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simeu

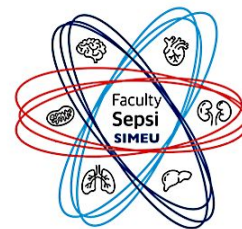
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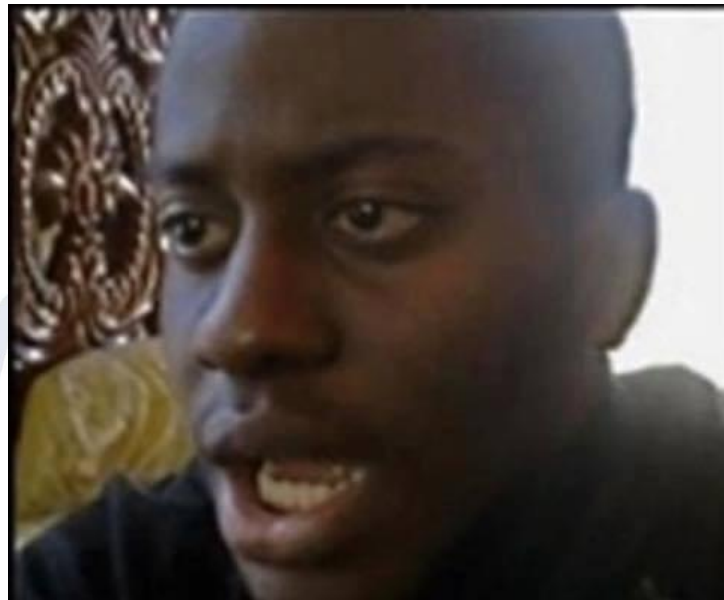


Antibiotici in Pronto Soccorso

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Emergency Medicine Clinics of North America

Volume 36, Issue 4, November 2018, Pages 853-872

Antimicrobial Stewardship in the Emergency Department

INDICATIONS

- Sepsis / Septic shock
- Meningitis
- Necrotizing Fascitis
- Open fracture



SEPSIS AND SEPTIC SHOCK

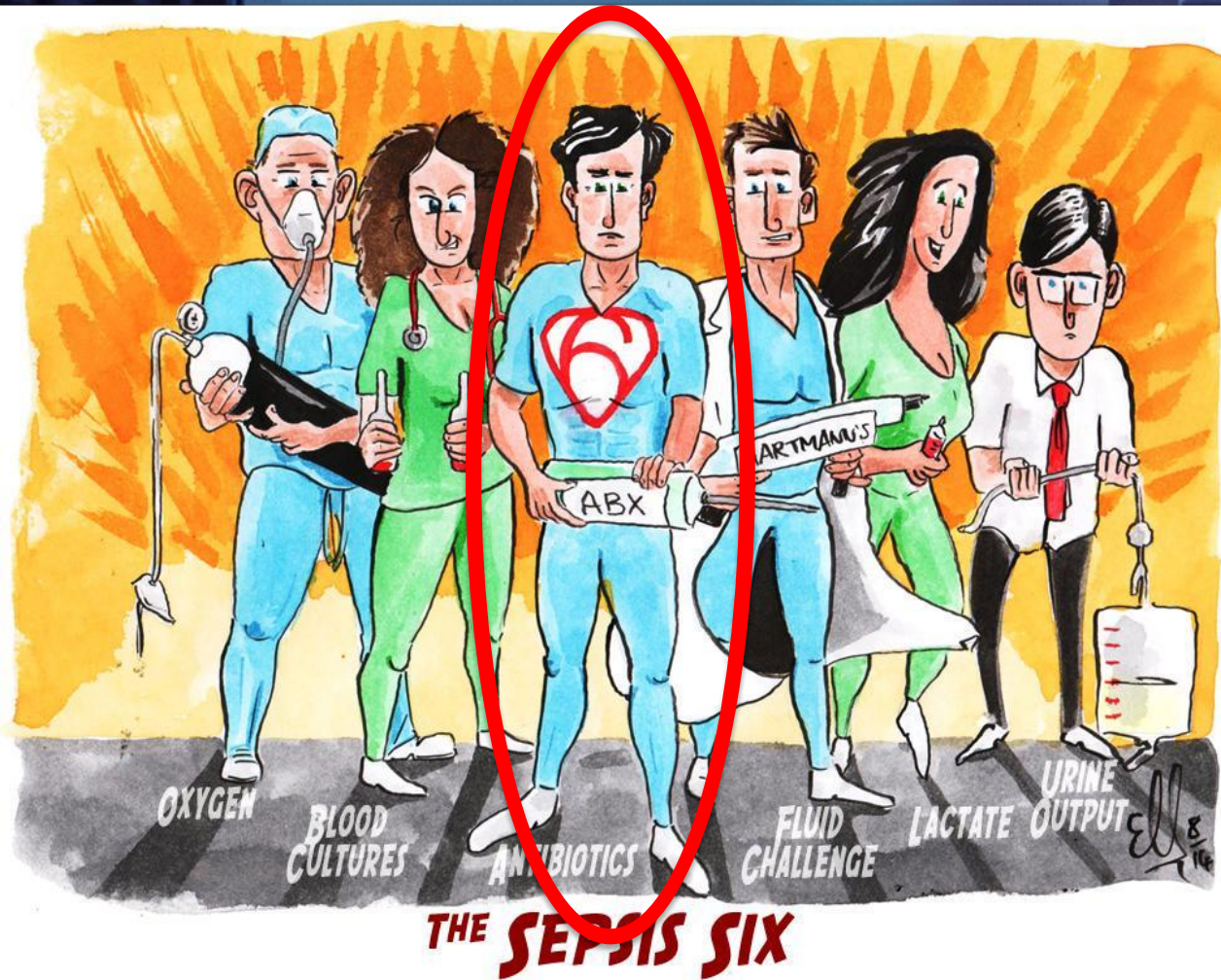
Sepsis

Septic shock

**Sepsis and septic shock
are medical emergencies**

wide range of infections.

associated with a greater risk of
mortality than sepsis alone.



Sepsis six

Seymour CW et al. *N Engl J Med*
2017;376:2235-44.

ANTIMICROBIAL TREATMENT

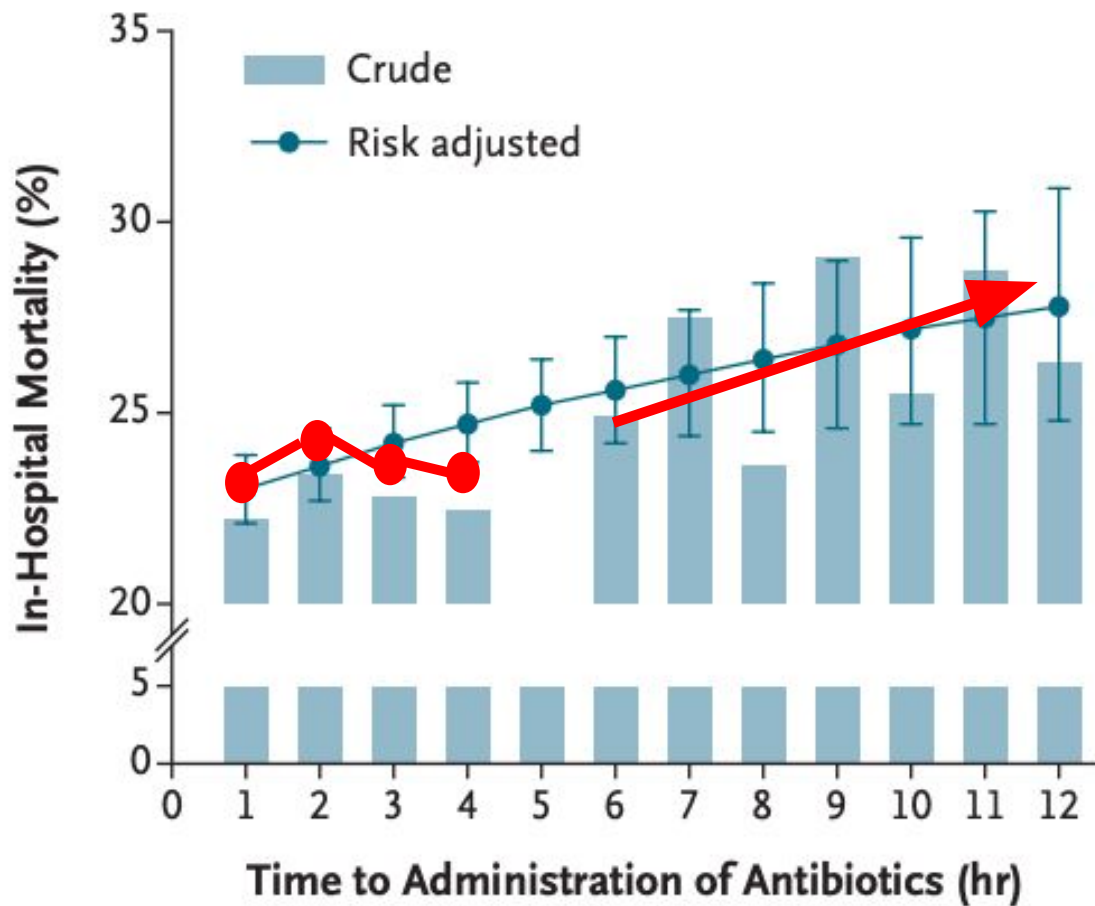
For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 h of recognition.

Strong recommendation, low quality of evidence (Septic shock)

Strong recommendation, very low quality of evidence (Sepsis without shock)

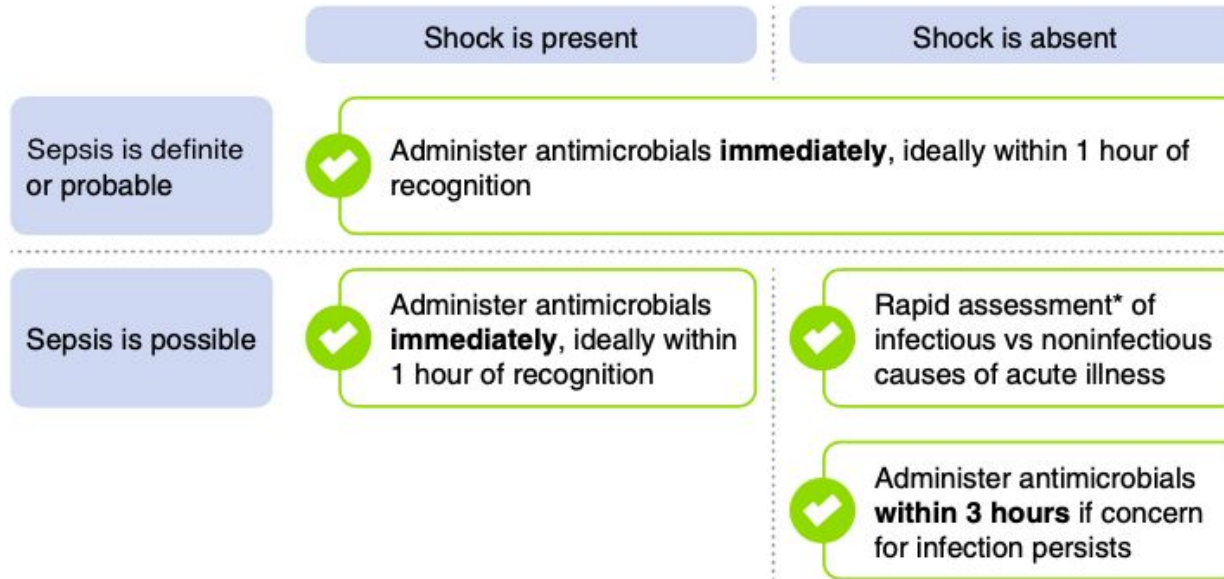


EMPIRIC BROAD SPECTRUM THERAPY



Seymour et al. *N Engl J Med.* 2017; 376:2235-2244.

Antibiotic Timing



*Rapid assessment includes history and clinical examination, tests for both infectious and non-infectious causes of acute illness and immediate treatment for acute conditions that can mimic sepsis. Whenever possible this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.

Fig. 1 Recommendations on timing of antibiotic administration



Gram positive cocci			Gram negative bacilli					Gram-negative cocci		Anaerobes	Atypicals
MRSA	MSSA	Streptococci	<i>E. coli</i>	<i>P. mirabilis</i>	<i>Klebsiella</i>	<i>Pseudomonas</i>	ESCAPPM	<i>N. gonorrhoeae</i>	<i>N. meningitidis</i>		e.g. <i>Mycoplasma</i>
		Penicillin G									
		Nafcillin/Oxacillin									
		Ampicillin/Amoxicillin						Amp/Amox			
		Cefazolin, cephalexin									
		Cephotetan, Cefoxitin								Cephotetan, Cefoxitin	
		Ceftriaxone						Ceftriaxone			
		Ceftazidime									
		Cefepime									
		Amoxicillin + clavulanate (Augmentin)								Amox-clav	
		Ampicillin + sulbactam (Unasyn)								Amp-sul	
		Piperacillin + tazobactam (Zosyn)						Piperacillin + tazobactam (Zosyn)			
		Ertapenem						Ertapenem			
		Imipenem, Meropenem									
		Aztreonam									
Ciprofloxacin		Ciprofloxacin									
		Levofloxacin									Levofloxacin
		Moxifloxacin						Moxifloxacin			
		Gent/Tobra/Amikacin									
Clindamycin										Clindamycin	
		Azithromycin						Azithromycin			Azithromycin
		Doxycycline						Doxycycline			Doxycycline
		Vancomycin									
		TMP/SMX (Bactrim)						TMP/SMX			
										Metronidazole	

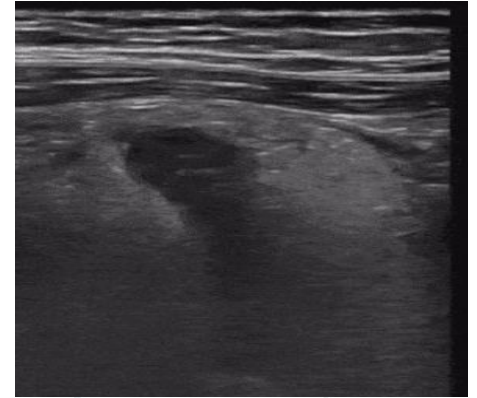
FOCUS



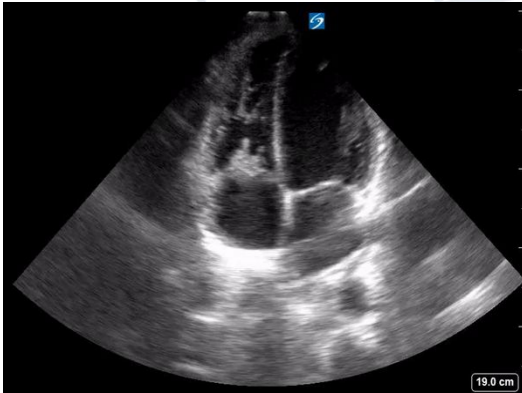
Pneumoniae



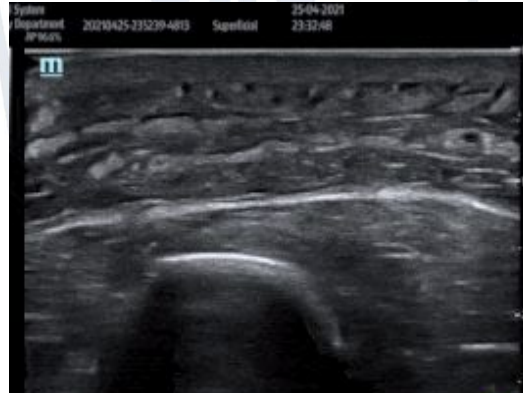
Cholecystitis with gallstone



Appendicitis



Endocarditis

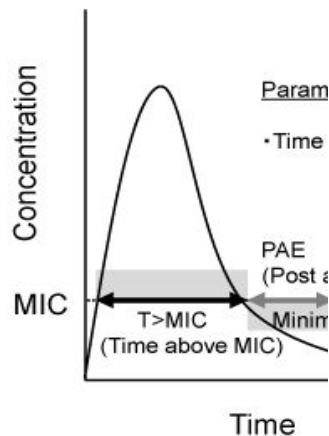


Cellulitis

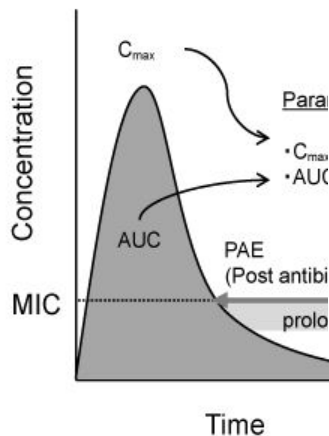


Abscess

Time-dependent antibiotics



Concentration-dependent



C_{max}

CONCENTRATION (mg / L)

MIC

AUC_{0-24} / MIC

fC_{max} / MIC

SERUM LEVELS OVER A DOSING INTERVAL

TIME (hours)

C_{min}



Antibiotic Class - Antibiotic

Killing Characteristic

Pharmacodynamic Parameter*

CONCENTRATION DEPENDENT

Daptomycin
Aminoglycosides

(Gram-negatives)

antibacterial activity, Gram-negatives)
bactericidal activity, Gram-negatives)
antibacterial activity, Gram-negatives)

TIME AND CONCENTRATION DEPENDENT

Vancomycin
Fluoroquinolones
Linezolid
Tigecycline

(Gram-negatives)
(Gram-positives)

(Gram-negatives)
(Gram-positives)

TIME DEPENDENT

β -lactams
Clindamycin

(*Staphylococcus aureus*)
(*Streptococcus* spp.)

(*Streptococcus fragilis*)

(*Staphylococcus aureus*)

Tabah A et al. *Antibiotics*. 2022; 11:362

* Exposures are total drug unless otherwise noted

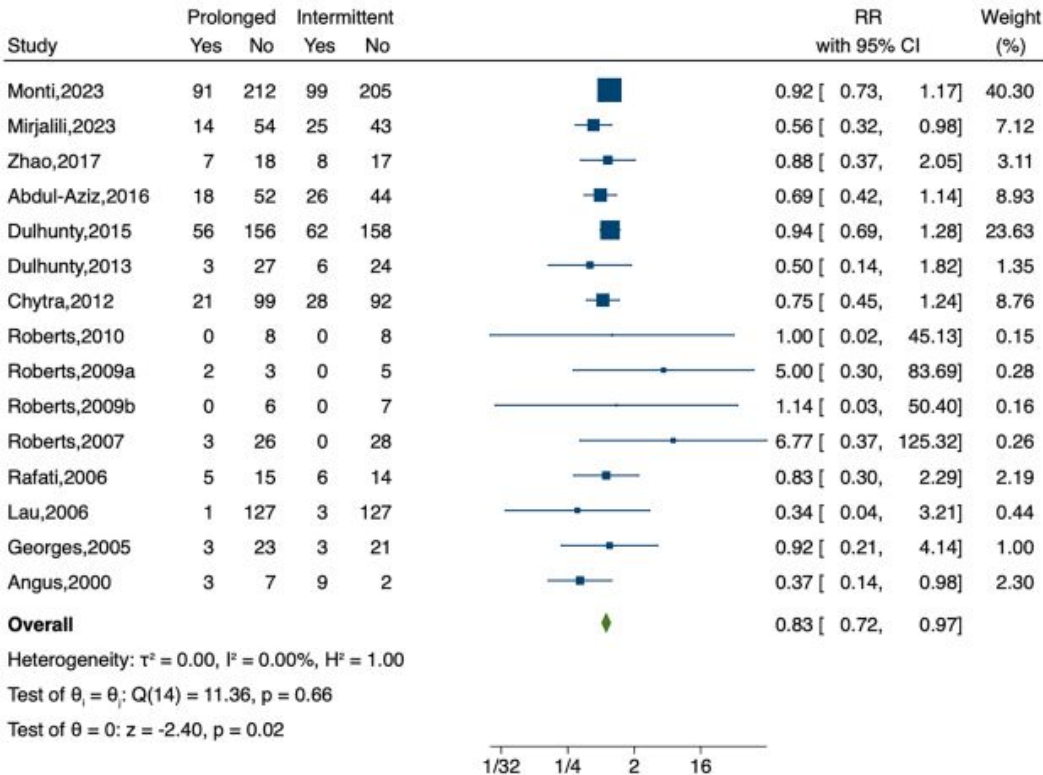
Fujii M et al. *Expert Opin Drug Metab Toxicol*. 2020; 16:415-430.



Prolonged versus intermittent β -lactam infusion in sepsis: a systematic review and meta-analysis of randomized controlled trials

The study demonstrated a statistically significant reduction in all-cause mortality with prolonged infusion compared to intermittent infusion (RR, 0.83; 95% CI 0.72–0.97; $P=0.02$).

The use of a loading dose for prolonged β -lactam infusion resulted in a significant reduction in mortality (RR, 0.84; 95% CI 0.72–0.97; $P=0.02$).

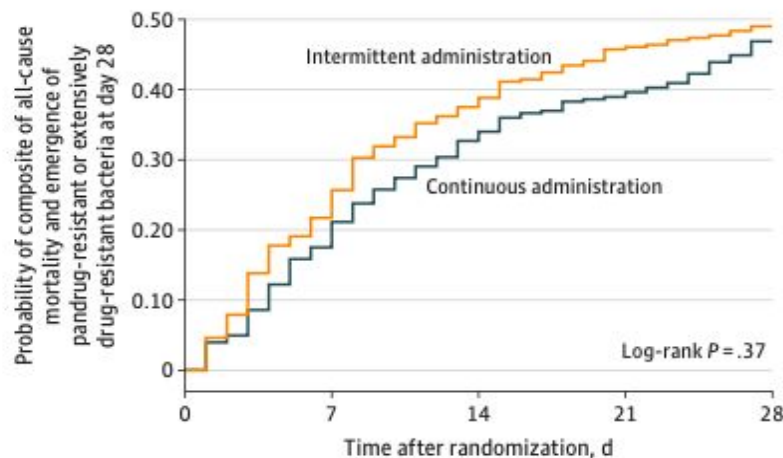


Random-effects DerSimonian-Laird model

Continuous vs Intermittent Meropenem Administration in Critically Ill Patients With Sepsis

The MERCY Randomized Clinical Trial

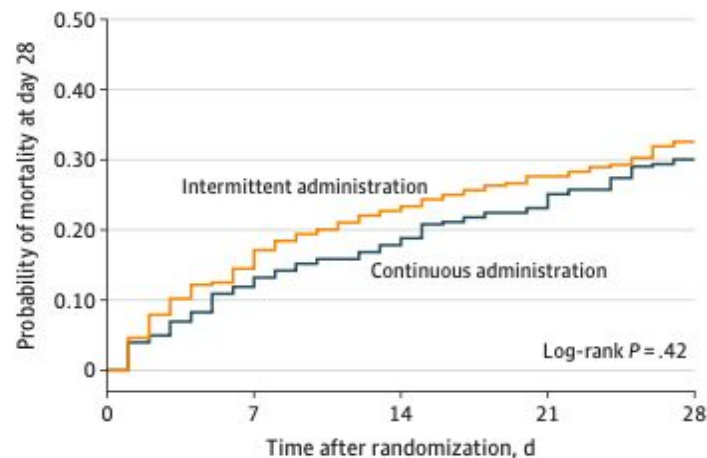
A Composite primary outcome



No. at risk

Continuous administration	303	250	204	185	161
Intermittent administration	304	238	190	165	155

B Secondary outcome



303	267	249	233	212
304	260	235	220	205

CONCLUSIONS AND RELEVANCE In critically ill patients with sepsis, compared with intermittent administration, the continuous administration of meropenem did not improve the composite outcome of mortality and emergence of pandrug-resistant or extensively drug-resistant bacteria at day 28.

ANTIMICROBIAL TREATMENT DURATION

Duration of antibiotics

Recommendation

30. For adults with an initial diagnosis of sepsis or septic shock and adequate source control, we **suggest** using shorter over longer duration of antimicrobial therapy

Weak recommendation, very low quality of evidence

DSA
Diseases Society of America

hivma
hiv medicine association

OXFORD

Antimicrobial Treatment Infections

Lindsay M. Busch and Sameer S. Kadri

Biomarkers to discontinue antibiotics

Recommendation

31. For adults with an initial diagnosis of sepsis or septic shock and adequate source control where optimal duration of therapy is unclear, we **suggest** using procalcitonin AND clinical evaluation to decide when to discontinue antimicrobials over clinical evaluation alone

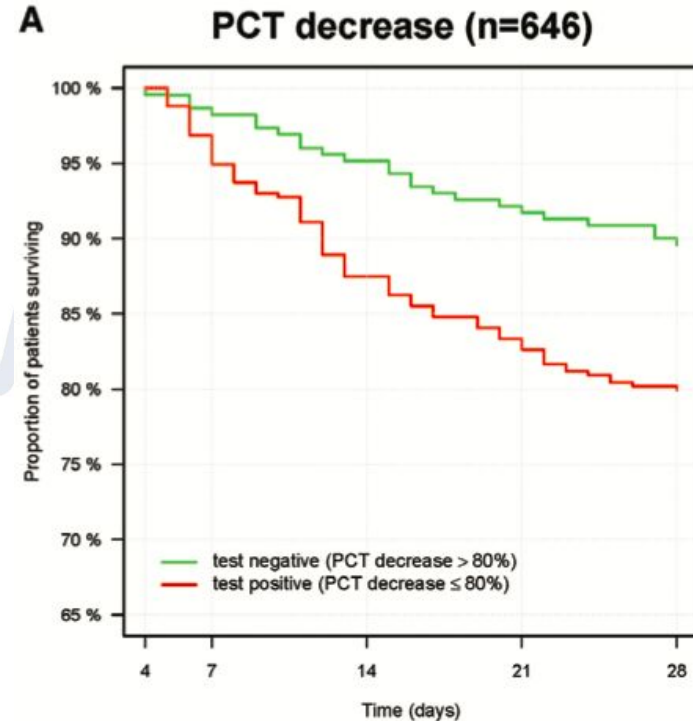
Weak recommendation, low quality of evidence

PROCALCITONIN

Serial Procalcitonin Predicts Mortality in Severe Sepsis Patients: Results From the Multicenter Procalcitonin MONitoring SEpsis (MOSES) Study

Philipp Schuetz, MD, MPH¹; Robert Birkhahn, MD²; Robert Sherwin, MD³; Alan E. Jones, MD⁴; Adam Singer, MD⁵; Jeffrey A. Kline, MD⁶; Michael S. Runyon, MD, MPH⁶; Wesley H. Self, MD⁷; D. Mark Courtney, MD⁸; Richard M. Nowak, MD⁹; David F. Gaieski, MD¹⁰; Stefan Ebmeyer, MD¹¹; Sascha Johannes, PhD¹¹; Jan C. Wiemer, PhD¹¹; Andrej Schwabe, PhD¹¹; Nathan I. Shapiro, MD, MPH¹²

**Reduction to less
than 80% of basal
PCT at day 4
significantly reduces
28-day mortality**



ANTIMICROBIAL DE-ESCALATION

Clinical Infectious Diseases

REVIEW ARTICLE



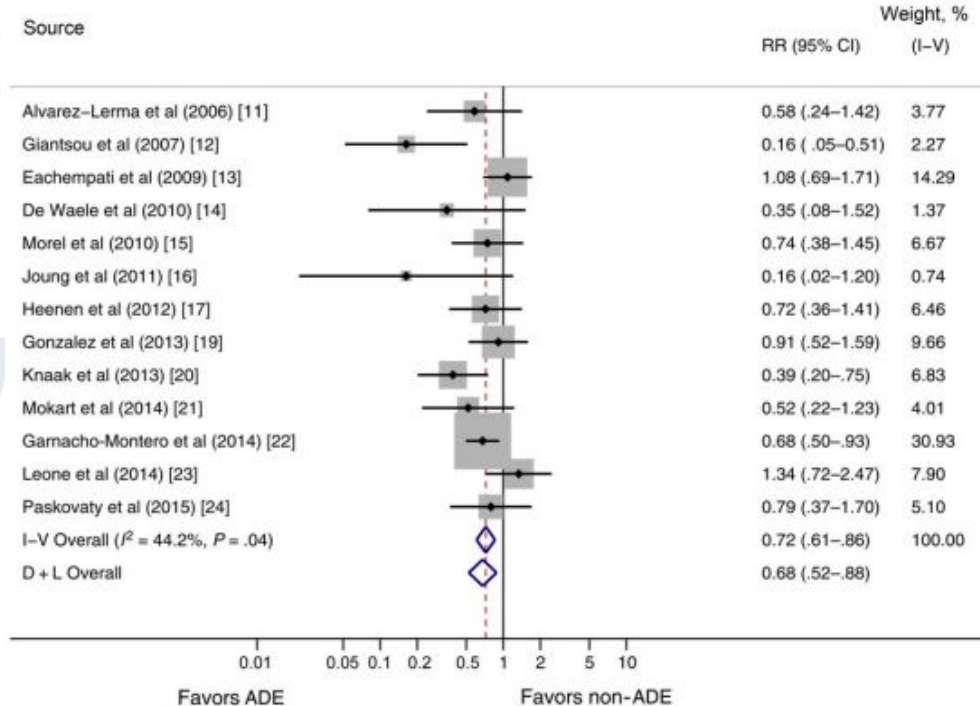
A Systematic Review of the Definitions, Determinants, and Clinical Outcomes of Antimicrobial De-escalation in the Intensive Care Unit

Alexis Tabah,^{1,2,a} Menino Osbert Cotta,^{1,2,3,a} Jose Garnacho-Montero,⁴ Jeroen Schouten,⁷ Jason A. Roberts,^{1,2,3} Jeffrey Lipman,^{1,2,4} Mark Tacey,⁵ Jean-François Timsit,^{8,9} Marc Leone,¹⁰ Jean Ralph Zahar,¹¹ and Jan J. De Waele¹²; for the Working Group for Antimicrobial Use in the ICU

Table 3. Factors Associated With Antimicrobial De-escalation

Factors Associated With ADE	
Positively associated	
Initially appropriate empiric antimicrobial therapy	
Broad-spectrum empiric therapy	
Compliance with national prescribing guidelines	
Treatment with multiple and "companion" antimicrobials	
Positive microbiological cultures	
Lower severity of illness scores at	
Baseline	
Time of ADE	
Day 5 of therapy	
Negatively associated	
Isolation of a multiresistant pathogen	
Polymicrobial infections	
Intra-abdominal infections	

Abbreviation: ADE, antimicrobial de-escalation.



Tabah A. Clin Infect Dis. 2016; 62:1009-1017.



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- Sepsis / Septic shock
- Meningitis
- Necrotizing Fascitis
- Open fracture



MENINGITIS

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

ANTIMICROBIAL AGENTS: BACTERIAL/FUNGAL: EDITED BY MONICA A. SLAVIN

Dose optimisation of antibiotics used for meningitis

Heffernan, Aaron J.^{a,b}; Roberts, Jason A.^{a,c,d}

<50 years Ceftriaxone 2 g/die
 +
 ±
 Acyclovir 10
 mg/kg/tid

>50 years Ceftriaxone 2 g/die
 +
 Ampicillin 12 g/die
 ±
 Acyclovir 10
 mg/kg/tid

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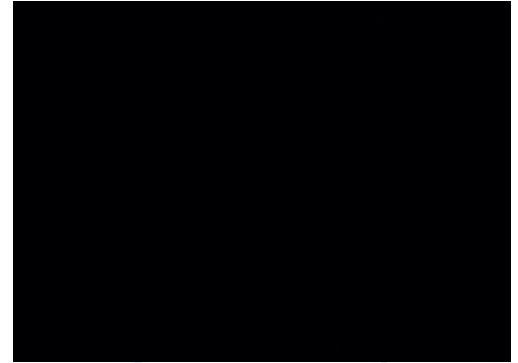


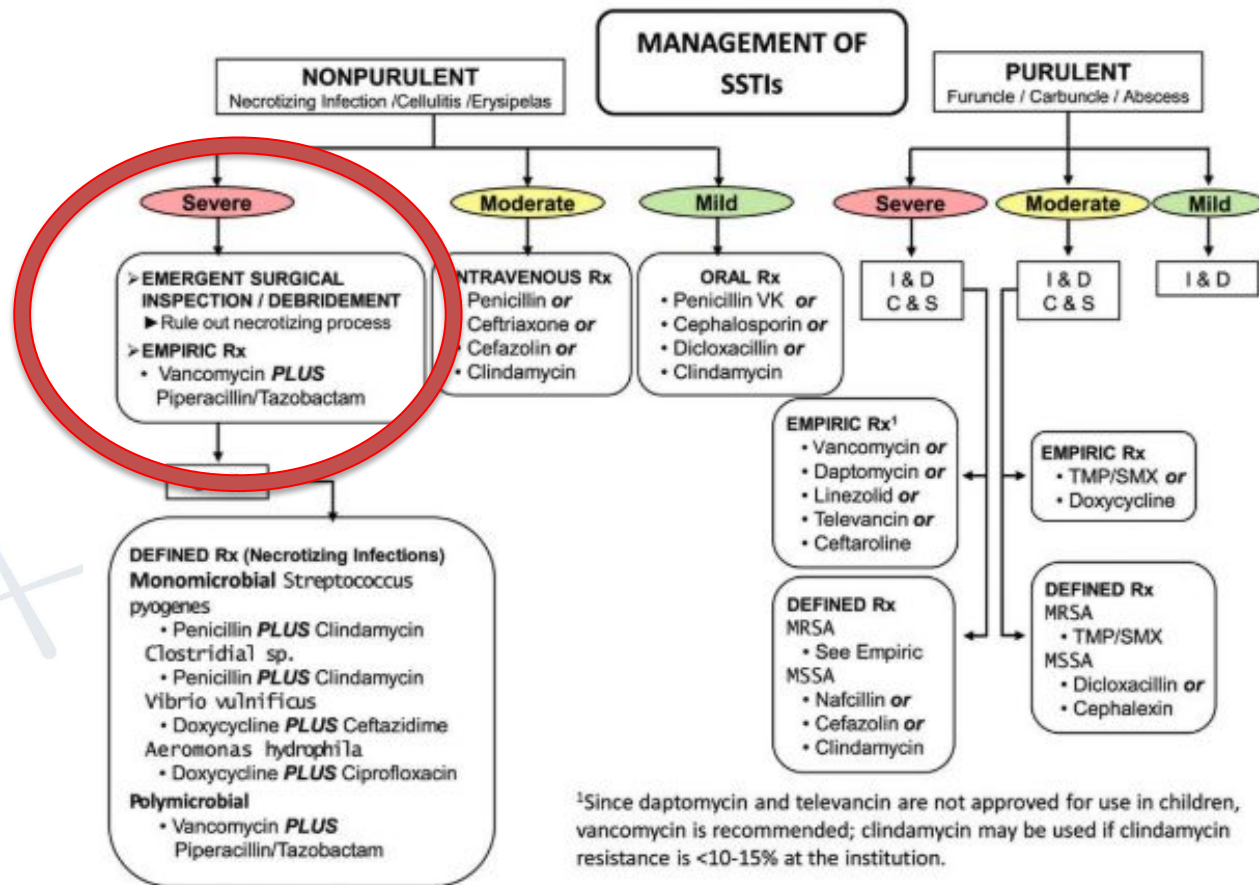
NECROTIZING FASCITIS

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Table 1 The Laboratory Risk Indicator for Necrotising Fasciitis		
Parameter	Range	Score ^a
Hb (g/dl)	>13.5	0
	11–13.5	1
	<11	2
White cells (10 ⁹ /L)	<15	0
	15–25	1
	>25	2
Sodium (mmol/L)	<135	2
Creatinine (μmol/L)	>141	2
Glucose	>10	1
C-reactive protein	>150	4
^a Score ≤5 = <50% risk (low); 6–7 = intermediate risk; ≥8 = >75% risk (high).		

LRINEC score





¹Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

INDICATIONS

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- Necrotizing Fascitis
- Open fractures



OPEN FRACTURES

Review Article

Antibiotic Prophylaxis in Open Fractures: Evidence, Evolving Issues, and Recommendations

Table 1

Gustilo-Anderson Classification of Open Fractures^{1,2}

Type	Details
I	Open fracture with a wound less than 1 cm long, low energy, without gross contamination
II	Open fracture with a wound 1–10 cm long, low energy, without gross contamination or extensive soft-tissue damage, flaps, or avulsions
III	A: Open fracture with a wound greater than 10 cm with adequate soft-tissue coverage, or any open fracture due to high-energy trauma or with gross contamination, regardless of the size of the wound B: Open fracture with extensive soft-tissue injury or loss, with periosteal stripping and bone exposure that requires soft-tissue coverage in the form of muscle rotation or transfer C: Open fracture associated with arterial injury requiring repair

The Eastern Association for the Surgery of Trauma recommends **coverage for gram-positive bacteria** with systemic antibiotics **at the time of presentation for patients with an open fracture.** **Gram-negative coverage should be added for type III open fractures,** and high-dose penicillin should be added for barnyard injuries.

HOME TREATMENTS

Type of Infection	First Line Treatment	Allergies to Penicillin
CAP	Amoxicillin/Clavulanate 1 g tid + Clarithromycin 500 mg bid	Levofloxacin 750 mg od
Uncomplicated UTIs	Trimethoprim / Sulphamethoxazole 160+800 mg bid	
Pyelonephritis	Ceftriaxone 2 g followed by Trimethoprim / Sulphamethoxazole 160+800 mg bid	
Abdominal Infections	Amoxicillin/Clavulanate 1 g tid	
Soft Tissue Infections	Amoxicillin/Clavulanate 1 g tid \pm Clindamycin 600 mg qid	

CONCLUSIONS

- Antimicrobial management is a life-saving treatment.
- It should be firstly performed with empiric broad-spectrum regimens based on local epidemiology.
- Short course a preferred to long ones (no changes in mortality).
- The team-work with other specialists should be always considered.





QUESTIONS? QUESTIONS?
OH!