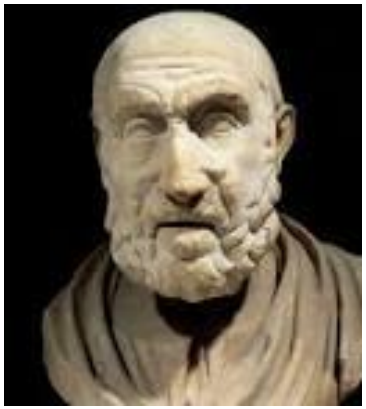
UWTASP tele-antimicrobial stewardship program | echo

September 20th, 2022

Agenda

- Speaker: *Antibiotics and Sepsis*
  Zahra Kassamali-Escobar + Jeannie Chan
- Case Discussions
- Open Discussion

Sepsis- Early definition



Sepsis is the process by which flesh rots, swamps generate foul airs, and wounds fester

https://www.nejm.org/doi/full/10.1056/nejmra1208623

Ancient times

Early ^ Management

Make sacrifices to the goddess, Febris

(Fever) - the goddess to dry up swamps and protect from malaria

Honey

Sought by ancient Egyptians looking for materials that never decay as a wound salve

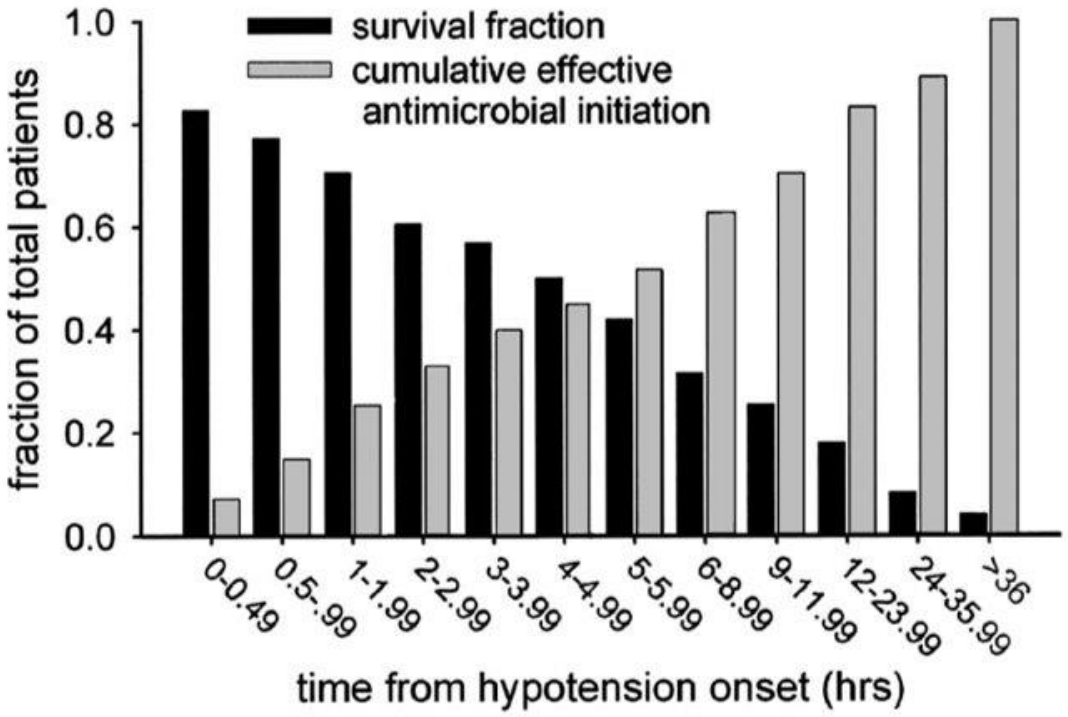
https://www.nejm.org/doi/full/10.1056/nejmra1208623

The Journal of Infectious Diseases Vol. 163, No. 5 (May, 1991), pp. 937-945


Thanks to PENICILLIN
...He Will Come Home!


A RACE AGAINST DEATH!
The Faster this building is completed...the quicker our wounded men get
Penicillin
THE NEW LIFE-SAVING DRUG
Give this job EVERYTHING You've got!

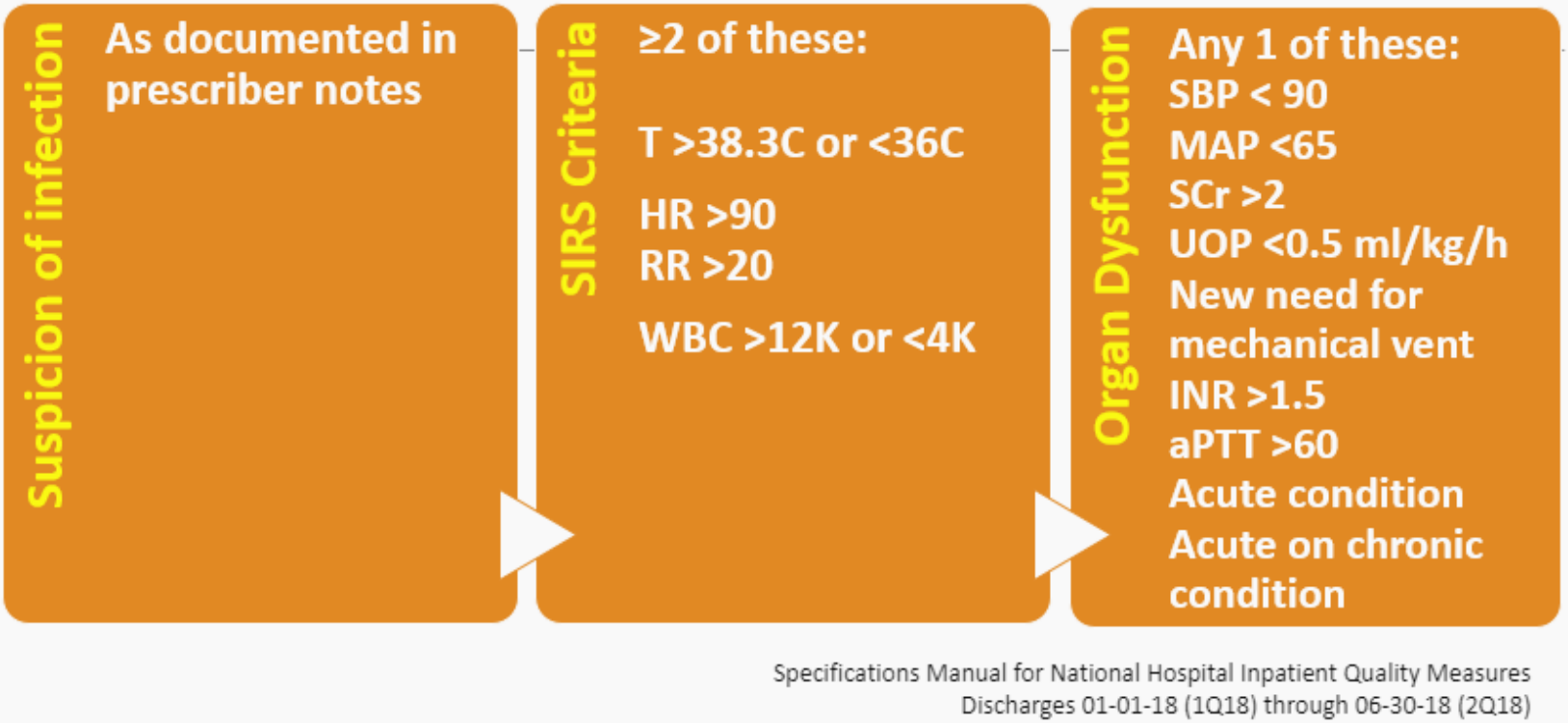
The importance of *Early* Antibiotic Therapy



Each hour of delay in antimicrobial administration over the ensuing 6 hrs was associated with an average decrease in survival of 7.6%

Kumar A, Roberts D, Wood KE, et al. Crit Care Med 2006;34(6):1589-96.

But not ALL sepsis is septic *Shock*



Severe Sepsis	Suspicion of infection + Signs of infection + Acute organ dysfunction
Septic Shock	Suspicion of infection + Signs of infection + Hypotension refractory to fluid resuscitation

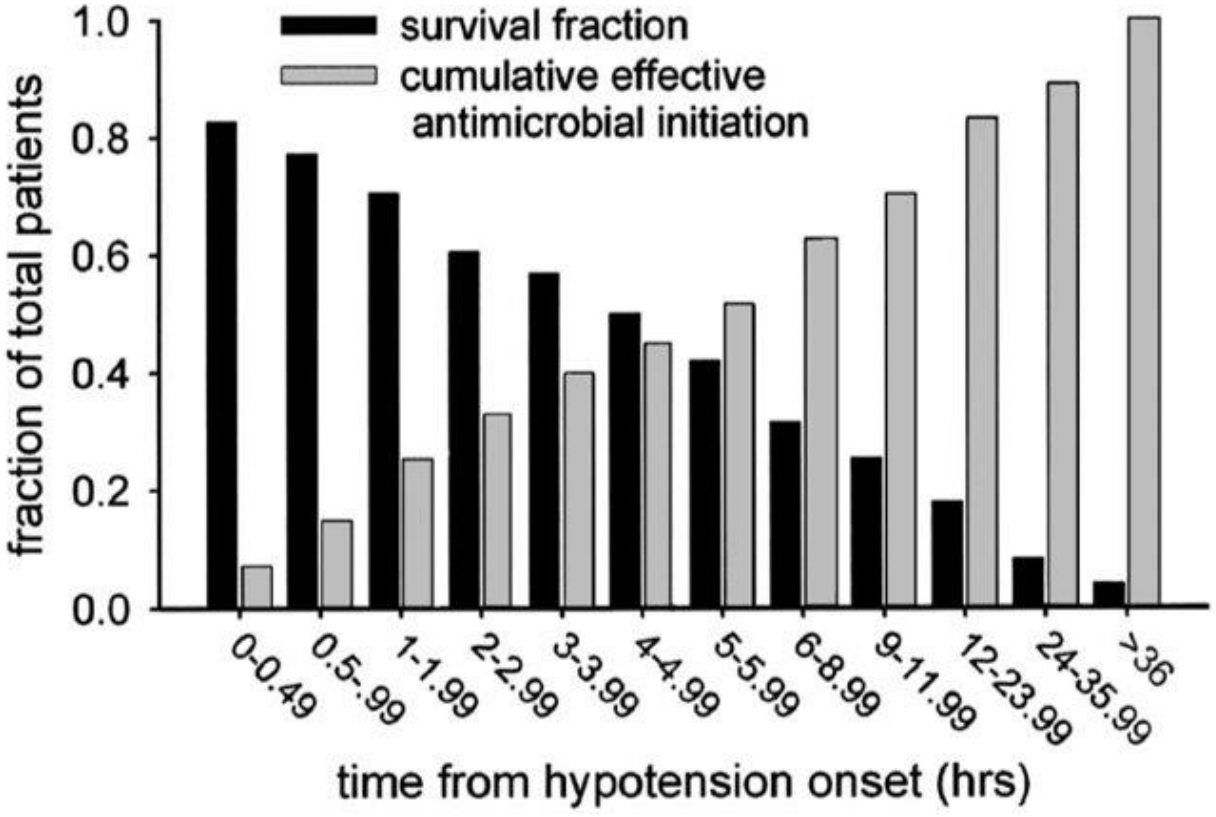
https://www.nejm.org/doi/full/10.1056/nejmra1208623

2021:
New Surviving Sepsis Campaign Guidelines

Specifies antibiotic decisions should be made in the context of patient presentation

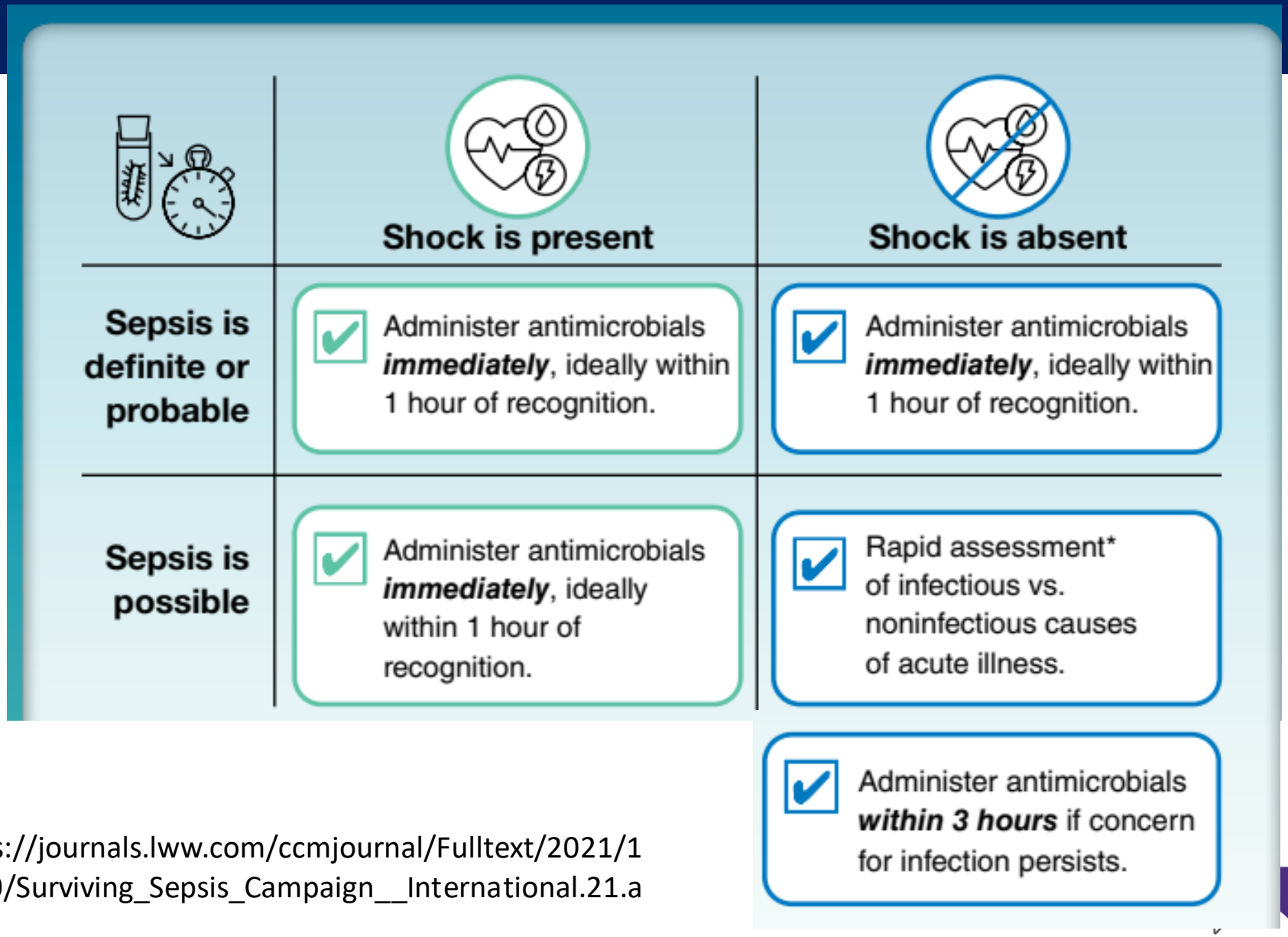
https://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

Antibiotics for Septic Shock: Be Brisk, Be Broad



https://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

New Guidelines allow for nuance



	Shock is present	Shock is absent
Sepsis is definite or probable	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.
Sepsis is possible	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Rapid assessment* of infectious vs. noninfectious causes of acute illness.
		✔ Administer antimicrobials ***within 3 hours*** if concern for infection persists.

https://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

Whoa Nelly Window

When to hold your horses to reassess infectious vs. noninfectious causes

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s://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

Whoa Nelly Window

Holding your Horses to reassess infectious vs. noninfectious causes

	Shock is present	Shock is absent
Sepsis is definite or probable	Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.
Sepsis is possible	Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	Rapid assessment* of infectious vs. noninfectious causes of acute illness. Administer antimicrobials ***within 3 hours*** if concern for infection persists.

Rapid assessment (ideally within 3 hours) =

- History and clinical exam
- Tests for infectious and noninfectious causes of acute illness
- Immediate treatment of acute conditions that mimic sepsis

https://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

What Antibiotics to Start?

High risk for multidrug (MDR) resistant organisms?

- Recent broad-spectrum antimicrobial use
- Infection or colonization with antibiotic resistant organisms in the last year
- Travel to an endemic country in the past 90 days
- Hospitalization abroad within 90 days

Yes

Suggest 2 antimicrobial agents with gram-negative coverage empirically

No

Suggest against 2 antimicrobial agents with gram-negative coverage empirically

Weak recommendation, very low quality of evidence

What Antibiotics to Start?

High risk for multidrug (MDR) resistant organisms?

- Recent broad-spectrum antimicrobial use

LOCAL INFORMATION ABOUT THE RESISTANCE PATTERNS OF THE MOST COMMON CAUSATIVE AGENTS OF SEPSIS IS ESSENTIAL TO CHOOSE THE MOST APPROPRIATE EMPIRIC ANTIBIOTIC THERAPY

Weak recommendation, very low quality of evidence

Q: Where to get your local information?

A: The Antibiogram

Hospital XXX Antibiogram

Bacteria	Number of isolates tested (n)
E. cloacae	192
E. coli	1462
K. pneumoniae	379*
A. baumannii	117
P. aeruginosa	928
S. aureus	1178
E. faecalis	572
E. faecium	206

LOCAL INFORMATION ABOUT THE RESISTANCE PATTERNS OF THE MOST COMMON CAUSATIVE AGENTS OF SEPSIS IS ESSENTIAL TO CHOOSE THE MOST APPROPRIATE EMPIRIC ANTIBIOTIC THERAPY

- A LOT of enterobacterales (=E.coli + K. pneumoniae + E. cloacae)
- A good amount of S. aureus > 1K
- Some *Pseudomonas aeruginosa*

Antibiotic selection: What about spectrum of coverage?

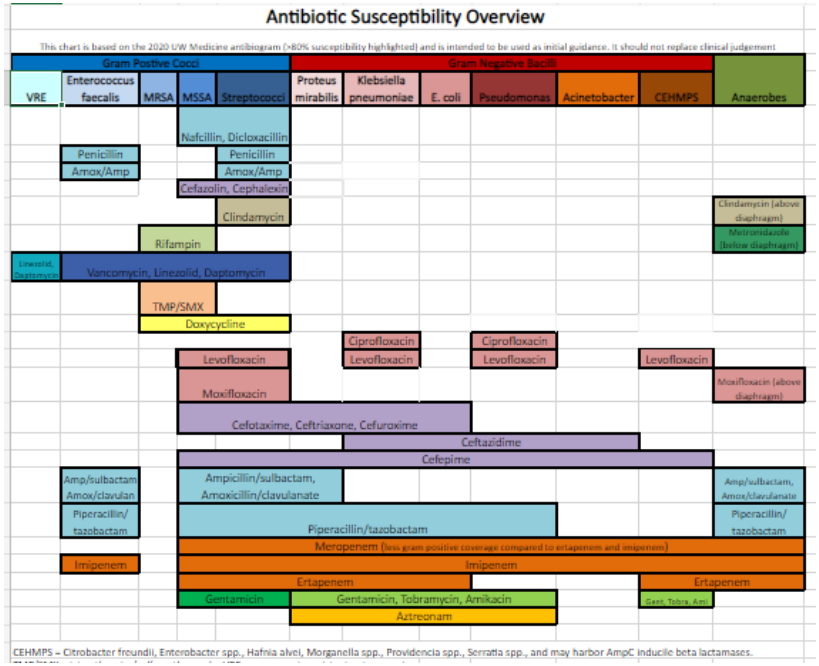
Antibiogram

Hospital XXX Antibiogram

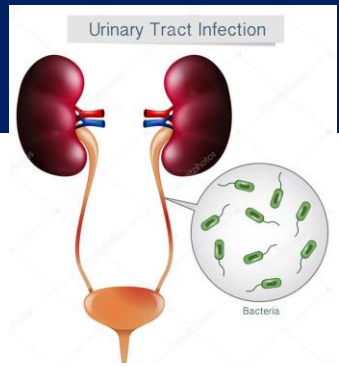
Bacteria	Number of isolates tested (n)	% of n isolates susceptible to each antibiotic listed								
		TOB	CFP	CTZ	PTZ	IMI	CIP	OXA	VAN	DAP
E. cloacae	192	65	77	66	79	96	85			
E. coli	1462	86	94	90	90	99	65			
K. pneumoniae	379*	78	80	79	86	97	81			
A. baumannii	117	63	61	57	69	73	66			
P. aeruginosa	928	65	73	71	88	76	44			
S. aureus	1178						44	41	100¥	100
E. faecalis	572								99	100
E. faecium	206								43	96

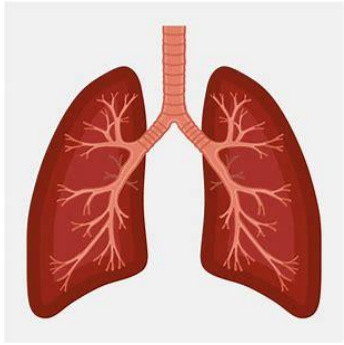
*20% of isolates are ESBL-positive
¥23% of isolates have vancomycin MIC = 2mcg/mL
TOB = tobramycin; CFP = cefepime; CTZ = ceftazidime; PTZ = piperacillin/tazobactam; IMI = imipenem; CIP = ciprofloxacin; OXA = oxacillin; VAN = vancomycin; DAP = daptomycin
Example adapted from Utilization of the Antibiogram in Clinical Practice accessed at http://www.bugsvsdrugs.com

Antibiotic Chart



Antibiotic Selection Considerations





- Suspected source of infection
- Likely pathogens
- Host factors, comorbidities
  - DM, HIV, splenectomy, neutropenia
- Concern for resistant organisms
  - community vs. nosocomial, nursing homes, previous hospitalization/antibiotics, colonization (MRSA, MDRO)
  - Use your antibiogram!

citations

Which antibiotic to give FIRST?

- Differentials often involved both Gram-positive and Gram-negative organisms
- Gram-negative BSI with increased risk of early mortality
- β-lactam can be infused rapidly whereas vancomycin requires longer infusion
- Additional lines are preserved for fluids, vasopressors, or other medications

citations

Which antibiotic to give FIRST?

Clinical Infectious Diseases

MAJOR ARTICLE

Administration of a β-Lactam Prior to Vancomycin as the First Dose of Antibiotic Therapy Improves Survival in Patients With Bloodstream Infections

Joe Amoah,[1] Eili Y. Klein,[2] Kathleen Chiotos,[3] Sara E. Cosgrove,[4,©] and Pranita D. Tamma[1]; for the Centers for Disease Control and Prevention's Prevention Epicenters Program

[1]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; [2]Department of Emergency Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; [3]Department of Anesthesia and Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; and [4]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

- Observational study of patients ≥ 13yo with a bacterial bloodstream infection admitted to any of the 5 hospitals in the Johns Hopkins Health System between 2016-2020
- Receipt of a β-lactam agent before vancomycin vs. vancomycin before a β-lactam agent based on timestamp of administration
- Primary outcome – mortality within 7 days from the time of blood culture collection

citations

Patient Population

Table 1. Mortality Associated With the Most Frequently Recovered Bacterial Organisms Causing Bloodstream Infections in a Cohort of 5514 Patients[a,b,c]

Organism	No. (%)	Mortality≤48 h	Mortality≤7 d	Mortality≤30 d
Gram-negative organisms	3658 (66.3)	102 (2.8)	256 (7.0)	614 (16.8)
Acinetobacter baumannii complex	104 (1.9)	7 (6.7)	17 (16.3)	31 (29.8)
Citrobacter freundii	142 (2.6)	3 (2.1)	5 (3.5)	13 (9.2)
Enterobacter cloacae complex	368 (6.7)	11 (3.0)	20 (5.4)	53 (14.4)
Escherichia coli	1148 (20.8)	14 (1.2)	41 (3.6)	158 (13.8)
Klebsiella aerogenes	148 (2.7)	5 (3.4)	13 (8.8)	30 (20.3)
Klebsiella oxytoca	172 (3.1)	14 (8.1)	17 (9.9)	40 (23.3)
Klebsiella pneumoniae	764 (13.9)	23 (3.0)	65 (8.5)	153 (20.0)
Proteus mirabilis	128 (2.3)	2 (1.6)	11 (8.6)	18 (14.1)
Pseudomonas aeruginosa	380 (6.9)	16 (4.2)	46 (12.1)	73 (19.2)
Serratia marcescens	168 (3.0)	5 (3.0)	16 (9.5)	25 (14.9)
Stenotrophomonas maltophilia	136 (2.5)	2 (1.5)	5 (3.7)	20 (14.7)
Gram-positive organisms	2476 (44.9)	84 (3.4)	162 (6.5)	295 (11.9)
Enterococcus faecalis	424 (7.7)	7 (1.7)	14 (3.3)	23 (5.4)
Enterococcus faecium	261 (4.7)	6 (2.3)	13 (5.0)	28 (10.7)
Methicillin-susceptible *Staphylococcus aureus*	715 (13.0)	35 (4.9)	69 (9.7)	121 (16.9)
Methicillin-resistant *Staphylococcus aureus*	524 (9.5)	14 (2.7)	29 (5.5)	60 (11.5)
Streptococcus anginosus	96 (1.7)	2 (2.1)	4 (4.2)	5 (5.2)
Streptococcus pneumoniae	160 (2.9)	4 (2.5)	8 (5)	16 (10)
Streptococcus agalactiae	164 (3.0)	5 (3.0)	9 (5.5)	15 (9.1)
Streptococcus pyogenes	132 (2.4)	11 (8.3)	16 (12.1)	27 (20.5)

citations

The odds of 7d mortality reduced by 52%

Suspect SEPSIS Save Lives

Table 3. Univariable and Multivariable Analysis of Mortality at 7 Days for 3376 Patients Aged 13 Years and Older With Bloodstream Infections, Using an Inverse Probability of Treatment–Weighted Cohort Based on Propensity Scores

Variable	Unadjusted Odds of Mortality Within 7 d (95% CI)	*P* Value	Adjusted Odds of Mortality Within 7 d[a] (95% CI)	*P* Value
Gram-negative agent administered first	0.68 (.50–.92)	.013	0.48 (.33–.69)	<.001
Pitt bacteremia score	1.39 (1.33–1.47)	<.001	1.26 (1.17–1.37)	<.001
Highest lactate	1.28 (1.24–1.33)	<.001	1.28 (1.23–1.34)	<.001
Highest peripheral WBC count	1.00 (1.00–1.00)	.328	1.00 (1.00–1.00)	.273
Severe immunocompromise	0.83 (.53–1.30)	.412	1.18 (.69–2.03)	.544
Intensive care unit admission	3.38 (2.53–4.52)	<.001	1.30 (.88–1.92)	.188
Charlson comorbidity index	0.99 (.95–1.00)	.138	0.96 (.92–1.00)	.051
Active antibiotic therapy	1.47 (1.05–2.05)	.025	1.25 (.84–1.86)	.275
Combination gram-negative therapy	1.48 (.72–3.04)	.283	0.94 (.44–1.99)	.865

Abbreviations: CI, confidence interval; WBC, white blood cell.

[a]Doubly robust analysis using the inverse probability of treatment–weighted cohort based on propensity scores, with additional adjustment for all covariates included in the table.

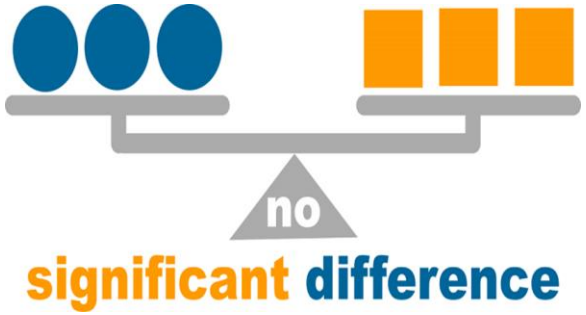
- SENTRY Antimicrobial Surveillance Program: 13,245 BSIs per year
- Prioritizing initial β-lactam administration has the potential to save **737** lives per year!

citations

What about patients with MRSA bacteremia?

- MRSA BSI Subset: 524 patients
  - 380 (73%) received a β-lactam first
  - 144 (27%) received vancomycin first

- The aOR of 7d mortality for patients who received β-lactam prior to vancomycin was 0.93 (95% CI: 0.3 –2.6).



citations

Sepsis care in 2022:

Things that have not changed

- Early recognition still key
- Antibiotics are still important

Goddess Febris

Sepsis care in 2022

Things that are new:

- Holding our horses in cases of hemodynamic stability + lower suspicion of infectious source

- Tailoring empiric antimicrobial therapy based on local resistance patterns

Antibiogram

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E. cloacae	192	65	77	66	79	96	85			
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Example adapted from Utilization of the Antibiogram in Clinical Practice accessed at http://www.bugsvsdrugs.com

Sepsis in September:
Stay tuned for Dr. Laura Evans

ONLINE SPECIAL ARTICLE

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

Evans, Laura[1]; Rhodes, Andrew[2]; Alhazzani, Waleed[3]; Antonelli, Massimo[4]; Coopersmith, Craig M.[5]; French, Craig[6]; [illegible]hado, Flávia R.[7]; Mcintyre, Lauralyn[8]; Ostermann, Marlies[9]; Prescott, Hallie C.[10]; Schorr, Christa[11]; [illegible] Steven[12]; Wiersinga, W. Joost[13]; Alshamsi, Fayez[14]; Angus, Derek C.[15]; Arabi, Yaseen[16]; Azevedo, Lucian[illegible][17]; Beale, Richard[18]; Beilman, Gregory[19]; Belley-Cote, Emilie[20]; Burry, Lisa[21]; Cecconi, Maurizio[22]; Centofanti, John[23]; Coz Yataco, Angel[24]; De Waele, Jan[25]; Dellinger, R. Phillip[26]; Doi, Kent[27]; Du, Bin[28]; Estenssoro, Elisa[29]; Ferrer, Ricard[30]; Gomersall, Charles[31]; Hodgson, Carol[32]; Hylander Møller, Morten[33]; Iwashyna, Theodore[34]; Jacob, Shevin[35]; Kleinpell, Ruth[36]; Klompas, Michael[37]; Koh, Younsuck[38]; Kumar, Anand[39]; Kwizera, Arthur[40]; Lobo, Suzana[41]; Masur, Henry[42]; McGloughlin, Steven[43]; Mehta, Sangeeta[44]; Mehta, Yatin[45]; Mer, Mervyn[46]; Nunnally, Mark[47]; Oczkowski, Simon[48]; Osborn, Tiffany[49]; Papathanassoglou, Elizabeth[50]; Perner, Anders[51]; Puskarich, Michael[52]; Roberts, Jason[53]; Schweickert, William[54]; Seckel, Maureen[55]; Sevransky, Jonathan[56]; Sprung, Charles L.[57]; Welte, Tobias[58]; Zimmerman, Janice[59]; Levy, Mitchell[60]

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