Shock and inotropes
JMO teaching
20220224

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Septic Shock - Identification

New definition of sepsis and septic shock – JAMA Feb 23, 2016

Sepsis (Formal Definition – Not very useful to make diagnosis of sepsis)

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
  - Organ dysfunction defined by change in SOFA score (Sequential Organ Failure Assessment)

Identification of patients with high risk of dying or prolonged ICU stay

Presumed infection

- 2 out of 3 from the quick SOFA (qSOFA) (HAT)
  - Hypotension (SBP < 100)
  - Altered mental status
  - Tachypnea (>22/minute)

- SOFA – Refers to Sequential Organ Failure Assessment.
- 2021 Surviving Sepsis Guidelines – qSOFA no longer recommended as a SINGLE TOOL to screen for patients with septic shock.

New definition of sepsis and septic shock – JAMA Feb 23, 2016

Septic shock

Clinical construct of sepsis with

1. persisting hypotension requiring vasopressors to maintain MAP 65mmHg **AND**
2. Having a serum lactate level >2 mmol/L (18mg/dL) despite adequate* volume resuscitation.
   - With these criteria, hospital mortality is in excess of 40%.

   - * Adequacy of resuscitation is easier said than assessed.

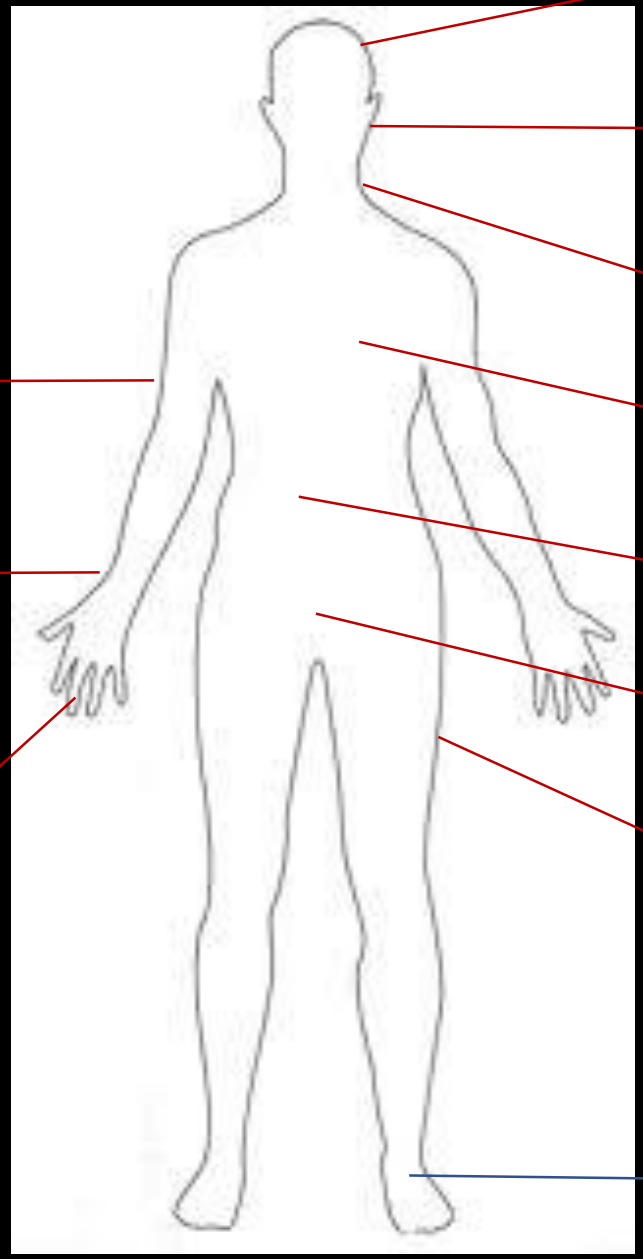
A case in the ward

Mrs. FT is 49 years old female, who was admitted to ED on 03/01/2018 with one day history of fever (39C), burning micturition, right flank pain and foul-smelling urine. Her blood culture from the time of admission has grown E. coli (6 hours after incubation).

- Previous medical problems:
  - Rheumatoid arthritis, on steroids and methotrexate.
- Clinical examination:
  - BP 70/40 mm Hg
  - PR: 120/min, sinus rhythm
  - Peripheries cold
  - Poor capillary refil
  - T – 39.8°C

Focused clinical assessment in shock

Hands to shoulders, head to toe



Mental Status

Oral and conjunctival mucosa, Chemosis

JVP

Blood Pressure

Crackles, heart sounds, pl effusion

Pulse rate

Hepatomegaly, ascites

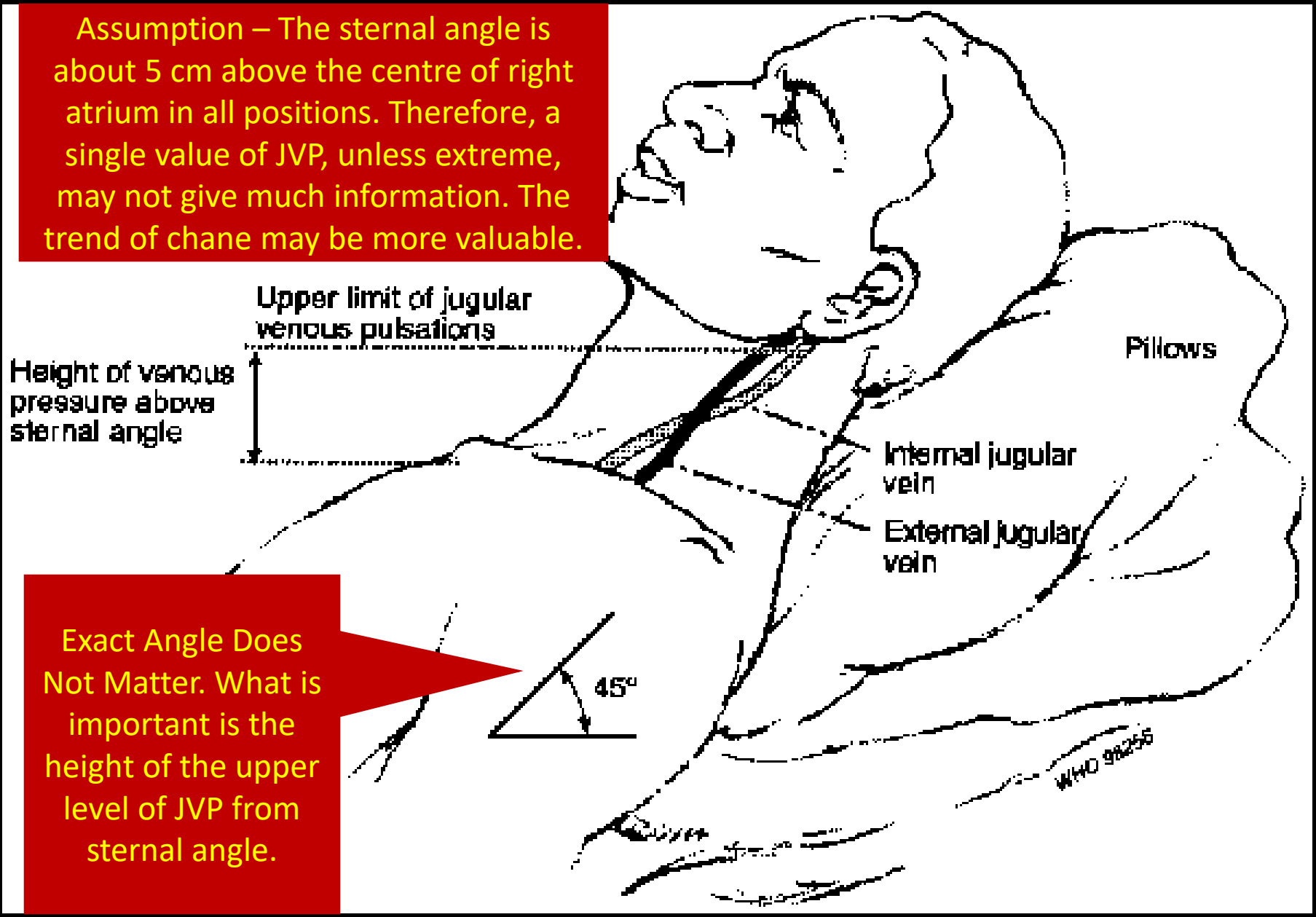
Urine output

Temperature, Capillary refill time, Pallor, edema

Edema

Edema

Assumption – The sternal angle is about 5 cm above the centre of right atrium in all positions. Therefore, a single value of JVP, unless extreme, may not give much information. The trend of chane may be more valuable.



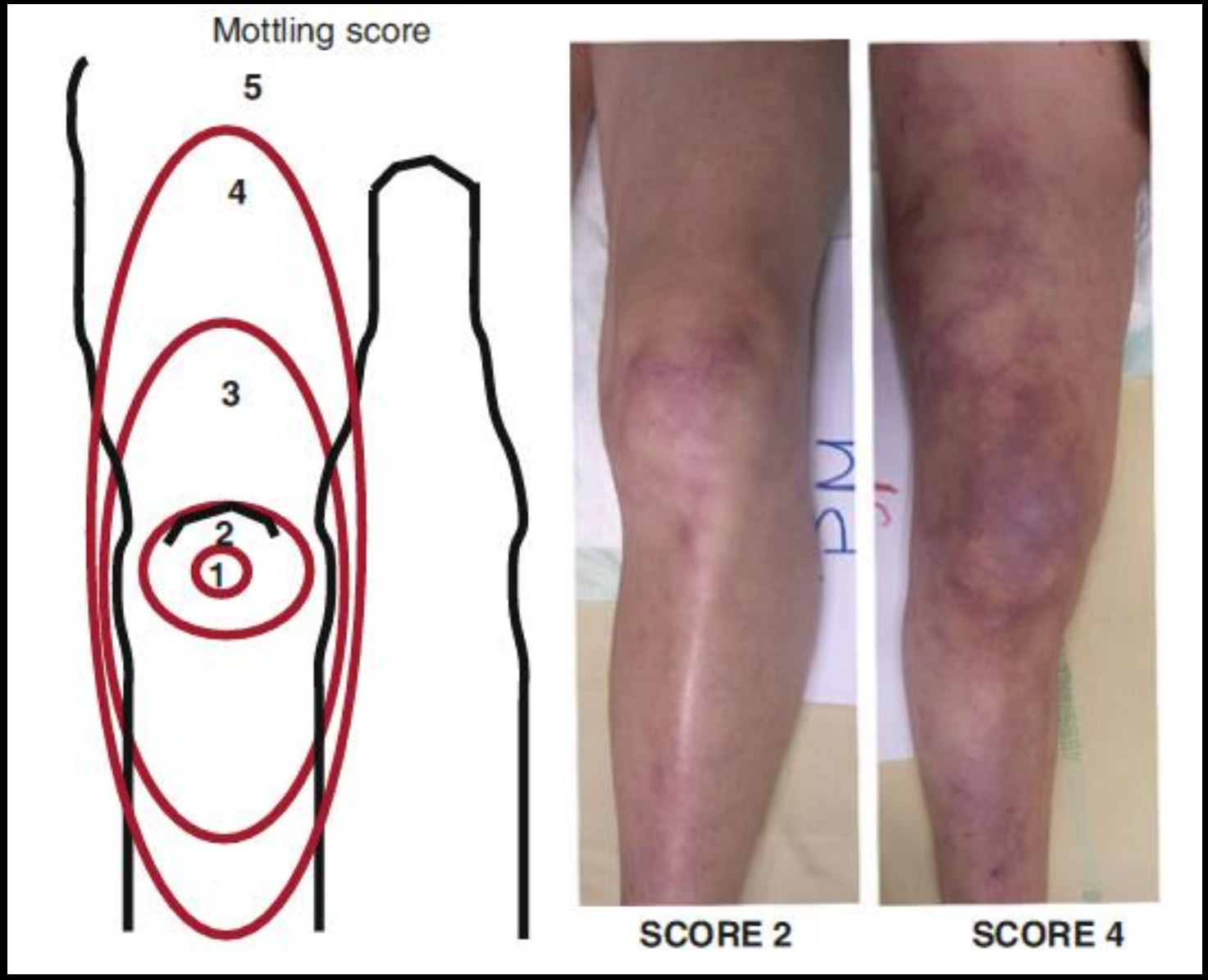
Exact Angle Does Not Matter. What is important is the height of the upper level of JVP from sternal angle.

Microvascular perfusion

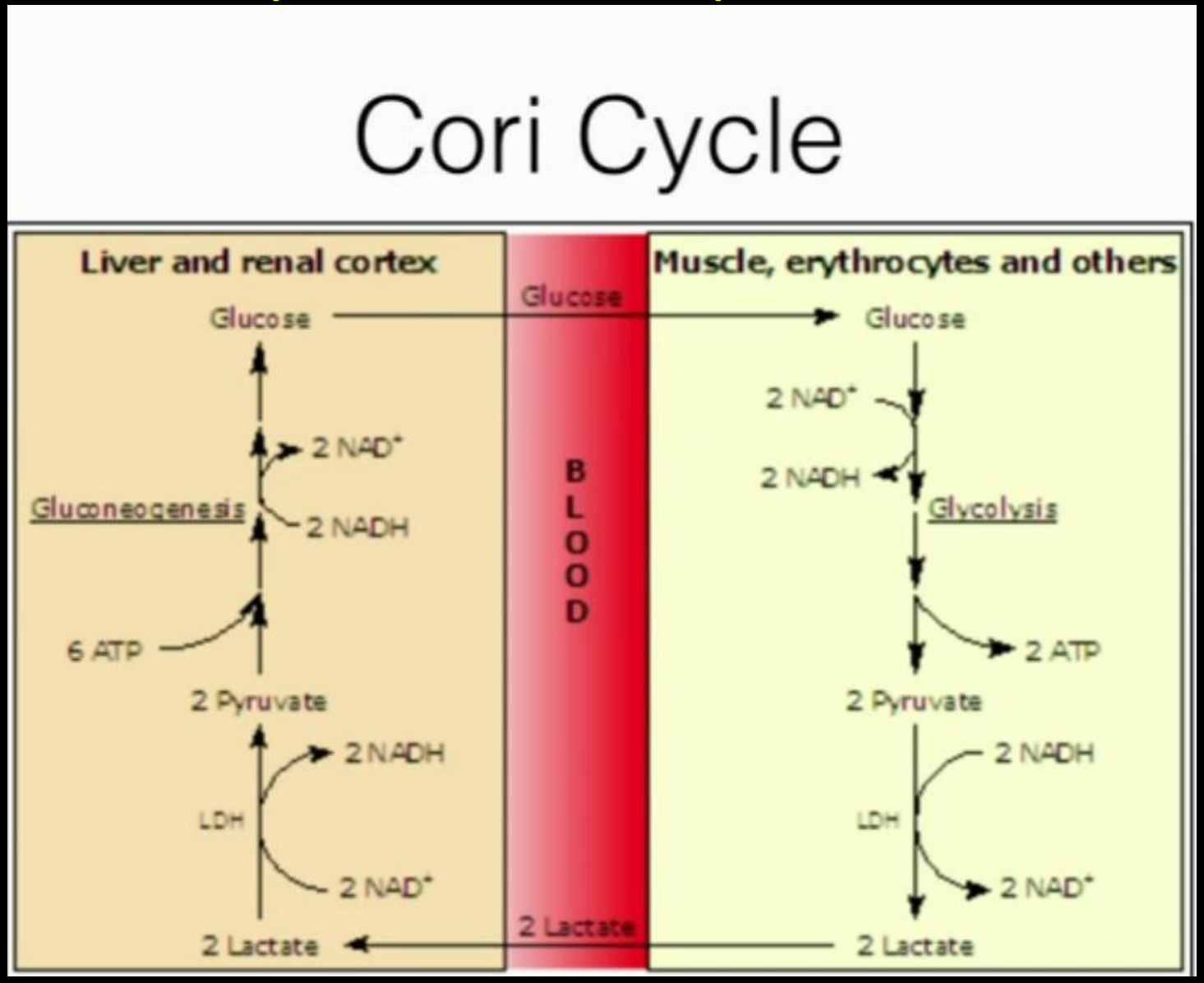
Table 1. Different methods used to measure peripheral perfusion

Method	Variable	Main advantage	Main limitation	Suggested cut-offs
Clinical assessment	Cold/warm	Depends only on the physical examination; valuable adjunct for haemodynamic monitoring in circulatory shock	Observer dependent. Digitalized and perhaps automated measurements may overcome this limitation	
	Capillary refill time			>4.5 s, related to higher morbidity and mortality
	Mottle score	Mottling is widely described and is an easily assessable clinical sign	The score cannot be used in patients with black skin.	Score 4–5, related to mortality
Body temperature gradient	Forearm-to-finger	Validated method for estimating microcirculatory skin perfusion	Does not reflect peripheral perfusion variations in real time	>4°C, related to higher morbidity and mortality
	Central-to-toe			>7°C, related to higher morbidity and mortality

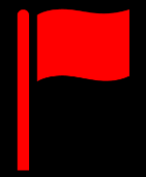
Current Opinion in Critical Care. 18(3):273-279, June 2012


Mottling score
5
4
3
2
1
SCORE 2
SCORE 4

Why is Lactate produced?



Lactate – A red flag



- In the setting of critical illness, even modest elevation of lactate is associated with worse outcome.
- Lactate clearance is associated with improved outcome in the setting of early resuscitation
- Lactate may be persistently elevated despite venous oxygen saturation of > 70%, suggesting that it may be a better indicator of septic shock.
- Lactate itself is not bad. It is only a marker of poor perfusion

Role of Echocardiography

In septic shock, echo may be helpful if primary cardiac pathology is contributory

Role of echo in assessment of fluid responsiveness is rapidly expanding

- End diastolic LV area
- End systolic LV area
- IVC diameter and changes with respiration

Should JMO call cardiology for assessment of cardiac function in septic shock –

No definite guideline

Judgement call

Premorbid cardiac dysfunction, suspicion of AMI/Pulmonary edema/CCF/Endocarditis

That someone will question your judgement on phone should not be a reason to not call for help. This is a very important learning point. JMOs will of course become more confident with time (POWH Cardiology is fantastic - My personal opinion).

Management of septic shock – Time Critical

The first hour

Hour-1 Bundle

Surviving Sepsis Campaign®

Initial Resuscitation for Sepsis and Septic Shock (begin immediately):

Time Zero/Time Presentation

*"Time zero" or "time of presentation" is defined as 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 sepsis (formerly severe sepsis) or septic shock ascertained through chart review.

1 **Measure lactate level.**

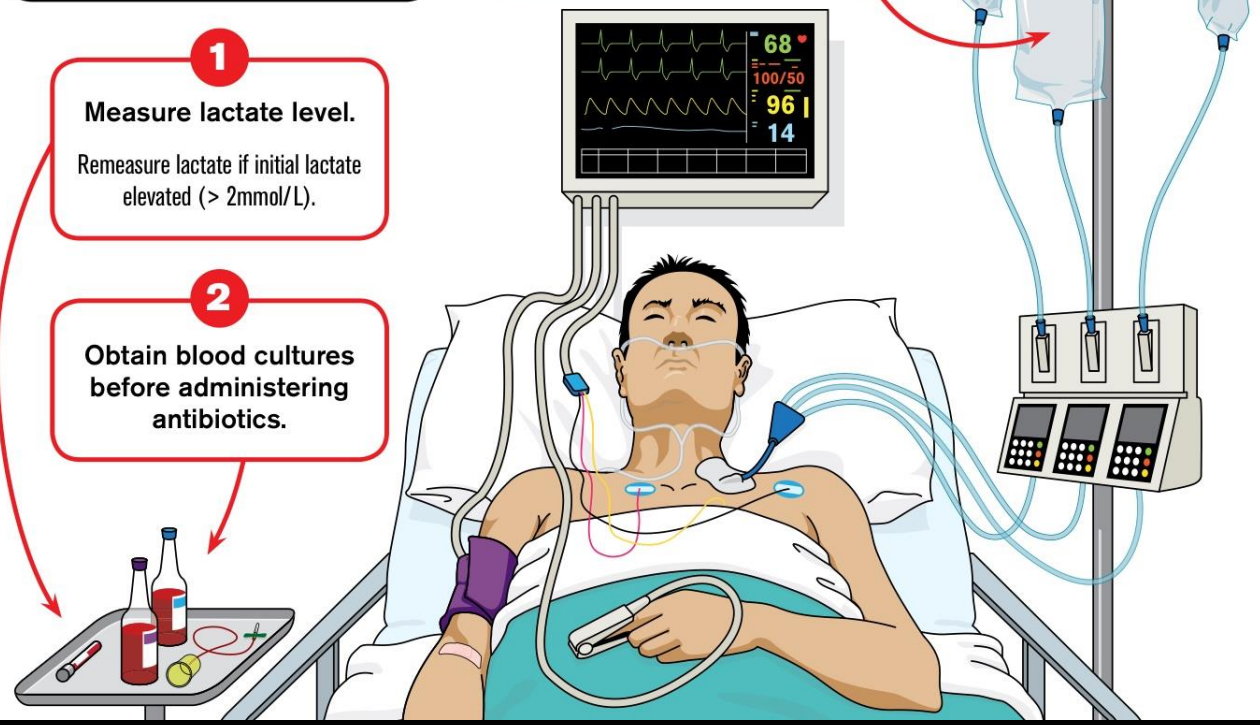
Remeasure lactate if initial lactate elevated (> 2mmol/L).

2 **Obtain blood cultures before administering antibiotics.**

3 **Administer broad-spectrum antibiotics.**

4 **Begin rapid administration of 30 ml/kg crystalloid for hypotension or lactate > 4 mmol/L**

5 **Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg.**



Fluid resuscitation

- Which Fluid?
  - Albumin?
  - NS?
  - Hartmann's/Plasmalyte (Non-inferior to saline)
  - Blood?
  - Dextrose?, N/5?
- How much? (sepsis bundle – 30ml/kg)
- What are the end points of resuscitation?
  - BP target/HR/CVP/UO/
  - Lactate/Base deficit (May lag behind)
  - Watch out for worsening oxygenation!
- Patients who appear volume replete may become intra-vascularly dry again in a few hours.

What size cannula is good enough?
Blood pump sets

You have given 2 L of iv fluids. BP is still 80/40 mm Hg.

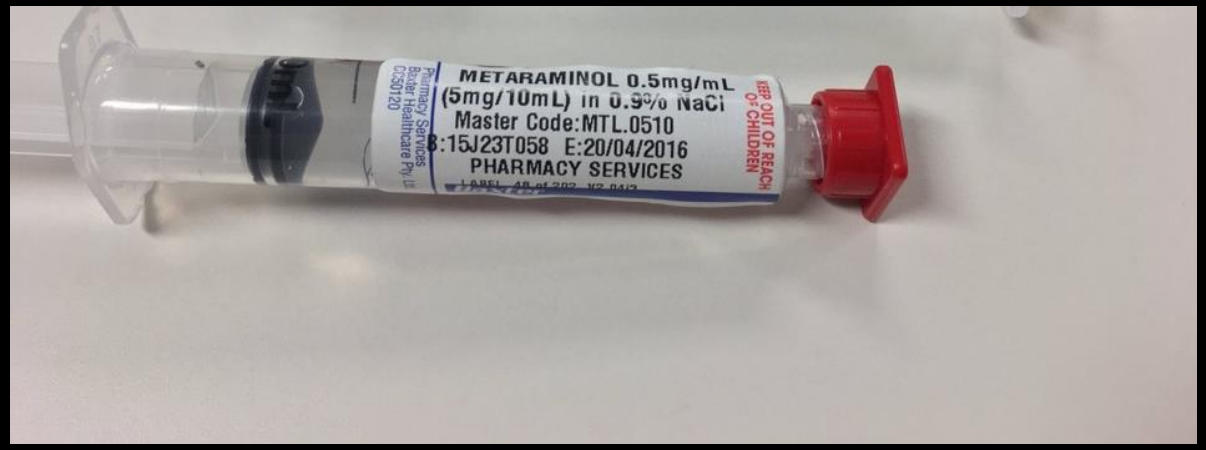
Why is the Mrs. FT still hypotensive?

Myocardial depression

Third space fluid loss

Mrs. FT needs vasopressors. She does not have a central line.

What will you do?



Aramine Prefilled Syringe
0.5 ml/ml.
Total volume = 6 ml.

10 mg/ampoule
Dilute in 20 ml
Give 1-2 ml as required
May use as infusion 0-10 ml/hr, through peripheral line

Where should you put a central line?

SCV/IJV/FV

Mrs FT now has a CVC. Pick your choice of vasopressor/inotrope

1. Nor adrenaline
2. Dopamine
3. Dobutamine
4. Adrenaline
5. Metaraminol

Vasopressors

- Noradrenaline
- Vasopressin
- Phenylephrine

Inotropes

- Adrenaline
- Dobutamine
- Isoprenaline
- Levosimendan
- Milrinone
- Digoxin

Noradrenaline and adrenaline

- Noradrenaline
  - usually the first line vasopressor for hypotension.
  - Predominantly alpha and some beta effects
  - Administer through central line. Extravasation from a peripheral line may cause skin necrosis.
- Adrenaline
  - Predominantly beta agonist, more alpha action at higher doses
  - Tachycardia, lactic acidosis common.
  - No outcome difference when compared to nor-adrenaline

Vasopressin

- Synthesized by posterior pituitary. (Terlipressin is a synthetic analogue: Active metabolite: Vasopressin)
- V1 receptor stimulation promotes vasoconstriction.
- Usually used when noradrenaline requirement is moderate to high.
- 40 units in 40 ml, administer through a central line, maximum dose 2.4 units/hour.
- Usual threshold – Noradrenaline 0.2 microgm/kg/min. No definitive guideline to starting point.
- VASST trial *(N Engl J Med 2008;358:877-87): No mortality benefit, Vasopressin vs. Noradrenaline.*

Dobutamine – Inotrope and peripheral vasodilator (Inodilator)

- In the setting of hypotension, I would consider dobutamine if:
  - I know that LV function is not good.
  - Poor peripheral perfusion
  - Persistent lactic acidosis
  - Persistent oliguria
- Avoid if:
  - Tachyarrhythmias

Milrinone

- Inotrope and vasodilator similar to dobutamine
- Works as a phospho-diesterase III inhibitor.
- Consider milrinone instead of dobutamine if:
  - Pulmonary hypertension
  - Tachyarrhythmia

Digoxin

- Not commonly used as an inotrope of first choice due to side effects and pure renal clearance.
- Consider digoxin if:
  - AF with fast heart rate and poor LV function or hypotension, when beta blockers or CCB can not be used.
  - AF with fast heart rate, not controlled by beta blocker or CCB alone; as a second line agent.
- MY PRACTICE
  - If patient not on digoxin usually, and has hypotension with AF with fast ventricular rate –
  - Single dose, 500 microgm iv (IN ICU)
  - Oral digoxin may be given in the ward.

Levosimendan

- Calcium sensitizer
- You have to fill a form to obtain levosimendan
- Main role in cardiogenic shock
- 2021 surviving sepsis guidelines recommended against use of Levosimendan in patients with septic shock and cardiac dysfunction.

What advance monitoring is commonly done?

PiCCO [CI, SVR, EVLWI useful parameters]

PA catheter

Mrs. FT is now on 0.4 microgm/kg/min Nor-adrenaline and vasopressin. His BP is 88/50 mm Hg. She appears to be adequately fluid resuscitated.

What can be done to improve BP

Is there a role for steroids?

Depends who you talk to!

- Early resolution of shock
- Increased risk of superinfection
- Shock + Hypoxia

Role of short synacthen test

Choice of agent

ADRENAL study – Just completed

Vitamin C

- High dose vitamin C has been shown in one study to improve outcome in septic shock.
- 2021 Surviving sepsis guideline recommended against the use of Vitamin C.

Principles of antibiotic treatment

1. Early antibiotic save lives (Urgency often disregarded). Culture before antibiotics if possible
2. Right antibiotics
3. Right dose (Don’t do renal adjustment for day 1)
4. Rationalize in 48-72 hrs

In ICU, UO for first 6 hrs has been < 20 ml/hr

Why?

Role of diuretics

Timing of dialysis

Blood purification

Experimental

Polymyxin hemoperfusion to bind endotoxin.

Other supportive treatment

- DVT prophylaxis
- Glycemia control

Source control

Think again about source control if patient is not improving

Mr AP, 65 yrs, diabetic, presents to ED with chest pain for last 2 hrs.

BP: 80/40

HR: 92/min, SR

Chest: Minor crackles over bases

ECG: ST elevation V2-V6

Trop I: 50000

Cardiogenic shock

Inadequate perfusion and hypoxia

Due to impairment of cardiac output

Adequate intravascular volume

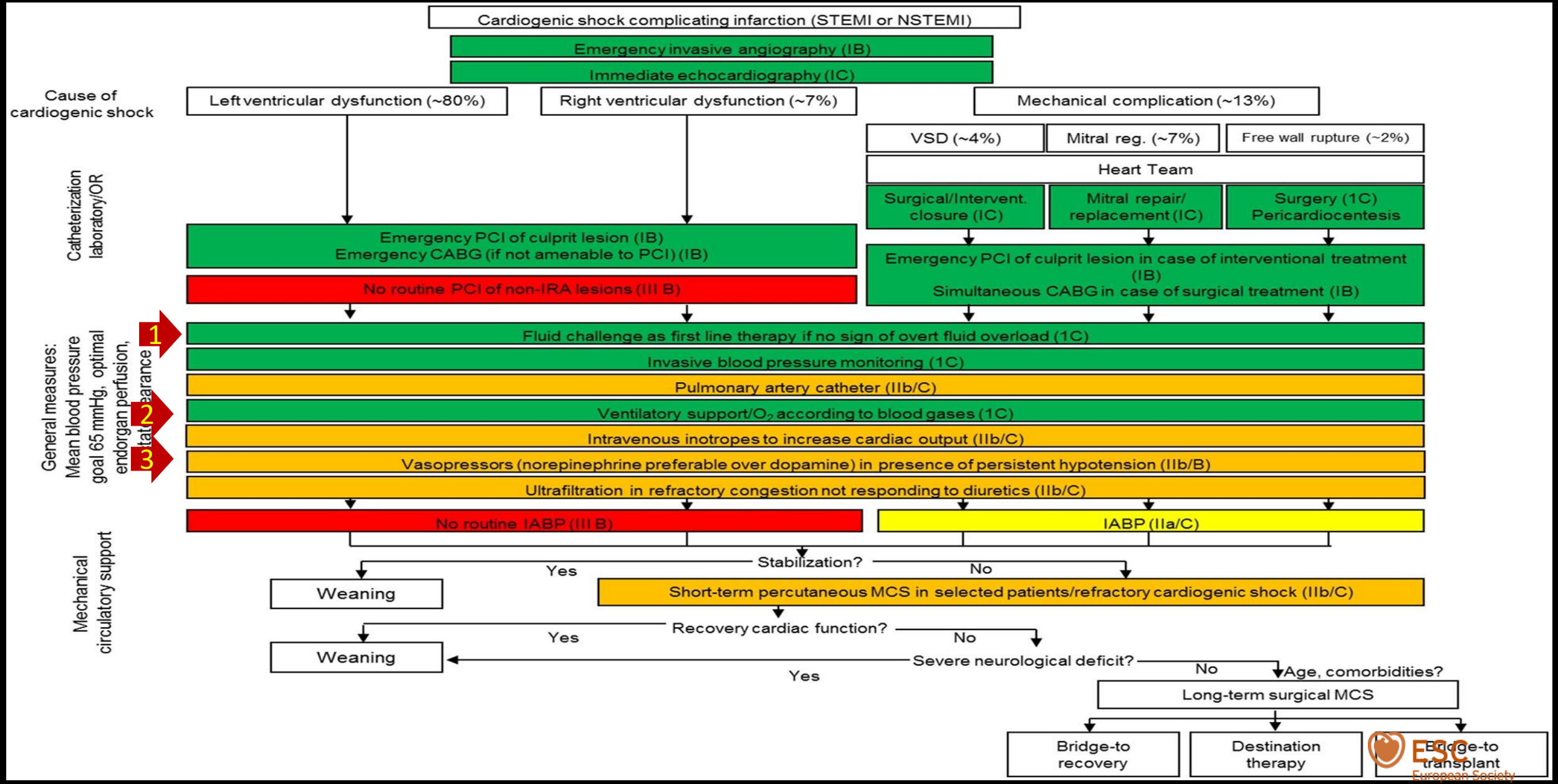
Usually with SBP < 90, MAP <60, CI < 2.2

No standard definition of cardiogenic shock

Table 1. Pragmatic and Clinical Trial Definitions of CS

Clinical Definition	SHOCK Trial[9]*	IABP-SHOCK II[1]†	ESC HF Guidelines[15]
Cardiac disorder that results in both clinical and biochemical evidence of tissue hypoperfusion	Clinical criteria: SBP <90 mm Hg for ≥30 min OR Support to maintain SBP ≥90 mm Hg AND End-organ hypoperfusion (urine output <30 mL/h or cool extremities) Hemodynamic criteria: CI of ≤2.2 L·min^{-1}·m^{-2} AND PCWP ≥15 mm Hg	Clinical criteria: SBP <90 mm Hg for ≥30 min OR Catecholamines to maintain SBP >90 mm Hg AND Clinical pulmonary congestion AND Impaired end-organ perfusion (altered mental status, cold/clammy skin and extremities, urine output <30 mL/h, or lactate >2.0 mmol/L)	SBP <90 mm Hg with adequate volume and clinical or laboratory signs of hypoperfusion Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure Laboratory hypoperfusion: Metabolic acidosis, elevated serum lactate, elevated serum creatinine

CI indicates cardiac index; CS, cardiogenic shock; ESC, European Society of Cardiology; HF, heart failure; IABP-SHOCK II, Intraaortic Balloon Pump in Cardiogenic Shock II; LV, left ventricular; MI, myocardial infarction; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; and SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock.



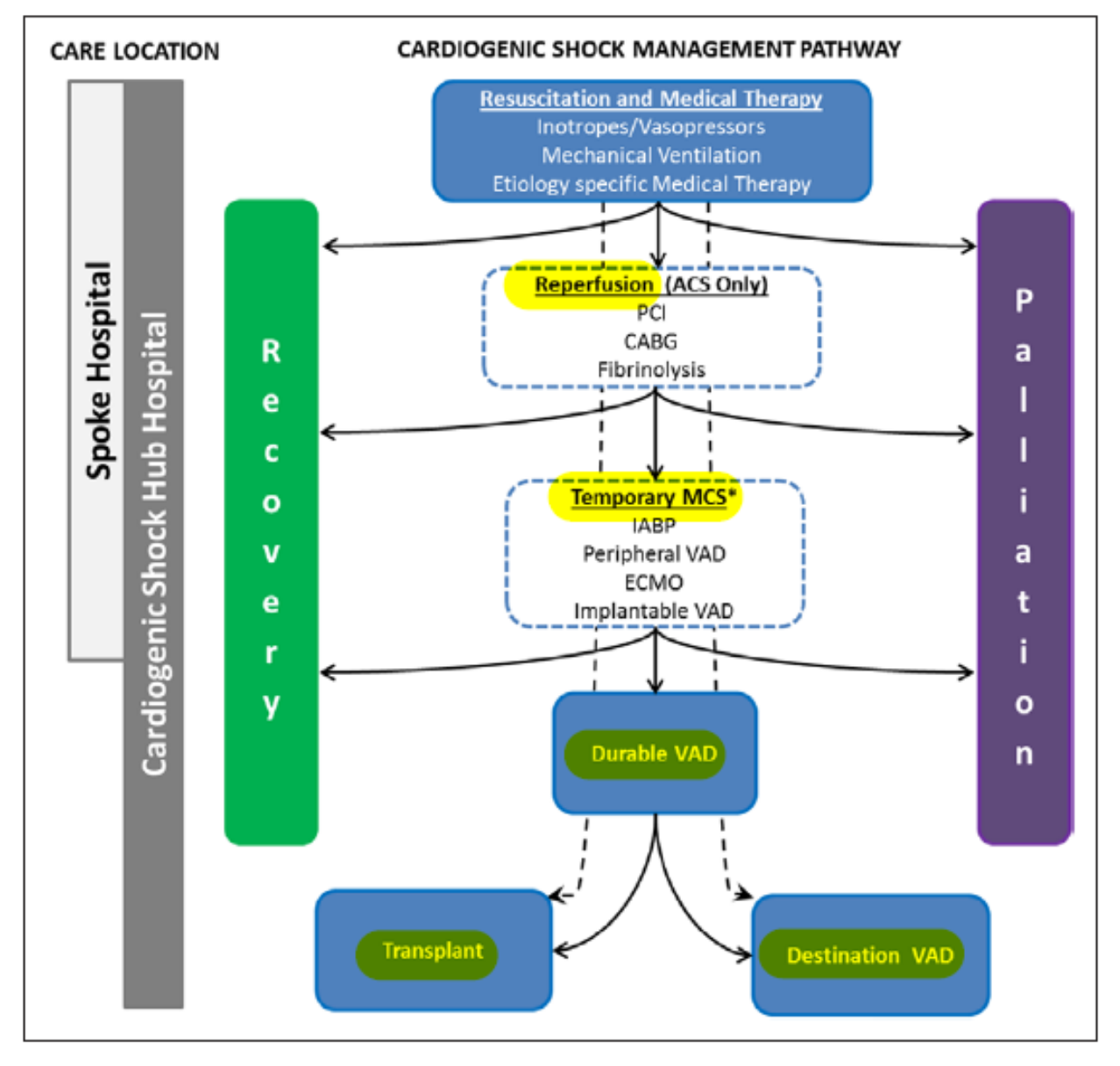
Eur Heart J, Volume 40, Issue 32, 21 August 2019, Pages 2671–2683, https://doi.org/10.1093/eurheartj/ehz363

Causes

- STEMI: 8% (60% of patients have TVD, 20% L Main)
- NSTEMI 2.5%
- RVI: 3%

Management of cardiogenic shock

Focus of early diagnostics - ACS



What is the cause of hypotension in Mr. AP?

Poor LV contractility

Hypovolemia

MR/VSD/free wall rupture

SIRS

Poor catecholamine mediated vasoconstriction

Can we give more fluids to increase BP?

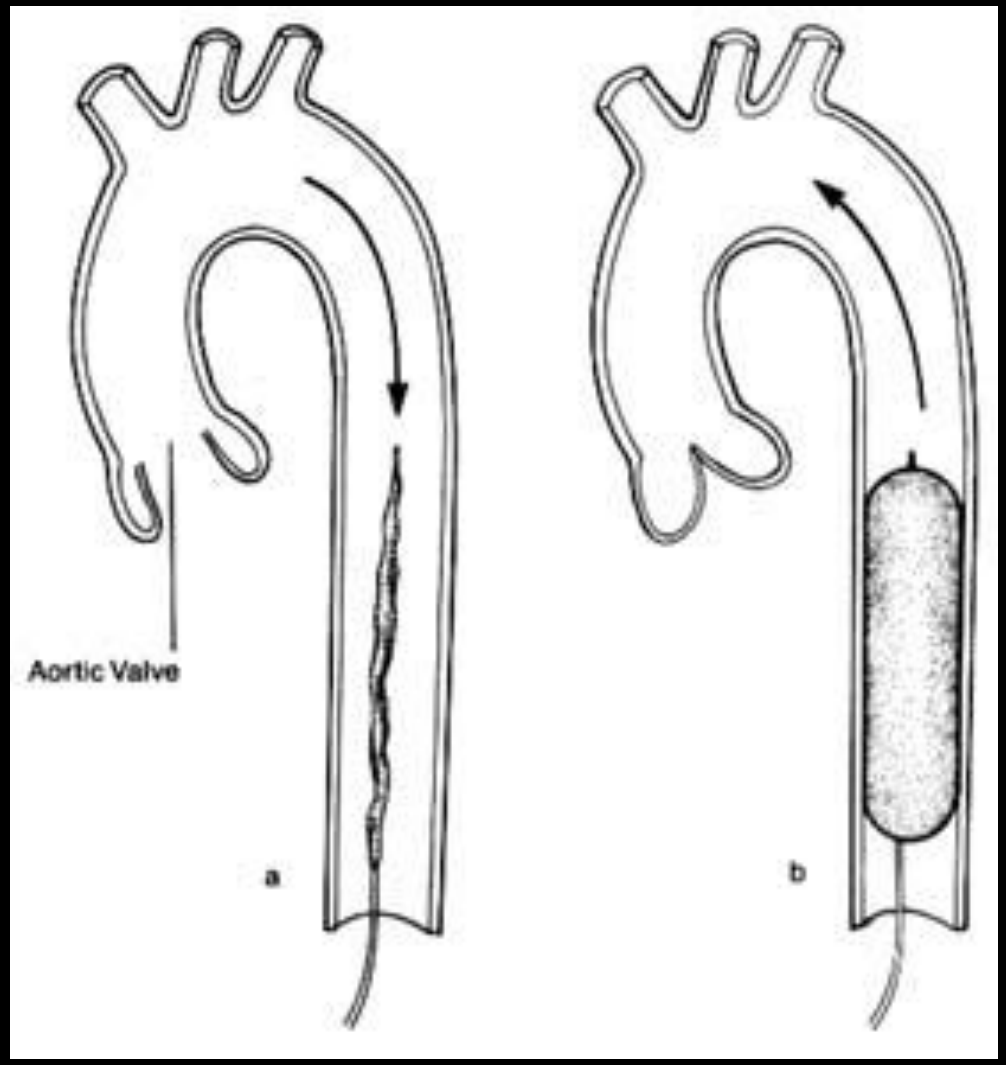
Crystalloids vs. colloids vs. blood

Target Hb?

BP remains 80/40 despite 500 ml fluid. You do not want to give more fluid. Which vasopressor will you use?

CVC in acute MI: Be very careful!

Role of IABP in cardiogenic shock



Management of pulmonary edema in presence of hypotension

Dobutamine, Nor adrenaline

NIV/intubation

Haemorrhagic shock

- Has the bleeding been controlled?
- Is the patient coagulopathic (Check Fibrinogen)
- Fluid: PRBC/crystalloid/Colloid. Hypotensive Resuscitation?
- Hemostatic agents: FFP, platelets, Cryoprecipitate, Prothrombinex, Factor VII
- Antifibrinolytics (aprotinin, EACA, Tranexamic acid)
- Reverse heparin

Anaphylactic shock

- Adrenaline 500 microgm im or 50 microgm iv. Use iv only if experienced with IV adrenaline.

Anaphylactic shock

2 Adrenaline *(give IM unless experienced with IV adrenaline)*
IM doses of 1:1000 adrenaline (repeat after 5 min if no better)

- Adult 500 micrograms IM (0.5 mL)
- Child more than 12 years: 500 micrograms IM (0.5 mL)
- Child 6 -12 years: 300 micrograms IM (0.3 mL)
- Child less than 6 years: 150 micrograms IM (0.15 mL)

Adrenaline IV to be given **only by experienced specialists**
Titrate: Adults 50 micrograms; Children 1 microgram/kg

3 IV fluid challenge:
Adult - 500 – 1000 mL
Child - crystalloid 20 mL/kg

Stop IV colloid
if this might be the cause
of anaphylaxis

	4 Chlorphenamine (IM or slow IV)	5 Hydrocortisone (IM or slow IV)
Adult or child more than 12 years	10 mg	200 mg
Child 6 - 12 years	5 mg	100 mg
Child 6 months to 6 years	2.5 mg	50 mg
Child less than 6 months	250 micrograms/kg	25 mg

Thank you