Evidence-Based Clinical Care: Surviving Sepsis





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Disclosures



Narrators

Eduardo Martinez-DuBouchet, M.D., indicated that neither he nor his spouse/partner has relevant financial relationships with commercial interest companies, and he will not include off-label or unapproved product usage in his presentation or discussion.

Katia Jimenez, M.D., CCDS, indicated that neither she nor her spouse/partner has relevant financial relationships with commercial interest companies, and she will not include off-label or unapproved product usage in her presentation or discussion

Design Team

All content contributors, including all sepsis and design team members, have indicated that neither they nor their spouses/partners have relevant financial relationships with commercial interest companies, and they will not include off-label or unapproved product usage in their presentations or discussions.

All other team members and those involved in the narration, planning, development and editing/review of the content have no relevant financial relationships to disclose.

Objectives



- Discuss factors used to identify patients presenting with sepsis.
- Review evidence-based best-practice management of sepsis.
- Describe our team role in time-sensitive sepsis management.

Sepsis Stone Age



- Life-threatening organ dysfunction caused by a dysregulated host response to infection
- Yet no individualized treatment to date for that host response (Treatment is similar across all phenotypes)
- Current management is infection control and organ support

Case



62 y.o. female brought by family to the ED with history of syncope at home. She states she has felt a dull full feeling in her left lower abdomen for 4 days, and this morning had 3 bloody bowel movements, leaving her feeling weak and dizzy. She has taken nothing by mouth except sips of tea today.



- PMHX- hypertension managed with metoprolol, diet controlled DM with a hgba1c 7.1 three months ago and a BMI of 36, breast cancer this year postmastectomy and last chemotherapy 4 weeks ago
- Allergy- penicillin (rash after taking it for a few days 30 years ago for a dental procedure)



- VS BP 100/60, HR 98, R 22, and O2 sat 100% on room air, T 99.4 F (standing BP 90/51, HR 110)
- Pale conjunctiva
- Abdomen- palpable discomfort left lower quadrant, no rebound or guarding
- Rectal normal exam except noted blood on glove
- Extremities warm with easily palpable pulses



- Chest X-ray normal findings with chemo port in good position
- EKG- sinus tachycardia, nonspecific lateral ST changes and high lateral R waves in AVL, V5, V6 consistent with LVH
- Troponin 2.1
- Lab calls with a critical hemoglobin 6.2



- Labs- glucose 195, creatinine 1.5, BUN 47, hgb 6.5, WBC 3.5
- Despite IVF and blood transfusion, her BP deteriorates to 88/50, repeat hgb 8.5 after 2 units PRBC.
- Her urine output remains low at 30ml/hr.
- Bedside echocardiogram reports EF 30% globally depressed with LVH



- Rapid micro results with positive gene expression for MRSA in blood cultures done in triage and E. coli 2/2
- CT abdomen and pelvis- some thickening of the sigmoid colon wall, with possible small adjacent collection



SIRS

| Signs of systemic inflammatory response syndrome (SIRS) | | | |
|---|---------------------------|--|--|
| SIRS—defined by presence of two or more criteria of following | | | |
| Heart rate | >90 beats/min | | |
| Core temperature | <36°C or >38°C | | |
| White blood count | <4000 or >12000/mm3 | | |
| Respirations | >20/min or PCO2 <32 mm Hg | | |

How Do We Screen for Sepsis?



| Table 2. Definitions of Sepsis, Severe Sepsis, and Septic Shock | | | |
|---|---|--|---|
| Sepsis Category | Sepsis-3 | 2001 Sepsis | CMS SEP-1 |
| Sepsis | SOFA score ≥ 2 + suspected infection | 2 of 4 SIRS criteria + suspected infection | 2 of 4 SIRS criteria + suspected infection |
| Severe sepsis | Not applicable | Sepsis + organ dysfunction, hypoperfusion, or hypotension | Sepsis + sepsis-induced organ dysfunction* |
| Septic shock | Vasopressor requirement to maintain MAP ≥ 65 mm Hg + serum lactate level > 2 mmol/L in the absence of hypovolemia | Sepsis-induced hypotension persisting after adequate IV fluid resuscitation + presence of perfusion abnormalities or organ dysfunction | Lactate > 4 mmol/L SBP < 90 mm Hg, not responsive to IV fluids or MAP < 70 mm Hg, not responsive to IV fluids |

Organ dysfunction variables according to CMS SEP-1 include: SBP < 90 mm Hg or MAP < 70 mm Hg, or a SBP decrease > 40 mm Hg or < 2 SD below normal for age or known baseline; creatinine > 2.0 mg/dL (176.8 mmol/L) or urine output < 0.5 mL/kg/hr for > 2 hr; bilirubin > 2 mg/dL (34.2 mmol/L); platelet count < 100,000; coagulopathy (INR > 1.5 or aPTT > 60 sec); lactate > 2 mmol/L (18.0 mg/dL).

Abbreviations: aPTT, activated partial thromboplastin time; CMS, Centers for Medicare and Medicaid Services; INR, international normalized ratio; MAP, mean arterial pressure; SBP, systolic blood pressure; SD, standard deviation; SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment.

qSOFA Vs. SIRS



- 46.7% sensitive in ED
- Pooled specificity 72%
- 2/3 of AMS, RR≥22, SBP≤100
- Identifies patients at high risk of death

- 83.6% sensitive in ED
- Specificity 25.8%
- Superior screening

Encephalopathy = High Risk

Fernando SM, Tran A, Taljaard M, et al. Prognostic accuracy of the Quick Sequential Organ Failure Assessment for mortality in patients with suspected infection: A systematic review and metaanalysis. *Ann Intern Med* 2018;168:266-275.

Severe Sepsis = Organ Dysfunction



- 1. Lactate > 2 mmol/L
- 2. INR > 1.5 or aPTT > 60 seconds
- 3. Platelet count < 100,000
- 4. Bilirubin > 2 mg/dL
- 5. Creatinine > 2, or urine output < 0.5 mL/kg/hour for 2 hours
- 6. Systolic blood pressure (SBP) < 90 mmHg, or mean arterial pressure (MAP) < 65 mmHg, or decrease in SBP more than 40 mmHg from last previously recorded SBP "normal" for patient

Or



 Numeric criteria for severe sepsis are not met; however, there is physician/ARNP/PA documentation of sepsis, severe sepsis or septic shock.

CMS Requirement



Two initiatives for improvement in sepsis management come from the Surviving Sepsis Campaign and the Centers for Medicare & Medicaid (CMS).

In 2002, the Surviving Sepsis Campaign began with a goal to reduce mortality from severe sepsis and septic shock worldwide. It was a joint collaboration of the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. The campaign focused on using bundles (a selected set of elements used together within a specified time frame) to improve the treatment and survival of patients diagnosed with sepsis. Here are the current recommendations.

To be completed within 3 hours of presentation*:

- Measure lactic acid level.
- 2 Obtain blood cultures before administering antibiotics.
- 3 Administer broad-spectrum antibiotics.
- 4 Administer 30 mL/kg crystalloid for hypotension or lactic acid ≥ 4 mmol/L.

To be completed within 6 hours of presentation:

5 Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mmHg.

- 6 In the event of persistent hypotension after initial fluid administration (MAP < 65 mmHg) or if initial lactic acid was ≥ 4 mmol/L, reassess volume status and tissue perfusion and document findings.</p>
- 7 Remeasure lactic acid if initial level elevated.

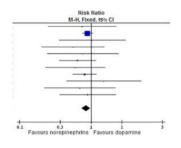
*Time of presentation is the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.

The CMS Severe Sepsis/Septic Shock Early Management Bundle (SEP-1) took effect in 2015. The bundle consists of core measures that must be completed within 3- and 6-hour time frames. Hospitals are required to achieve 100% compliance with all the bundle elements. The CMS bundle has been criticized by clinicians; Aaronson and colleagues note its "ambiguous definition of severe sepsis and septic shock, prescriptive fluid volume requirements, rigid reassessment, and complex abstraction logic."

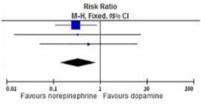
Sources: Surviving Sepsis Campaign. Updated bundles in response to new evidence. April 2015. survivingsepsis.org/SiteCollectionDocuments/SSC_Bundle.pdf; Aaronson EL, Filbin MR, Brown DF, Tobin K, Mort EA. New mandated Centers for Medicare and Medicaid Services requirements for sepsis reporting: Caution from the field. J Emerg Med. 2017;52(1):109-116.



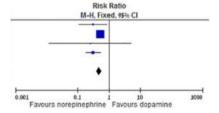
Norepinephrine vs. Dopamine







Adverse Events

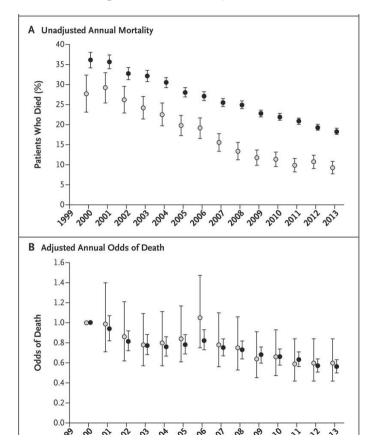


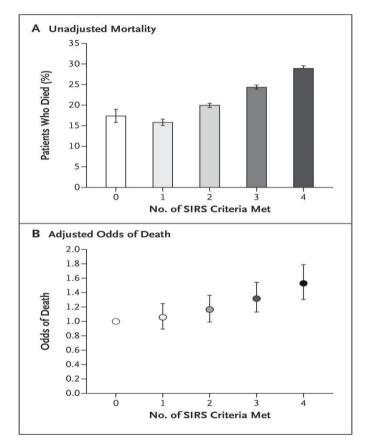
Cardiac Arrythmias

Vasopressors for the Treatment of Septic Shock: Systematic Review and Meta-Analysis Avni T, Lador A, Lev S, Leibovici L, Paul M, Grossman A. PLoS One. 2015 Aug 3;10(8)



Kaukonen KM et al. Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis. NEJM 2015. PMID: 25776936



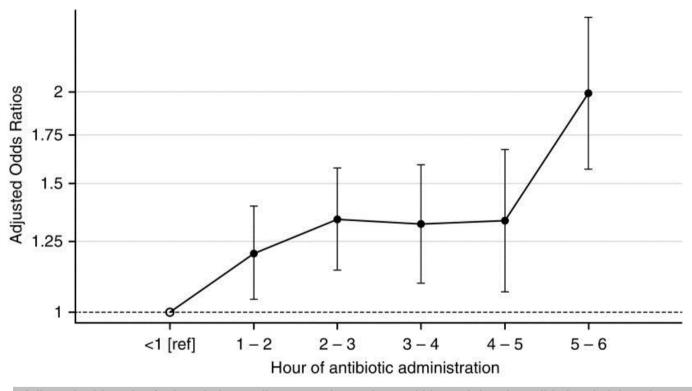


Blood Culture Results Before and After Antimicrobial Administration in Patients With Severe Manifestations of Sepsis: A Diagnostic Study Ann Intern Med. 17 September 2019 Matthew P. Cheng et al.



- Severe sepsis with SBP<90 or lactate ≥ 4 mmol/L
- Pre-antibiotic blood cultures 31.4% positive
- Post-antibiotic blood cultures 19.4% positive
- Absolute difference 12.0% (95% CI, 5.4% to 18.6%;
 P < 0.001)





Adjusted odds ratios for hospital mortality comparing patients within each hourly antibiotic administration group with the reference group of patients given antibiotics in <1 hour. The *y-axis* is on logarithmic scale and the *error bars* represent 95% confidence intervals.

Vincent X. Liu et al. Am J Respir Crit Care Med. 2017 Oct 1;196(7):856-863. The Timing of Early Antibiotics and Hospital Mortality in Sepsis.



Severe Sepsis and Septic Shock Trials Rivers EGDT 2001 vs. (ProCESS, ARISE, ProMISe) 2014-2015: What Is Optimal Resuscitation?

Improving Sepsis Treatment by Embracing Diagnostic Uncertainty



- Surviving Sepsis Campaign released a new 1-hour treatment bundle, strengthening the recommendation that antibiotics be delivered within 60 minutes
- ???Indiscriminate use of broad-spectrum antibiotics
- Decision to administer antibiotics must often be made when the diagnosis is still uncertain



Framework for Timing and Broadness of Initial Antimicrobials

Shock Lactic Acidosis Altered Mentation Respiratory Failure

> Illness Severity (Risk of Death)

Empiric antibiotics within 1 hour, unless definitive alternative diagnosis.

Antibiotics within 3 hours, targeted to site if possible.

Intensive search for alternative diagnoses and confirmation of infection prior to starting any antibiotics.

Targeted antibiotics only after obtaining additional information to guide antibiotic selection.

Likelihood of Bacterial Infection

30-Day Mortality (%) Sepsis and Intermediate Lactic Acid



Prebundle 2012

Postbundle 2013

- Hx CHF 18.8%
- Hx CKD 15.9%

- 17.8%
- 13.3%



The NEW ENGLAND JOURNAL of MEDICINE

Time to Treatment and Mortality During Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D., Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D., Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H., Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

June 8, 2017 N Engl J Med 2017; 376:2235-2244

Rate of Fluid Bolus



 There is less evidence that the rate of bolus or completion within the time frame changes mortality

 Found no association between the time to completion of the initial bolus of intravenous fluids and outcome



0.9% Saline

- Increased volume expansion +++
- Diuresis ++
- Hyperchloremia
- Metabolic acidosis
- Chloride causes tubuloglomerular feedback with constrictive adenosine and worse GFR

Balanced solutions

- Volume expansion ++
- Diuresis +++
- Renal artery flow velocity
- Renal cortical perfusion

Balanced crystalloids for septic shock resuscitation Thiago Domingos Corrêa, Alexandre Biasi Cavalcanti, and Murillo Santucci Cesar de Assunção Rev Bras Ter Intensiva. 2016 Oct-Dec; 28(4): 463–471

SMART



- Semler MW et al. Balanced Crystalloids Versus Saline in Critically III Adults. N Engl J Med 2018; 378:829-839
- Critically ill adults
- (Balanced crystalloids vs. saline)
- Lower rate composite outcome death, new RRT, or persistent renal dysfunction than the use of saline.

Fluid Responsiveness



- The ability to increase cardiac output after fluid administration
- Requires functional hemodynamic monitoring

Fluid Creep



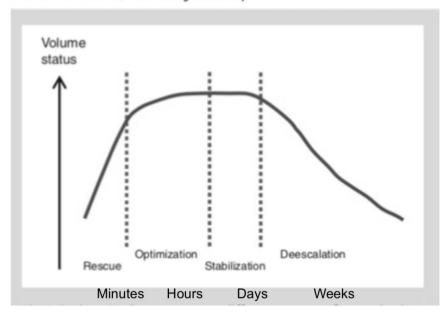




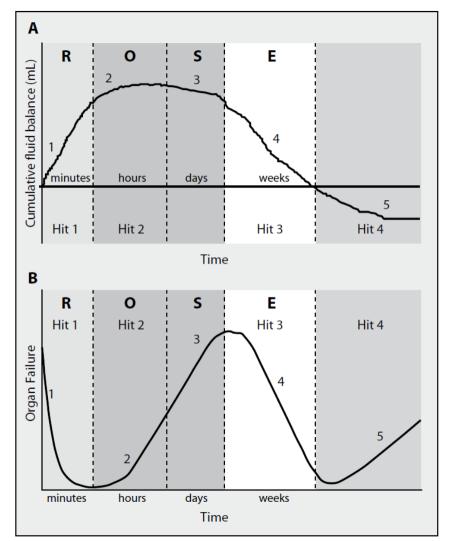
SPECIAL ARTICLES

Four phases of intravenous fluid therapy: a conceptual model[†]

E. A. Hoste^{1,2}, K. Maitland^{3,4}, C. S. Brudney⁵, R. Mehta⁶, J.-L. Vincent⁷, D. Yates⁸, J. A. Kellum⁹, M. G. Mythen¹⁰ and A. D. Shaw¹¹ for the ADQI XII Investigators Group







Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice

Manu L.N.G. Malbrain, Paul E. Marik, Ine Witters, Colin Cordemans, Andrew W. Kirkpatrick, Derek J. Roberts, Niels Van Regenmortel Anaesthesiology Intensive Therapy 2014, vol. 46, no 5, 361–380

After Hemodynamic Stabilization

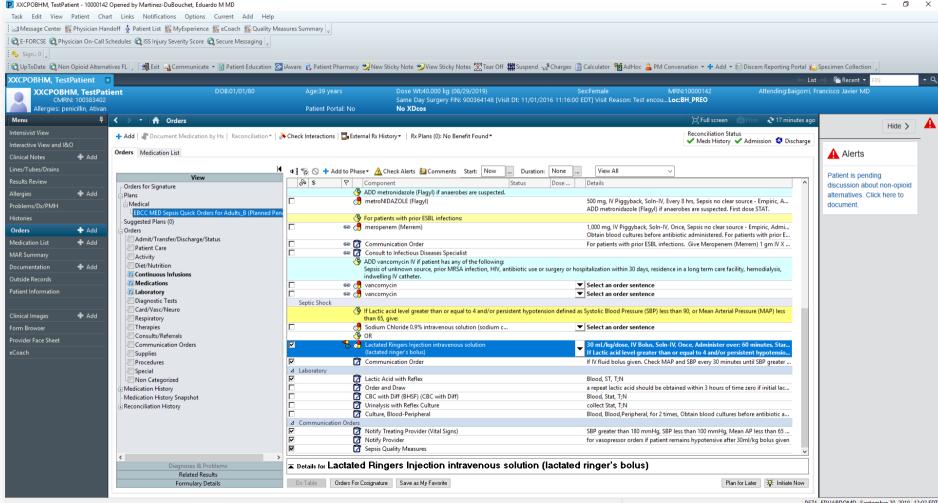


- Conserve fluids
- Diurese
- May need RRT

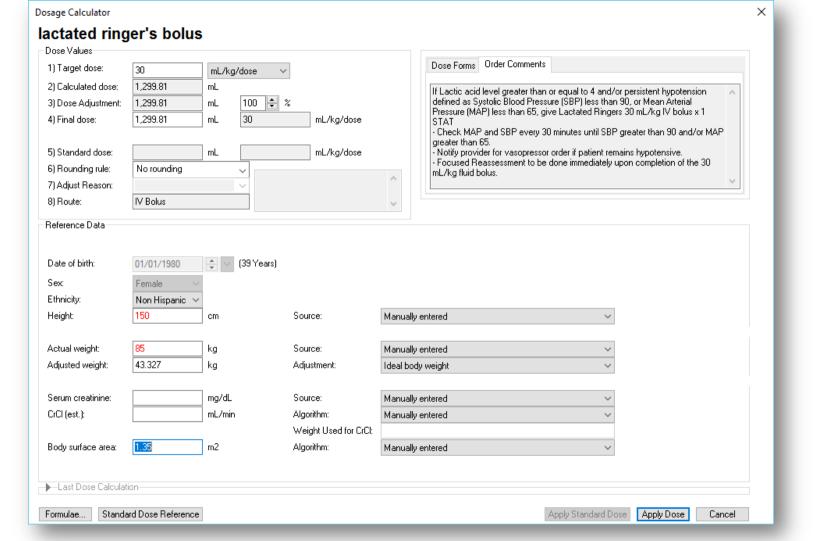
Deresuscitation

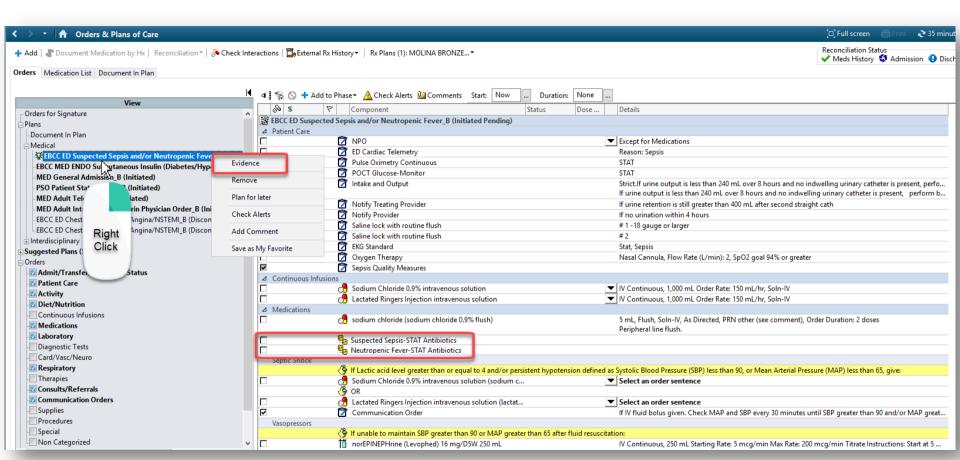


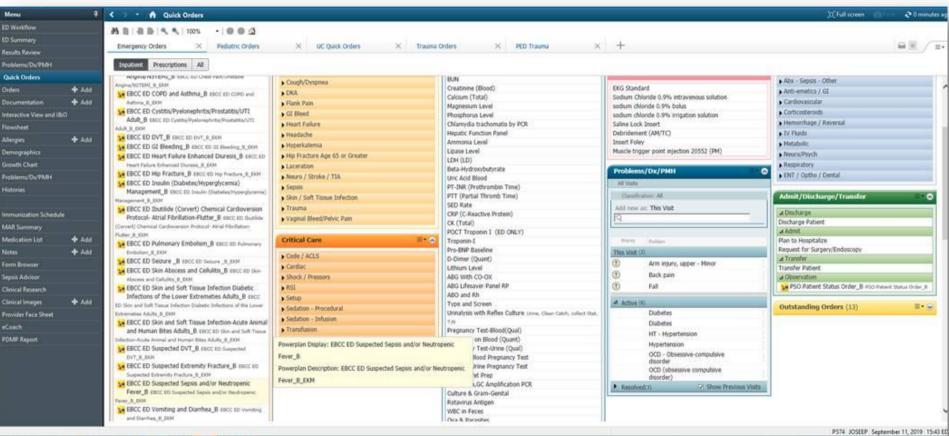
In ARDS, sepsis or SIRS, a conservative or deresuscitative fluid strategy results in an increased number of ventilator-free days and a decreased length of ICU stay compared with a liberal strategy or standard care



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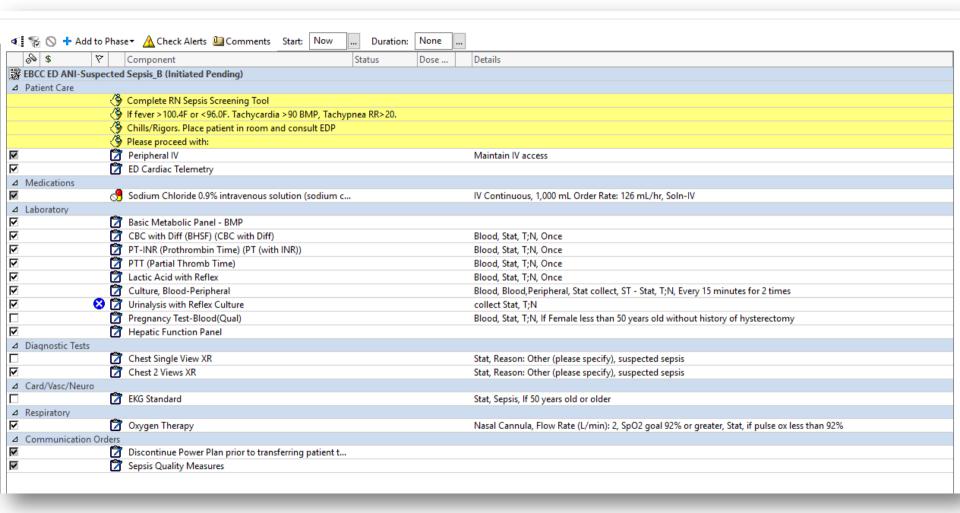












Summary of "Pearls"



- Call the VSU x79802 on new sepsis cases or when in doubt.
- There are criteria to be excluded from the 6-hour bundle that require documentation. (ex. Palliative)
- Always think "Could this be sepsis?" (cultures, lactate, antibiotics)
- Use IBW to calculate fluids in BMI>30 for shock.
- Manage hypoperfusion in timely fashion. (Pressors if not responding to fluids)
- Assess fluid responsiveness if continuing fluids past bolus.
- Beware of the fluid CREEP. Think deresuscitation.
- Get reperfusion exam done in time.
- Beware of transition points of care "handoff tool"

VSU Team





Thank you to the Sepsis Steering Committee and EBCC Group for all their efforts toward improving sepsis outcomes at Baptist Health South Florida!

Sepsis Documentation



- Coders are not clinical, they are translators.
- The data that is coded is the data that is reported.
- Data impact: financial, quality, public reporting.
- Documentation is not showing how "sick" our patients are; no
 justification for the amount of resources geared toward their care.

Sepsis Documentation



- If you think it, document! Terminology such as "suspected," "possible," "probable," "likely," "questionable," or other similar terms is accepted.
- If condition is *ruled out,* please document in the medical record and remove diagnosis from problem list.
- DO NOT USE "sepsis syndrome," "urosepsis" or "SIRS."
- Always document POA status.
- Link the sepsis with the source of infection, and if microorganism known, also document.
- Link the organ dysfunctions to the sepsis.

Sepsis Documentation



- Stay away from signs, symptoms, and lab values. Document diagnoses!
- Instead of hypoxia...is this a <u>respiratory failure</u>?
- Instead of confusion, altered mental status...is this a <u>metabolic or</u> <u>septic encephalopathy?</u>
- Instead of bedridden...is this a <u>functional quadriplegia</u>?
- Instead of frailty, debility, cachexia...does this patient have malnutrition? What degree?
- Instead of hypotension...is this patient in <u>shock</u>? What type?



Questions?

Thank You!