Sepsis:
What to do and when to do it

Tiffany Samples, DO
Hospitalist
St. Francis Medical Center
Cape Girardeau, MO

Disclosure

No conflicts of interest to disclose.

Objectives

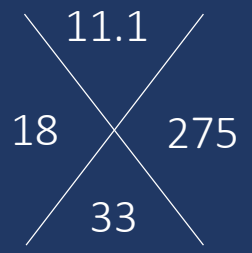
- Recognizing patients at high risk of decompensation from sepsis and how to intervene early to prevent decompensation.
- Pathogenesis and pathophysiology of sepsis, how interventions help correct pathophysiologic mechanisms.
- Formulating and implementing a treatment strategy for the septic patient.
- Identifying appropriate treatment algorithms based on current guidelines and trials.

Timeline of Sepsis Management

- Sepsis-1 (1991/1992)
- Early Goal Directed Therapy - Rivers Trial (2001)
- Sepsis-2 (2001)
- Surviving Sepsis Campaign (2004/2008/2012)
- ARISE/ProMISE/ProCESS (2014/2015)
- Sepsis-3 (2016)
- Surviving Sepsis Campaign 2016
- PRISM Investigators (2017)
- Surviving Sepsis Campaign 2021

Patient Case

- 67 year old female presents to the ER from home with 3 days of shortness of breath, productive cough, subjective fevers, and chills.
- PMH: Diabetes, Hypertension, Coronary Artery Disease
- Vital Signs: HR 120, RR 26, 115/72, Temp 100.8° F, 87% on room air



Procalcitonin – 7 ng/mL
Lactic Acid – 4.5 mmol/L
Flu A/B – Negative
COVID - Negative

Initial Evaluation

- Stabilize the patient – ABCs
- IV access
- Labs: CBC, CMP, Coagulation studies, lactic acid, ABG, blood cultures
  - Consider Procalcitonin
- Imaging

Recognizing decompensation risk

- Modified Early Warning Score (MEWS)
- National Early Warning Score 2 (NEWS)
- Quick Sequential Organ Failure Assessment Score (qSOFA)
- Systemic Inflammatory Response Syndrome Criteria (SIRS)

Recognizing decompensation risk

- Modified Early Warning Score (MEWS)
- National Early Warning Score 2 (NEWS)
- ~~Quick Sequential Organ Failure Assessment Score (qSOFA)~~
- Systemic Inflammatory Response Syndrome Criteria (SIRS)

MEWS

Physiologic Parameter	3	2	1	Score 0	1	2	3
Respiratory rate		<9		9-14	15-20	21-29	>30
Systolic Blood Pressure	≤70	71-80	81-100	101-199		≥200	
Pulse		<40	41-50	51-100	101-110	111-129	≥130
Consciousness				Alert			AVPU
Temp		<35 (95)		35-38.4		≥38.5 (101.3)	

https://www.mdcalc.com/calc/1875/modified-early-warning-score-mews-clinical-deterioration

NEWS2

Physiologic Parameter	3	2	1	Score 0	1	2	3
Respiratory rate	≤8		9-11	12-20		21-24	≥25
SpO2 (1)	≤91	92-93	94-95	≥96			
SpO2 (2)	≤83	84-85	86-87	88-92 ≥93 on RA	93-94 on Oxygen	95-96 on Oxygen	≥97 on Oxygen
Air or O2		Oxygen					
Systolic Blood Pressure	≤90	91-100	101-110	111-219			≥220
Pulse	≤40		41-50	51-90	91-110	111-130	≥131
Consciousness				Alert			CVPU
Temp	≤35		35.1-36	36.1-38	38.1-39	≥39.1	

https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2

NEWS2

NEWS Score	Clinical Risk	Response
Aggregate Score 0-4	Low	Ward-based response
Red Score (score of 3 in any individual parameter)	Low-Medium	Urgent ward-based response
Aggregate Score 5-6	Medium	Key threshold for urgent response
Aggregate Score $\geq$ 7	High	Urgent or emergency response

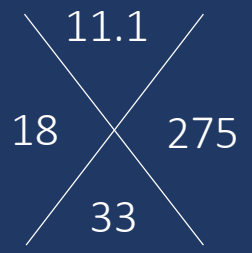
https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2

SIRS

- Temperature >38^{o} C (100.4^{o} F) or <36^{o} C (96.8^{o} F)
- Heart Rate >90
- Respiratory Rate >20 or $PaCO_2$ <32mmHg
- WBC >12,000 or <4,000 or >10% bands

Patient Case

- 67 year old female presents to the ER from home with 3 days of shortness of breath, productive cough, subjective fevers, and chills.
- PMH: Diabetes, Hypertension, Coronary Artery Disease
- Vital Signs: HR 120, RR 26, 115/72, Temp 100.8° F, 87% on room air



Procalcitonin – 7 ng/mL
Lactic Acid – 4.5 mmol/L
Flu A/B – Negative
COVID - Negative

Patient Case

- MEWS - 4
- NEWS2 - 9

NEWS2

NEWS Score	Clinical Risk	Response
Aggregate Score 0-4	Low	Ward-based response
Red Score (score of 3 in any individual parameter)	Low-Medium	Urgent ward-based response
Aggregate Score 5-6	Medium	Key threshold for urgent response
Aggregate Score $\geq$ 7	High	Urgent or emergency response

https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2

Risk Factors for Decompensation

- Advanced Age
- Bacteremia
- Community Acquired Pneumonia (CAP)
- Diabetes (DM)
- Genetic Polymorphisms
- Immunosuppressed
- ICU Admission
- Obesity
- Previous Hospitalization

Pathogenesis of Sepsis

- Immune System
- Inflammatory Cascade
- Alterations in Hemostasis
- Microcirculatory and Mitochondrial Dysfunction

Pathogenesis of Sepsis

- Immune System
  - Innate – initial response (minutes-hours)
  - Adaptive – delayed response (days)

Pathogenesis of Sepsis

- Inflammatory Cascade
  - Pro-inflammatory cytokines: TNF-α, IL-1β, NF-$\kappa\beta$
    - Fever
    - Hypotension
    - Capillary leakage with decreased intravascular volume
    - Myocardial depression
  - Anti-inflammatory cytokines: IL-4 and IL-10
    - Still not fully understood

Pathogenesis of Sepsis

- Alterations in Hemostasis
  - Increase in procoagulant factors and decrease in anticoagulant factors

Pathogenesis of Sepsis

- Microcirculatory Dysfunction
  - Endothelial cell dysfunction
  - Increased Leukocyte Adhesion
  - Microthrombi
  - Inability of Red Blood Cells (RBC) to deform/change shape
  - Altered perfusion pressures

Pathogenesis of Sepsis

- Mitochondrial Dysfunction
  - Impaired cellular utilization of oxygen

Pathophysiology of Sepsis

- Central Nervous System
- Circulatory
- Gastrointestinal
- Hematologic
- Hepatic
- Metabolic
- Renal
- Respiratory

Pathophysiology of Sepsis

- Central Nervous System
  - Encephalopathy

Pathophysiology of Sepsis

- Circulatory
  - Hypovolemic Shock
  - Cardiogenic Shock
  - Distributive Shock

Pathophysiology of Sepsis

- Gastrointestinal

Pathophysiology of Sepsis

- Hematologic
  - Thrombocytopenia
  - Prolonged PT
  - DIC

Pathophysiology of Sepsis

- Hepatic
  - Cholestasis
  - Ischemic Hepatitis (Shock Liver)

Pathophysiology of Sepsis

- Metabolic
  - Loss of glycemic control
  - Metabolic acidosis

Pathophysiology of Sepsis

- Renal
  - Oliguria
  - Acute renal failure requiring dialysis

Pathophysiology of Sepsis

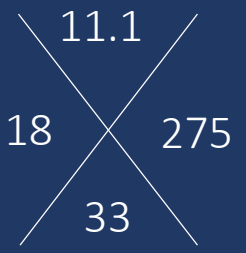
- Respiratory
  - Acute Lung Injury
  - Acute Respiratory Distress Syndrome (ARDS)

Initial Intervention

- IVF – 30mL/kg (ideal body weight)
- Empiric Antibiotics

Patient Case

- 67 year old female presents to the ER from home with 3 days of shortness of breath, productive cough, subjective fevers, and chills.
- Repeat Vital Signs: HR 127, RR 25, 105/79, Temp 100.8^{o} F, 93% on 2L NC



Procalcitonin – 7 ng/mL
Lactic Acid – 4.5 mmol/L
Flu A/B – Negative
COVID - Negative

Patient Case

- 30mL/kg IBW of Lactated Ringers
- Ceftriaxone + Azithromycin

Initial Intervention – Physiology

- Capillary leak → Intravascular Volume Loss → Hypotension
  - GOAL: Increase intravascular volume to obtain adequate cardiac filling pressures
  - CHALLENGE: Knowing the optimal intravascular volume

Initial Intervention – Monitoring

- Optimal Intravascular Volume?
  - MAP $\geq$ 65
  - Static Monitoring
  - Dynamic Monitoring

Initial Intervention – Monitoring

- Static Monitoring
  - Central Venous Pressure (CVP)
  - Central Venous Oxyhemoglobin Saturation ($ScvO_2$)

Initial Intervention – Monitoring

- Dynamic Monitoring
  - Stroke Volume
  - Stroke Volume Variation
  - Pulse Pressure Variation
  - Echocardiography
  - Passive Leg Raise

Initial Intervention – Monitoring

- Physical Exam
  - Temperature of extremities
  - Skin mottling
  - Capillary Refill Time (CRT)
- Labs
  - Serum Lactate
  - Arterial Blood Gases

Patient Case

- 67 year old female
- Received 2L LR + Antibiotics
- Repeat Vital Signs: HR 104, RR 18, 120/83, Temp 99^{o} F, 93% on 2L NC
- Repeat Lactic Acid – 2.5 mmol/L
- Admit to Hospitalist – closely monitored unit

Source Control

- Obtain source control as soon as possible
- Remove any potentially infected devices

Vasopressors

- Norepinephrine
- Vasopressin

Additional Treatment Considerations

- Bicarbonate
- Glucocorticoids
- Inotropes
- Red Blood Cells

Additional Treatment Considerations

- Bicarbonate
  - Should NOT be routinely administered for lactic acid induced acidosis
  - Can be considered with concomitant AKI or severe acidosis (pH < 7.1)

Additional Treatment Considerations

- Glucocorticoids – Hydrocortisone
  - Relative Adrenal Insufficiency
    - ACTH Stimulation Test and Serum Cortisol – unreliable
  - Consider administration in refractory shock

Questions???

References

Bone, Roger C. et al. “Definitions For Sepsis And Organ Failure.” *Chest*, vol 103, no. 2, 1993, p. 1644-1655. *Elsevier BV*, doi:10.1378/chest.103.2.656-c.

Dellinger RP. (2019). Severe Sepsis and Septic Shock. In JE Parillo & RP Dellinger (Eds), *CRITICAL CARE MEDICINE : Principles of Diagnosis and Management in the Adult* (5th Ed., pp. 323-345). Elsevier.

Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., Coopersmith, C. M., French, C., Machado, F. R., Mcintyre, L., Ostermann, M., Prescott, H. C., Schorr, C., Simpson, S., Wiersinga, W. J., Alshamsi, F., Angus, D. C., Arabi, Y., Azevedo, L., Beale, R., Beilman, G., & Belley-Cote, E. (2021). Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock 2021. *Critical Care Medicine*, *49*(11).

Kaufman, DA. Glucocorticoid therapy in septic shock in adults. In: UpToDate, Parsons, PE (Ed), Wolters Kluwer. (Accessed on December 10, 2023.)

References

Mouncey, Paul et al. “Trial of Early, Goal-Directed Resuscitation for Septic Shock.” *NEJM*, vol 372, no. 14, 2015, p. 1301-1311, *NEJM*. doi:10.1056/NEJMoa1500896.

Neviere, R. Pathophysiology of sepsis. In: UpToDate, Manaker, S., Sexton, DJ (Ed), Wolters Kluwer. (Accessed on December 10, 2023.)

Neviere, R. Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis. In: UpToDate, Gong, MN (Ed), Wolters Kluwer. (Accessed on December 10, 2023.)

Peake, Sandra et al. “Goal-Directed Resuscitation for Patients with Early Septic Shock.” *NEJM*, vol 371, no. 16, 2014, p. 1496-1506, *NEJM*. doi:10.1056/NEJMoa1404380.

Rivers, Emanuel et al. “Early Goal-Directed Therapy In The Treatment Of Severe Sepsis And Septic Shock.” *New England Journal of Medicine*, vol 345, no. 19, 2001, p. 168-1377. *New England Journal of Medicine*. doi:10.1056/nejmoa010307.

References

Schmidt, GA, Mandel, J. Evaluation and management of suspected sepsis and septic shock in adults. In: UpToDate, Sexton, DJ, Zachrison, KS, Gong, MN, Wolters Kluwer. (Accessed on December 10, 2023.)

Wiederkehr, M., Emmett, M. Bicarbonate therapy in lactic acidosis. In: UpToDate, Sterns RH (Ed), Wolters Kluwer. (Accessed on February 17, 2024.)

Yealy, Donald et al. “A Randomized Trial of Protocol-Based Care for Early Septic Shock.” *NEJM*, vol 370, no. 18, 2014, p. 1683-1693. *NEJM*. doi:10.1056/NEJMoa1401602.