

# Sepsis

Σκούρτης Ι. Σκούρτης

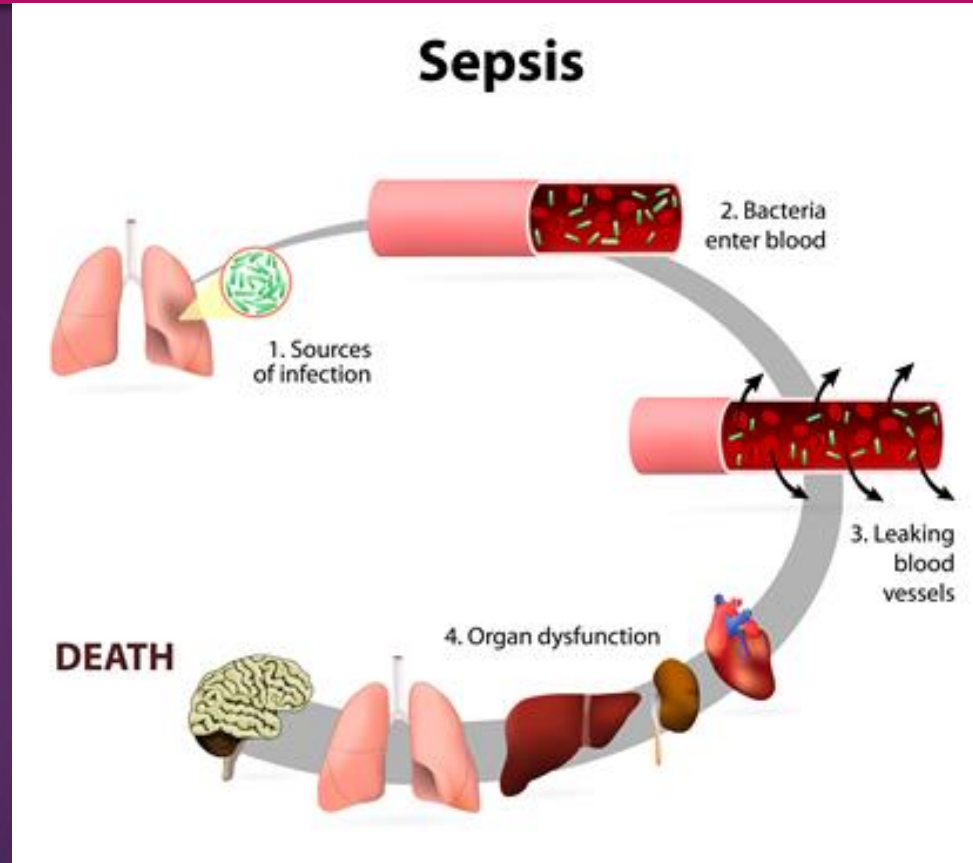
Επιμελητής Β' Παθολογίας-Τμήμα Επειγόντων Περιστατικών

ΓΝΑ «Ο Ευαγγελισμός»



**S E P S I S**

# Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection

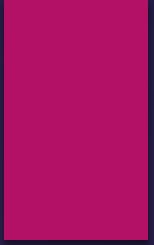


Singer M, Deutschman CS, Seymour CW, et al: The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315:801–810

# Septic shock

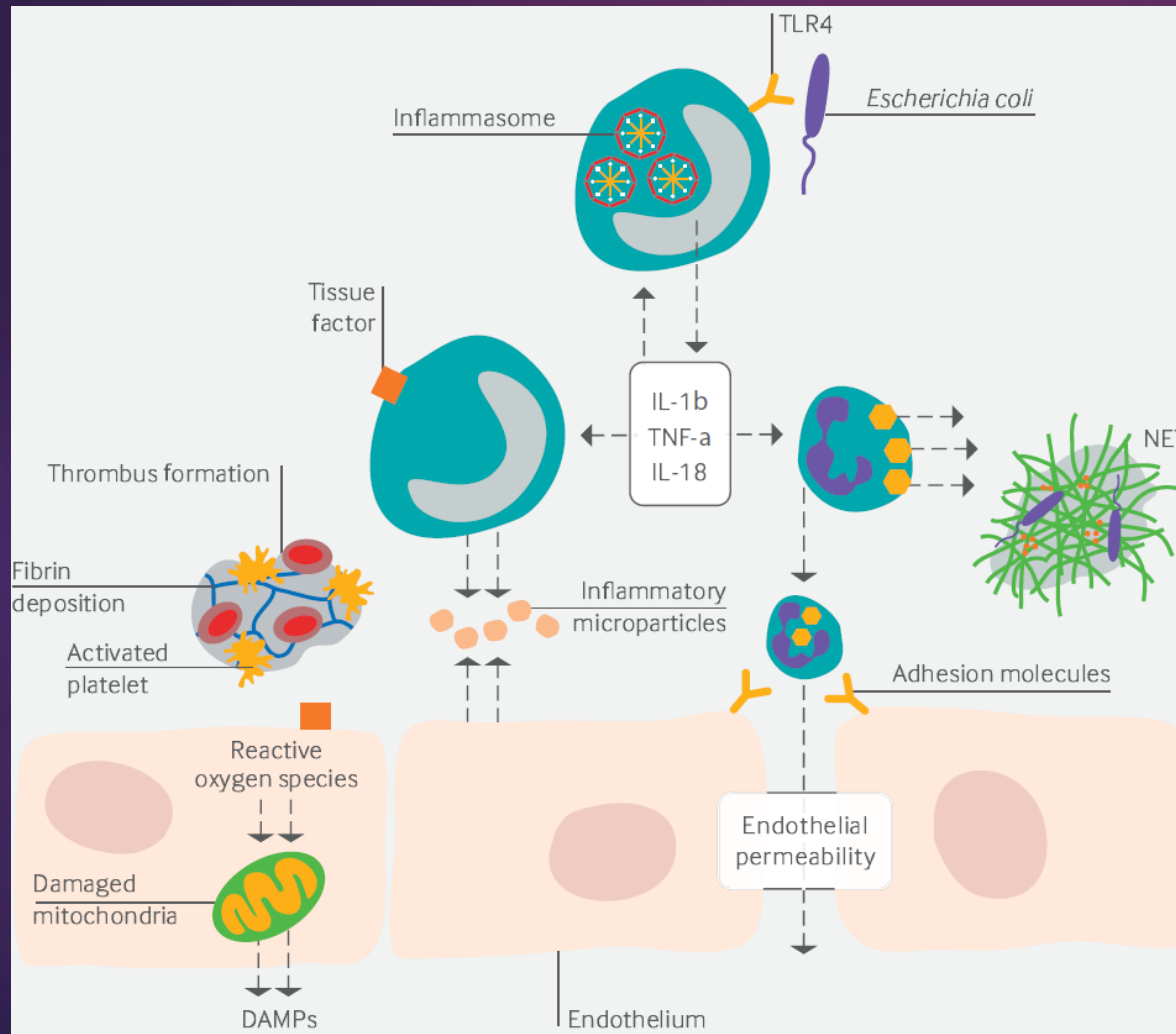
Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.

Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.



Sepsis and septic shock are major healthcare problems, impacting millions of people around the world each year and killing between one in three and one in six of those it affects

# Pathophysiology



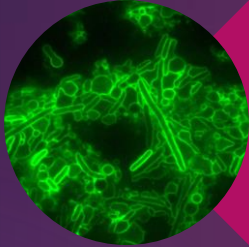
The self reinforcing pathophysiologic processes involved in sepsis.

Endothelial injury results in activation of monocytes and granulocytes, endothelial barrier breakdown, immunothrombosis, and disseminated intravascular coagulation.

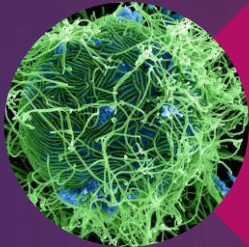
DAMPs= damage associated molecular patterns; IL= interleukin; TLR3= Toll-like receptor 3; TNF-4=tumor necrosis factor 4



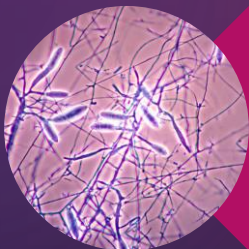
# Pathogens



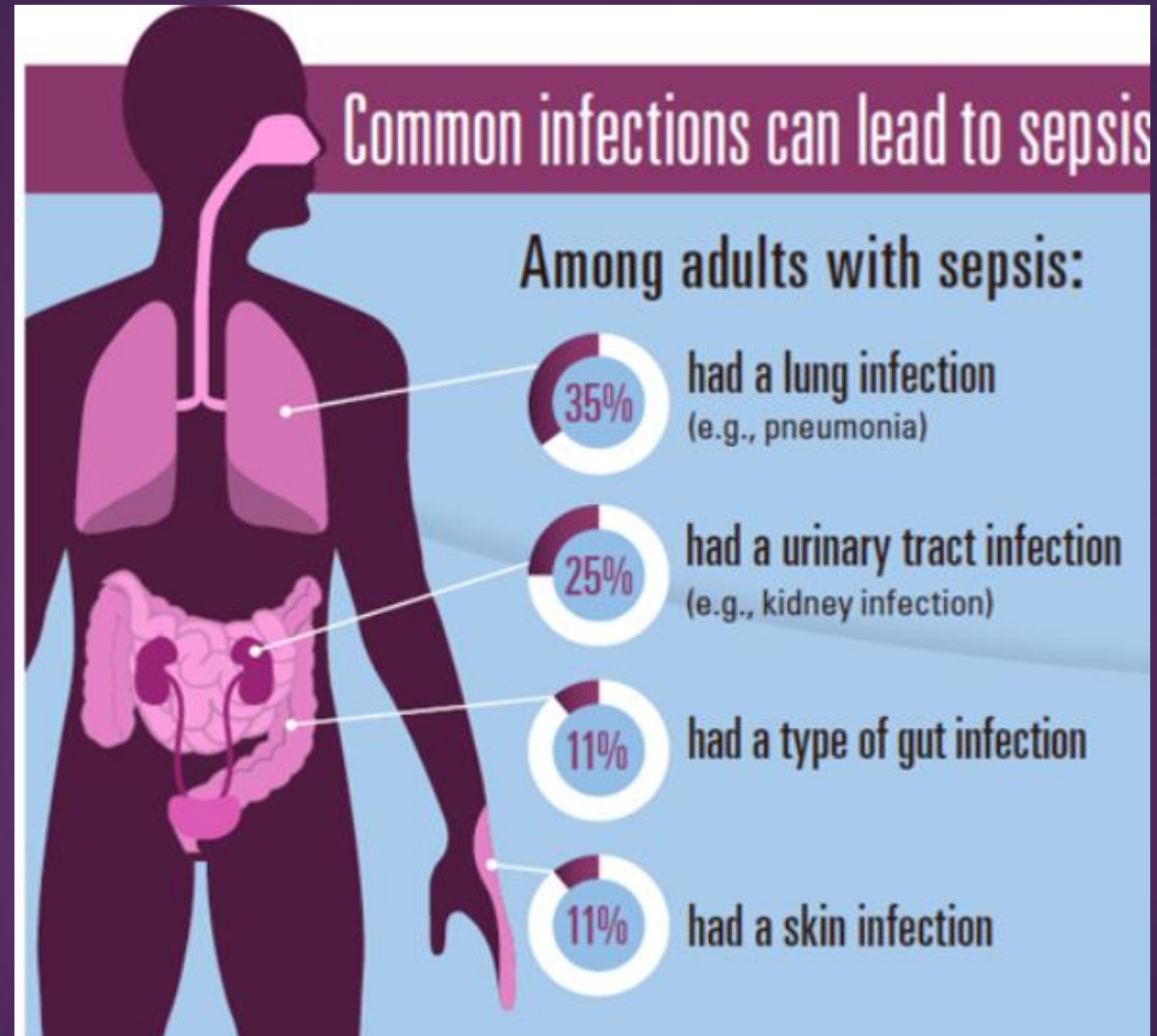
Bacteria have been shown to be the predominant pathogen of sepsis among patients with pathogens detected.



Sepsis caused by viruses is underdiagnosed worldwide



The incidence of fungal sepsis has increased over the past decade, but remains lower than bacterial sepsis





# Patient groups at higher risk of developing sepsis

Certain groups of people are more susceptible to developing sepsis:

- ✓ the very young (under 1 year) and older people (over 75 years) or people who are very frail
- people who have impaired immune systems because of illness or drugs, including:
  - people being treated for cancer with chemotherapy
  - people who have impaired immune function (for example, people with diabetes, people who have had a splenectomy, or people with sickle cell disease)
  - people taking long-term steroids
  - people taking immunosuppressant drugs to treat non-malignant disorders such as rheumatoid arthritis
- people who have had surgery, or other invasive procedures, in the past 6 weeks
- people with any breach of skin integrity (for example, cuts, burns, blisters or skin infections)
- people who misuse drugs intravenously
- people with indwelling lines or catheters.

# SEPSIS STEPS

## SIRS

T: >100.4 F  
< 96.8 F  
RR: >20  
HR: >90  
WBC: >12,000  
<4,000  
>10% bands  
PCO2 < 32 mmHg

## SEPSIS

2 SIRS

+

Confirmed  
or suspected  
infection

## SEVERE SEPSIS

Sepsis +

Signs of End  
Organ Damage

Hypotension  
(SBP <90)

Lactate >4 mmol

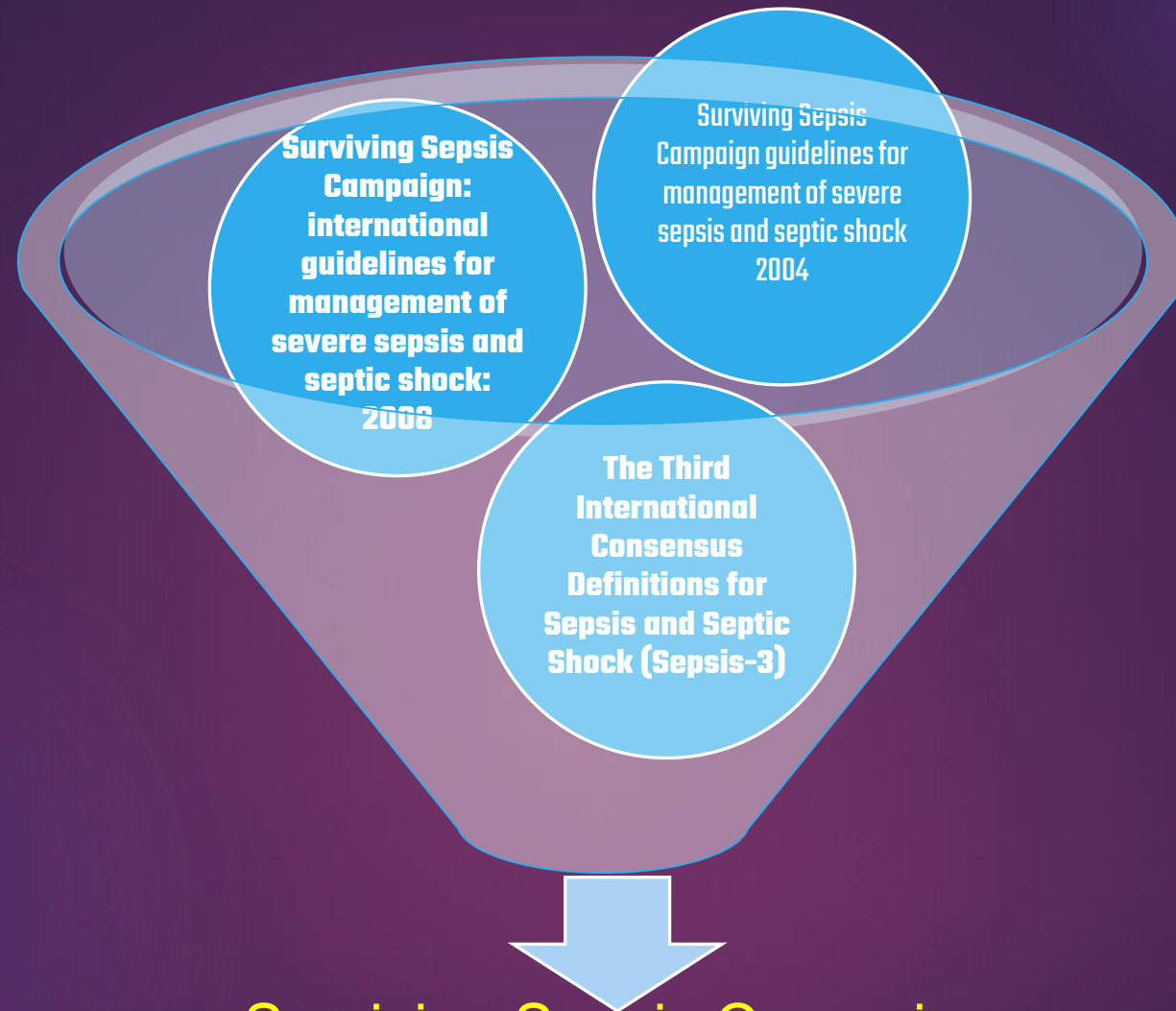
## SEPTIC SHOCK

Severe Sepsis  
with persistent:

Signs of End  
Organ Damage

Hypotension  
(SBP <90)

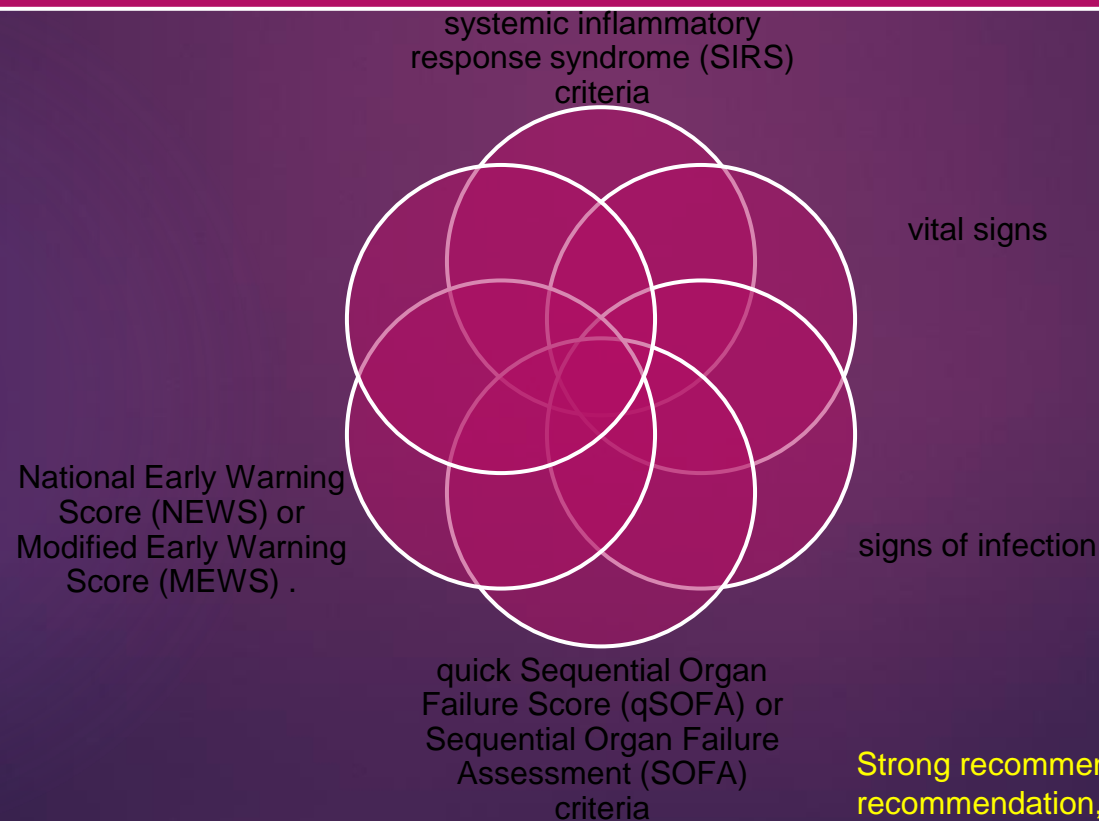
Lactate >4 mmol



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

# Screening for Patients With Sepsis and Septic Shock

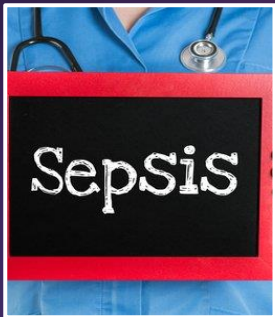
For hospitals and health systems, we recommend using a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients and standard operating procedures for treatment.



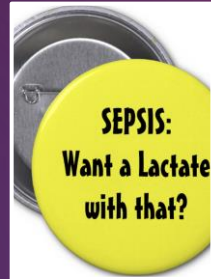
Strong recommendation, moderate quality of evidence for screening. Strong recommendation, very low-quality evidence for standard operating procedures

# Screening

Standard operating procedures for Sepsis, initially specified as Early Goal Directed Therapy have evolved to “usual care” which includes a standard approach with components of the sepsis bundle



early  
identification



lactate



cultures



antibiotics



fluids

Strong recommendation, moderate quality of evidence for screening. Strong recommendation, very low-quality evidence for standard operating procedures

We recommend **against** using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock.

Strong recommendation, moderate-quality evidence.



# qSOFA

uses three variables to predict death and prolonged ICU stay in patients with known or suspected sepsis:

a Glasgow Coma Score  $< 15$ ,

a respiratory rate  $\geq 22$  breaths/min and

a systolic blood pressure  $\leq 100$  mm Hg.

When any two of these variables are present simultaneously, the patient is considered qSOFA positive

# SIRS (Systemic Inflammatory Response Syndrome)

- ✓ Two or more of:
  - ✓ Temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$
  - ✓ Heart rate  $>90/\text{min}$
  - ✓ Respiratory rate  $>20/\text{min}$  or  $\text{PaCO}_2 <32 \text{ mm Hg}$  (4.3 kPa)
  - ✓ White blood cell count  $>12\,000/\text{mm}^3$  or  $<4000/\text{mm}^3$  or  $>10\%$  immature bands

Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med.* 1992;20(6):864-874.

## National Early Warning Score (NEWS) 2

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



# MEWS

| Score                   | 3   | 2     | 1      | 0       | 1       | 2       | 3            |
|-------------------------|-----|-------|--------|---------|---------|---------|--------------|
| Respiratory rate        |     | <9    |        | 9-14    | 15-20   | 21-29   | >30          |
| Heart rate              |     | <40   | 41-50  | 51-100  | 101-110 | 111-129 | >130         |
| Systolic blood pressure | <70 | 71-80 | 81-100 | 101-199 |         | >200    |              |
| Temperature             |     | <35   |        | 35-38,4 |         | >38,5   |              |
| Level of consciousness  |     |       |        | Alert   | Voice   | Pain    | Unresponsive |

Contact physician when MEWS score  $\geq 4$ , if oxygen saturation drops to  $<90\%$  with oxygen treatment and if you are concerned of the patients' condition.

| Color-code | MEWS score | Follow up/new measurements |
|------------|------------|----------------------------|
| Blue       | 0          | 24 hours                   |
| Yellow     | 1          | 8-12 hours                 |
| Orange     | 2          | 4-8 hours                  |
| Red        | 3-4        | 1-4 hours                  |
|            | $\geq 4$   | Contact physician          |



| SEPSIS SCREENING TOOL ACUTE ASSESSMENT   |   | AGE 12+      |
|--|---|--------------|
| <b>PATIENT DETAILS:</b><br><br>  | <b>DATE:</b><br><b>NAME:</b><br><b>DESIGNATION:</b><br><b>SIGNATURE:</b>  | <b>TIME:</b> |
| <h2 style="margin: 0;">01 START THIS CHART IF THE PATIENT LOOKS UNWELL OR NEWS2 IS 5 OR ABOVE</h2>   |   |              |
| <b>RISK FACTORS FOR SEPSIS INCLUDE:</b><br><div style="display: flex; justify-content: space-between;"> <div> <input type="checkbox"/> Age &gt; 75<br/> <input type="checkbox"/> Impaired immunity (e.g. diabetes, steroids, chemotherapy)         </div> <div> <input type="checkbox"/> Recent trauma / surgery / invasive procedure<br/> <input type="checkbox"/> Indwelling lines / IVDU / broken skin         </div> </div>  |   |              |
| <h2 style="margin: 0;">02 COULD THIS BE DUE TO AN INFECTION?</h2> <p><b>LIKELY SOURCE:</b></p> <div style="display: flex; justify-content: space-between;"> <div> <input type="checkbox"/> Respiratory<br/> <input type="checkbox"/> Brain         </div> <div> <input type="checkbox"/> Urine<br/> <input type="checkbox"/> Surgical         </div> <div> <input type="checkbox"/> Skin / joint / wound<br/> <input type="checkbox"/> Other         </div> <div> <input type="checkbox"/> Indwelling device         </div> </div>   | <div style="background-color: #ff0000; color: white; width: 20px; height: 20px; margin: 0 auto; transform: rotate(45deg);"></div> <p><b>SEPSIS UNLIKELY, CONSIDER OTHER DIAGNOSIS</b></p> |              |
| <h2 style="margin: 0;">03 ANY RED FLAG PRESENT?</h2> <div style="display: flex;"> <div style="flex: 1;"> <input type="checkbox"/> Objective evidence of new or altered mental state<br/> <input type="checkbox"/> Systolic BP ≤ 90 mmHg (or drop of &gt;40 from normal)<br/> <input type="checkbox"/> Heart rate ≥ 130 per minute<br/> <input type="checkbox"/> Respiratory rate ≥ 25 per minute<br/> <input type="checkbox"/> Needs O<sub>2</sub> to keep SpO<sub>2</sub> ≥ 92% (88% in COPD)<br/> <input type="checkbox"/> Non-blanching rash / mottled / ashen / cyanotic<br/> <input type="checkbox"/> Lactate ≥ 2 mmol/l<br/> <input type="checkbox"/> Recent chemotherapy<br/> <input type="checkbox"/> Not passed urine in 18 hours (&lt;0.5ml/kg/hr if catheterised)         </div> <div style="flex: 1; background-color: #ff0000; color: white; text-align: center; padding: 10px;"> <h1 style="margin: 0;">RED FLAG SEPSIS</h1> <p style="color: white; font-weight: bold;">START SEPSIS SIX</p> </div> </div>  |   |              |
| <h2 style="margin: 0;">04 ANY AMBER FLAG PRESENT?</h2> <div style="display: flex;"> <div style="flex: 1;"> <input type="checkbox"/> Relatives concerned about mental status<br/> <input type="checkbox"/> Acute deterioration in functional ability<br/> <input type="checkbox"/> Immunosuppressed<br/> <input type="checkbox"/> Trauma / surgery / procedure in last 8 weeks<br/> <input type="checkbox"/> Respiratory rate 21-24<br/> <input type="checkbox"/> Systolic BP 91-100 mmHg<br/> <input type="checkbox"/> Heart rate 91-130 or new dysrhythmia<br/> <input type="checkbox"/> Temperature &lt;36°C<br/> <input type="checkbox"/> Clinical signs of wound infection         </div> <div style="flex: 1; background-color: #ffcc00; text-align: center; padding: 10px;"> <h1 style="margin: 0;">FURTHER REVIEW REQUIRED:</h1> <p style="color: white; font-weight: bold;">- SEND BLOODS AND REVIEW RESULTS<br/>- ENSURE SENIOR CLINICAL REVIEW within 1HR</p> <p>TIME OF REVIEW: <span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span></p> <p>ANTIBIOTICS REQUIRED:<br/> <input type="checkbox"/> Yes   <input type="checkbox"/> No         </p> </div> </div> |   |              |
| <b>NO AMBER FLAGS = ROUTINE CARE / CONSIDER OTHER DIAGNOSIS</b>  |   |              |

| SEPSIS SCREENING TOOL - THE SEPSIS SIX  |  | AGE 12+      |
|---|--|--------------|
| <b>PATIENT DETAILS:</b><br><br>   | <b>DATE:</b><br><b>NAME:</b><br><b>DESIGNATION:</b><br><b>SIGNATURE:</b>   | <b>TIME:</b> |
| <h2 style="margin: 0;">COMPLETE ALL ACTIONS WITHIN ONE HOUR</h2>  |  |              |
| <h2 style="margin: 0;">01 ENSURE SENIOR CLINICIAN ATTENDS</h2> <p>NOT ALL PATIENTS WITH RED FLAGS WILL NEED THE 'SEPSIS 6' URGENTLY. A SENIOR DECISION MAKER MAY SEEK ALTERNATIVE DIAGNOSES/ DE-ESCALATE CARE. RECORD DECISIONS BELOW</p> <p>NAME: _____ GRADE: _____</p> | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <h2 style="margin: 0;">02 OXYGEN IF REQUIRED</h2> <p>START IF O<sub>2</sub> SATURATIONS LESS THAN 92% - AIM FOR O<sub>2</sub> SATURATIONS OF 94-98%<br/>IF AT RISK OF HYPERCARBIA AIM FOR SATURATIONS OF 88-92%</p>   | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <h2 style="margin: 0;">03 OBTAIN IV ACCESS, TAKE BLOODS</h2> <p>BLOOD CULTURES, BLOOD GLUCOSE, LACTATE, FBC, U&amp;Es, CRP AND CLOTTING<br/>LUMBAR PUNCTURE IF INDICATED</p>  | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <h2 style="margin: 0;">04 GIVE IV ANTIBIOTICS</h2> <p>MAXIMUM DOSE BROAD SPECTRUM THERAPY<br/>CONSIDER: LOCAL POLICY / ALLERGY STATUS / ANTIVIRALS</p>  | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <h2 style="margin: 0;">05 GIVE IV FLUIDS</h2> <p>GIVE FLUID BOLUS OF 20 ml/kg if age &lt;16, 500ml if 16+<br/>NICE RECOMMENDS USING LACTATE TO GUIDE FURTHER FLUID THERAPY</p>  | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <h2 style="margin: 0;">06 MONITOR</h2> <p>USE NEWS2. MEASURE URINARY OUTPUT: THIS MAY REQUIRE A URINARY CATHETER REPEAT LACTATE AT LEAST ONCE PER HOUR IF INITIAL LACTATE ELEVATED OR IF CLINICAL CONDITION CHANGES</p>   | <b>TIME</b><br><span style="border: 1px solid black; padding: 2px 5px;">  </span> : <span style="border: 1px solid black; padding: 2px 5px;">  </span> |              |
| <b>RED FLAGS AFTER ONE HOUR - ESCALATE TO CONSULTANT NOW</b>  |  |              |
| <b>RECORD ADDITIONAL NOTES HERE:</b><br>e.g. allergy status, arrival of specialist teams, de-escalation of care, delayed antimicrobial decision making, variance from Sepsis Six  |  |              |

In 2015, the UK Sepsis Trust (UKST) developed an operational tool called Red Flag Sepsis to empower junior professionals to act. This followed the development in 2007 of the Sepsis 6: a simplified care bundle including source control and antibiotics, escalation to critical care where needed, and treatment coordinated by senior clinician.

# NEWS 2

Respiratory rate  breaths/min ▼

Hypercapneic respiratory failure ☐ No (Scale 1)  
☐ Yes (Scale 2)

On supplemental O<sub>2</sub> ☐ No  
☐ Yes

O<sub>2</sub> saturation  % ▼

Systolic BP  mmHg ▼

Pulse  beats/min ▼

Consciousness ☐ Alert  
☐ CVPU

Temperature  degC ▼

**0 to 4 points:** 0 to 4 points (but no 3-point risk item): Low clinical risk: Ward-based response

3 or 4 points (including one 3-point risk item): Low-medium clinical risk: Urgent ward-based response

**5 to 6 points:** Medium clinical risk: Key threshold for urgent response

**7 to 20 points:** High clinical risk: Urgent or emergency response


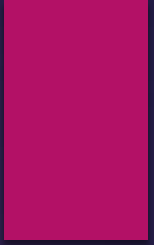
| NEWS key   |  | FULL NAME     |                             |        |
|--|--|---------------|-----------------------------|--------|
| 0 1 2 3  |  | DATE OF BIRTH | DATE OF ADMISSION           |        |
|  | DATE TIME  |               | DATE TIME                   |        |
| <b>A+B</b><br>Respirations<br>Breaths/min  | ≥25  | 3             | ≥25                         |        |
|  | 21-24  | 2             | 21-24                       |        |
|  | 18-20  |               | 18-20                       |        |
|  | 15-17  |               | 15-17                       |        |
|  | 12-14  |               | 12-14                       |        |
|  | 9-11   | 1             | 9-11                        |        |
|  | ≤8   | 3             | ≤8                          |        |
| <b>A+B</b><br>SpO <sub>2</sub> Scale 1<br>Oxygen saturation (%)  | ≥96  |               | ≥96                         |        |
|  | 94-95  | 1             | 94-95                       |        |
|  | 92-93  | 2             | 92-93                       |        |
|  | ≤91  | 3             | ≤91                         |        |
| <b>SpO<sub>2</sub> Scale 2</b><br>Oxygen saturation (%)<br>Use Scale 2 if range is 94-95%<br>40% hypercapnic respiratory failure | ≥97... O <sub>2</sub>  | 3             | ≥97... O <sub>2</sub>       |        |
|  | 95-96... O <sub>2</sub>  | 2             | 95-96... O <sub>2</sub>     |        |
|  | 93-94... O <sub>2</sub>  | 1             | 93-94... O <sub>2</sub>     |        |
|  | ≤93... 8l  |               | ≤93... 8l                   |        |
|  | 88-92  |               | 88-92                       |        |
|  | 86-87  | 1             | 86-87                       |        |
|  | 84-85  | 2             | 84-85                       |        |
|  | ≤83%   | 3             | ≤83%                        |        |
|  | *ONLY use Scale 2 under the direction of a qualified clinician |               |                             |        |
|  | <b>Air or oxygen?</b>  | As Air        |                             | As Air |
| O <sub>2</sub> L/min Device  |  | 2             | O <sub>2</sub> L/min Device |        |
| <b>C</b><br>Blood pressure<br>mmHg<br>Score uses systolic BP only  | ≥220   | 3             | ≥220                        |        |
|  | 201-219  |               | 201-219                     |        |
|  | 181-200  |               | 181-200                     |        |
|  | 161-180  |               | 161-180                     |        |
|  | 141-160  |               | 141-160                     |        |
|  | 121-140  |               | 121-140                     |        |
|  | 111-120  |               | 111-120                     |        |
|  | 101-110  | 1             | 101-110                     |        |
|  | 91-100   | 2             | 91-100                      |        |
|  | 81-90  |               | 81-90                       |        |
|  | 71-80  | 3             | 71-80                       |        |
| <b>C</b><br>Pulse<br>Beats/min   | ≥131   | 3             | ≥131                        |        |
|  | 121-130  |               | 121-130                     |        |
|  | 111-120  | 2             | 111-120                     |        |
|  | 101-110  |               | 101-110                     |        |
|  | 91-100   | 1             | 91-100                      |        |
|  | 81-90  |               | 81-90                       |        |
|  | 71-80  |               | 71-80                       |        |
|  | 61-70  |               | 61-70                       |        |
|  | 51-60  |               | 51-60                       |        |
|  | 41-50  | 1             | 41-50                       |        |
|  | 31-40  | 3             | 31-40                       |        |
|  | ≤30  |               | ≤30                         |        |
| <b>D</b><br>Consolousness<br>Score for ACU<br>Scale of confusion<br>(No score if drowsy)   | Alert  |               | Alert                       |        |
|  | Confusion  |               | Confusion                   |        |
|  | V  | 3             | V                           |        |
|  | P  |               | P                           |        |
|  | U  |               | U                           |        |
| <b>E</b><br>Temperature<br>°C  | ≥39.1°   | 2             | ≥39.1°                      |        |
|  | 38.1-39.0°   | 1             | 38.1-39.0°                  |        |
|  | 37.1-38.0°   |               | 37.1-38.0°                  |        |
|  | 36.1-37.0°   |               | 36.1-37.0°                  |        |
|  | 35.1-36.0°   | 1             | 35.1-36.0°                  |        |
|  | ≤35.0°   | 3             | ≤35.0°                      |        |
| <b>NEWS TOTAL</b>  |  |               | <b>TOTAL</b>                |        |
| Monitoring frequency   |  |               | Monitoring                  |        |
| Escalation of care Y/N   |  |               | Escalation                  |        |
| Initials   |  |               | Initials                    |        |



# Signs of altered tissue perfusion visualized through the three “windows” of the body:



Windows



**Sepsis and septic shock are medical emergencies,  
and we recommend that treatment and  
resuscitation begin immediately.**

**Best practice statement**

Lactate alone is neither sensitive nor specific enough to rule-in or rule-out the diagnosis on its own.

For adults suspected of having sepsis, we suggest measuring blood lactate.

Surviving Sepsis Campaign

## BUNDLE

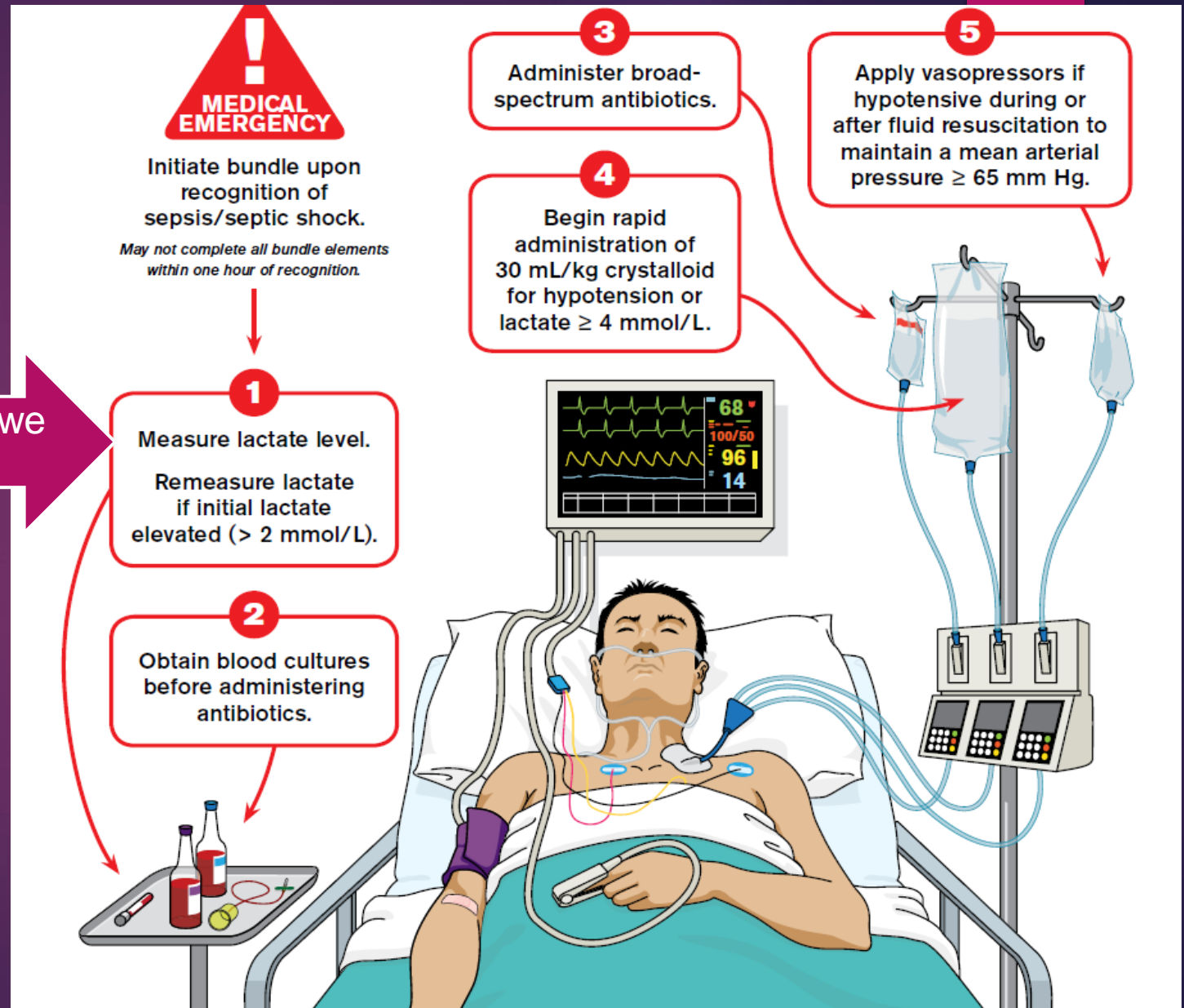
### HOURLY-1 BUNDLE: INITIAL RESUSCITATION FOR SEPSIS AND SEPTIC SHOCK:

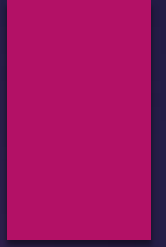
- 1) Measure lactate level.\*
- 2) Obtain blood cultures before administering antibiotics.
- 3) Administer broad-spectrum antibiotics.
- 4) Begin rapid administration of 30mL/kg crystalloid for hypotension or lactate  $\geq 4$  mmol/L.
- 5) Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure  $\geq 65$  mm Hg.

\*Remeasure lactate if initial lactate elevated ( $> 2$  mmol/L).

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[survivingsepsis.org](http://survivingsepsis.org)





- For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hours of resuscitation.

Weak recommendation, very low-quality evidence.

# Dynamic Measures

- For adults with sepsis or septic shock, we suggest using **dynamic measures** to guide fluid resuscitation over physical examination or static parameters alone.

Weak recommendation, very low quality evidence.

*include response to a passive leg raise or a fluid bolus, using*

*stroke volume (SV)*

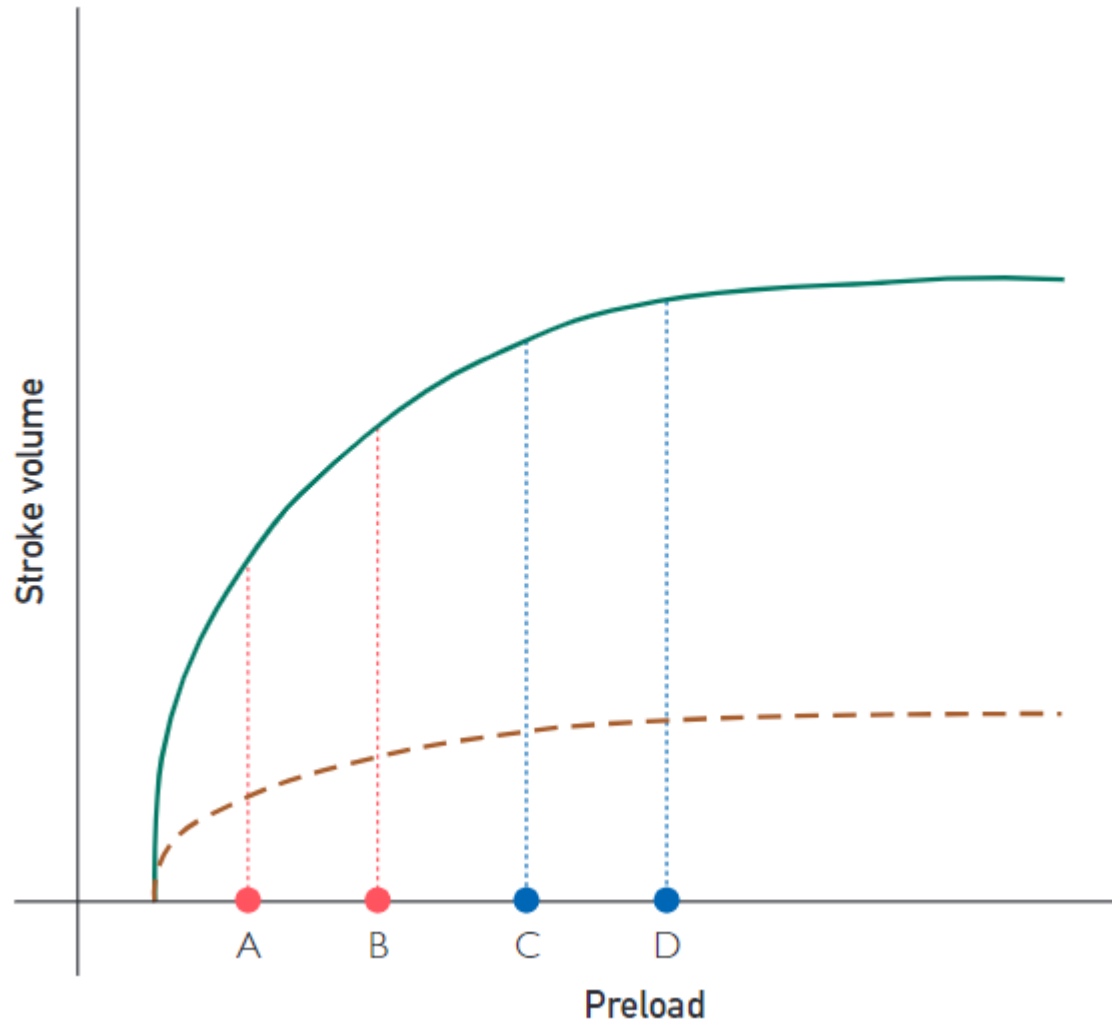
*stroke volume variation (SVV)*

*pulse pressure variation (PPV)*

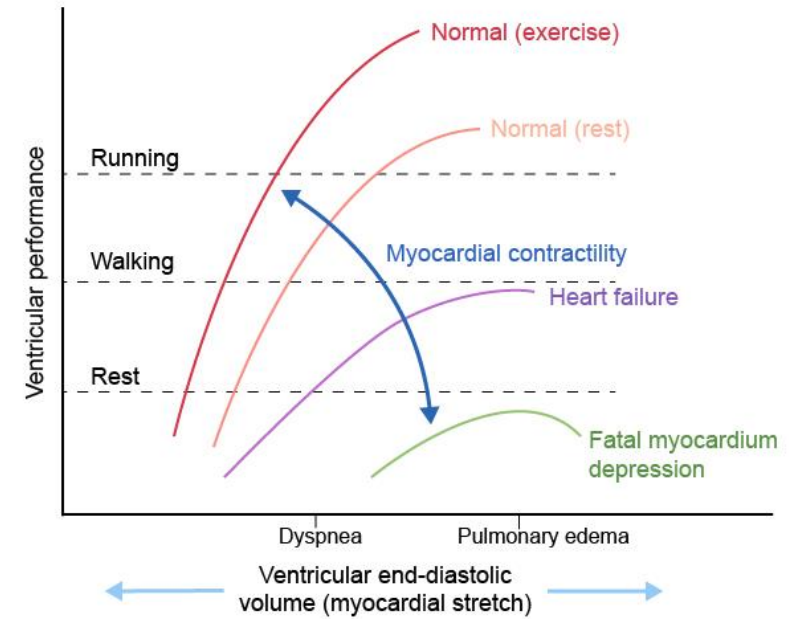
*echocardiography*



# The Frank-Starling Mechanism



## Frank-Starling Relationship



© Lineage

Lucy Liu

The ability of the heart to change its force of contraction and therefore stroke volume in response to changes in venous return is called **The Frank-Starling Mechanism**



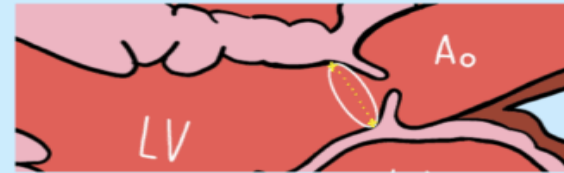
# Stroke Volume

$$\begin{aligned} \text{CO} &= \text{SV} \times \text{HR} \\ \text{SV} &= \text{EDV} - \text{ESV} \\ \text{LVEF} &= \text{SV} / \text{EDV} \end{aligned}$$

## MEASURING CARDIAC OUTPUT

### CALCULATE LVOT AREA

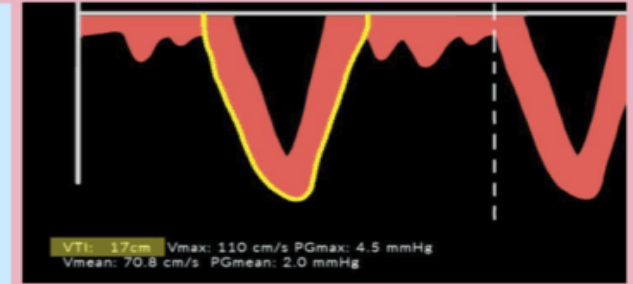
1. PARASTERNAL LONG AXIS VIEW
2. ZOOM INTO LVOT
3. MEASURE LVOT DIAMETER IN CM
4. CALCULATE LVOT AREA USING AREA OF A CIRCLE FORMULA



$$\text{LVOT AREA} = \pi \left( \frac{\text{cm}}{2} \right)^2$$

### CALCULATE LVOT VTI

1. APICAL 5 CHAMBER VIEW
2. PLACE PULSE WAVE DOPPLER GATE AT LVOT
3. ACTIVATE PW DOPPLER
4. TRACE AROUND EJECTION WAVE
5. RECORD VTI IN CM



### CALCULATE CARDIAC OUTPUT

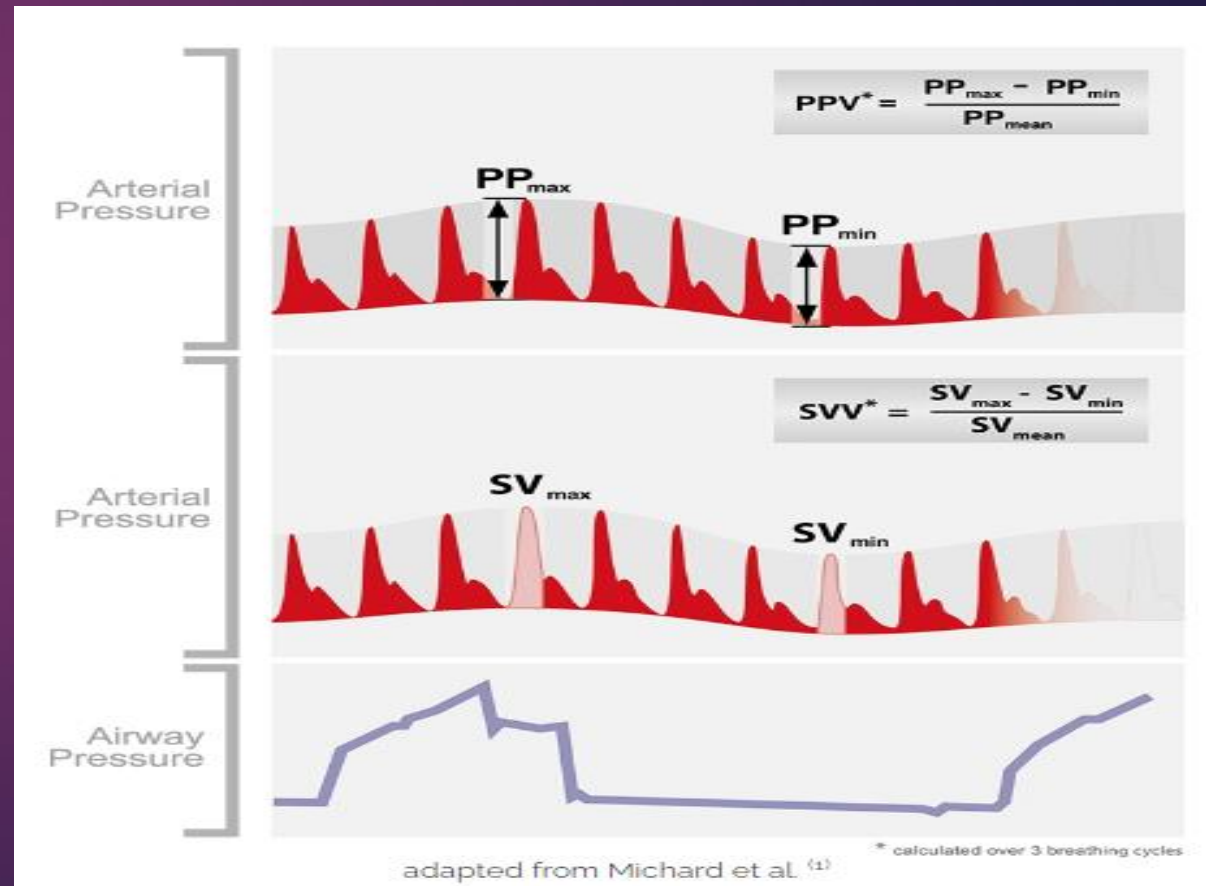
$$\text{SV} = \text{LVOT AREA} \times \text{LVOT VTI}$$

$$\text{CO} = (\text{LVOT AREA} \times \text{LVOT VTI}) \times \text{HR}$$

$$\text{CO (mL/min)} = \text{SV (mL/cycle)} \times \text{HR (bpm)}$$

# Stroke volume variation (SVV), Pulse pressure variation (PPV)

PPV as well as SVV are calculated from the minimum and maximum of pulse pressure (PPV) or stroke volume (SVV) during a respiratory cycle.



# Resuscitation

For patients with sepsis or septic shock, we suggest guiding resuscitation to

decrease  
serum  
lactate in  
patients  
with  
elevated  
lactate  
level,

over not using  
serum lactate.

Weak recommendation, low-quality evidence.

# Resuscitation

- ▶ During acute resuscitation, serum lactate level should be interpreted considering the clinical context and other causes of elevated lactate.

# Etiology of lactic acidosis

## Increased lactate production

Increased pyruvate production

Enzymatic defects in glycogenolysis or gluconeogenesis (as with type 1 glycogen storage disease)

Respiratory alkalosis, including salicylate intoxication

Pheochromocytoma

Beta-agonists

**Sepsis**

## Impaired pyruvate utilization

Decreased activity of pyruvate dehydrogenase or pyruvate carboxylase

- Congenital
- Possibly a role in diabetes mellitus, Reye syndrome

## Altered redox state favoring pyruvate conversion to lactate

## Enhanced metabolic rate

- Grand mal seizure
- Severe exercise
- Hypothermic shivering
- Severe asthma

## Decreased oxygen delivery

- **Shock**
- Cardiac arrest
- Acute pulmonary edema
- Carbon monoxide poisoning
- Severe hypoxemia ( $PO_2 < 25$  to 30 mmHg)
- Pheochromocytoma

## Reduced oxygen utilization

- Cyanide intoxication (decreased oxidative metabolism), which may result from cyanide poisoning or, during a fire, from smoke inhalation of vapors derived from the thermal decomposition of nitrogen-containing materials such as wool, silk, and polyurethane
- Drug-induced mitochondrial dysfunction due to zidovudine or stavudine

• **Sepsis**

## D-lactic acidosis

## Primary decrease in lactate utilization

Hypoperfusion and marked acidemia

Alcoholism

Liver disease

## Mechanism uncertain

Malignancy

Diabetes mellitus, including metformin in the absence of tissue hypoxia

Acquired immunodeficiency syndrome

Hypoglycemia

Idiopathic

# Resuscitation

For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.

Weak recommendation, low-quality evidence.



# Resuscitation

## MEAN ARTERIAL PRESSURE

For adults with septic shock on vasopressors,  
we recommend an initial target mean arterial pressure (MAP) of  
65 mm Hg  
over higher MAP targets.

Strong, moderate-quality evidence

# Resuscitation

**crystalloids as first-line fluid**

Strong, moderate-quality evidence

**no starches**

Strong, high-quality evidence

**no gelatin**

Weak, moderate-quality evidence

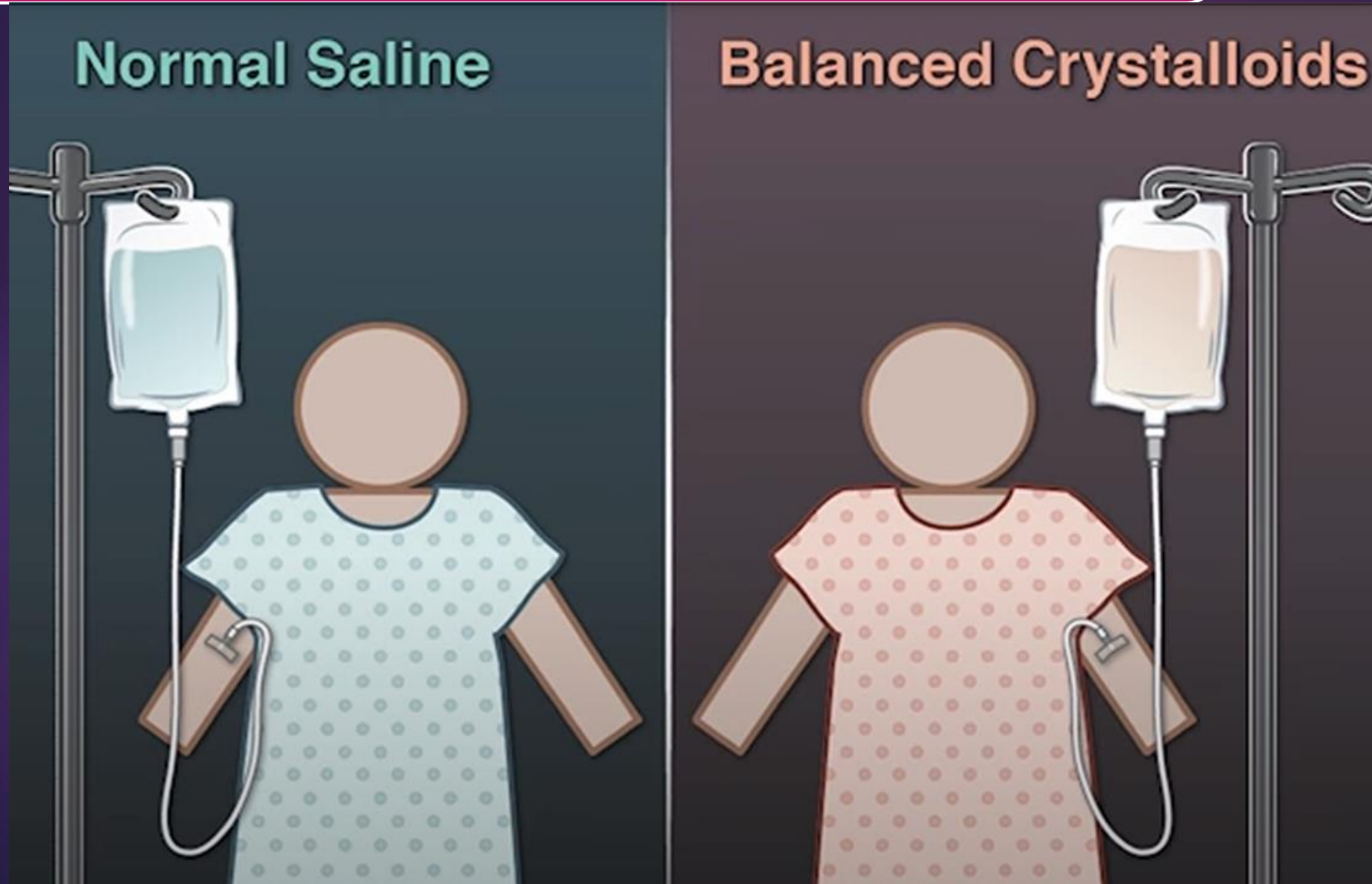
**albumin in patients who  
received large volumes  
of crystalloids.**

Weak, moderate-quality evidence

**Balanced crystalloids  
instead of N/S**

Weak, low quality of evidence

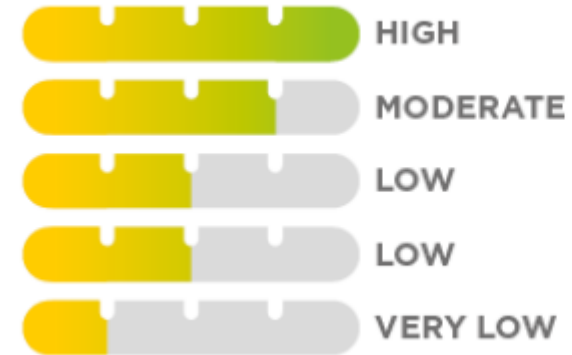
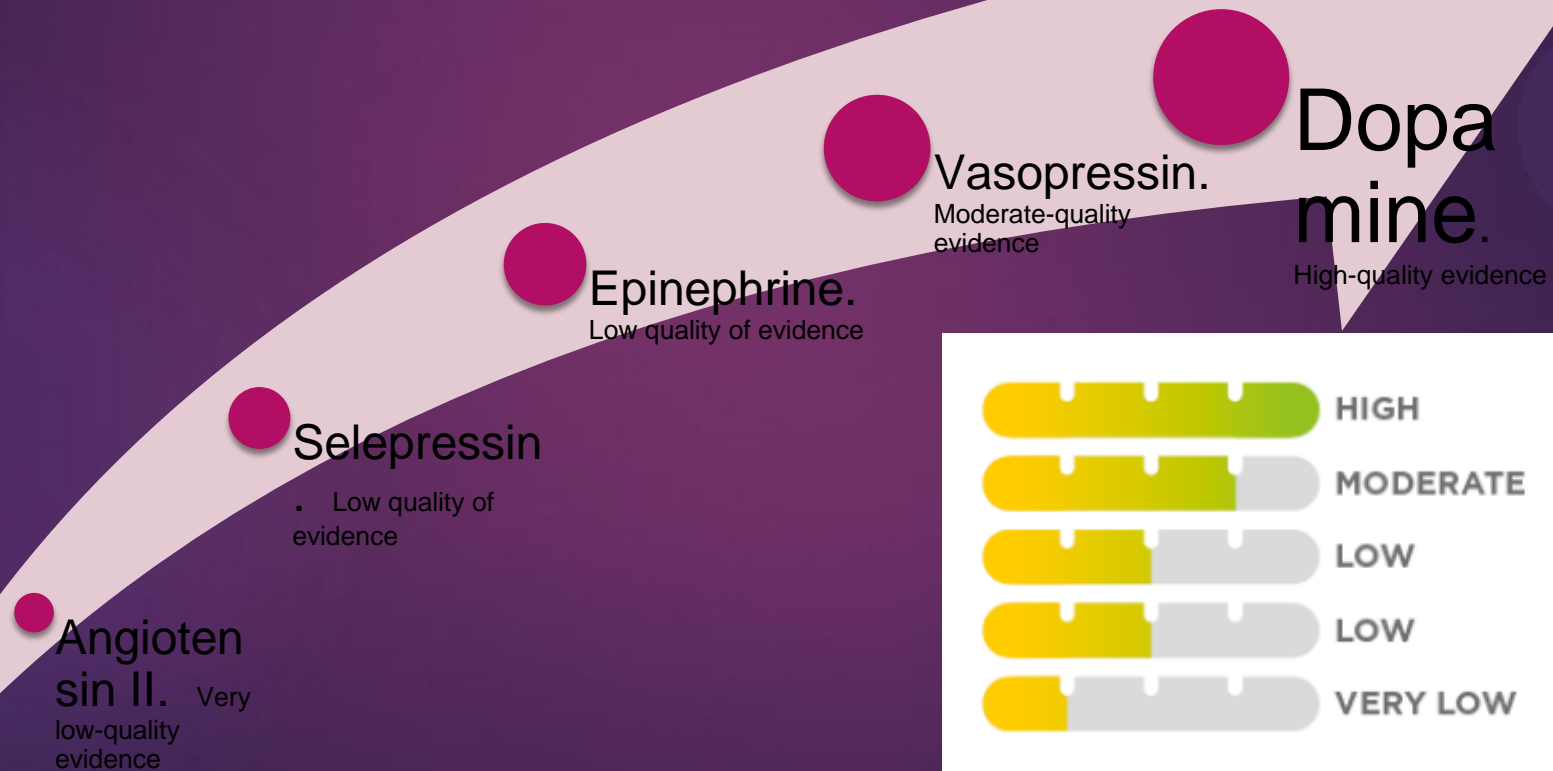
# Resuscitation



# Vasopressors

For adults with septic shock, we recommend using **Norepinephrine** as the first-line agent over other vasopressors.

**STRONG**



# Vasoactive Agent Management

Norepinephrine as the first-line agent over other vasopressors.

initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets.

Strong

Consider invasive monitoring of arterial blood pressure

If central line is not yet available

Consider starting vasopressors peripherally to restore mean arterial pressure rather than delaying initiation until a central venous access is secured.

If MAP is still inadequate despite low-to-moderate dose norepinephrine

Consider adding vasopressin instead of escalating the dose of norepinephrine

Inadequate mean arterial pressure levels despite norepinephrine and vasopressin,

Consider adding epinephrine.

Weak

# Vasopressors

For adults with septic shock, we suggest against using terlipressin.

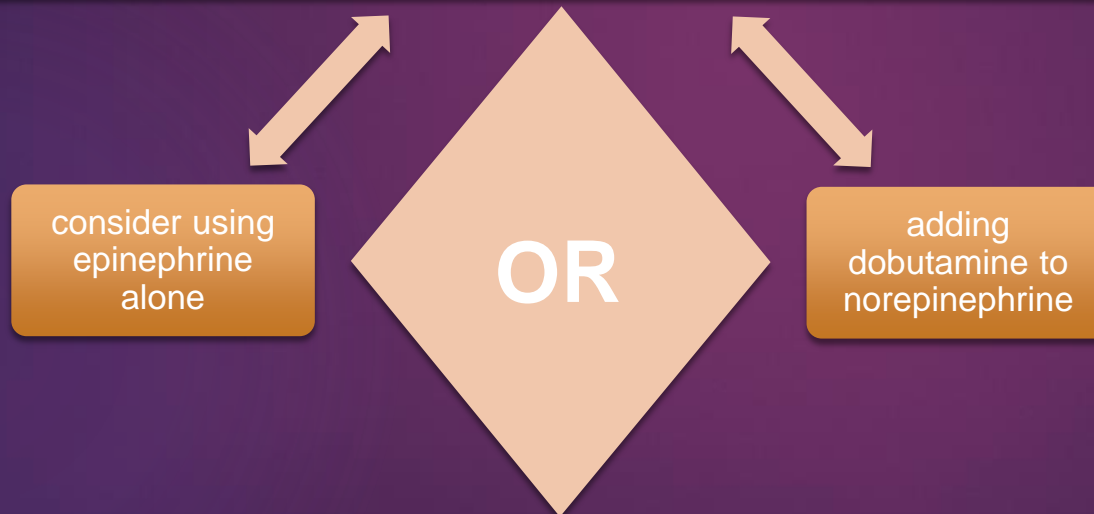
Weak, low quality of evidence



# Vasopressors

For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure

Weak, low quality of evidence






we suggest against using levosimendan.

Weak, low quality of evidence

# INFECTION

**For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.**

# INFECTION

|   | <br>Shock is present                  | <br>Shock is absent                   |
|---|--|--|
| <b>Sepsis is definite or probable</b>   | <input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition. | <input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition. |
| <b>Sepsis is possible</b>   | <input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition. | <input checked="" type="checkbox"/> Rapid assessment* of infectious vs. noninfectious causes of acute illness.           |
| <p><i>*Rapid assessment includes history and clinical examination, tests for both infectious and noninfectious causes of acute illness, and immediate treatment of 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.</i></p> |  | <input checked="" type="checkbox"/> Administer antimicrobials <b>within 3 hours</b> if concern for infection persists.   |

# INFECTION

For adults with suspected sepsis or septic shock but unconfirmed infection, we recommend continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected

For adults with possible sepsis without shock, we recommend rapid assessment of the likelihood of infectious versus noninfectious causes of acute illness.

# INFECTION

high risk of MRSA

- empiric antimicrobials with MRSA

high risk for multidrug  
resistant  
(MDR) organisms

- two antimicrobials with gram-negative coverage for empiric treatment

High risk of fungal  
infection, we suggest  
using

- empiric antifungal therapy

# INFECTION

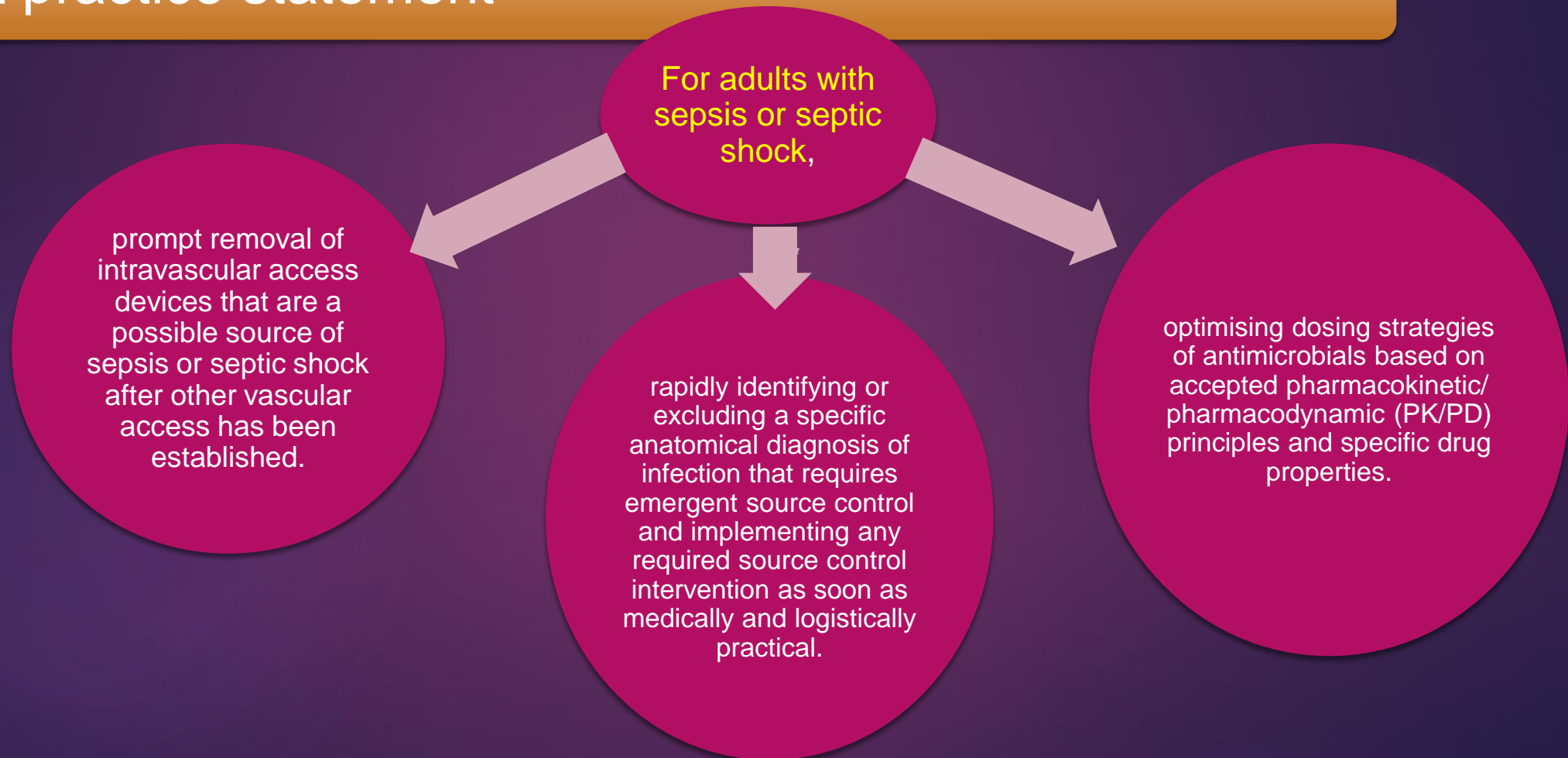
For adults with sepsis or septic shock, we suggest using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion.

Weak, moderate-quality evidence



# INFECTION

## Best practice statement



# INFECTION

For adults with sepsis or septic shock, we suggest daily assessment for de-escalation of antimicrobials over using fixed durations of therapy without daily reassessment for de-escalation.

For adults with an initial diagnosis of sepsis or septic shock and adequate source control, we suggest using shorter over longer duration of antimicrobial therapy.

Weak, very low quality  
of evidence

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.

# ADMISSION TO INTENSIVE CARE

For adults with sepsis or septic shock who require ICU admission, we suggest admitting the patients to the ICU within 6 hr.

Weak, low quality of evidence

## 2021 RECOMMENDATIONS ON ADDITIONAL THERAPIES



MODERATE

For adults with septic shock and an ongoing requirement for vasopressor therapy we **suggest** using IV corticosteroids.



LOW

For adults with sepsis or septic shock we **suggest against** using polymyxin B hemoperfusion.



There is insufficient evidence to make a recommendation on the use of other blood purification techniques.



MODERATE

For adults with sepsis or septic shock we **recommend** using a restrictive (over liberal) transfusion strategy.



LOW

For adults with sepsis or septic shock we **suggest against** using intravenous immunoglobulins.



MODERATE

For adults with sepsis or septic shock, and who have risk factors for gastrointestinal (GI) bleeding, we **suggest** using stress ulcer prophylaxis.



MODERATE

For adults with sepsis or septic shock, we **recommend** using pharmacologic venous thromboembolism (VTE) prophylaxis unless a contraindication to such therapy exists.



MODERATE

For adults with sepsis or septic shock, we **recommend** using low molecular weight heparin over unfractionated heparin for VTE prophylaxis.



LOW

For adults with sepsis or septic shock, we **suggest against** using mechanical VTE prophylaxis, in addition to pharmacological prophylaxis, over pharmacologic prophylaxis alone.



LOW

In adults with sepsis or septic shock and AKI, we **suggest** using either continuous or intermittent renal replacement therapy.



MODERATE

In adults with sepsis or septic shock and AKI, with no definitive indications for renal replacement therapy, we **suggest against** using renal replacement therapy.



MODERATE

For adults with sepsis or septic shock, we **recommend** initiating insulin therapy at a glucose level of  $\geq 180\text{mg/dL}$  ( $10\text{mmol/L}$ ).



LOW

For adults with sepsis or septic shock we **suggest against** using IV vitamin C.



LOW

For adults with septic shock and hypoperfusion-induced lactic acidemia, we **suggest against** using sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements.



LOW

For adults with septic shock and severe metabolic acidemia ( $\text{pH} \leq 7.2$ ) and acute kidney injury (AKIN score 2 or 3), we **suggest** using sodium bicarbonate therapy.





VERY LOW

For adult patients with sepsis or septic shock who can be fed enterally, we **suggest** early (within 72 hours) initiation of enteral nutrition.







## 2021 RECOMMENDATIONS ON VENTILATION



  LOW  
For adults with sepsis-induced hypoxemic respiratory failure, we **suggest** the use of high flow nasal oxygen over non-invasive ventilation.

  HIGH  
For adults with sepsis-induced ARDS, we **recommend** using a low tidal volume ventilation strategy (6 mL/kg), over a high tidal volume strategy (>10 mL/kg).



  MODERATE  
For adults with sepsis-induced severe ARDS, we **recommend** using an upper limit goal for plateau pressures of 30 cm H<sub>2</sub>O, over higher plateau pressures.



  LOW  
For adults with sepsis-induced severe ARDS, we **suggest** using Veno-venous (VV) ECMO when conventional mechanical ventilation fails in experienced centres with the infrastructure in place to support its use.

  MODERATE  
For adults with moderate to severe sepsis-induced ARDS, we **suggest** using higher PEEP over lower PEEP.

  LOW  
For adults with sepsis-induced respiratory failure (without ARDS), we **suggest** using low tidal volume as compared to high tidal volume ventilation.

  MODERATE  
When using recruitment maneuvers, we **recommend against** using incremental PEEP titration/strategy.

  MODERATE  
For adults with sepsis-induced moderate-severe ARDS, we **recommend** using prone ventilation for greater than 12 hours daily.

  MODERATE  
For adults with sepsis induced moderate-severe ARDS, we **suggest** using intermittent NMBA boluses, over NMBA continuous infusion.

# ΕΥΧΑΡΙΣΤΩ

