An Update to the Surviving Sepsis Campaign

OVERVIEW

1 Hour Bundle

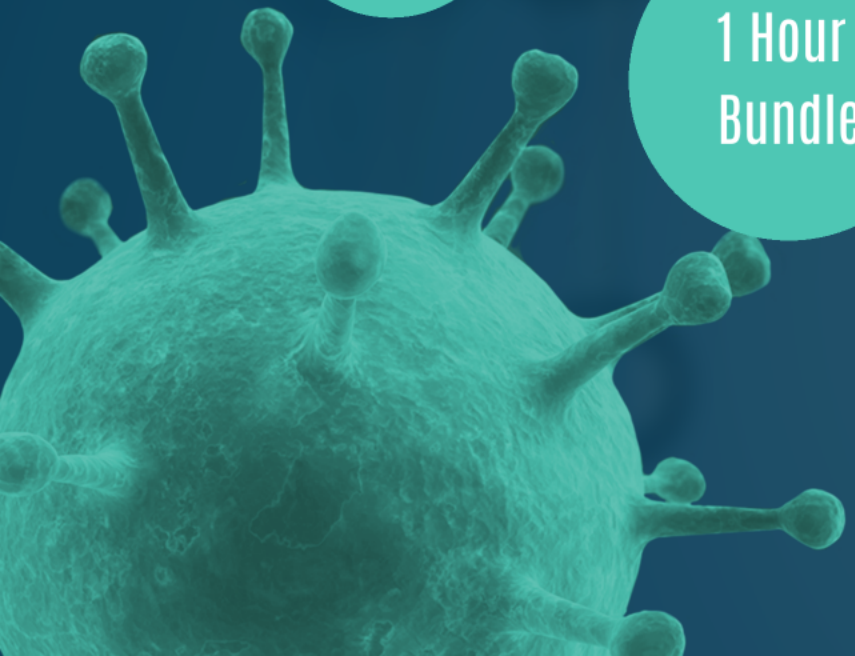
FLUIDS

ANTIBIOTICS

PRESSERS

STEROIDS & VITAMIN C

Additional Standards of Care



OVERVIEW

Sepsis

Life-threatening organ dysfunction caused by a dysregulated host response to infection

Septic Shock

Sepsis with underlying circulatory and cellular/ metabolic abnormality that is associated with increased mortality as a result of persistent hypotension

Historically

In Practice

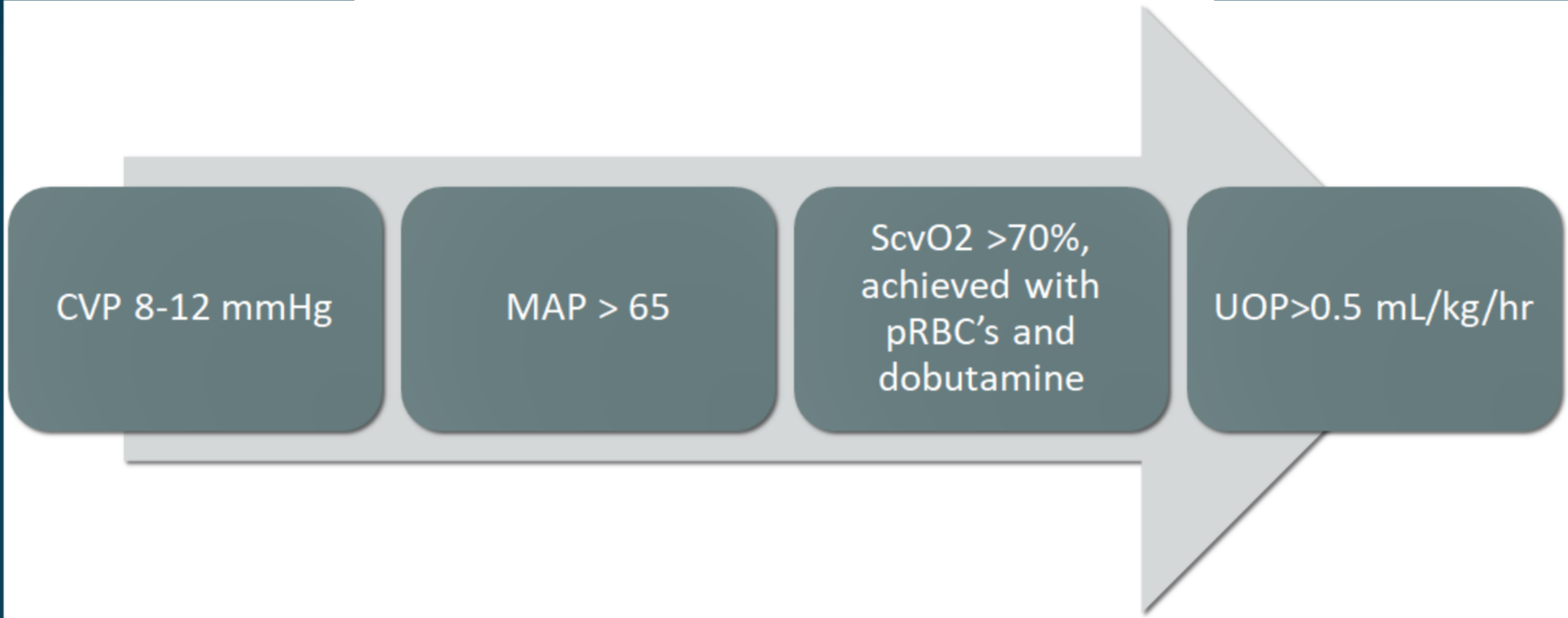
Evidence

Presentation

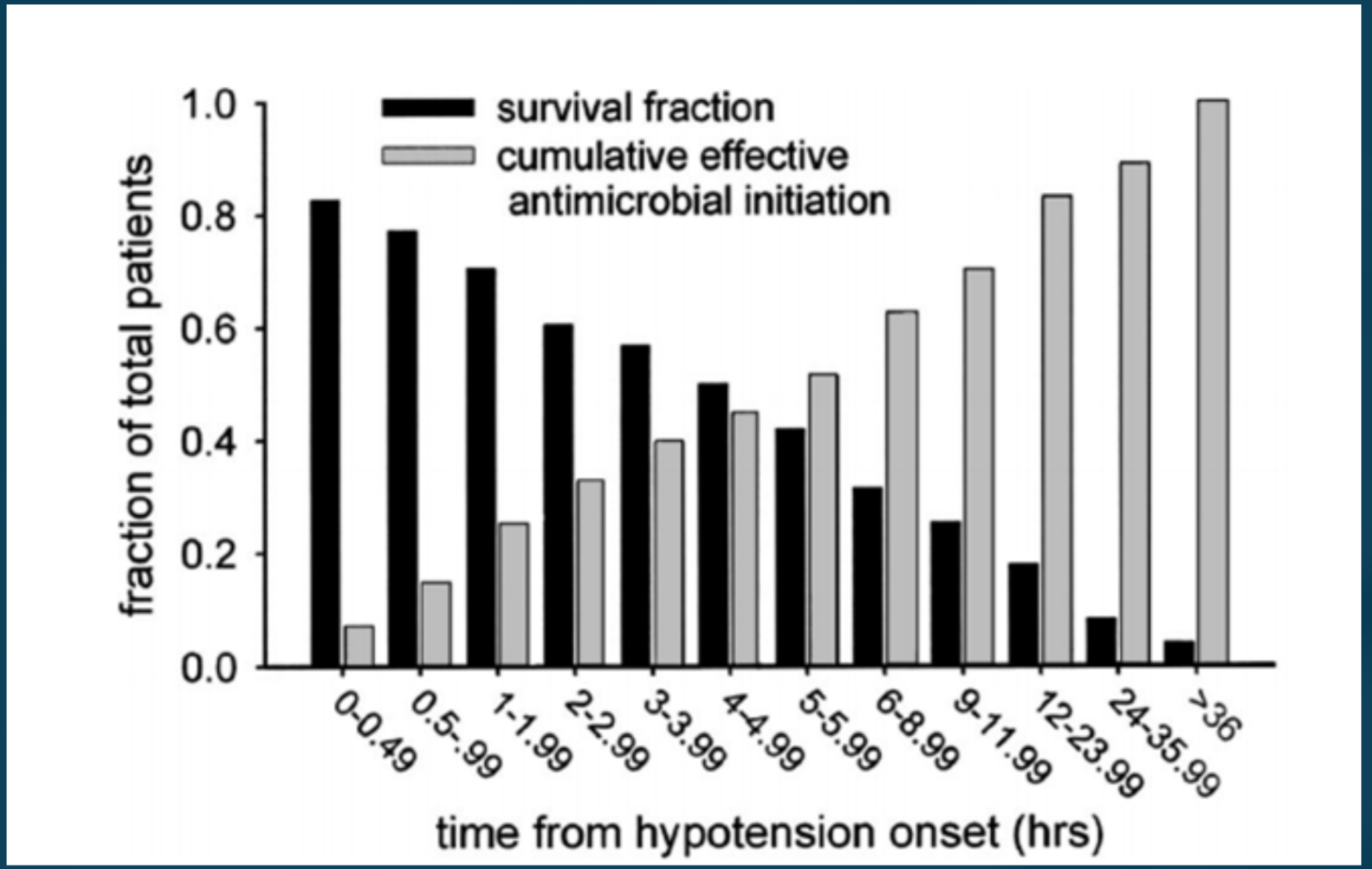
Signs & Symptoms

Fever	<36 or >38°C
Altered Mental Status	WBC <4 or >12,000 cells per mm
Chills	Respiratory Rate > 20 bpm
Pale-looking	Hypotensive
Site of Infection	Heart Rate > 90 bpm

Early Goal Directed Therapy (EGDT)



Rivers	EGDT decreases the risk of mortality (ARR 16%)
ProCESS	No difference in all-cause in-hospital mortality at 60 days • EGDT vs protocol-based vs usual care
ARISE	EGDT did not reduce all-cause morality at 90 days • EGDT vs standard care
ProMISe	EGDT did not improve mortality at 90 days • EGDT vs standard care



Source Control!

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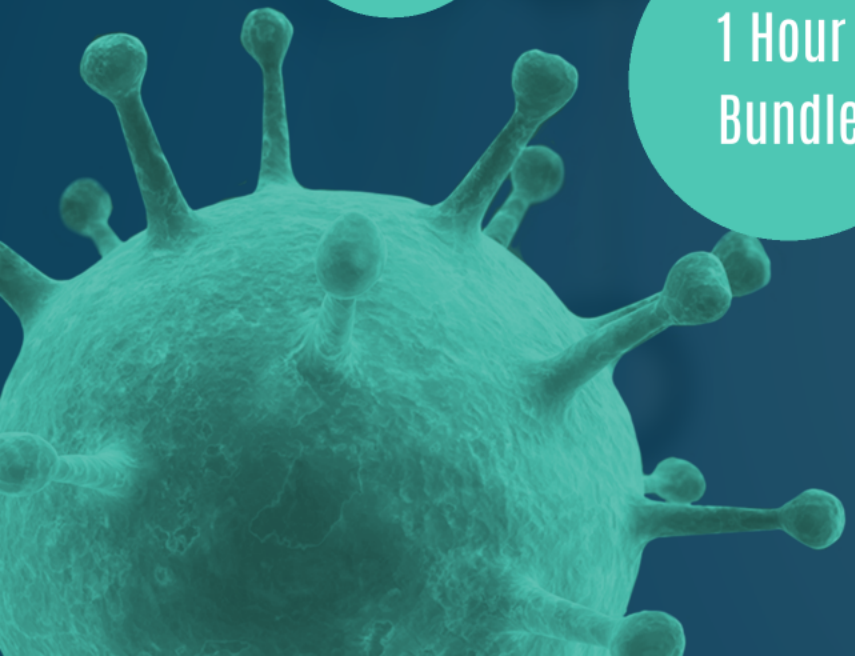

SCCM:
1 hour Bundle

Within the 1st Hour of Admission

- Measure Lactate
  (tissue hypoxia >1.6)
- Obtain Cultures
- Administer Antibiotics
- 30 mL/kg *(IBW)* crystalloid for hypotension or lactate >4 mmol/L within 3 hours
- Add vasopressors if persistently hypotensive to maintain a MAP atleast 65 mmHg
- "Remeasure lactate if initial lactate elevated (> 2mmol/L)

Mean Arterial Pressure (MAP)

$$MAP = {}^{2}/_{3}\,Systolic\ (SBP) + {}^{1}/_{3}\,Diastolic\ (DBP)$$

Ideal Body Weight

Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet
Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet

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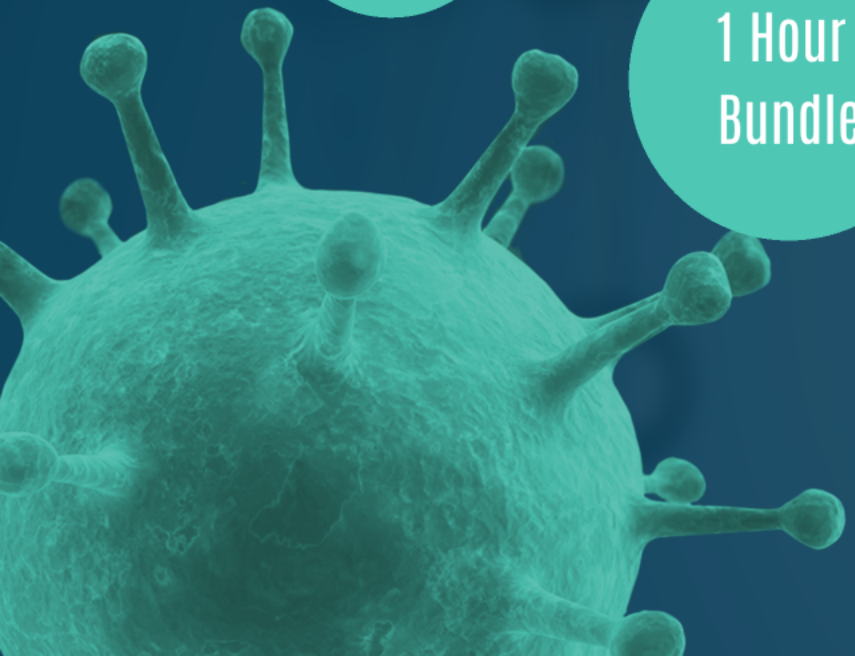


Balanced Crystalloids > Normal Saline

	CRISTAL (2013)
	SMART-MED (2018)
	SALT-ED (2018)

FLUIDS

30 mL/kg IBW

Albumin

Re-assess with 4 mL/kg bolus

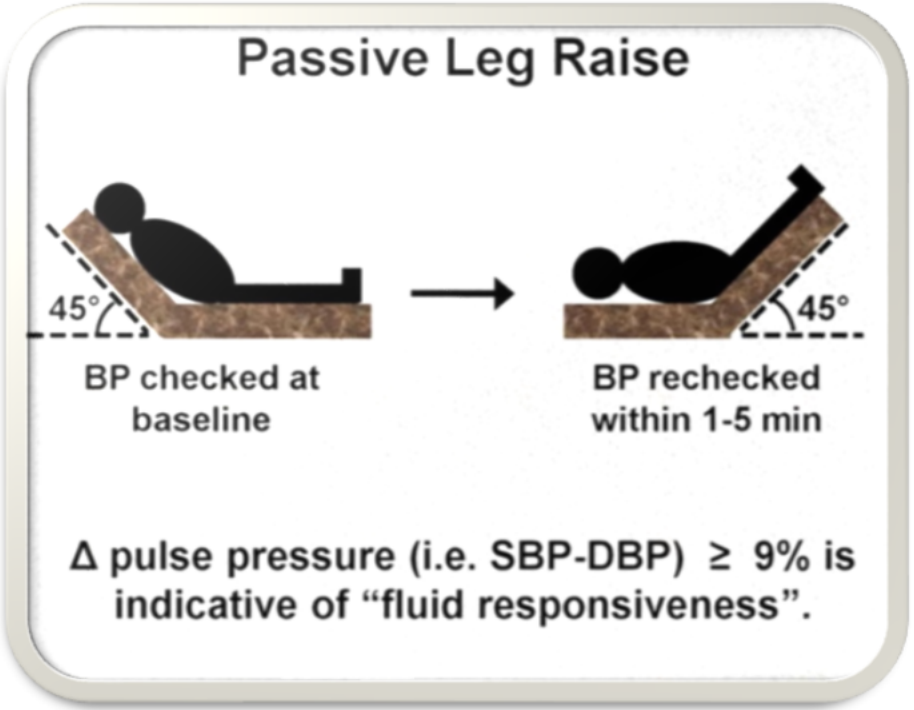
30 mL/kg of IBW

"For adults with sepsis or septic shock, we suggest using balanced crystalloids instead of normal saline for resuscitation."
Weak, *low quality of evidence*

Table 1 - Characteristics of the fluids used for resuscitation.

	Normal Saline	Lactated Ringer's Solution	Plasma-Lyte pH 7.4
Sodium (mEq/l)	154	130	140
Potassium (mEq/l)	0	4	5
Calcium (mEq/l)	0	3	0
Magnesium (mEq/l)	0	0	3
Chloride (mEq/l)	154	109	98
Lactate (mEq/l)	0	28	0
Gluconate (mEq/l)	0	0	23
Acetate (mEq/l)	0	0	27
Osmolarity (mOsm/l)	308	275	294
pH	5.50	6.75	7.40

Guided Resuscitation:
4 mL/kg

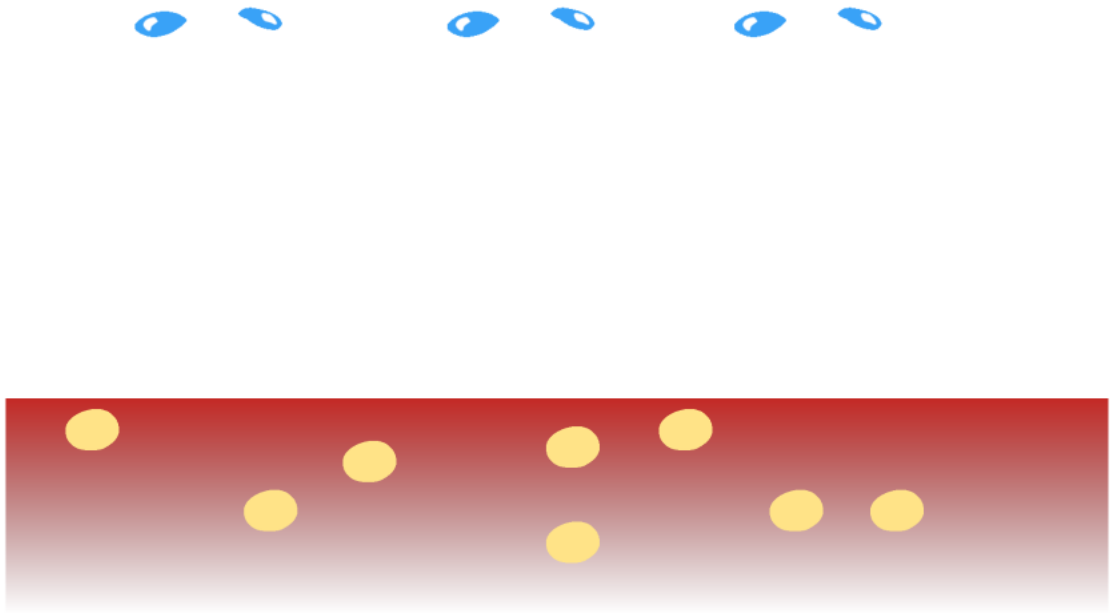


Physiology

Albumin

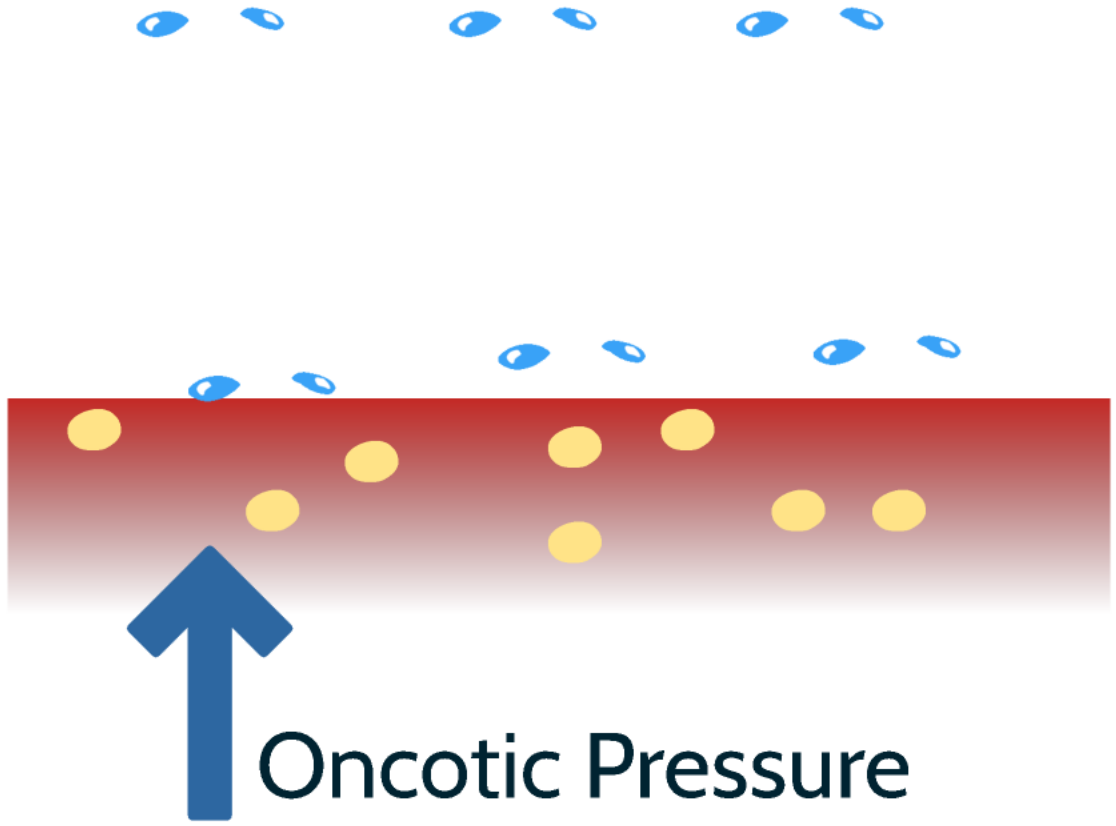
"For adults with sepsis or septic shock, we suggest using albumin in patients who received large volumes of crystalloids."
***Weak**, moderate quality evidence*

Oncotic Pressure



Oncotic Pressure


Oncotic Pressure


Oncotic Pressure

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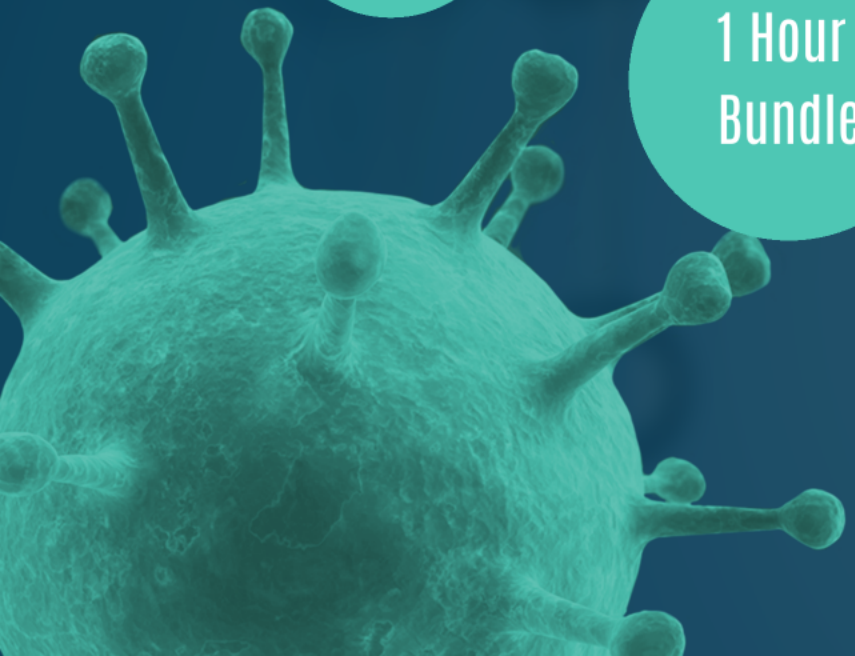

ANTIBIOTICS

De-escalation

Multi-drug Resistant (MDR)

Timing

MRSA

Pseudomonas

Antibiotic Timing

	Shock is present	Shock is absent
Sepsis is definite or probable	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 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.

Hospital vs Community

Risk Factors for MRSA

- Prior history of MRSA infection of colonization
- Recent IV antibiotics
- Chronic wounds
- Recurrent skin infections
- Invasive devices
- Hemodialysis
- Recent hospitalization
- Severity of Illness
- IV Drug Use*

MRSA Hospital Staples

Pharmacology

Vancomycin
Linezolid
Daptomycin

Pharmacology

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin				
Linezolid				
Daptomycin*				

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg			
Linezolid				
Daptomycin*				

LexiCompOnline. 2022

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg	Yes		
Linezolid				
Daptomycin*				

LexiCompOnline. 2022

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg	Yes	Cidal	
Linezolid				
Daptomycin*				

LexiCompOnline. 2022

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg	Yes	Cidal	
Inhibits bacterial cell wall synthesis by binding to D-alanyl-D-alanine and inhibits polymerization				
Linezolid				
Daptomycin*				

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg	Yes	Cidal	Otoxicity Acute Kidney Injury Red Man's Syndrome SJS/TENS
Inhibits bacterial cell wall synthesis by binding to D-alanyl-D-alanine and inhibits polymerization				
Linezolid				
Daptomycin*				

Pharmacology

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Daptomycin*				

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Daptomycin*				

LexiCompOnline. 2022

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Daptomycin*				

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Linezolid	600 mg BID	No	Both*	
Inhibits bacterial synthesis via binding to 23S Ribsomal RNA of the 50S subunit to inhibit cellular translation. **Static against Enterococcus & Staphylococcus* * *Endotoxin Inhibiting Properties*				
Daptomycin*				

LexiCompOnline. 2022

Pharmacology

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LexiCompOnline. 2022

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Daptomycin*	6-10 mg/kg	Yes		

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Pharmacology

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LexiCompOnline. 2022

Pharmacology

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Daptomycin*	6-10 mg/kg	Yes	Cidal	
Inhibits intracellular synthesis of DNA, RNA, & protein via depolarization of the cell membrane * *Inhibited by lung surfactant*				

Pharmacology

Antibiotic	Dose	Renal	Bacterio	Considerations
Vancomycin	15-20 mg/kg	Yes	Cidal	Otoxicity Acute Kidney Injury Red Man's Syndrome SJS/TENS
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Daptomycin*	6-10 mg/kg	Yes	Cidal	Eosinophilic pna Rhabdomyolysis
Inhibits intracellular synthesis of DNA, RNA, & protein via depolarization of the cell membrane * *Inhibited by lung surfactant*				

Pseudmonas Coverage

Pharmacology

Carbapenem's* (except Ertapenem)
Aminoglycosides
Monobactam
Polymyxin's
Flouroquinolones
Th**IR**d & Fourth Cephalopsorin's
Extended Spectrum Beta-lactamase Inhibitor

Class	Antibiotic	MOA	Renally Dose	Bacterio	Considerations
Carbapenems	Imipenem	Binds to Penicillin Binding Proteins on the cell wall to inhibit bacterial wall synthesis via transpeptidation	Yes	Cidal	**Seizures!!** DRESS
	Meropenem				
	Doripenem				
Aminoglycosides	Gentamicin	Binds to the 30S ribosomal subunit to inhibit bacterial protein synthesis	Yes	Static	Bronchospasm Ototoxicity Nephrotoxicity Myasthenia Gravis NMBA
	Tobramycin				
	Amikacin				
Monobactam	Aztreonam	Binds to Penicillin Binding Proteins on the cell wall to inhibit bacterial wall synthesis via transpeptidation	Yes	Cidal	TEN
Polymyxin	Colistin	Acts as a detergent to damage the cytoplasmic membrane	Yes	Cidal	Nephrotoxic Neurotoxic
	Polymyxin B				
Fluroquinolones	Levofloxacin	Inhibits DNA gyrase (Topo II) to prevent relaxation of supercoiled DNA and cause DNA strand breaking	Yes	Cidal	QT prolongation Tendon Rupture CNS Effects Myasthenia Gravis
	Ciprofloxacin				
Third & Fourth Generation Cephalosporins	Ceftazidime	Binds to Penicillin Binding Proteins on the cell wall to inhibit bacterial wall synthesis via transpeptidation	Yes	Cidal	Thrombocytopenia Seizures Encephalopathy
	Cefepime				
Extended Spectrum Beta Lactam	Piperacillin-Tazobactam	Binds to Penicillin Binding Proteins on the cell wall to inhibit bacterial wall synthesis via transpeptidation	Yes	Cidal	Thrombocytopenia Seizures

MDR Organisms

Recommendations
19. For adults with sepsis or septic shock and high risk for multidrug resistant (MDR) organisms, we **suggest** using two antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent *Weak recommendation, very low quality of evidence*
20. For adults with sepsis or septic shock and low risk for MDR organisms, we **suggest against** using two Gram-negative agents for empiric treatment, as compared to one Gram-negative agent *Weak recommendation, very low quality of evidence*
21. For adults with sepsis or septic shock, we **suggest against** using double gram-negative coverage once the causative pathogen and the susceptibilities are known *Weak recommendation, very low quality of evidence*

High-Risk

High Risk for MDRO's

- History of MDR organism in the preceding year
- Broad-spectrum antibiotic use within 90 days
- Travel to high endemic ountry within 90 days
- Hospitalization abroad within 90 days
- Local prevalence of antibiotic-resistant organisms based on local susceptibilities

De-escalation

"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."

Low quality evidence

Procalcitonin?

Procalcitonin

- Acute phase reactant
- Primarily found in the thyroid, lungs, and intestine
  - Half life roughly 30 hours
- Synthesized in response to inflammatory mediated bacterial infections as a result of TNF-alpha and Interleukin-6
  - May be higher in patients with gram negative infections compared to gram positive infections

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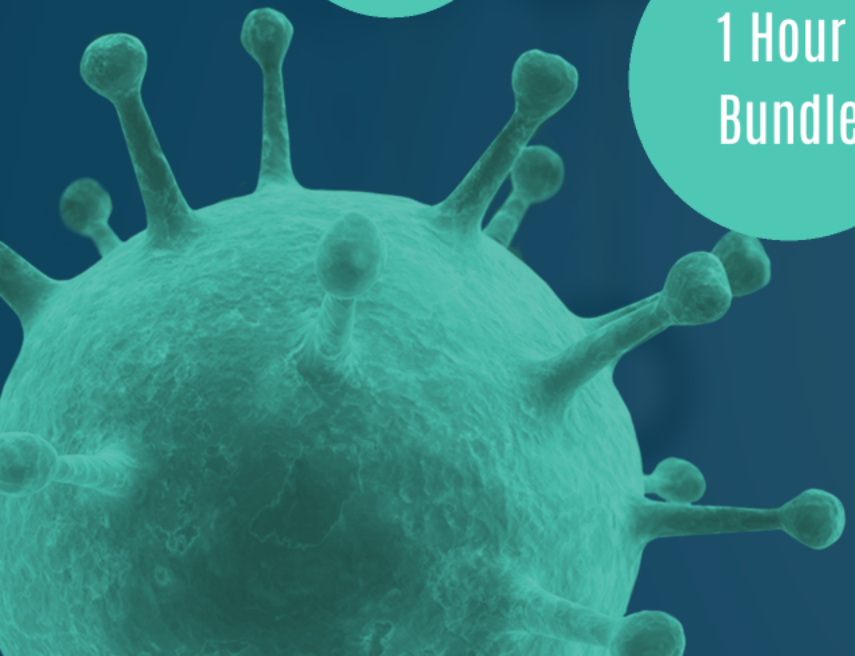

Presser Choice

- **Norepinephrine**
- **Vasopressin**
  Initiate when NE 0.25 - 0.5 ug/kg/min
- **Epinephrine**
  Epinephrine or dobutamine preferred if cardiac component
- **Dopamine**

Visit SCCM for the most up-todate recommendations

Vasopressors	Max Dose	α	β1	β2	DA	MAP	HR	SVR	CO	Indication
Norepinephrine	100 mcg/min	++++	++	+	-	↑↑	↑	↑↑	↑	Septic Shock (1st line) Cardiogenic Shock
Epinephrine	30 mcg/min	+++	+++	+++	-	↑	↑↑	↓↑	↑↑	Septic Shock, Cardiogenic Shock, Bronchospasm, Anaphylaxis
Vasopressin	0.03 units/min	Stimulate v1 receptors in vascular smooth muscle				↑	↔	↑↑	↔	Adjunct for Septic Shock (never used as monotherapy)
Dopamine (mcg/kg/min)	1 – 3	-	+	-	++	↔	↔	↔	↑	Cardiogenic Shock Symptomatic Bradycardia
	3 – 10	+	++	+	++	↑	↑	↑	↑↑	
	>10 - 20	+++	+++	-	++	↑	↑	↑↑	↑	

What about Methylene Blue?

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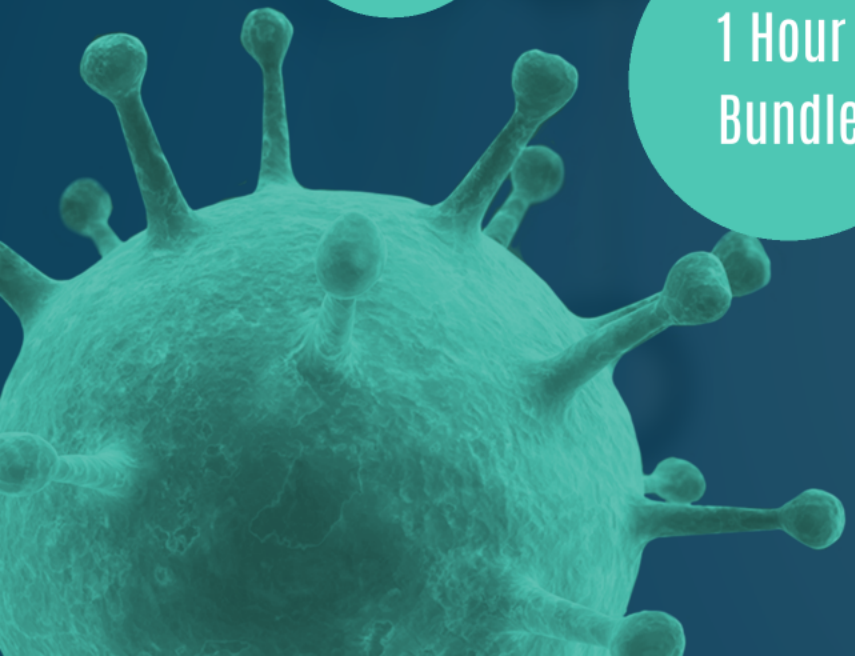


STEROIDS

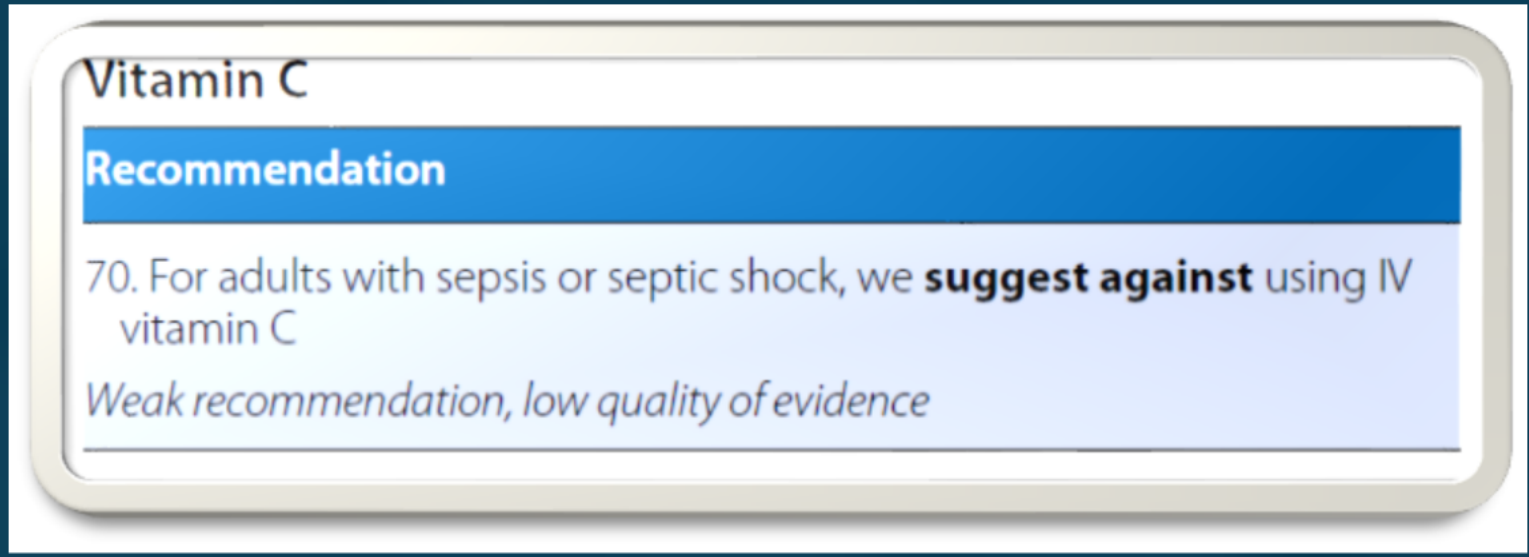
VITAMINS?

ANNANE (2002)
CORTICUS (2008)
ADRENAL & APPROCHSS (2018)

Hydrocortisone 200 - 300 mg IV per day

Commenced at a dose of Norephinephrine >0.25 mcg/kg/min at least 4 hours aft

Vitamins?



Vitamin C

Recommendation
70. For adults with sepsis or septic shock, we **suggest against** using IV vitamin C *Weak recommendation, low quality of evidence*

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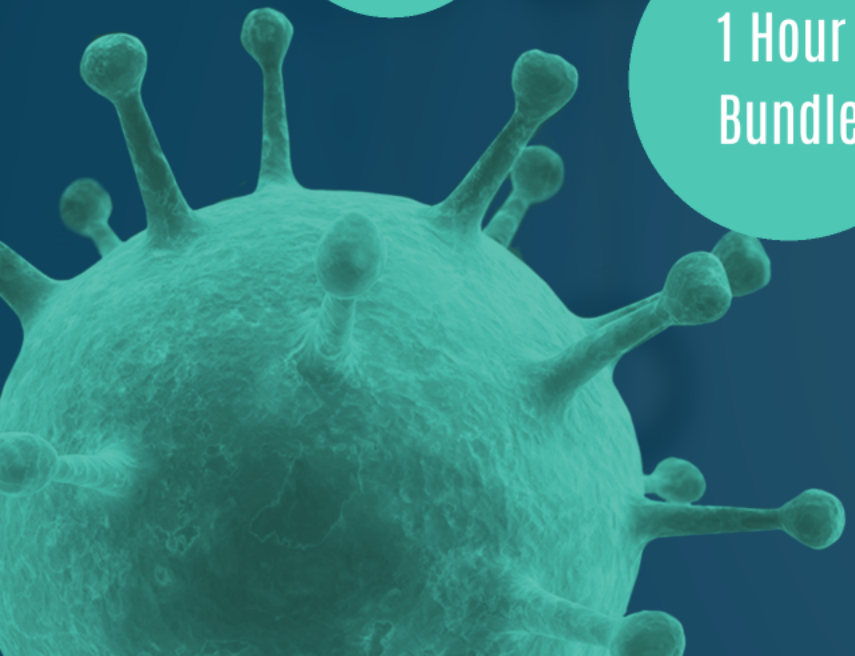


Additional Standards of Care

Acidosis

FASTHUG

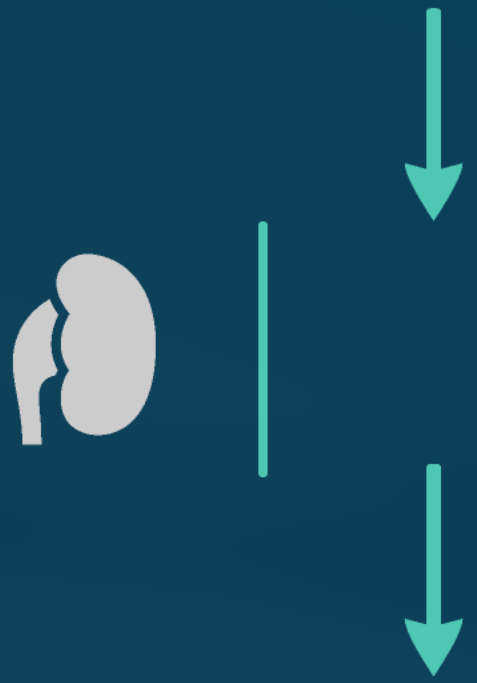
Metabolic Acidosis

Metabolic Acidosis

Severe Metabolic Acidosis pH <7.2

Metabolic Acidosis

Severe Metabolic Acidosis pH <7.2



Metabolic Acidosis

Severe Metabolic Acidosis pH <7.2

Sodium Bicarbonate Therapy Recommended

Metabolic Acidosis

Severe Metabolic Acidosis pH <7.2

AKIN score of 2 or 3

Sodium Bicarbonate Therapy Recommended

FAST HUG

FAST HUG

Feeding

FAST HUG

Feeding

Analgesia

FAST HUG

Feeding

Analgesia

Sedation

FAST HUG

Feeding

Analgesia

ZZZ Sedation

Thromboprophylaxis

FAST HUG

Feeding

Head of Bed

Analgesia

Sedation

Thromboprophylaxis

FAST HUG

Feeding

Head of Bed

Analgesia

Ulcer Prophylaxis

Sedation

Thromboprophylaxis

FAST HUG

Feeding

Head of Bed

Analgesia

Ulcer Prophylaxis

Sedation

Glucose Control

Thromboprophylaxis

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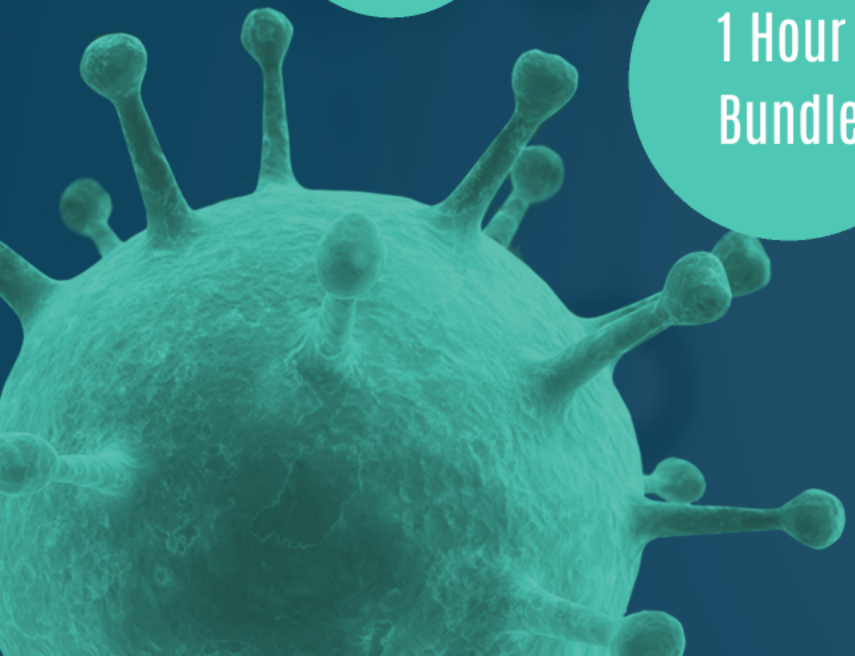

Designed by

Jen McKay, PharmD, BCPS

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