

Sepsis Wave II

Balancing Antibiotics Stewardship with Sepsis







Presenters



Jessica Whittle, Phd, MD



Lauren Epstein, MD, MSc





Antibiotics.

Easy.

Jessica Whittle, MD, PhD, FACEP

Research Director, Department of Emergency Medicine
University of Tennessee College Of Medicine, Chattanooga
Erlanger Health System

ACEP E-QUAL SEPSIS Steering Committee

ACEP liaison to IDSA for workgroup on antibiotic selection in sepsis

I have no financial relationships of any kind with any of the manufacturers of the drugs or the software discussed in this presentation and the opinions expressed are mine alone.

PT. 2015 Apr; 40(4): 277-283.

The Antibiotic Resistance Crisis

Part 1: Causes and Threats

C. Lee Ventola, MS

Nausea / Vomiting
Diarrhea



Medication Increased Follows



Increased Risk of Sepsis During Hospital Readmission Following Exposure to Certain Antibiotics During Hospitalization 3

James Baggs, PhD; John Jernigan, MD, MS; Kelly McCormick, MSPH; Lauren Epstein, MD, MSc; Alison S. Laufer-Halpin, PhD; L. Clifford McDonald, MD, FSHEA

Open Forum Infect Dis (2016) 3 (suppl_1): 73. **DOI:** https://doi.org/10.1093/ofid/ofw194.08 **Published:** 24 October 2016

Ventola CL. The Antibiotic Resistance Crisis: Part 1: Causes and Threats. *Pharmacy and Therapeutics*. 2015;40(4):277-283.

Things we all need

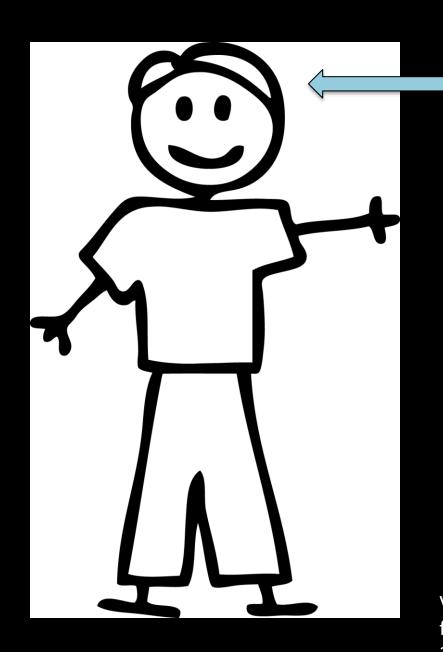
Working knowledge (How to get smart) overview today

Pearls and Pitfalls (How to practice smart) high risk and common mistakes

Resources (How to stay smart)
antibiograms and pocket brain resources

Updated Information (How to look smart) new antibiotics in the news

GETTING SMART - OVERVIEW



Meningitis:

vancomycin cefdinir (Rocephin) +/- ampicillin

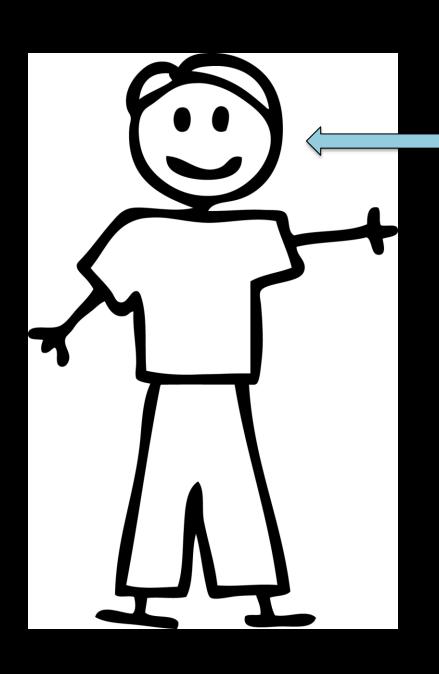
Pearl:

acyclovir steroids prior to antibiotics

Pitfall:

delay early bacterial meningitis can look viral

Van de Beek, D et. al. Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med. 2004 Oct 28;351(18):1849-59.



Ears/ Sinuses/ Pharynx:

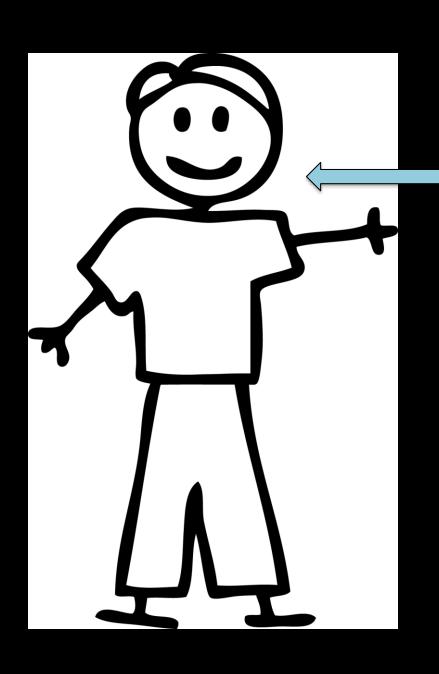
amoxicillin/ clavulanate (Augmentin)
cephalosporins
trimethoprim/sulfamethoxazole (Bactrim)
doxycycline
macrolides (*) / azithromycin/ clarithromycin

Pearl:

Steroids make people feel better

Pitfall:

Growing resistance against azithromycin MRSA



Mouth:

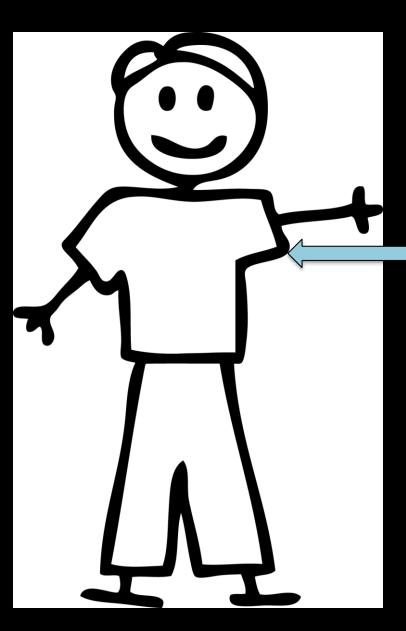
amoxicillin/ clavulanate (Augmentin) clindamycin pen Vee K cefdinir (Rocephin)

Pearl:

Source control

Pitfall:

MRSA



Lungs:

Bronchitis:

doxycycline

azithromycin, clarithromycin

Pneumonia: (above +)

amoxicillin/ clavulanate (Augmentin)

cephalosporins

trimethoprim/sulfamethoxazole (Bactrim)

Or levofloxacin (Levaquin) / moxifloxacin

Hospital Acquired: (*Pseudomonas*, MRSA)

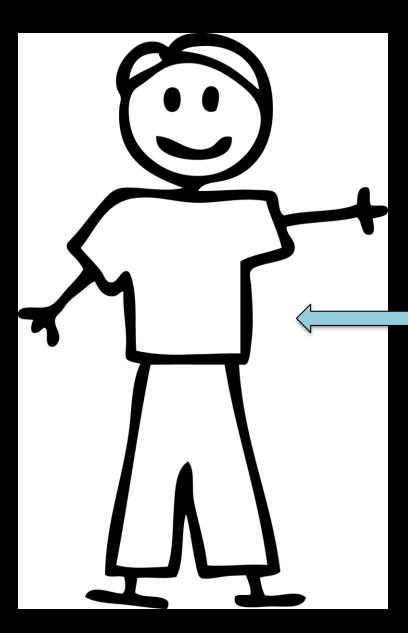
Zosyn/ Levaquin/ Meropenem/ cefepime

Pearl:

remember atypicals (Mycoplasm)

Pitfall:

PE



Abdomen:

pipercillin + tazobactam (Zosyn)

levofloxacin (Levaquin)/ cipro

+ metronidazole (Flagyl)

amoxicillin/ clavulanate (Augmentin)

+ metronidazole (Flagyl)

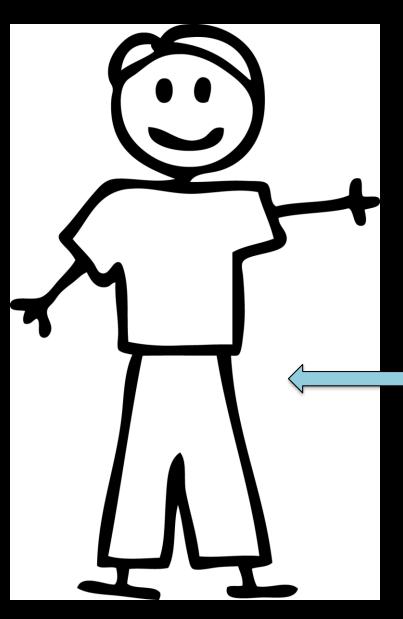
metronidazole (Flagyl) / oral vancomycin for C. Diff

Pearl:

probiotics

Pitfall:

appendicitis is an infection; may be sepsis



Bladder:

trimethoprim/sulfamethoxazole (Bactrim) macrobid cephalosporins amoxicillin/ clavulanate (Augmentin)

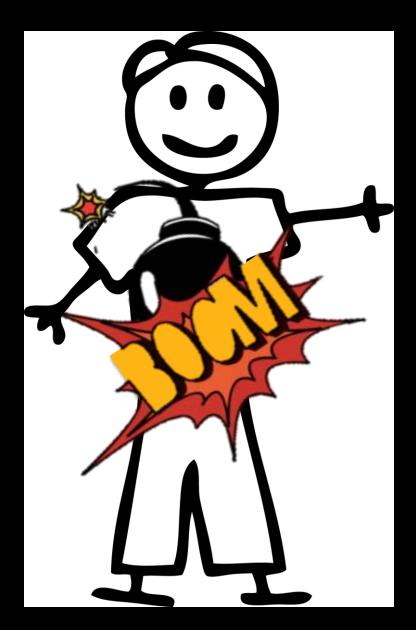
Pearl:

Consider doxycycline or azithromycin

Pitfall:

fluoroquinolones NOT recommended 1st line

"Guidelines for Antimicrobial Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women" Clin Inf Dis; 2011; 52: e103-e120



When you have no idea what's going on....

... then use vancomycin and pipercillin + tazobactam (Zosyn)

OR

Carbapenem +/- MRSA coverage



Don't forget fungal infections, viral infections, autoimmunity

trimethoprim/sulfamethoxazole (Bactrim)– renal failure, SJS azithromycin – long QT

fluoroquinolones – tendinopathies, long QT, seizures

clindamycin – C. Diff

metronidazole (Flagyl) – disulfiram-like reaction

STAYING SMART – ANTIBIOGRAMS AND RESOURCES

Antibiogram



BEH ANTIBIOGRAM 2016 PERCENT SUSCEPTIBLE

Usually obtain through pharmacy

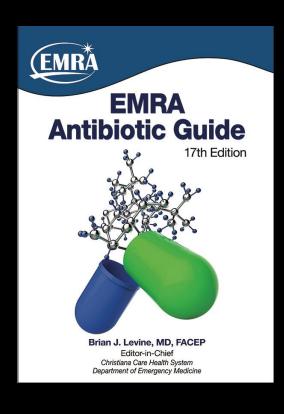
Gram Positive																		
Organism	# Isolates Tested	% Interpretation	Penicillin	Ampicillin	Oxacillin	Amox/Clav & Amp/Sulb	Cefazolin	Ceftriaxone	Ciprofloxacin	Levofloxacin	Trimeth/sulfa	Clindamycin	Daptomycin	Azithromycin	Nitrofurantoin	Linezolid	Vancomycin	Tetracycline
MSSA	411	S	21	-	100	100	100	100	81	85	100	85	99	100	100	100	100	93
MRSA	535	S	-	-	ı	1	-	ł	46	42	95	63	99	33	100	100	100	92
Total Staph aureus	946	S	9	_	43	44	43	43	61	61	97	73	99	60	100	100	100	92
Staph (coag. neg.)	239	S	15	-	42	43	42	42	52	54	65	66	82	36	100	100	100	82
Strep pneumoniae	88	S	59	1	ł	98	1	98	Ī	91	69	88	1	50	1	1	99	74
E. faecalis	283	S	98	98	ł	ı	-	ł	61	70	ı	ł	100		98	99	96	26
E. faecium	27	s	30	30	-	_		-	19	22	_	-	67		50	100	33	15

Gram Negative

Organism	# Isolates Tested	% Interpretation	Ampicillin	Amp/Sulb	Pip/Tazo	Cefazolin	Cefuroxime	Ceftazidime	Ceftriaxone	Cefepime	Cefoxitin	Aztreonam	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Levofloxacin	Trimeth/sulfa	Nitrofurantoin	Tetracycline
Escherichia coli	966	s	44	50	96	84	80	85	85	87	95	85	100	99	88	88	62	63	68	96	74
Klebsiella pneumoniae	270	S	3	84	97	100	90	98	99	99	100	97	100	99	99	99	95	98	94	48	81
Klebsiella oxytoca	67	S	6	75	95	ı	81	98	97	100	1	90	100	100	97	97	94	98	94	92	90
Proteus mirabilis	136	S	69	78	98	ı	79	85	85	84	100	83	99	100	89	90	50	59	63	1	
E. aerogenes	52	S	12	66	92	ı	62	72	84	100	1	84	100	100	96	96	96	96	98	17	90
E. cloacae	140	S	13	28	83	100	38	78	77	93	1	81	100	100	98	98	92	95	92	25	83
Serratia marcescens	67	S	5	3	83	1	1	72	91	100	ı	78	97	97	95	91	95	95	95	ı	3
P. aeruginosa	239	S	-	-	95	1	-	87	-	84	-	70	91	98	78	89	70	70	-	-	-
A. baumannii	49	S	-	60	1	1	-	48	27	42	-	-	50	52	50	46	46	48	42	1	46
Stenotrophomonas	41	S		_	1	1		45	- 1	1	-	-	-			1	1	88	100	_	

Favorite Resources

(Tools for staying smart)



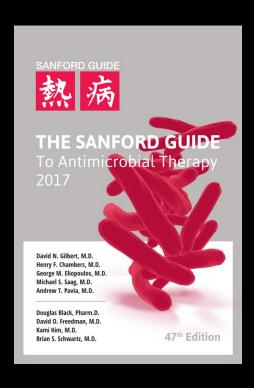
Why I love it:

Clear and concise evaluate by organism, body part or drug not overwhelming accurate

\$17 app

Favorite Resources

(Tools for staying smart)



Why I love it:

comprehensive
accurate

Why I don't love it:
overwhelming
difficult to navigate

\$30 app subscription 1 yr

Favorite Resources

(Tools for staying smart)



Why I love it:

comprehensive evaluate by disease or drug read more about disease

Why I don't love it: sometimes buggy/ updates

free

LOOKING SMART – NEW STUFF

New Stuff

(Tools for looking smart)

Dalbavancin (Dalvance)

Glycopeptide (same class as vancomycin)

Approved for treatment of uncomplicated soft tissue infections by Gram + bacteria

Effective against MRSA

Dilute in sterile water or D5W; can dialyze

Estimated CrCl	Single Dose Regimen	Two-Dose Regimen				
≥ 30 mL/min or on regular hemodialysis	1500 mg	1000 mg followed one week later by 500 mg				
< 30 mL/min and not on regular hemodialysis	1125 mg	750 mg followed one week later by 375 mg				



New Stuff

(Tools for looking smart)

Oritavancin (Orbactiv)

Glycopeptide (same class as vancomycin)

Approved for treatment of uncomplicated soft tissue infections by Gram + bacteria

Effective against MRSA

1200mg single dose in 3 hour infusion

No adjustment for mild/ mod renal impairment Never studied in severe renal or hepatic impairment Must be in D5W Falsely elevated pTT for 5 days



New Stuff

(Tools for looking smart)

ESBL

Extended Spectrum Beta-Lactamase Producing *E. coli Enterobacteriaceae*

Resistant to penicillins, cephalosporins, aztreonam, and Fluoroquinolones

Usually susceptible to Carbapenems, fosfomycin

National Center for Emerging and Zoonotic Infectious Diseases



Sepsis, Antibiotic Stewardship and the Emergency Department

Lauren Epstein, MD, MSc

Sepsis Lead

Epidemiology Research and Innovations Branch
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention

Objectives

- Review the importance of antibiotic stewardship
- Discuss how antibiotic stewardship and sepsis treatment align
- Discuss public health and sepsis prevention and identification activities

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Antibiotics

- More than half of all hospitalized patients receive an antibiotic during their hospitalization
- However, 20-50% of all antibiotics prescribed in U.S. acute care hospitals are either unnecessary or inappropriate
- ED has a role to play in improving antibiotic prescribing

Inpatient Antibiotics

- 4 antibiotics made up approximately 45% of all antibiotic treatment
 - Vancomycin
 - Piperacillin-tazobactam
 - Ceftriaxone
 - Levofloxacin

What is Antibiotic Stewardship?

- Measure antibiotic prescribing
- Improve antibiotic prescribing so that antibiotics are only prescribed and used when needed
- Minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics
- Ensure that the right drug, dose, and duration are selected when an antibiotic is needed

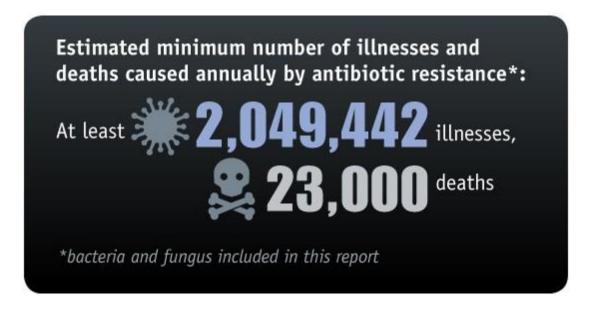


It's about patient safety and delivering high-quality healthcare.

Antibiotic Stewardship – why?

- In the context of other medications, antibiotics are generally welltolerated medications
 - Difficult to stop antibiotics if a patient is doing well or if a patient is doing poorly
 - Antibiotics are life-saving medicines that have risks and benefits

Antibiotic Resistance



\$20 billion in excess direct healthcare costs annually

Antibiotics and Patient Safety

- 1. Antibiotic adverse events can be **severe**, examples:
 - Antibiotic-associated diarrhea (e.g., C. difficile infection)
 - Life-threatening allergic reactions (e.g., anaphylaxis)
- 2. Antibiotic adverse events can lead to **ER visits**
 - 1 in 1000 antibiotic prescriptions leads to an ER visit for an adverse event
 - ~200,000 estimated ER visits/year in U.S.
- 3. Antibiotic may have long-term consequences through disruption of microbiome

Antibiotic Stewardship Infrastructure

- Infrastructure within a facility should help providers choose appropriate antibiotic therapy and facilitate rapid administration of antibiotics:
 - There are hospitals that have pharmacy protocols that position antibiotics within units to facilitate rapid release

Antibiotic Stewardship vs Infection Control

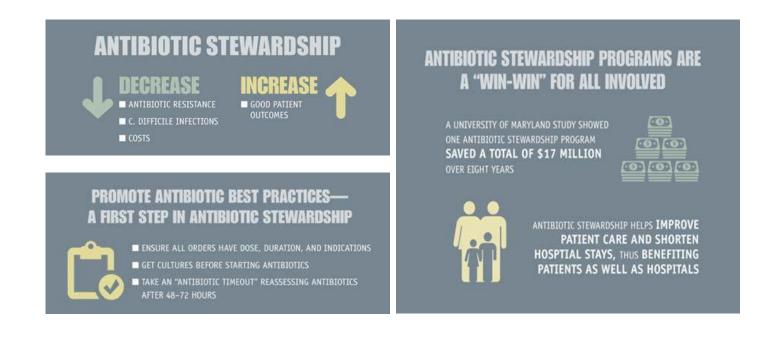
	Infection Control	antibiotic Stewardship Program
Patient safety	Optimize environment and protocols within the hospital to prevent infections	Optimize antibiotic therapy
Treatment?	Not responsible for diagnosis and treatment	Not responsible for diagnosis and treatment

What Antibiotic Stewardship is NOT?

- It is not a mechanism to restrict or prevent antibiotics among patients with infections or suspected infections that need antibiotics
- If there is an issue in any facility where antibiotic stewardship programs are impeding urgent antibiotic release for patients with sepsis or septic shock, this should be assessed and modified

Antibiotic Stewardship Programs and Public Health

 Antibiotic stewardship interventions have been proven to improve individual patient outcomes, reduce the overall burden of antibiotic resistance, save healthcare dollars, and ultimately save lives



Appropriate Antibiotic Use & Challenges in the ED

- ED's role in appropriate antibiotic use
 - Diagnose sepsis and serious bacterial infections
 - Start empiric antibiotic therapy
 - Obtain appropriate cultures prior to treatment (e.g. blood cultures)
 - Prescribe antibiotics for discharged patients
- ED's challenges in stewardship
 - Hard to capture all ED clinicians
 - Need for quick decision making
 - Lack of follow-up
 - Patient satisfaction & demand



Antibiotic Stewardship and Sepsis

- No single template for a program to optimize antibiotic prescribing in hospitals
- Complexity of medical decision making and variability in the type and care among U.S. hospitals require flexibility in implementation
 - Adapting to ED is especially challenging
- Antibiotic stewardship has been successful in many different healthcare settings (i.e. long term care facilities, telemedicine)

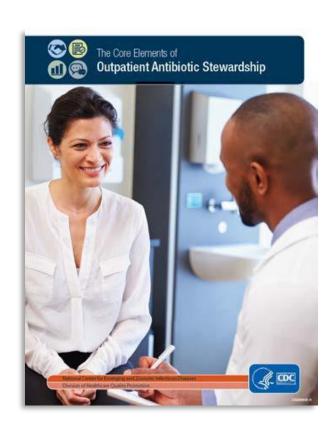
Antibiotic Stewardship: Hospital Core Elements



- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at http://www.cdc.gov/getsmart/healthcare/ implementation/core-elements.html.ucation

Antibiotic Stewardship: Outpatient Core Elements



- Commitment
- Action for policy and practice
- Tracking and reporting
- Education and expertise

ED and Antibiotic Stewardship

- Engaging ED as first stop in inpatient care
 - Have an ED clinician sit on the hospital antibiotic stewardship program
 - Leverage the ED pharmacist (<5% of EDs have a dedicated pharmacist)
 - Guide ED empiric treatment with clinical pathways, clinical decision support, antibiotic order forms
 - Collect cultures prior to starting antibiotics to help the inpatient team optimize therapy
 - Optimize antibiotic dosing

Objectives

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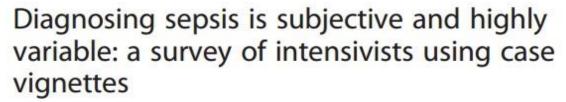
Sepsis: Challenges to Diagnosis and Treatment

- Difficult to diagnose, no specific pathogen or clinical test for sepsis
- Lack of sepsis diagnostic specificity and the importance of initiating early antibiotic therapy likely contributes to inappropriate broad spectrum use of antibiotics
- A pathogen is not identified in most cases of sepsis and septic shock
- Viral infections also contribute to a significant amount to sepsis
- Sepsis can mimic other types of conditions

Sepsis: Challenges to Diagnosis and Treatment

RESEARCH Open Access

(CrossMark



Chanu Rhee^{1,2*}, Sameer S. Kadri³, Robert L. Danner³, Anthony F. Suffredini³, Anthony F. Massaro², Barrett T. Kitch⁴, Grace Lee¹ and Michael Klompas^{1,2}

- 5 case vignettes of patients with suspected or confirmed infection and possible organ dysfunction distributed to 94 academic intensivists
 - Respondents classified cases as SIRS alone, sepsis, severe sepsis, septic shock, or none of the above

Antibiotic Stewardship and Sepsis: ED

- Front line practitioners are important for addressing antibiotic resistance
- Broad spectrum antibiotic use is often the most appropriate initial regimen for life-threatening infections
 - Ensuring the most appropriate empiric treatment is a major focus of stewardship
 - Appropriate culture and diagnostics performed in the ED ensures antibiotics are tailored

Sepsis and Septic Shock vs Infections

- Imperative for early antibiotic administration in sepsis and septic shock
 - Antibiotics and source control are the backbone of sepsis treatment
- However, among patients with infections (without signs of sepsis) –
 further work can be performed prior to initiation of antibiotics
 - Getting a 'true' history of allergies from a family member or medical records if possible
 - Making sure appropriate tests are performed to localize the source of infection, including cultures if needed

Sepsis Treatment: Antibiotic Stewardship

- The initial choice of an antibiotic in the ED is perhaps the most important dose the patient receives
 - Should be based on suspected infection, host factors and prior antibiotic exposure
- The antibiotic choice in the ED has significant influence on what therapy is continued in the inpatient setting
 - Represents an important opportunity for antibiotic stewardship

Sepsis Treatment: Antibiotic Stewardship

 ED plays an important role in obtaining cultures prior to administration of antibiotics that allows for tailoring of antibiotic therapy during hospitalization

Specimen Collection

- Swabs are discouraged since swabs usually have insufficient material for gram stain and culture;
 - if swabs must be used be sure quantity is adequate for both culture and gram stain
- Do not culture chronic superficial wounds or sinus drainage since superficial cultures correlate poorly with deep cultures
- Stool:
 - Multiple specimens per day are not indicated
 - Formed stools in general should not be submitted

Objectives

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Sepsis Prevention Framework

Pathogens

Identifiable Pathogen Prevention

- Support vaccine development + promotion
- · Antimicrobial stewardship
- · Disease surveillance
- Outbreak response
- · Infection prevention for HAIs





Pathogen not identified in >50% sepsis





Host Susceptibility

Demographics (eg. Age, SES, access to care)

Health Behaviors (eg. smoking)

Microbiome

Immune and Genetic Factors

Comorbidities (eg. COPD, CHF, Cancer, Diabetes)

Healthcare Factors (eg. indwelling devices)

Sepsis

Death

Sepsis Questions: Public Health Perspective

- Who develops sepsis or infections that often lead to sepsis?
- How many persons get sepsis each year in the United States? How many die?
- How can CDC work to improve education for healthcare providers, patients and caregivers about sepsis?
- How can other research microbiome disruption, patient skin or nasal disinfection, improved management of medical devices, etc. – contribute to sepsis prevention?

Vital Signs: Sepsis (August, 2016)



Thank You!

For more information, contact CDC 1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.







Questions? Contact the E-QUAL team at equal@acep.org



