Fluid and Vasopressor in Shock

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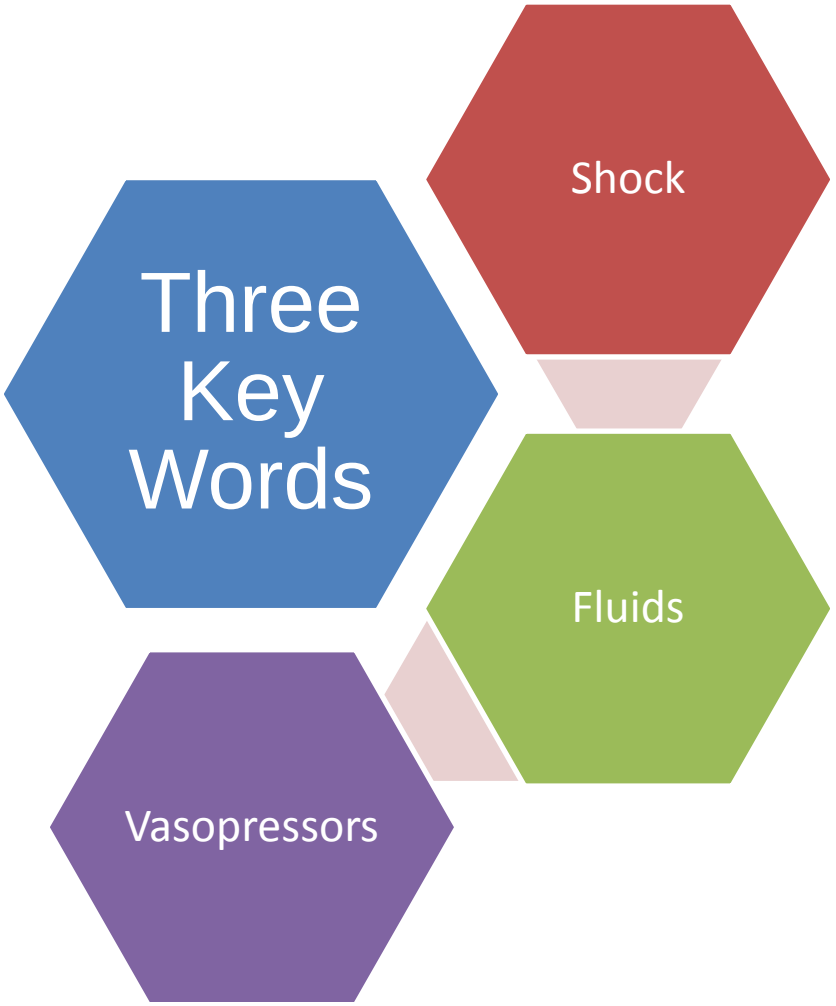
Fluid and Vasopressor therapy in Shock



Shock

- Discrepancy between demand and supply of oxygen to the vital organs of the body
- Reduced Oxygen supply (from atmosphere)
- Reduced uptake/exchange of Gases by Lungs
- Reduced Oxygen flow from lungs to tissues

Shock

- Transport of Oxygen from Lungs depends on
  - Circulating Volume the vehicle which carries Oxygen to Vital organs
  - Hemoglobin Level
  - Myocardial Function

These can be achieved only by smart use of fluids and \vasopressors in conditions of shock

Shock Types

- Cardiogenic
- Obstructive
- Hypovolemic
- Distributive

- First two types, shock can be treated only by treating the cause , we can only buy some time with fluids and vasopressors
- Hypovolumic shock is either because of loss of Fluid or Blood replacement of either will do the job

Distributive shock

- This Group includes
  - Neurogenic Shock
  - Anaphylaxis
  - Ac Adrenal Insufficiency
  - Septic Shock

- The First three again will require treatment of Cause

The Challenge

- The real challenge has been to treat Sepsis and Septic shock
- Fluid and Vasopressor therapy have been the most challenging issues in Management of these patients , therefore my focus on this topic

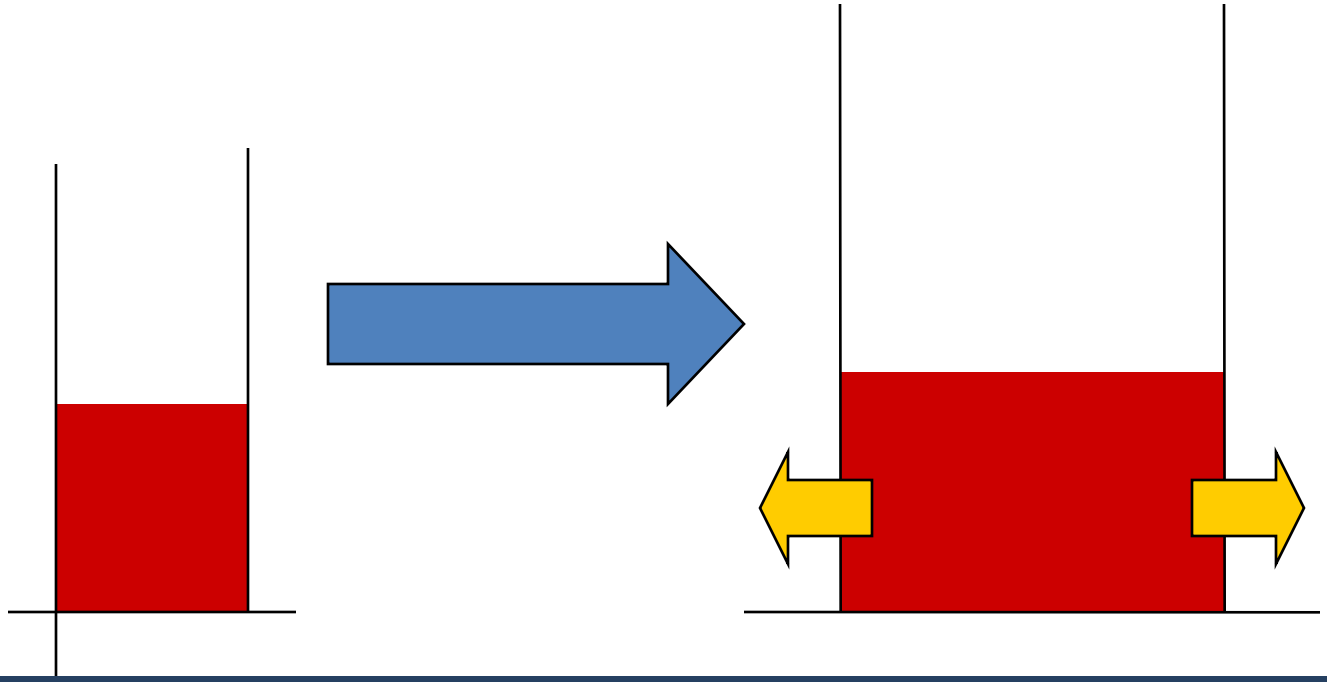
Objectives

- 1.To consider type of fluid for resuscitation in septic shock
- 2. To discuss the administration and monitoring fluid therapy in shock
- 3 .To discuss vasopressors therapy in brief in shock

Fluid Challenge Requires

- The type of fluid to be administered
- The rate of infusion
- Achieving the end points
- Work within the safety limits

Septic Shock – Pathophysiology



Dilatation and Increased Permeability of Capillary Bed- there is net net massive deficiency of circulating volume which needs to be replaced

Type of Fluid Selection?

- Has been debated more than world economy over the years .
- However , Crystalloids (0.9% saline) remain the fluid of choice
- Colloids (Albumin) have some place in resuscitation
- Starches , gelatins seem to losing the fight after recent reportings
- However the debate is likely to continue

The studies –
The CRYSTMAS study

- Reported significantly less requirement of 6% HES to achieve hemodynamic stabilization without differences in safety parameters

  (Study lost ground on technical flaws)

The CRISTAL trial

- Showed colloid resuscitation tended to reduce 28-day mortality and significantly reduced 90-day mortality.
- .

CRYCO Study Group (1,013 ICU patients)

- The use of artificial hyperoncotic colloids and hyper-oncotic albumin was significantly associated with renal event.
- ICU mortality was 27.1%
- Hyper-oncotic albumin increased risk of ICU death

The 2014 Albumin Italian Outcome Sepsis (ALBIOS) trial

- Randomized (100 centers) 1,818 patients with severe sepsis or septic shock .

- In this study all cause mortality at 28 days and 90 days were not different either in 20% albumin and crystalloid solution group.

Albumin – As Resuscitation Fluid

- Albumin infusion may be a useful substitute to crystalloids in hypoalbuminemic patients with septic shock.

- In patients with cirrhosis and peritonitis with hypoalbuminemia, albumin should be considered for volume resuscitation.

Crystalloids vs Colloids

- Colloids
- They are Expensive
- May cause coagulopathy
- May cause Renal dysfunction

ProCESS Trial – 2014

- .
- At 60 days, 90 days, and 1 year there was no differences in mortality between the three arms. The protocol-based care (Starch) was associated with higher degree of renal failure.

Hence the Type of Fluid

- Crystalloids remain fluid of choice until further evidence However –large volume is required.
- Though it's cheap but can cause hyperchloremic acidosis
- While Ringer Lactate may be inappropriate in patients with raised ICP, hyperkalaemia, or procoagulant state.

Speed and amount of Fluid -Therapeutic Strategies in Sepsis

To Optimize Organ Perfusion

Early goal-directed therapy (The First universally accepted fluid and vasopressor trial recommendation)

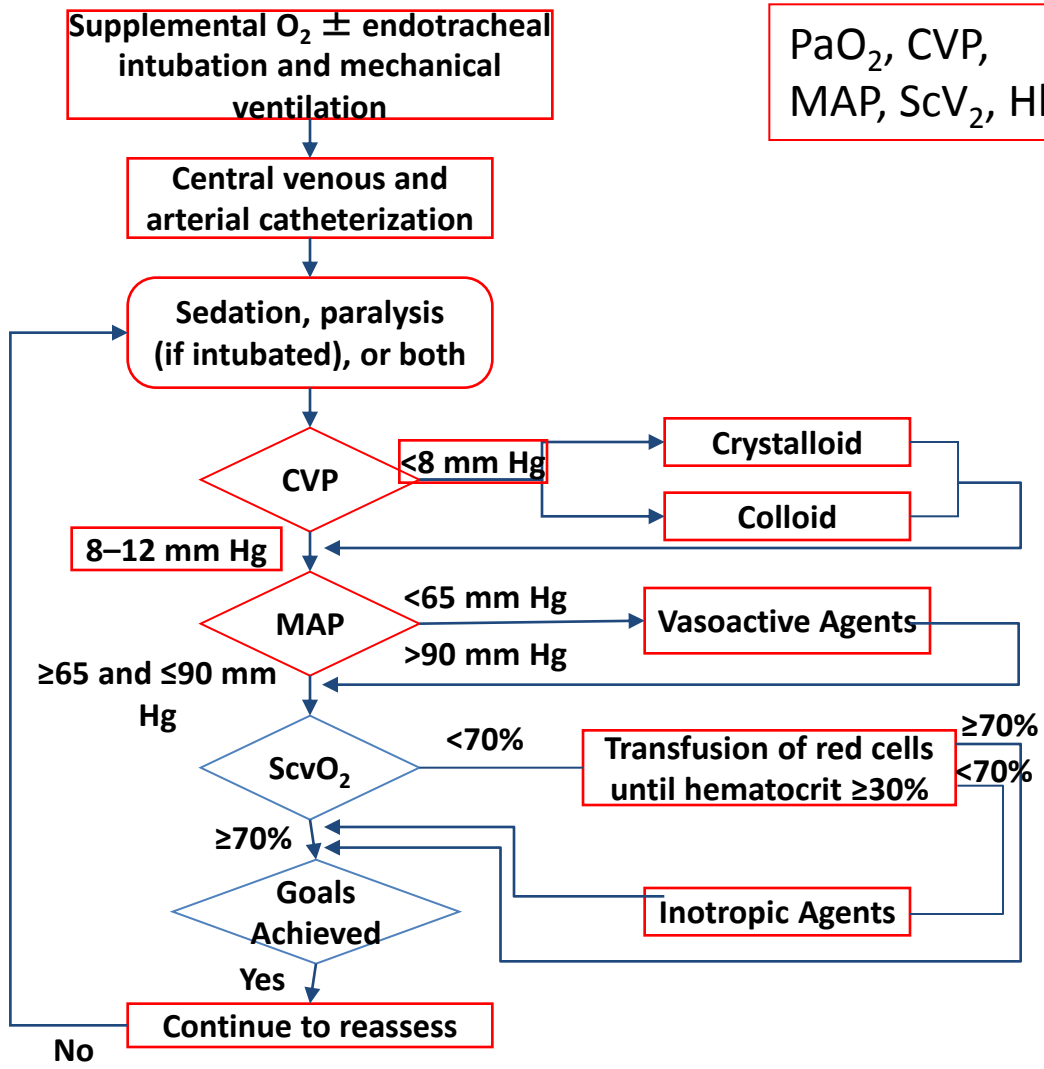
- 16% reduction in absolute risk of in-house mortality
- 39% reduction in relative risk of in-house mortality
- Decreased 28 day and 60 day mortality
- Less fluid volume
- less blood transfusion
- less vasopressor support
- less hospital length of stay

End points in –EGDT in 6 hours

- MAP >65
- CVP 8 to12
- SVO2>70%
- Hb 8.5gm%
- SPO2 >90%

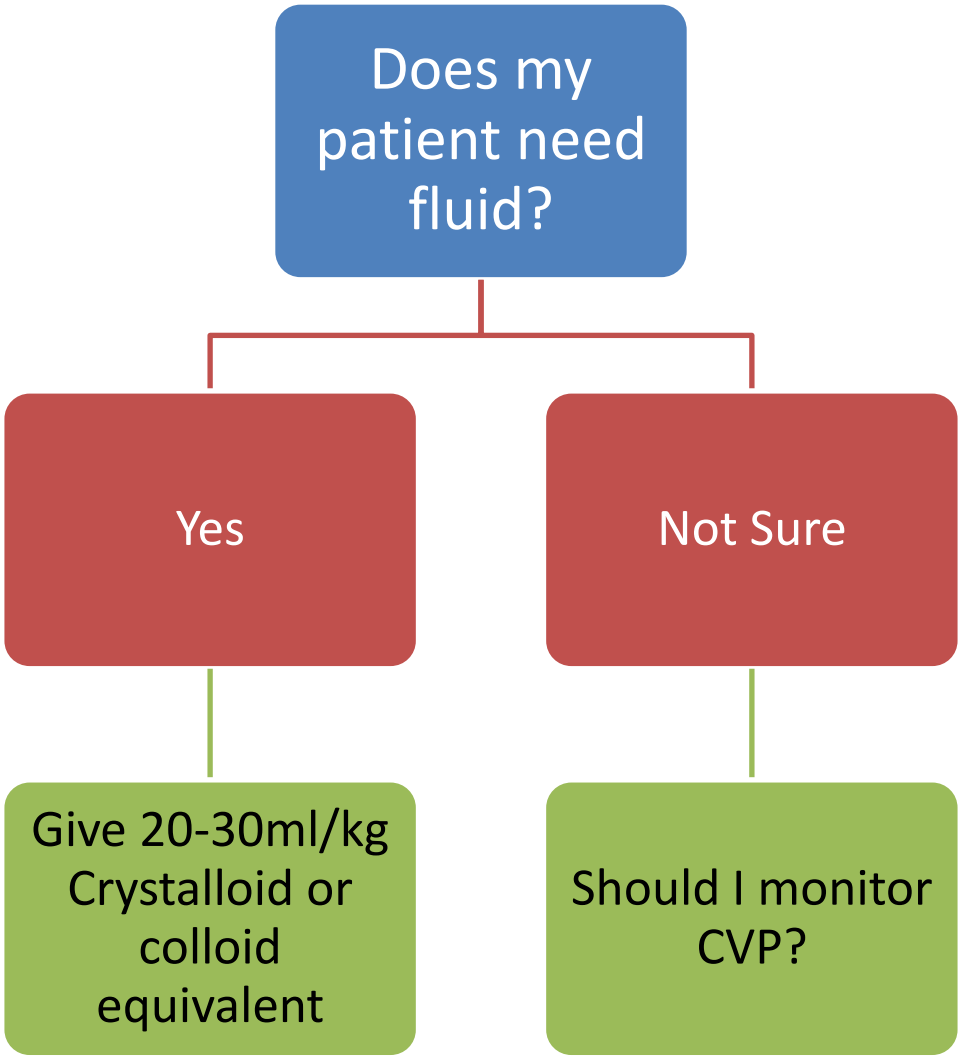
Rivers E, et al. N Engl J Med 2001;345:1368-77.

EGTD- based algorithm of septic shock management



PaO_2, CVP, MAP, ScV_2, Hb

However many a times dilemma continues



Bed side Strategies

Patient	Fluid challenge
MAP 60, HR 130 CVP 14, uo-20ml/hr	NS 500 ml Over 30 min

MAP = 65, HR = 120; CVP = 08 → Continue

MAP = 70, HR = 110; CVP = 14 → Stop

MAP = 65, HR = 120; CVP = 20 → Stop

Tight Rope walk – when to stop

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- Restore organ perfusion
- Correct hypotension
- Adequate for vasoactive drugs

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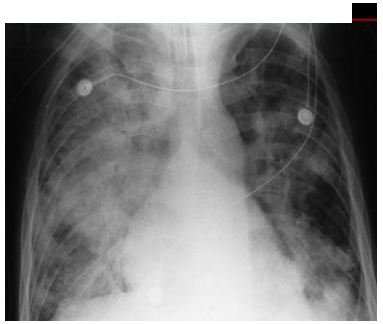
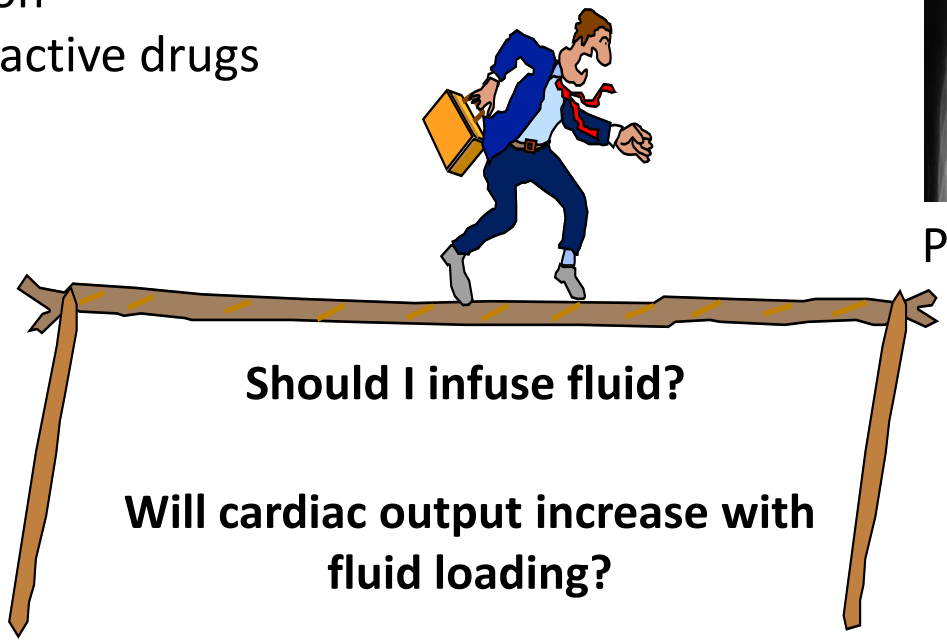


Pulmonary edema

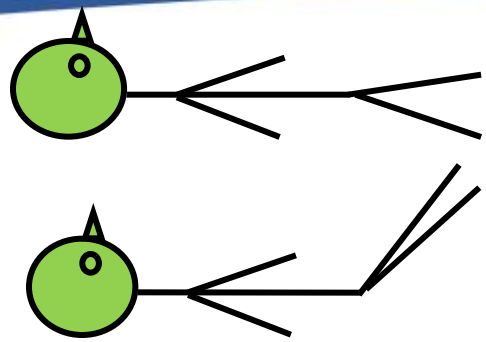


Should I infuse fluid?

Will cardiac output increase with fluid loading?

How much fluid?
When should I stop?

Passive Leg Raising



PLR recruits a part of blood contained in the venous reservoir.
Transfers ~150 ml blood into the central compartment

Hypovolemia vasoconstriction

↓

Increases right cardiac preload

↓

Increase in right cardiac output

RV preload reserve, RV function

↓

Increased left ventricular filling

LV preload reserve; LV function

↓

Increase in Cardiac output

ICM 2008;34:659-63

Bedside Vena-caval collapsibility indices

- A superior vena caval collapsibility of greater than36%predicted an increase in Cardiac out put at least 11%with 90% sensitivity and 100% specificity.
- They found that IVC index of more than 18% predicted an increase in cardiac out put of at least 15% with90% sensitivity

A very reliable and Popular Bedside method

Oesophageal Doppler probe

- McKendry et al used oesophageal doppler to assess fluid resuscitation protocol
- They stop further fluid resuscitation when aortic flow velocity no longer increased in response to bolus volume.
- Oesophageal Doppler may become a major tool in future for fluid resuscitation protocols.

End Point of Fluid Challenge

Indices of tissue perfusion should improve :

- Arterial pressure
- Urine output
- Sensorium
- Pulse rate SVO2

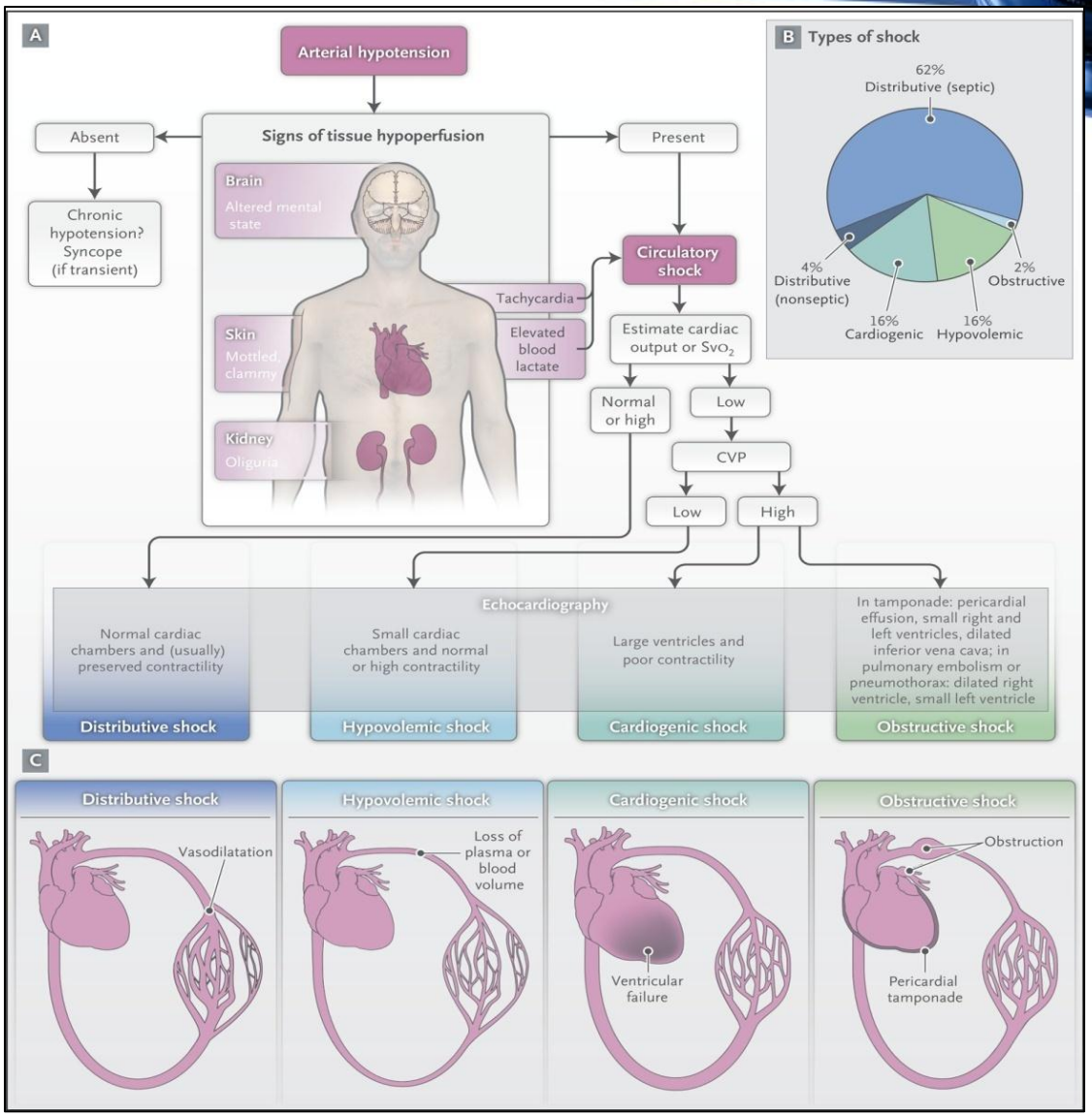
The Vasopressor Therapy

When?

What?

How Much?

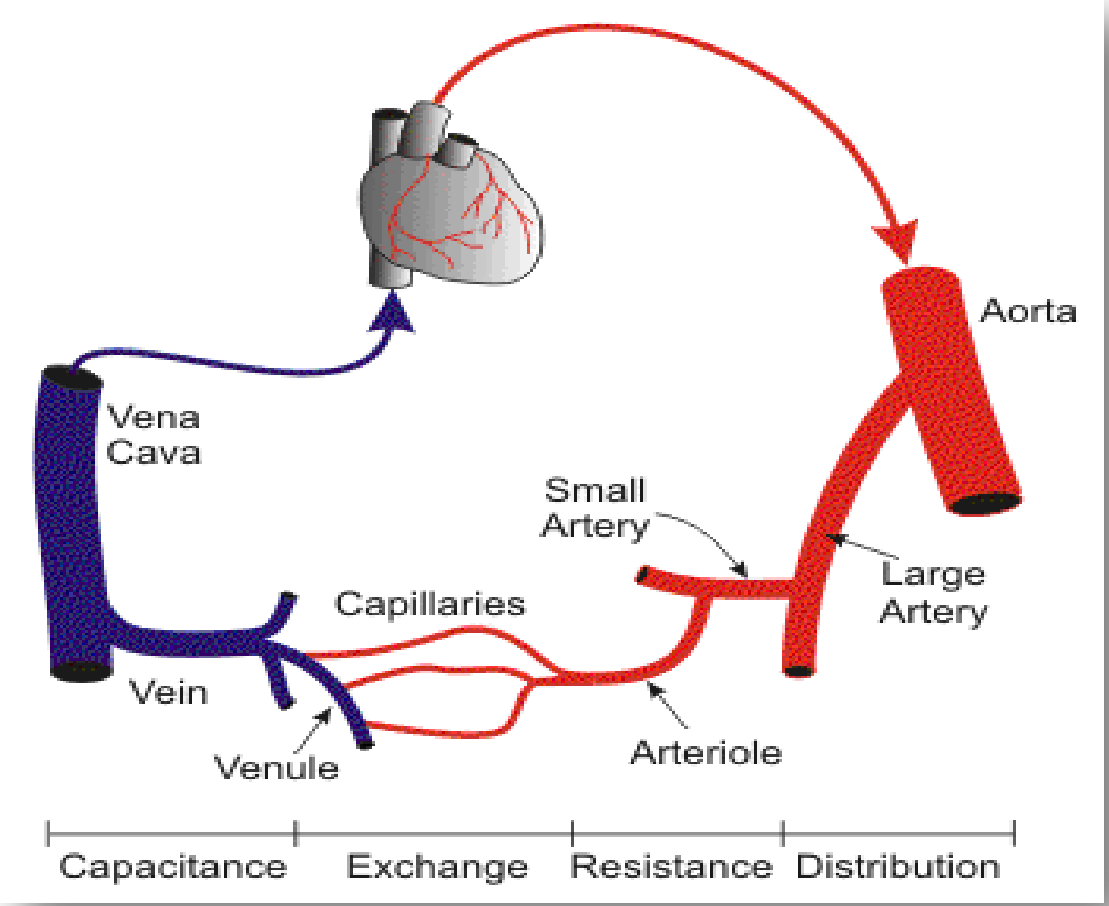
How Long?



Vasopressors in shock

- When fluid administration fails to restore an adequate arterial pressure and organ perfusion in patients with septic shock
- Therapy with vasopressor agents should be initiated.
- The ultimate goals of such therapy in patients with shock are to restore effective tissue perfusion and to normalize cellular metabolism.

When to start Vasopressors



When The Intravascular Space is filled up significantly

Vasopressors & Inotropes

- **Noradernaline** – The First choice
- **Aderaline** – The second Choice
- **Dopamine** – Given up
- **Vasopresin** – The second/Third Choice
- **Phenyl ephrine** – Now available in India
- **Dobutamine** – Limited choice

Dosage and Action

Drug	Dose/Mixture	Action	Cardiac Stimulation	Vasoconstriction	Vasodilation	Cardiac Output
Norepinephrine	2-20 μg/min 4 mg/250 mL	Primarily α-1, some β-1	++	++++	0	Slight increase or no change
Dopamine	0.5-20 μg/kg/min 400 mg/250 mL	α, β, and dopaminergic	++ at 5–10 μg/kg/min	++ at 7 μg/kg/min	+ at 0.5–5.0 μg/kg/min	Usually increases
Phenylephrine	40-200 μg/min 10 mg/250 mL	Pure α	0	++++	0	Decrease
Vasopressin	0.01–0.04 U/min 20 U/100 mL	α and V1	0	++++	+	Decrease
Epinephrine	1–10 μg/min 1 mg/250 mL	α and β	++++ at 0.03–0.15 μg/kg/min	++++ at 0.15–0.30 μg/kg/min	+++	Increases
Dobutamine	2.5–20 μg/kg/min 250 mg/250 mL	β-1, Some β-2 and α-1 in large dosages	++++	+	++	Increase

De Backer D, Biston P, Devriendt J, et al. Comparison of Dopamine and Norepinephrine in the treatment of shock. N Engl J Med 2010;362:779-89.

- RCT 1679 patients with shock
- Dopamine or norepinephrine as first-line therapy
- No significant difference in the primary endpoint of 28-day mortality
  - More arrhythmic events with dopamine
  - Pre-specified analysis by etiology of shock
- Mortality was lower with use of norepinephrine than dopamine in the subgroup with cardiogenic shock

Myburgh JA, Higgins A, Jovanovska A, Lipman J, Ramakrishnan N, Santamaria J. A comparison of Epinephrine and Norepinephrine in critically ill patients. Intensive care medicine 2008;34:2226-34.

- A randomized clinical trial comparing epinephrine to norepinephrine in 280 critically ill patients with shock
- Conclusion: No difference
  - Time to achieve arterial pressure goals
  - 28-day, or 90-day mortality
    - 13% of the patients in the epinephrine group were withdrawn from the study due to lactic acidosis or tachycardia.

Annane D, Vignon P, Renault A, et al. Norepinephrine plus Dobutamine versus Epinephrine alone for management of septic shock: a randomised trial. Lancet 2007;370:676-84.

- Fairly large (n=330) RCT compared epinephrine to norepinephrine with or without dobutamine
  - Titrated to maintain a mean arterial pressure above 70 and a cardiac index above 2.5 L/min
- There was no significant difference in
  - Time to hemodynamic success
  - Vasopressor withdrawal
  - 28-day, ICU, or hospital mortality
- Metabolic abnormalities were transient in this trial, and no patients were withdrawn for this reason.

Russell JA, Walley KR, Singer J, et al. Vasopressin versus Norepinephrine infusion in patients with septic shock. N Engl J Med 2008;358:877-87.

- A multicenter clinical trial (VASST) randomized 776 patients with pressor dependent septic shock
  - Vasopressin (0.03 U/min) or 15 μg/min norepinephrine (+ original vasopressor infusion)
  - The primary endpoint was 28-day mortality
  - No difference in mortality or adverse effects
- Vasopressin appeared to be better in the less severe (pre-hoc) subgroup
- Vasopressin should be thought of as replacement therapy for relative deficiency rather than as a vasopressor agent to be titrated to effect. Should be used only at low doses

Vasopressin

- Not a replacement for norepinephrine or dopamine as a first-line agent
- Consider in refractory shock despite high-dose conventional vasopressors
- If used, administer at 0.01-0.04 units/min in adults Grade E

Conclusions

Vasopressors may be used based on physiological principles

- After obtaining adequate volume & flow
- Different agents have differing effects on flow and pressure

Outcome based RCTs have not shown superiority of any of first line agents

- Noradrenaline, adrenaline, dopamine, dobutamine & vasopressin

Sub-group differences

- Noradrenaline better than dopamine in cardiogenic shock
- Dopamine more arrhythmogenic than Noradrenaline
- Adrenaline causes more metabolic disturbances

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