae, Acinetobacter* species, *Mycobacterium tuberculosis*
COPD and/or smoking	*Haemophilus influenzae, Pseudomonas aeruginosa, Legionella* species, *S. pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae*
Aspiration	Gram-negative enteric pathogens, oral anaerobes
Lung abscess	CA-MRSA, oral anaerobes, endemic fungal pneumonia, *M. tuberculosis*, atypical mycobacteria
Exposure to bat or bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydophila psittaci* (if poultry: avian influenza)
Exposure to rabbits	*Francisella tularensis*
Exposure to farm animals or parturient cats	*Coxiella burnetti* (Q fever)
HIV infection (early)	*S. pneumoniae, H. influenzae, M. tuberculosis*
HIV infection (late)	The pathogens listed for early infection plus *Pneumocystis jirovecii, Cryptococcus, Histoplasma, Aspergillus,* atypical mycobacteria (especially *Mycobacterium kansasii*), *P. aeruginosa, H. influenzae*
Hotel or cruise ship stay in previous 2 weeks	*Legionella* species
Travel to or residence in southwestern United States	*Coccidioides* species, *Hantavirus*
Travel to or residence in Southeast and East Asia	*Burkholderia pseudomallei,* avian influenza, SARS
Influenza active in community	Influenza, *S. pneumoniae, Staphylococcus aureus, H. influenzae*
Cough >2 weeks with whoop or posttussive vomiting	*Bordetella pertussis*
Structural lung disease (e.g., bronchiectasis)	*Pseudomonas aeruginosa, Burkholderia cepacia, S. aureus*
Injection drug use	*S. aureus*, anaerobes, *M. tuberculosis, S. pneumoniae*
Endobronchial obstruction	Anaerobes, *S. pneumoniae, H. influenzae, S. aureus*
In context of bioterrorism	*Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)

NOTE. CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus;* COPD, chronic obstructive pulmonary dis-

CAP

- Non-ICU
  - Ceftriaxone + azithromycin
  - Respiratory fluoroquinolone
- ICU
  - Ceftriaxone + respiratory fluoroquinolone +/- MRSA therapy
  - If pseudomonas risk factors consider either cefepime or piperacillin/tazobactam

Original Investigation | LESS IS MORE

Duration of Antibiotic Treatment in Community-Acquired Pneumonia
A Multicenter Randomized Clinical Trial

Ane Uranga, MD; Pedro P. España, MD; Amaia Bilbao, MSc, PhD; Jose María Quintana, MD, PhD; Ignacio Arriaga, MD; Maider Intxausti, MD; Jose Luis Lobo, MD, PhD; Laura Tomás, MD; Jesus Camino, MD; Juan Nuñez, MD; Alberto Capelastegui, MD, PhD

IMPORTANCE The optimal duration of antibiotic treatment for community-acquired pneumonia (CAP) has not been well established.

OBJECTIVE To validate Infectious Diseases Society of America/American Thoracic Society guidelines for duration of antibiotic treatment in hospitalized patients with CAP.

DESIGN, SETTING, AND PARTICIPANTS This study was a multicenter, noninferiority randomized clinical trial performed at 4 teaching hospitals in Spain from January 1, 2012, through August 31, 2013. A total of 312 hospitalized patients diagnosed as having CAP were studied. Data analysis was performed from January 1, 2014, through February 28, 2015.

INTERVENTIONS Patients were randomized at day 5 to an intervention or control group. Those in the intervention group were treated with antibiotics for a minimum of 5 days, and the antibiotic treatment was stopped at this point if their body temperature was 37.8°C or less for 48 hours and they had no more than 1 CAP-associated sign of clinical instability. Duration of antibiotic treatment in the control group was determined by physicians.

MAIN OUTCOMES AND MEASURES Clinical success rate at days 10 and 30 since admission and CAP-related symptoms at days 5 and 10 measured with the 18-item CAP symptom questionnaire score range, 0-90; higher scores indicate more severe symptoms.

RESULTS Of the 312 patients included, 150 and 162 were randomized to the control and intervention groups, respectively. The mean (SD) age of the patients was 66.2 (17.9) years and 64.7 (18.7) years in the control and intervention groups, respectively. There were 95 men (63.3%) and 55 women (36.7%) in the control group and 101 men (62.3%) and 61 women (37.7%) in the intervention group. In the intent-to-treat analysis, clinical success was 48.6% (71 of 150) in the control group and 56.3% (90 of 162) in the intervention group at day 10 (P = .18) and 88.6% (132 of 150) in the control group and 91.9% (147 of 162) in the intervention group at day 30 (P = .33). The mean (SD) CAP symptom questionnaire scores were 24.7 (11.4) vs 27.2 (12.5) at day 5 (P = .10) and 18.6 (9.0) vs 17.9 (7.6) at day 10 (P = .69). In the per-protocol analysis, clinical success was 50.4% (67 of 137) in the control group and 59.7% (86 of 146) in the intervention group at day 10 (P = .12) and 92.7% (126 of 137) in the control group and 94.4% (136 of 146) in the intervention group at day 30 (P = .54). The mean (SD) CAP symptom questionnaire scores were 24.3 (11.4) vs 26.6 (12.1) at day 5 (P = .16) and 18.1 (8.5) vs 17.6 (7.4) at day 10 (P = .81).

Editorial

Supplemental content at jamainternalmedicine.com

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Urinary Tract Infections

- Sepsis due to a UTI
  - Prior cultures and antibiotic exposures is key
  - Ceftriaxone for community acquired infections is an excellent option
  - Discourage quinolone use
    - Especially for antibiotic exposed and ECF patients
  - For antibiotic exposed or patients with history of MDR pathogens
    - Piperacillin/tazobactam OR a carbapenem is reasonable
- Deescalate once cultures are available!

Asymptomatic Bacteriuria Treatment Is Associated With a Higher Prevalence of Antibiotic Resistant Strains in Women With Urinary Tract Infections

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(See the Editorial Commentary by Wagenlehner and Naber on pages 1662–3.)

Background. Women suffering from recurrent urinary tract infections (rUTIs) are routinely treated for asymptomatic bacteriuria (AB), but the consequences of this procedure on antibiotic resistance are not fully known. The aim of this study was to evaluate the impact of AB treatment on antibiotic resistance among women with rUTIs.

Methods. The study population consisted of 2 groups of women who had previously been enrolled in a randomized clinical trial: group A was not treated, and group B was treated. All women were scheduled for follow-up visits every 6 months, or more frequently if symptoms arose. Microbiological evaluation was performed only in symptomatic women. All women were followed up for a mean of 38.8 months to analyze data from urine cultures and antibiograms.

Results. The previous study population consisted of 673 women, but 123 did not attend the entire follow-up period. For the final analysis, 257 of the remaining 550 patients were assigned to group A, and 293 to group B. At the end of follow-up, the difference in recurrence rates was statistically significant ($P < .001$): 97 (37.7%) in group A versus 204 (69.6%) in group B. Isolated *Escherichia coli* from group B showed higher resistance to amoxicillin–clavulanic acid ($P = .03$), trimethoprim-sulfamethoxazole ($P = .01$), and ciprofloxacin ($P = .03$) than that from group A.

Conclusions. This study shows that AB treatment is associated with a higher occurrence of antibiotic-resistant bacteria, indicating that AB treatment in women with rUTIs is potentially dangerous.

Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America

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Table 2. Agents and Regimens that May Be Used for the Initial Empiric Treatment of Extra-biliary Complicated Intra-abdominal Infection

Regimen	Community-acquired infection in pediatric patients	Community-acquired infection in adults	
		Mild-to-moderate severity: perforated or abscessed appendicitis and other infections of mild-to-moderate severity	High risk or severity: severe physiologic disturbance, advanced age, or immunocompromised state
Single agent	Ertapenem, meropenem, imipenem-cilastatin, ticarcillin-clavulanate, and piperacillin-tazobactam	Cefoxitin, ertapenem, moxifloxacin, tigecycline, and ticarcillin-clavulanic acid	Imipenem-cilastatin, meropenem, doripenem, and piperacillin-tazobactam
Combination	Ceftriaxone, cefotaxime, cefepime, or ceftazidime, each in combination with metronidazole; gentamicin or tobramycin, each in combination with metronidazole or clindamycin, and with or without ampicillin	Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a]	Cefepime, ceftazidime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a]

[a] Because of increasing resistance of *Escherichia coli* to fluoroquinolones, local population susceptibility profiles and, if available, isolate susceptibility should be reviewed.

Intra-abdominal infections

- Source control is key
- Need broad spectrum coverage including anaerobic activity
- MRSA is NOT a concern / empiric antifungals are not routinely indicated
- Options
  - Piperacillin/tazobactam
  - Ceftriaxone/metronidazole
  - Levofloxacin/metronidazole
  - Carbapenem (for PCN allergic OR history of MDR pathogens)

Cellulitis / Abscesses

- Staph and Strep are the most common pathogens
- Diabetes does NOT necessitate broad spectrum gram negative coverage
  - Only needed for diabetic foot ulcers with cellulitis / vascular ulcers
- Covering for MRSA is reasonable unless it is erysipelas or an cellulitis associated with lymphedema
- Clindamycin is used for toxic appearing patients
- Options
  - Vancomycin
  - Cefazolin
  - Linezolid

Gram Negative SSTI

- Risk Factors
  - Animal bites
  - Water exposure
  - Immunocompromised
  - Necrotizing fasciitis
  - Diabetic ulcers
  - Arterial insufficiency
  - Pelvic infections
  - Cirrhosis
  - LE orthopedic hardware infections

CNS Infections

- Community-acquired meningitis
  - Ceftriaxone 2 grams every 12 hours + vancomycin
- Nosocomial meningitis
  - Vancomycin + cefepime (or meropenem)
- Shunt related meningitis
  - Vancomycin and cefepime (or meropenem)
- Key points
  - Piperacillin/tazobactam does NOT treat meningitis
  - At ampicillin if risks for Listeria (elderly, alcoholics, immunocompromised, etc)

Sepsis of unclear etiology

- Broad spectrum of your choice with appropriate deescalation
- Imaging studies are often negative the first 24 hours, so please repeat imaging in a timely manner
- Consider Procalcitonin testing

Duration of antibiotic therapy: shorter = better

Diagnosis	Short (d)	Long (d)	Result
CAP	3 or 5	7,8 or 10	Equal
HAP	7	10-15	Equal
VAP	8	15	Equal
Pyelonephritis	5 or 7	10 or 14	Equal
Intra-abd	4	10	Equal
AECB	<5	>7	Equal
Cellulitis	5 or 6	10	Equal
Osteomyelitis	42	84	Equal

Summary

- Know your antibiogram
  - What works for me may not work for you!
- Era of "triples" has to end!
  - Outside of septic shock and heavily antibiotic exposed patients
- Optimize the antibiotic dosing
- Deescalate antibiotics once cultures are available
- Choose antibiotics based on location of infection
- Cross reactivity of the penicillin allergic patient is not as significant as once thought
  - Many patients will tolerate cephalosporins