Sepsis:
Diagnosis & Management

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Disclosures

Grant funding

CIHR, NIH, Research Manitoba, CancerCare Manitoba Foundation, Victoria General Hospital Foundation, Peter Munk Cardiac Centre, LifeArc, Thistledown, Ontario Together

Commercial interests

Grants/Research Support:	None
Speakers Bureau/Honoraria:	None
Consulting Fees:	None

Case

49 year old with, recent 4 admission to hospital for CVA. Recent falls at home. Presents with confusion, fever, no urine output for 24 hours.

On exam: BP 90.50. HR 110. RR 21, 96% on room air

Left leg cellulitis. No evidence of necrotising fasciitis

What's the diagnosis?

How would you treatment this patient?

Objectives

By attending this session, the attendee will have an appreciation for:

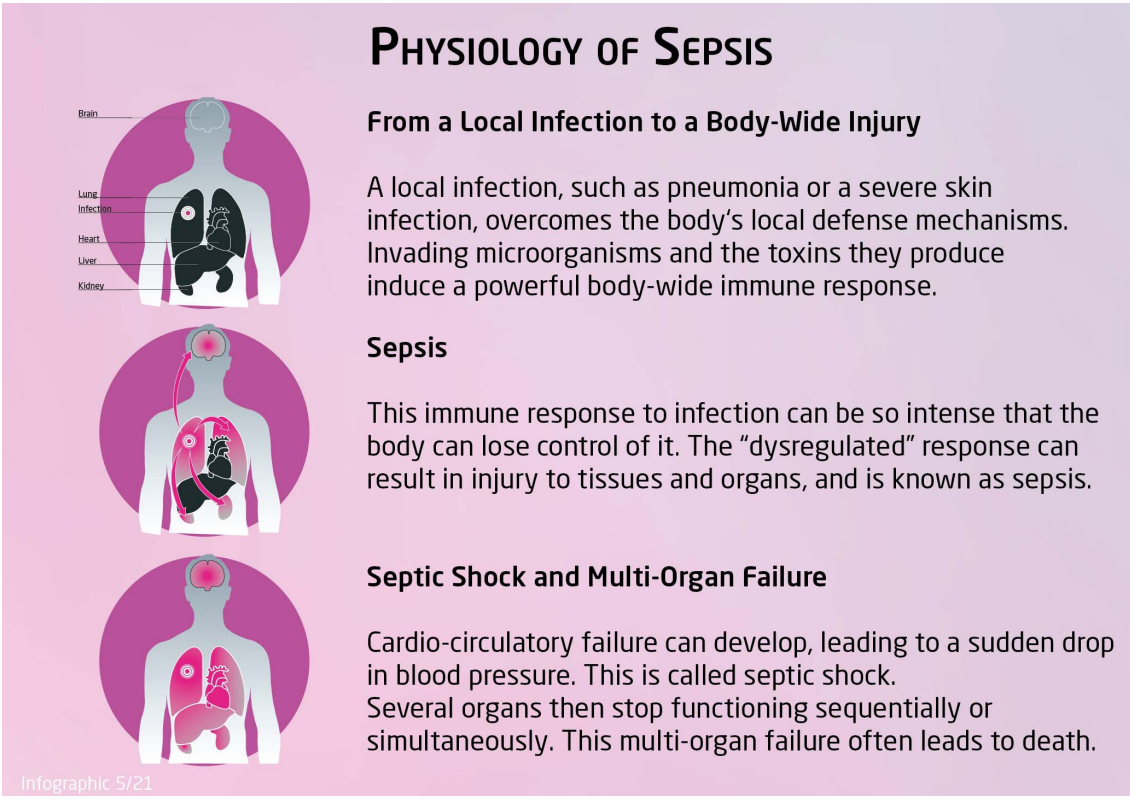
1. Signs and symptoms of sepsis
2. What constitutes appropriate initial therapies for patients with sepsis
3. Adjunctive or emerging therapies in sepsis beyond antimicrobials
4. Long term consequences of sepsis

Background

- 47-50 million cases of sepsis worldwide annually
- 1 in 5 deaths worldwide is associated with sepsis
- Most common preventable cause of death
- Up to 50% of survivors suffer long term physical or psychological effects

Defining sepsis

- Life-threatening organ dysfunction caused by a dysregulated host response to infection *(Sepsis 3 definition)*
- Organ dysfunction = change of ≥2 in SOFA score
- Represents a progression:
  - Infection
  - Sepsis
  - Septic Shock



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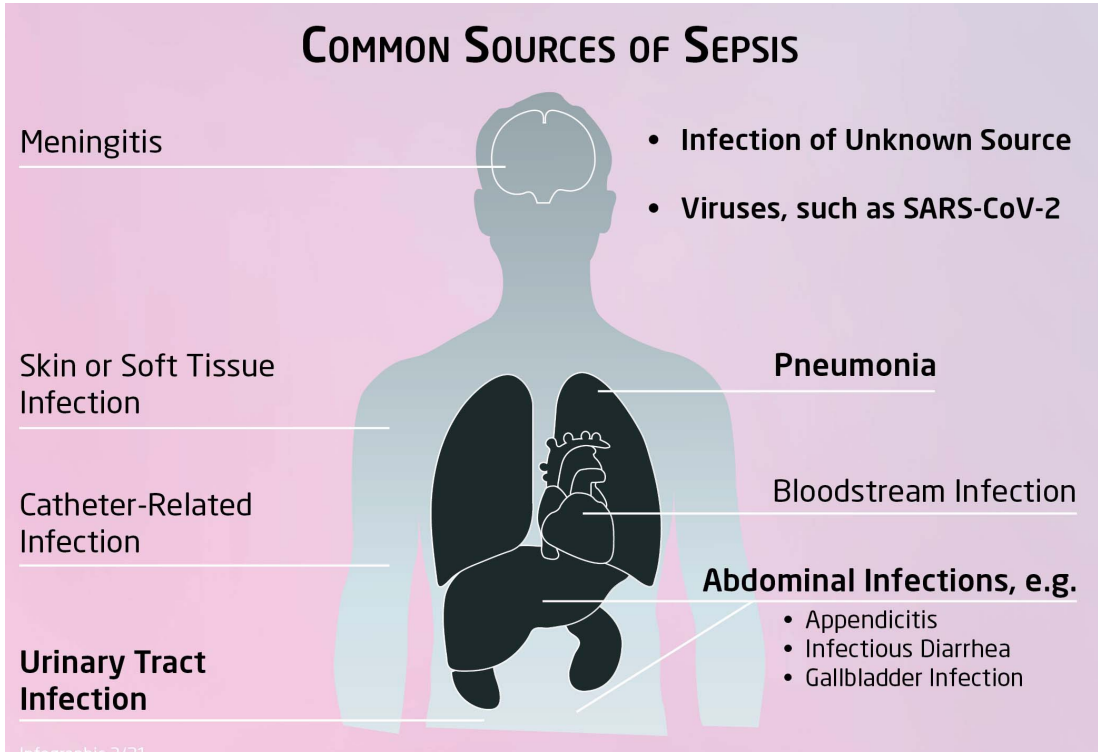
Common causes & sources of sepsis

- Infection
- Infection
- Infection
- Pancreatitis
- Burns



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Who's at risk for sepsis?

- **People with chronic diseases**
  - e.g., lung, heart, liver, kidney
- **People with weakened immune systems**
  - e.g., Diabetes, chemotherapy, immunosuppressives, AIDS
- Children under 1 year
- Adults over 60
- People with no spleen

"The patient in the next bed is highly infectious. Thank God for these curtains."

Signs & symptoms of sepsis

- **S**lurred speech or confusion
- **E**xtreme shivering or muscle pain
- **P**assing no urine all day
- **S**evere Breathlessness
- **I**mpending doom / feels like you're going to die
- **S**kin Mottled or discoloured

**Hypotension is a late sign = septic shock

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When to suspect sepsis? – Signs & Symptoms

- **Look for signs and symptoms of SEPSIS**
- Use an early warning scoring system to help identify unwell patients
  - NEWS2 – National Early Warning Score
  - Score of 5 should make you think ‘could this be sepsis’

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When to suspect sepsis? – Early Warning Score

- Look for signs and symptoms of SEPSIS
- **Use an early warning scoring system to identify unwell patients**
  - **NEWS2 – National Early Warning Score**
  - A News score of 5 should make you think ‘could this be sepsis!’

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

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When to suspect sepsis? – Think think of the organs!

- Look for signs and symptoms of SEPSIS
- Use an early warning scoring system to identify unwell patients
  - NEWS2 – National Early Warning Score
  - A News score of 5 should make you think ‘could this be sepsis!’
- **SOFA score change of ≥2 strongly supports a diagnosis of sepsis**
  - Score is primarily used in clinical research

Organ System, **Measurement**	**SOFA Score**				
	0	1	2	3	4
Respiration PaO_2/FiO_2, mmHg	Normal	<400	<300	<200 (with respiratory support)	<100 (with respiratory support)
Coagulation Platelets $x10^3/mm^3$	Normal	<150	<100	<50	<20
Liver Bilirubin, mg/dL (µmol/l)	Normal	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (<204)
Cardiovascular Hypotension	Normal	MAP<70 mmHg	Dopamine ≤5 or dobutamine (any dose)**	Dopamine >5 or epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Central Nervous System Glasgow Coma Score	Normal	13-14	10-12	6-9	<6
Renal Creatinine, mg/dL (µmol/l) or Urine output	Normal	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440) or <500 mL/day	>5.0 (>440) or <200 mL/day

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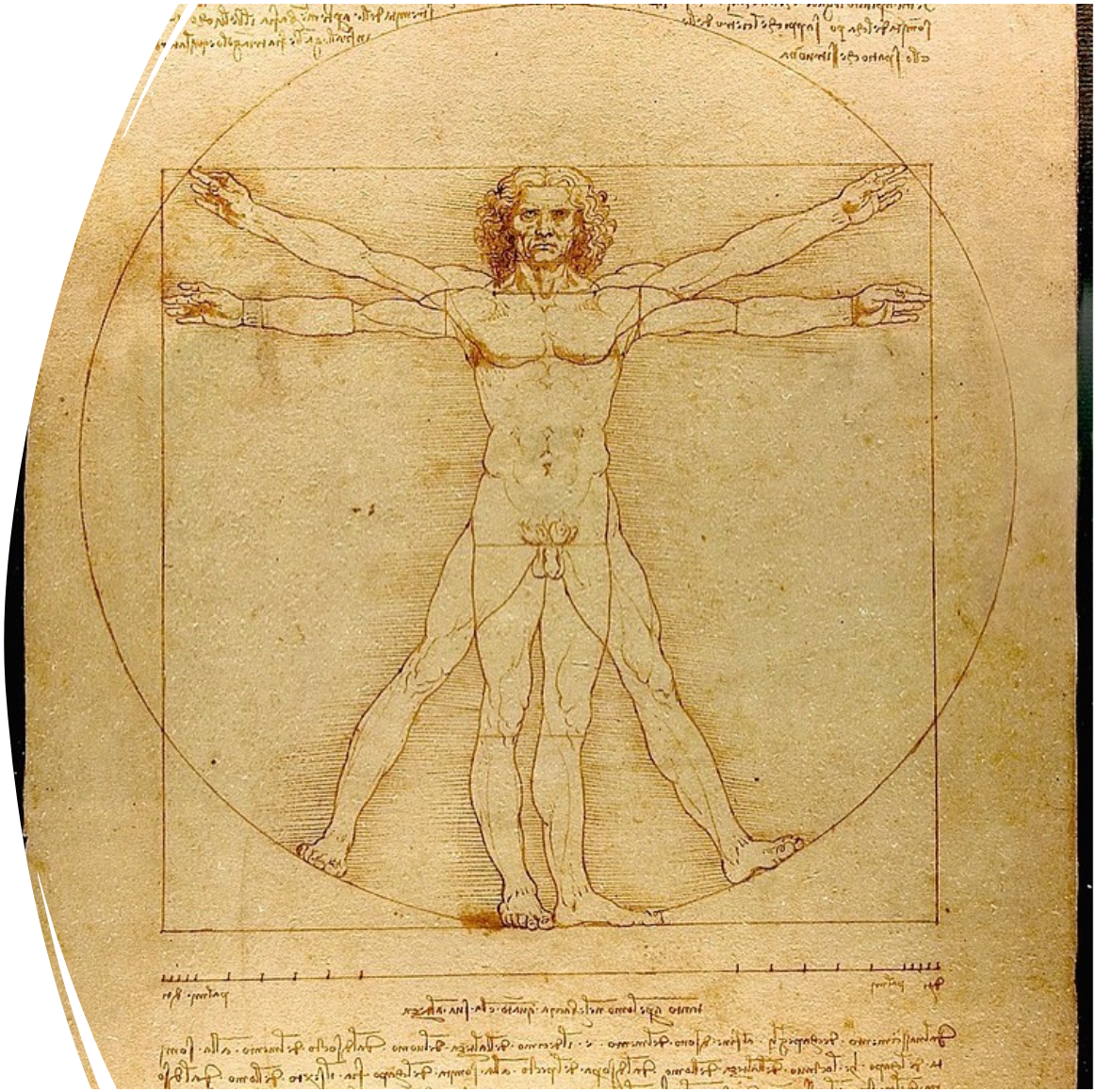
The art & science of suspecting sepsis

- No scoring system is perfect
- Use your clinical judgement
- Look for organ function
- Pay attention to markers of perfusion
  - capillary refill, lactate, urine output, mental status
- Find the source!



Tenants of Sepsis management

Sepsis is a medical emergency

- Resuscitation
- Antimicrobial therapy
- Source control
- Prevention future infections

Diagnosis & Management – 1 to 3 hours
For septic adults **NOT** in shock (MAP >65 mmHg/lactate < 2 mmol/L)

1. **Establish goals of care**
2. **Identify the source of infection**
   - Take cultures from the site(s) of suspected infection
   - Obtain blood cultures **(2 bottles from 2 sites)** PLUS from indwelling lines that are >48 hrs old
   - Urine, sputum, wound, and/or line cultures as appropriate
3. **Administer antibiotics – Ideally tailored to the infectious source**
4. Consider fluids if signs of hypoperfusion (30 mL/kg of crystalloid within 3 hrs)

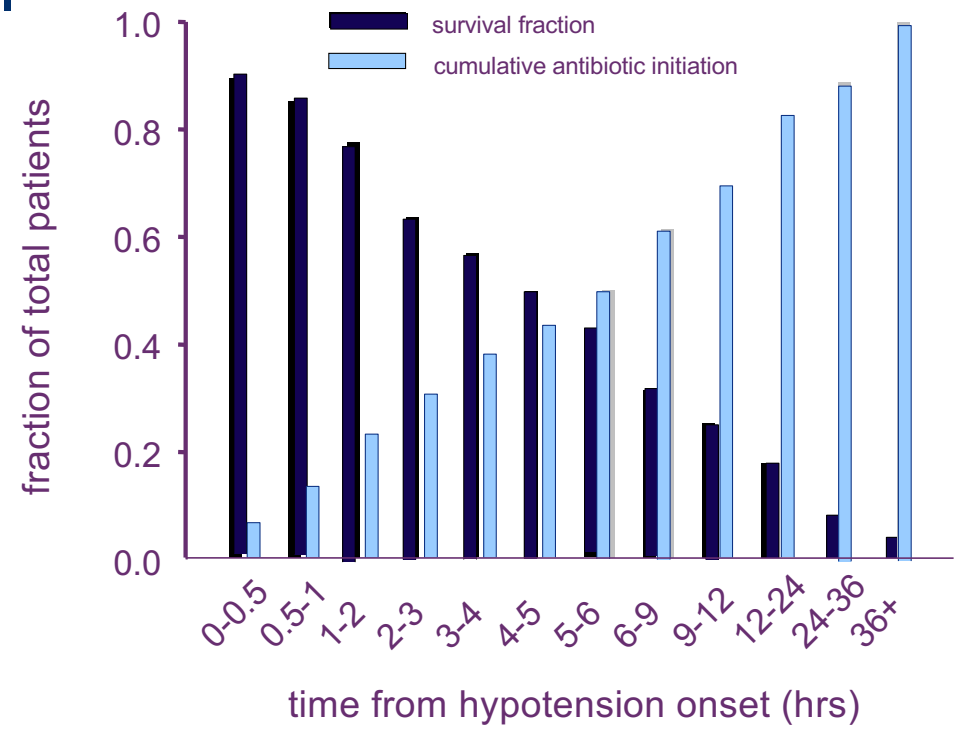
Diagnosis & Management – the 1st hour
For septic adults **WITH** shock (MAP < 65 mmHg OR lactate >2 mmol/L)

1. **Establish goals of care**
2. **Resuscitate**
   - If MAP <65 or lactate > 2 mmol/L, give 30 mL/kg of crystalloid within 3 hrs
3. **Identify the source of infection**
   - Take cultures from the site(s) of suspected infection
   - Obtain blood cultures **(2 bottles from 2 sites)** PLUS from indwelling lines that are >48 hrs old
   - Urine, sputum, wound, and/or line cultures as appropriate
4. **Administer broad-spectrum antibiotics**

*Transfer to an acute care facility. Obtain an ICU consult if hypotension persists despite fluid administration

Antibiotics: Time is survival

- Every hour delay of effective antibiotics equals 7.6% reduction in survival in septic shock



Kumar et al. *CCM*. 2006:34:1589-96.

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Effective antibiotics – 1st hour if shock

Undifferentiated Source	Piperacillin-tazobactam + vancomycin Meropenem + vancomycin (if βeta-lactam allergy)
CNS	Ceftriaxone + vancomycin (community infections) Meropenem + vancomycin (if βeta-lactam allergy; (hospital acquired or hardware related) If >50 yrs or immunosuppressed, add ampicillin
GI/GU source	Piperacillin-tazobactam
Skin and soft tissue	Vancomycin + ceftriaxone Meropenem + vancomycin (if β-lactam allergy, ESBL, diabetic wounds)
Community acquired pneumonia (CAP)	Ceftriaxone and azithromycin Levofloxacin (if beta-lactam allergy)

* Final decision of antimicrobials depends on clinical specifics, patient & microbial history, and local ecology

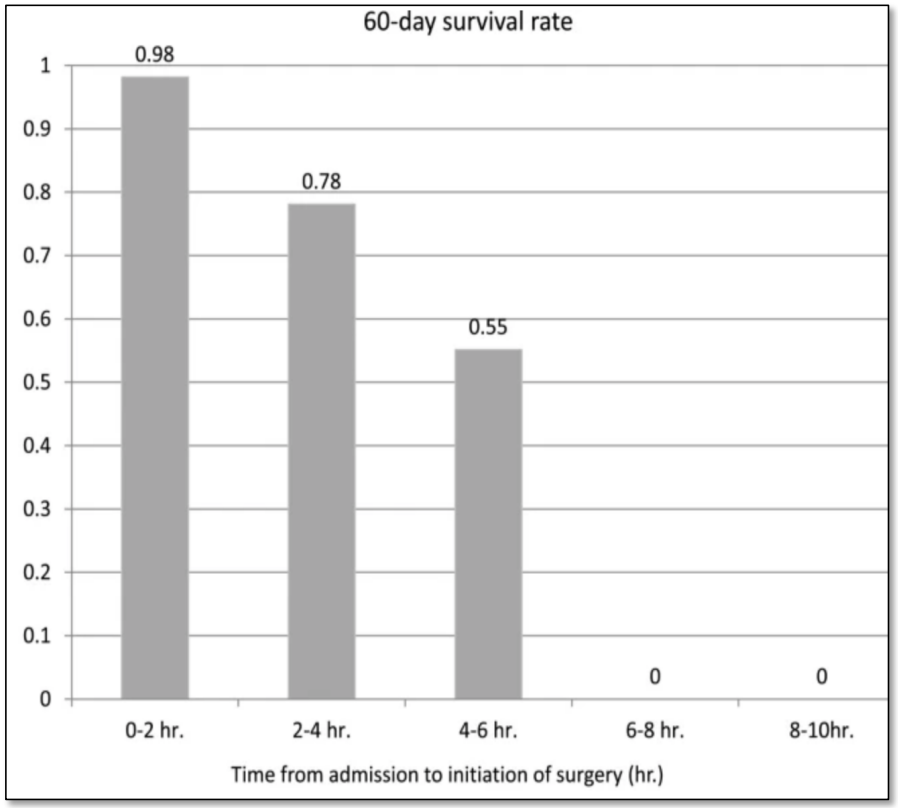
Risk factors for pathogens that require specific antimicrobial considerations

Multi-drug resistant (MDR) Gram-negative pathogens	MRSA	Candida
• Prior history of infection with MDR organism • Prior history of colonization with MDR organism • Local prevalence of MDR gram-negative pathogens • Hospital-acquired infection • Use of broad-spectrum antibiotics within the past 90 days • Selective digestive decontamination • Hospitalization abroad within the past 90 days • Travel within the past 90 days to a country highly endemic with MDR gram-negative pathogens	• Prior history of MRSA infection • Prior history of MRSA colonization • Recent use of intravenous antibiotics History of recurrent skin infections • History of chronic wounds • Presence of invasive devices • End-stage renal disease, receiving renal replacement therapy • Recent hospital admission • Severe critical illness	• Extended ICU length of stay • Renal failure • Mechanical ventilation • Parenteral nutrition • Neutropenia • Recent abdominal surgery • Immunocompromised • Candida colonization at multiple sites • Use of broad-spectrum antibiotics • Gastrointestinal perforations • Anastomotic leaks • Severe thermal injuries

Adapted from: Lother S et. al. Antibiotic, Antifungal, & Anti-viral therapies. In Comprehensive Critical Care. 2017.

Source Control

- Establish source control
  - Ideally within 6 hours
- Remove, debride, drain, wash, amputate, as required



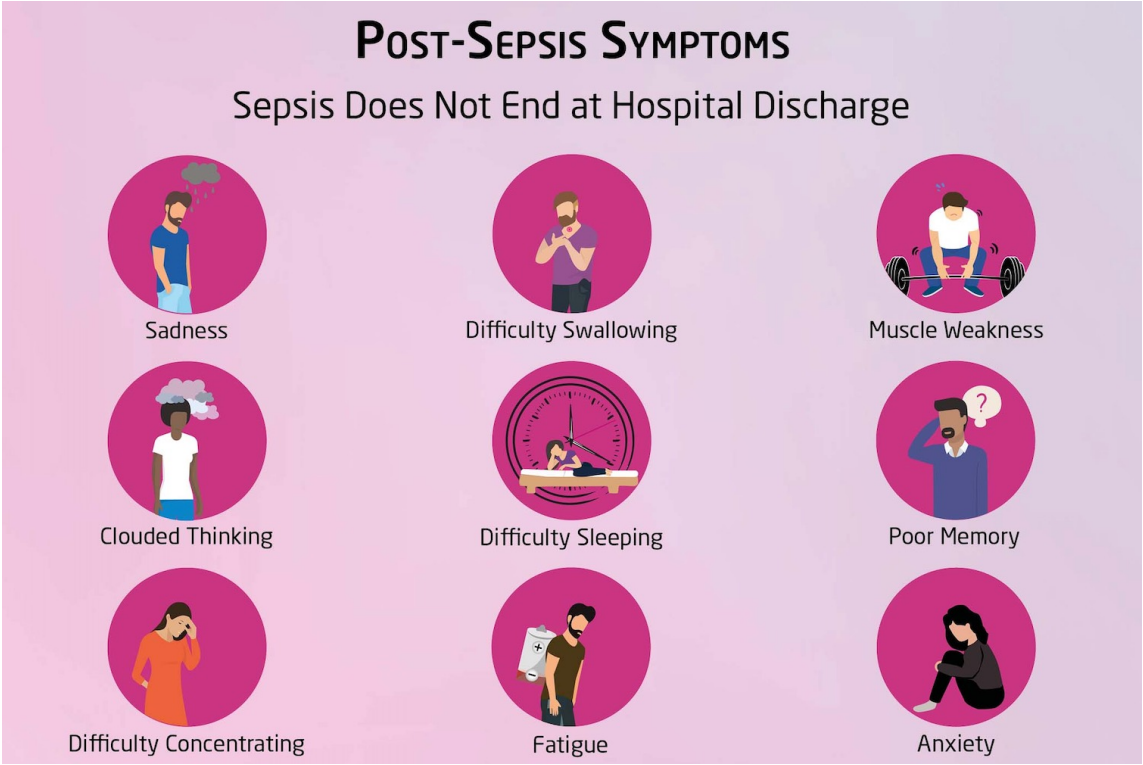
Azuhata. Crit Care. 2014

Potential adjunctive therapies in sepsis
Only after consultation with ID/ICU

Steroids	**Sometimes** – where blood pressure has responded poorly to adequate fluid resuscitation and vasopressors
Vitamin C	**NO** – harmful in RCTs
Therapeutic-dose heparin	*Insufficient evidence in undifferentiated sepsis. RCTs needed*
Plasma Exchange	*Insufficient evidence in undifferentiated sepsis. RCTs needed*
COVID-19 specific adjunctive treatments (hospitalized patients)	Steroids Therapeutic-dose heparin Tocilizumab } Standard of care in COVID-19

Sepsis outcomes

- Death
- Limb loss
- Post-sepsis symptom
  - Up to 50% of survivors
  - Higher risk if critically ill
- PTSD



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Sepsis with organ dysfunction

Case

How would you treatment this patient?

Resuscitation:	2 L of normal saline bolus
Antimicrobial therapy:	ceftriaxone + vancomycin
Source control:	N/A
Prevention future infections:	Encouraged use of walker

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Reference material

Surviving sepsis Campaign Guidelines for the Management of Sepsis and Septic Shock.
https://journals.lww.com/ccmjournal/Fulltext/2021/11000/Surviving_Sepsis_Campaign__International.21.aspx

National Early Warning Score (NEWS 2)

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

https://www.sepsiscanada.ca

https://www.worldsepsisday.org

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