

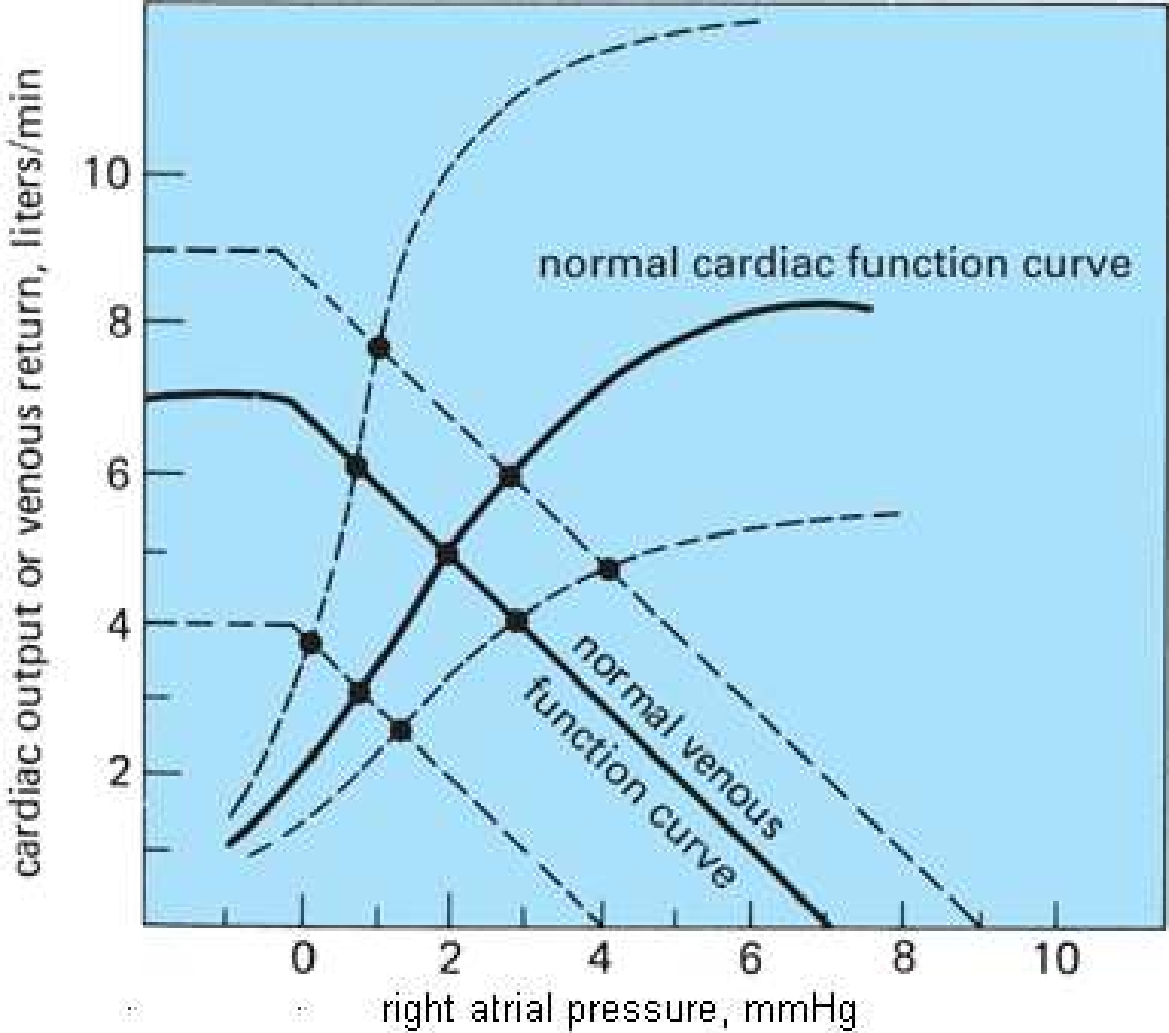


Pathophysiology of circulatory shock

Shock - definition

- Severe tissue hypoperfusion resulting in low supply of oxygen to the organs
- Systemic hypotension (of various causes) is present
- $P = Q \times R$
- $Q \sim CO = SV \times f$
- CO depends on
 - a) cardiac function
 - b) venous return (\rightarrow preload)
- R – systemic resistance (mostly arterioles) - afterload

Cardiac function and venous function



Vascular resistance

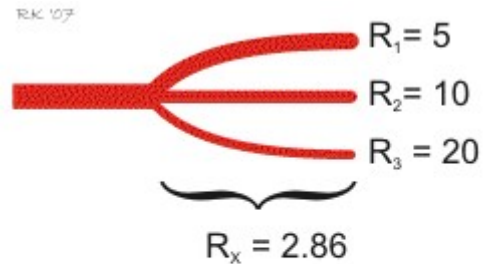
✘ R [$\text{kg}\cdot\text{s}^{-1}\cdot\text{m}^{-4}$]: can be obtained from Hagen-Poiseuill law:

$$R = 8 \times \eta \times d / \pi \times r^4, \text{ where:}$$

η = viscosity

d = length of the segment

r = radius



$$R_x = \frac{1}{\frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3}}$$

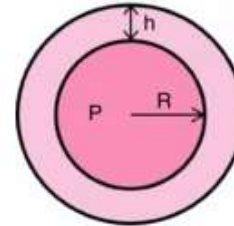
Preload and afterload in heart

- Law of Laplace for wall tension in a hollow sphere: $\sigma = \frac{P \times r}{2h}$,
where:

P....pressure inside the sphere

r....inner radius

h....wall thickness



- Preload – wall tension ($\text{N.m}^{-2} = \text{Pa}$ – force per area) before the systole
 - The main factor is venous return → filling of cardiac ventricles
- Afterload – increase in wall tension during the systole
 - The main factor is a peripheral resistance, or pulmonary vascular resistance in a case of the right ventricle
- Preload is higher in the right ventricle, afterload is higher in the left one

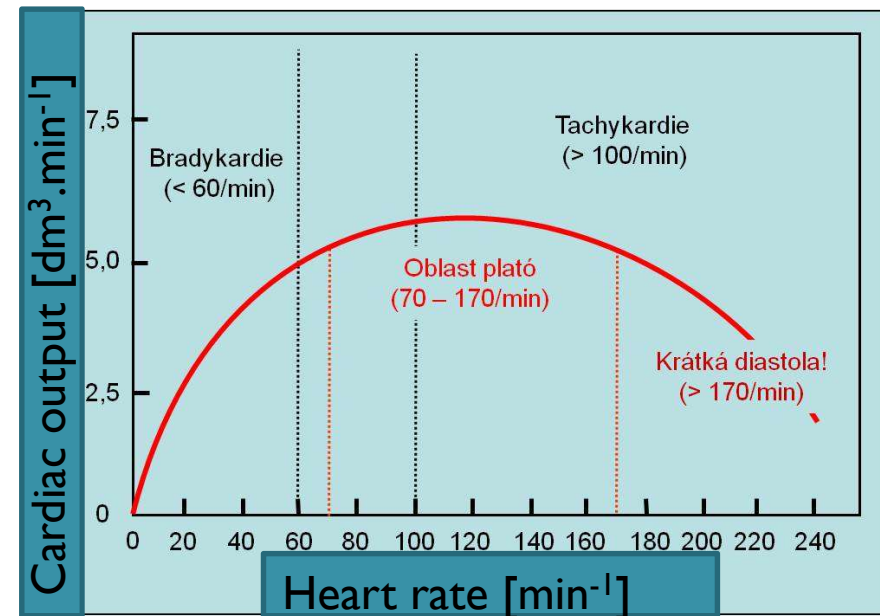


Phases of shock

- Compensation of initiating cause
- Decompensation
- Refractory shock

Compensatory mechanisms and their limits

- Activation of sympathetic nervous system (tens of seconds)
- Activation of RAAS (cca 1 hour)
- Vasoconstriction (if possible) – but it leads into lower blood supply
- Vasodilatation in some tissues (esp. myocardium)
- Positively inotropic effect of SNS (if possible) – but at cost of higher metabolic requirements of the heart
- Increased heart rate – but CO decreases in high HR (>150 bpm)
- Keeping circulating volume by lower diuresis – but at cost of acute renal failure
- Shift to anaerobic metabolism – but at cost of ↓ ATP a ↑ lactate (acidosis)
- Increased respiratory rate (but shallow breathing results in ↑ relative deadspace)
- Shift of saturation curve of hemoglobin to right (↑2,3-DPG)
- Hyperglycemia – but there is decreased utilization of Glc in the periphery



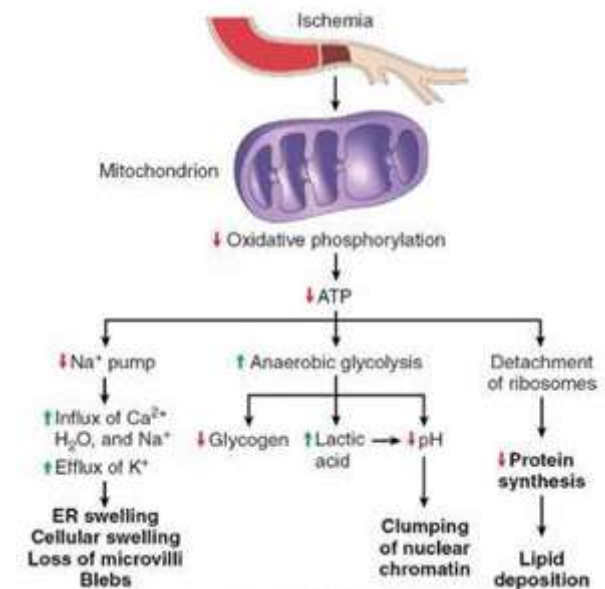


Decompensated shock

- ↓ BP
- ↓ diuresis
- Brain hypoperfusion – involvement of mental functions
- Acrocyanosis
- Tachypnea
- “Golden hour“

Shock at cellular level

- Mitochondrial dysfunction (result of hypoxia) – lower production of ATP
- ↑ ROS production by dysfunctional mitochondria
- Failure of ion pumps (e.g. Na/K ATP-ase → ↑ intracellular Ca^{2+})
- Activation of Ca^{2+} -dependent proteases
- Lysosomal abnormalities – release of lysosomal proteases
- ↓ intracellular pH, ↑ lactate
 - promote hyperpolarization of muscle cells by opening K^+ channels → ↓ Ca^{2+} entry → ↓ smooth muscle cell and cardiomyocyte contraction



Refractory shock

- Vicious circles

- 1) Vasodilatation ↔ hypoperfusion

- Endothelial cells contain two isoforms of nitric oxid synthase – constitutive (eNOS) and inducible (iNOS)
- In lasting hypoxia of endothelial cells there is increased iNOS activity (primarily physiological mechanism)
- ↑NO increases vasodilation and hypoperfusion
- Lactate acidosis → hypotension (lactate – prognostic factor)

- 2) Myocardial hypoxia ↔ lower contractility

- Lower myocardial perfusion leads into ↓CO, which further reduces coronary flow
- Myocardium does not benefit from the shift of Hb saturation curve – efficiency of O₂ extraction is already at its maximum

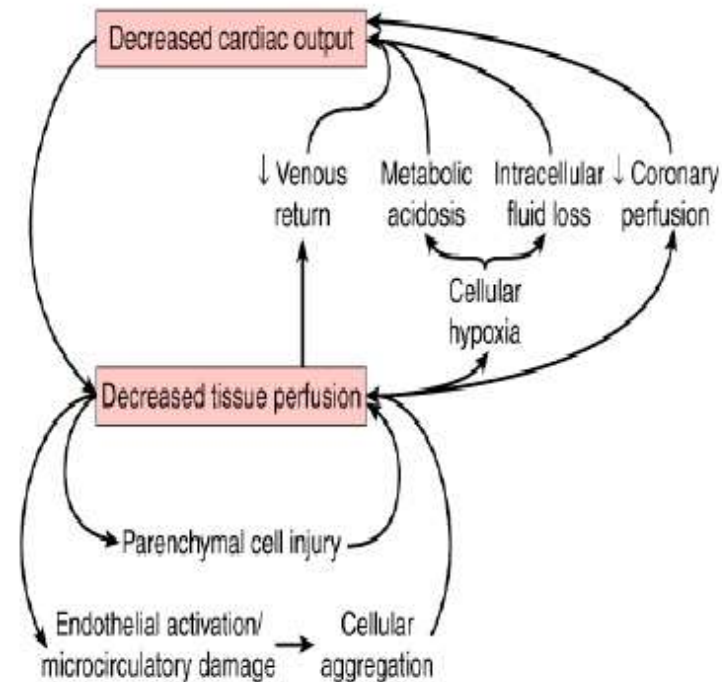
- 3) Brain hypoperfusion ↔ ↓SNS activity

- Lower perfusion of vasomotor centre leads first into SNS hyperactivity, which is then followed by its supression
- That leads into ↓brain perfusion

Other vicious circles in refractory shock

Vicious cycle of shock

- * SIRS
(systemic inflammation)
- * DIC
(systemic activation of coagulation)



Source: Brunicaudi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition*: <https://www.accessmedicine.com>. Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

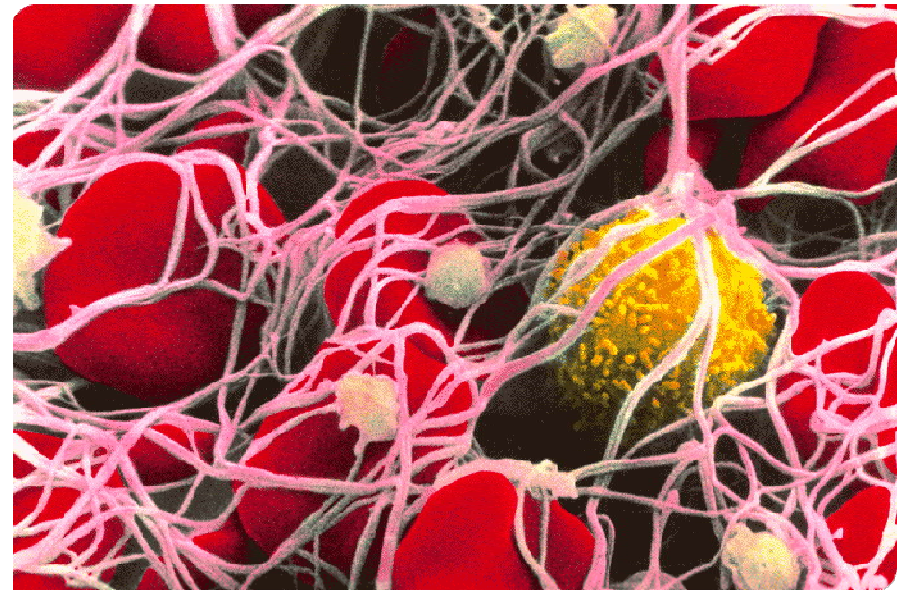


Systemic Inflammatory Response Syndrome (SIRS)

- Systemic activation of immune mechanisms
- Causes:
 - infections (sepsis)
 - Shock caused by non-infectious causes (diffuse tissue damage in hypoxia)
 - Non-compatible blood transfusions
 - Radiation syndrome (esp. GIT form)

Disseminated intravascular coagulopathy (DIC)

- Systemic exposure to thrombin
- Two phases:
 - 1) Formation of microtrombi (with local ischemia)
 - 2) Bleeding as a result of consummation of coagulation factors
- Consequence of the vessel wall damage
- Moreover, slower blood flow contributes to the extent of coagulation reactions
- DIC is especially frequent in septic shock





Signs of shock (benchmark)

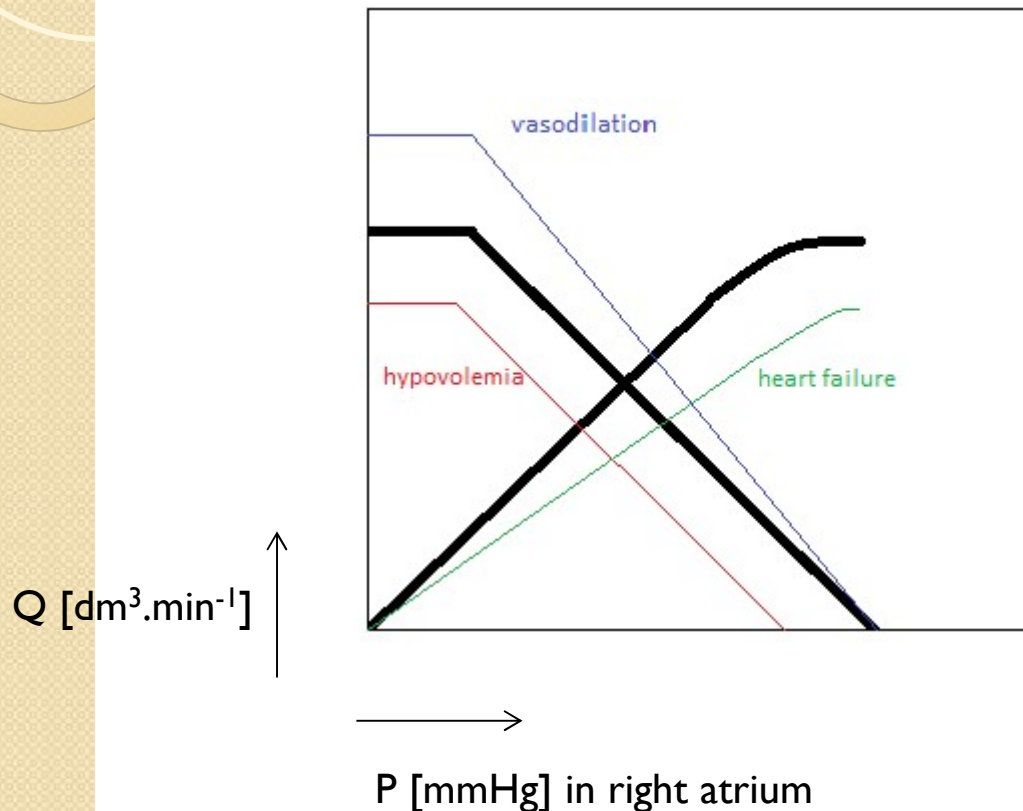
- systolic BP < 90 mmHg
- mean TK < 65 mmHg
- lactate > 4 mmol/l
- diuresis < 0.5 ml/kg/h
- often:
 - CI (= CO/body surface area) < 1.8 (not in septic shock)
 - HR > 100/min (not in shock with bradycardia, neurogenic shock)



Forms of shock

- a) Hypovolemic (“cold and dry”) shock – low circulating volume, low preload
- b) Distributive (“warm”) shock – low resistance, low afterload, CO might be increased
- c) Cardiogenic (“wet”) shock – low CO in bad cardiac function, fluid congestion
- d) Obstructive shock – low preload of one ventricle in normovolemia and subsequent lowering of CO + congestion – pathophysiology similar to cardiogenic shock (but congestion occurs in one half of the circulation)

Cardiac and venous function in shock



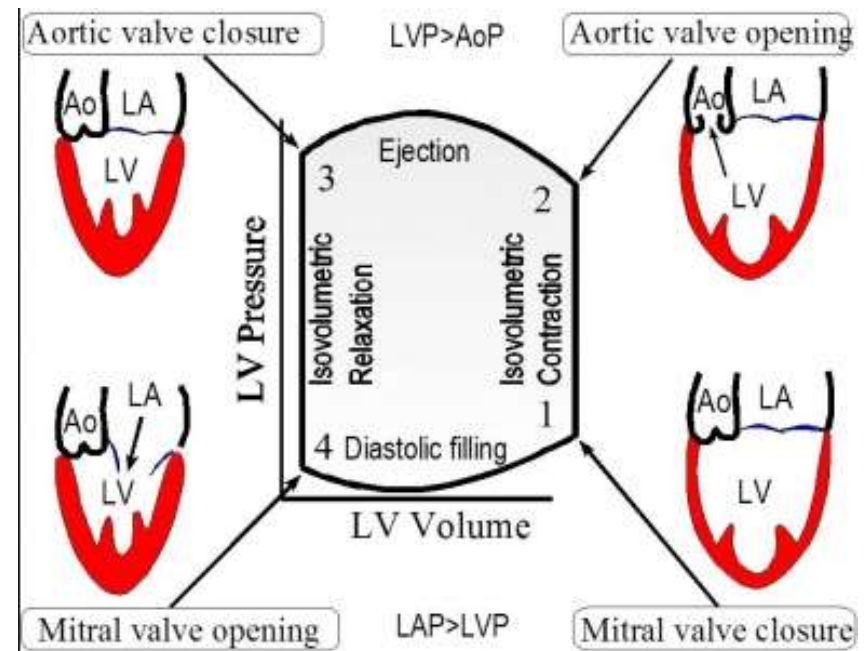
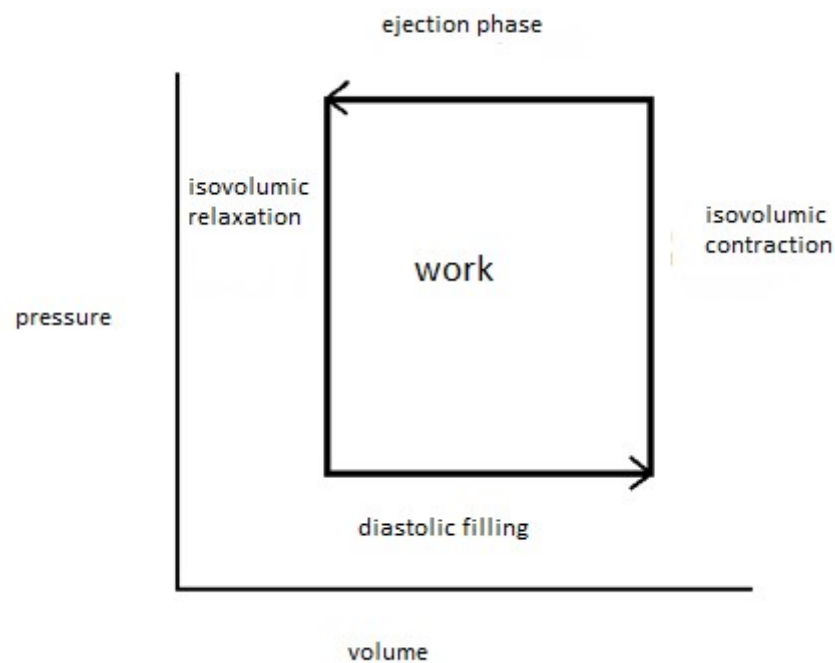
- Hypovolemic shock: compensation by the vasoconstriction and cardiac mechanisms (but: CO is limited by low venous return)
- Distributive shock: compensation by cardiac mechanisms (vasoconstriction is usually impossible)
- Cardiogenic (and obstructive) shock: compensation by vasoconstriction

| Type of shock | CO | SVR | PWP | CVP |
|---------------|----|-----|-----|-----|
| Hypovolemic | ↓ | ↑ | ↓ | ↓ |
| Cardiogenic | ↓ | ↑ | ↑ | ↑ |
| Distributive | ↑ | ↓↓ | ↓ | ↓ |

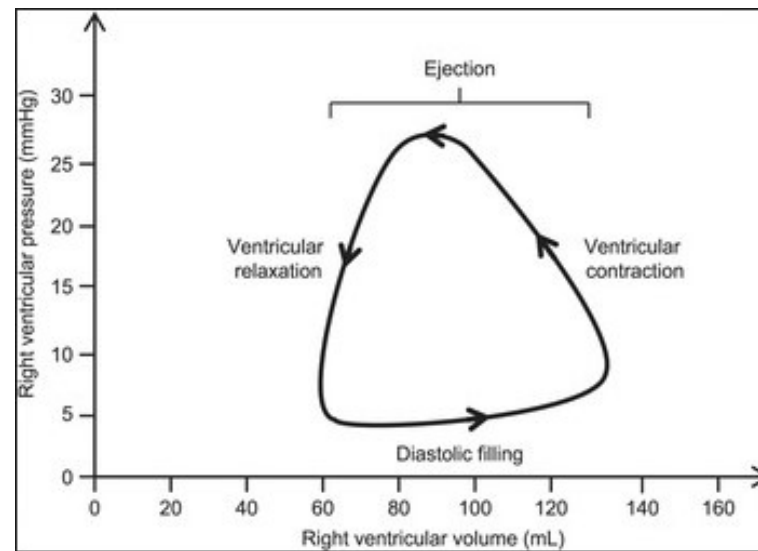
„Interests“ of the heart and perfused tissues

- Hypovolemic shock - ↓ preload
- Distributive shock - ↓ afterload
- From the heart's viewpoint, ↓ preload and ↓ afterload are advantageous, regarding the blood supply to key organs they may be linked to circulatory failure (shock states) – the cause is, however, an extracardiac insult → ↓ preload or ↓ afterload (or both – polytrauma)
 - But: heart must ensure its own perfusion
- Cardiac causes of shock
 - ↓ inotropy
 - ↓ lusitropy
 - ↓ HR

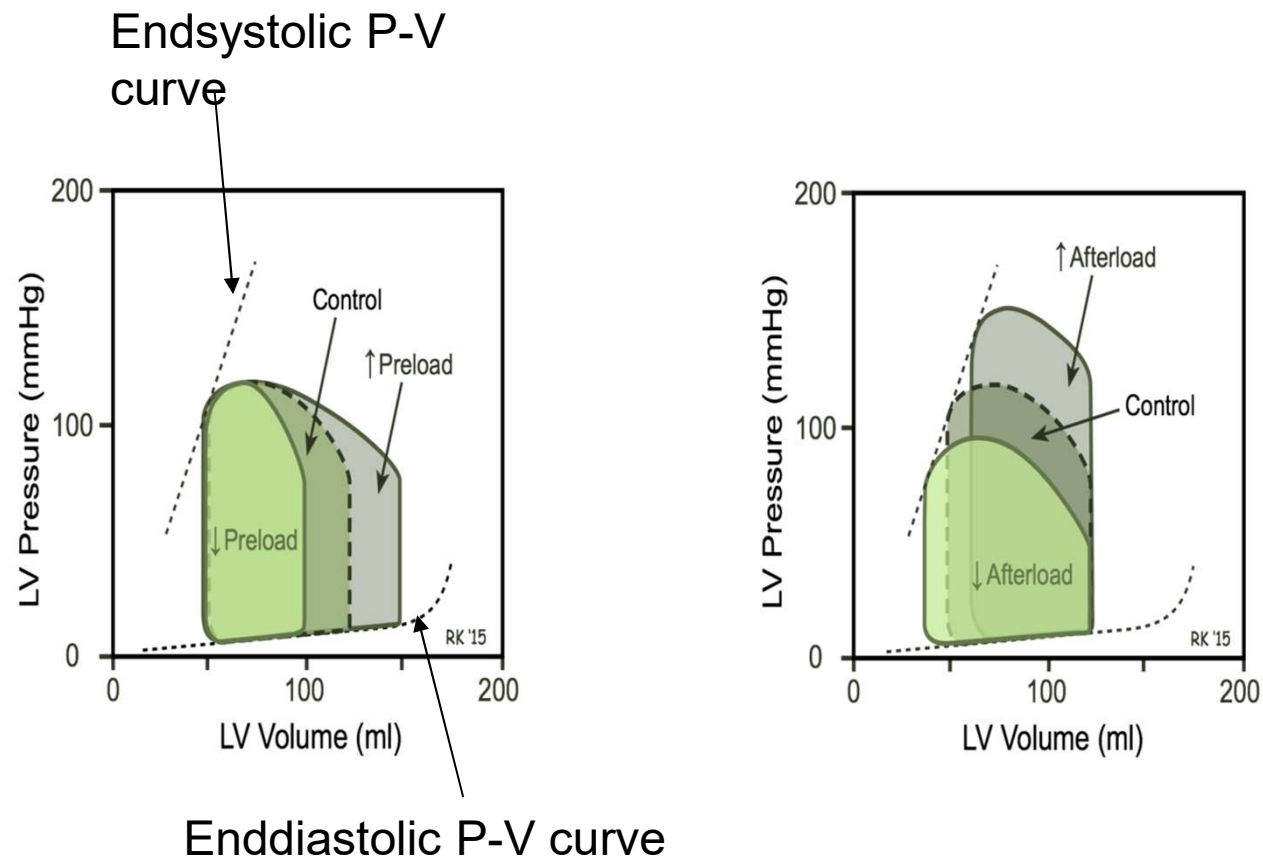
Muscular work of the heart – P-V diagram:



P-V diagram in the right ventricle

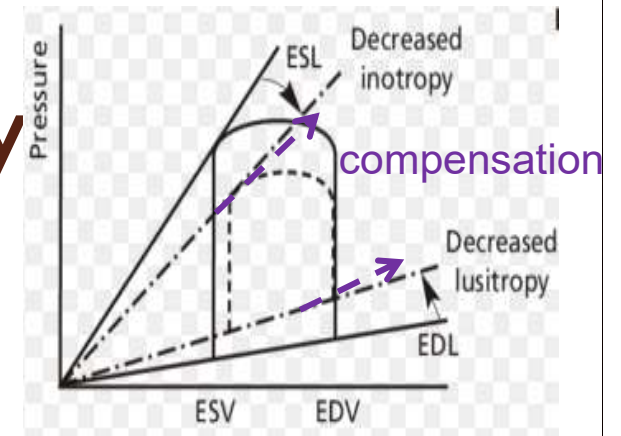


P-V diagram during changes of preload or afterload

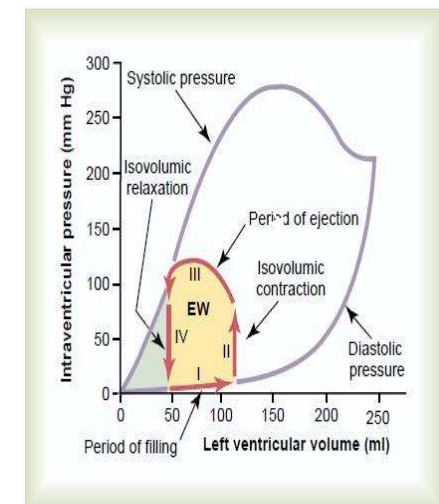


Inotropy and lusitropy

- ↑ inotropy („ability to contract“) of the heart – shifts the endsystolic P-V curve up
- ↑ lusitropy („ability to relax“) of the heart – shifts the enddiastolic P-V curve down
 - The relaxation process is ATP-dependent – as well as it is enabled by pumping out the cytosolic Ca^{2+}
- ↓ inotropy or lusitropy decrease an area of P-V diagram (i.e. the cardiac work decreases – compensation by RAAS and SNS linked to an increase of preload and afterload follows)



Limit of Frank-Starling mechanism (active muscular force decreases)



Passive contraction by elastic fibres (relaxation ability decreases)



Hypovolemic shock - causes

- Acute bleeding
- Burns, trauma
- Rapid development of ascites
- Acute pancreatitis
- Severe dehydration
 - Vomiting, diarrhoea
 - Excessive diuresis (e.g. in diabetes insipidus)

Acute blood loss

- Circulatory disorder (SBP < 100 mmHg, HR > 100/min) following the loss of 15% of circulating volume, shock in 30% of circulating volume
- Immediate priorities are to maintain the tissue perfusion (crystalloids, colloids) and to stop bleeding (if possible), then blood derivatives (erythrocytes + plasma + thrombocytes)



Distributive shock - causes

- Anaphylactic shock
- Anaphylactoid shock
 - Mediators of mast cells, but without IgE
 - E.g. snake venoms, radiocontrasts
- Septic shock
 - Role of bacterial lipopolysaccharides
 - Bacterial toxins
 - IL-1, TNF- α – stimulate synthesis of PGE₂ and NO
- Neurogenic shock
 - Vasodilatation as a result of vasomotoric centre (or its efferent pathways) impairment

Development of anaphylactic reaction

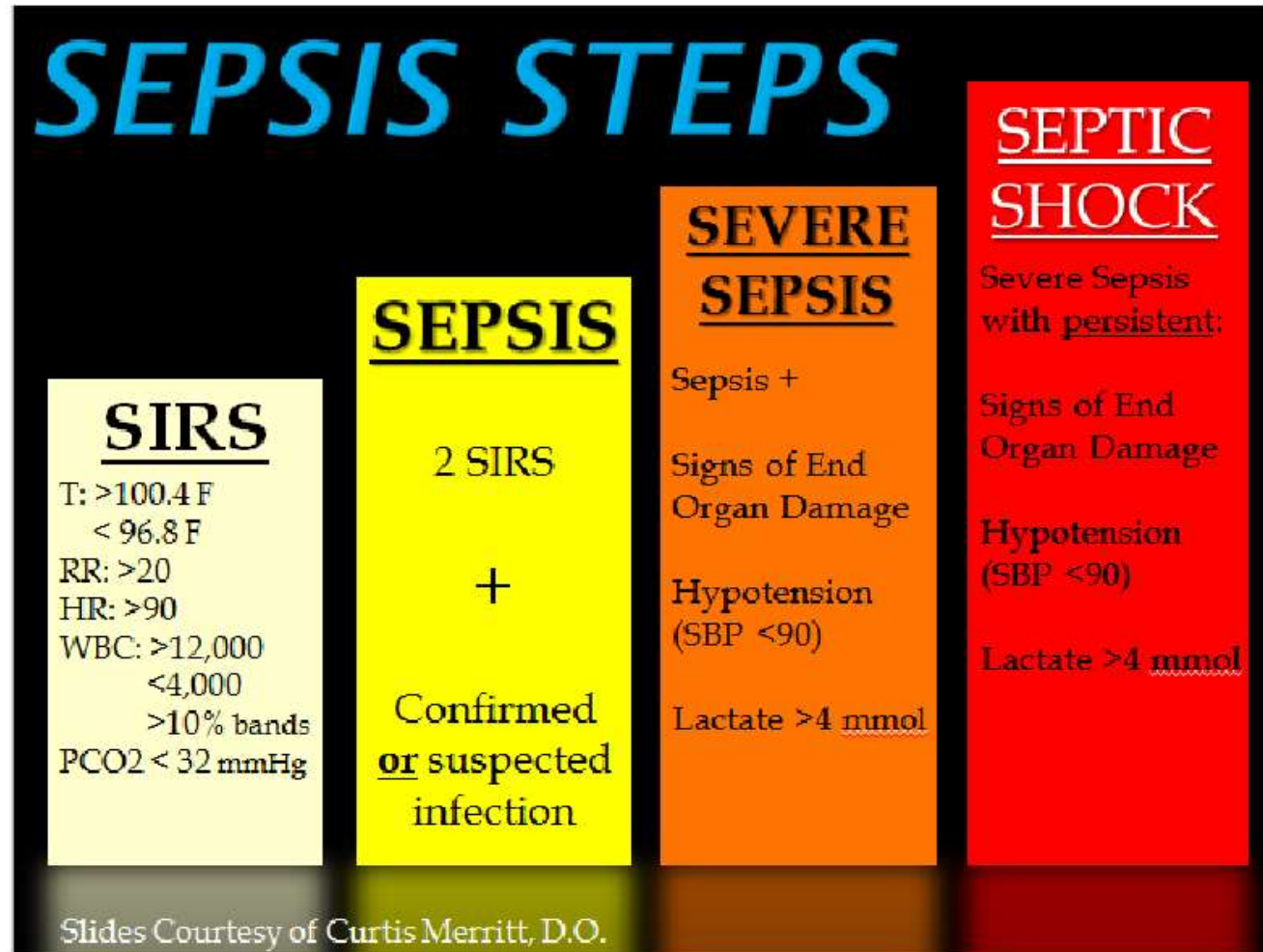
- **Sensibilization** of Th- and B-cells and IgE production
- **Opsonization** of basophils a mastocytes
 - IgE binds to FcεR (I a II)
- IgE-mediated **degranulation** of the mast cell and basophils following the repeated contact with an antigen
 - mediator release
 - primary (stored)– HISTAMIN (dominantly H₁ receptors)
 - secondary (newly formed) – PG, LTA, PAF, bradykinin, cytokines, ...
 - effects
 - vazodilatation, SMC contraction (incl. bronchoconstriction), ↑capillary permeability, chemotaxis, ↑mucus secretion, platelet aggregation

Anaphylactic and anaphylactoid reaction

- **Anaphylaxis**

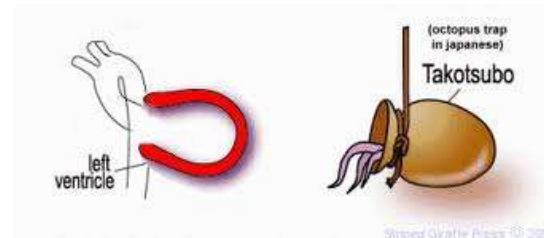
- Severe, systemic, potentially life-threatening reaction following systemic exposition to an allergen
- Medication, food, insects, allergen extracts, latex
- Manifestation
 - mucous membrane, derm: erythema, exanthema, pruritus, oedema
 - resp. system: acute rhinitis, nasal obstruction, sneezing, irritation to cough, breathing problems, foreign body sensation in throat
 - GIT: vomitus, colic, diarrhoea
 - CV system: palpitation, tachycardia, hypotension, arrhythmia
 - urogenital system: urine incontinence
 - CNS: consciousness disorders, spasms
- Anaphylactoid reaction:
 - Participation of mast cell mediators, but without IgE
 - IgG, immune complexes, anaphylatoxins (C3a, C5a), myorelaxants, opiates, contrast matters, snake venoms...

SIRS and sepsis

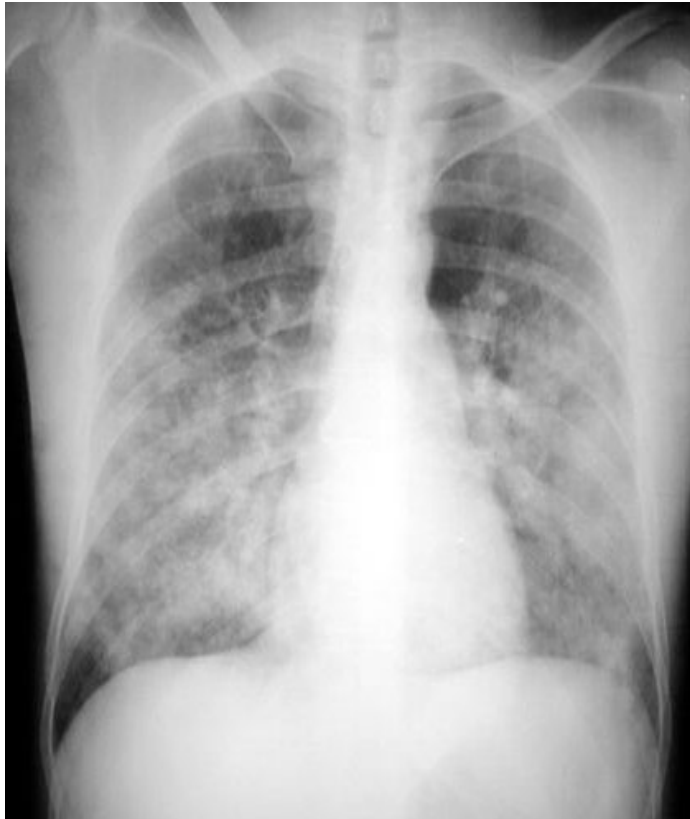


Cardiogenic shock - causes

- Myocardial infarction
 - Arrhythmias
 - Valvular disease (e.g. rupture of papillary muscles)
 - Decompensation of heart failure in dilated/restrictive cardiomyopathy, amyloidosis
 - Overload by catecholamines (“tako-tsubo syndrome“ – apical akinesia + basal hyperkinesia)
-
- Rupture of ventricular septum
 - Obstructive shock – e.g. cardiac tamponade, massive pulmonary embolism, aortic dissection



„Backward“ acute heart failure – X-ray



Pulmonary oedema



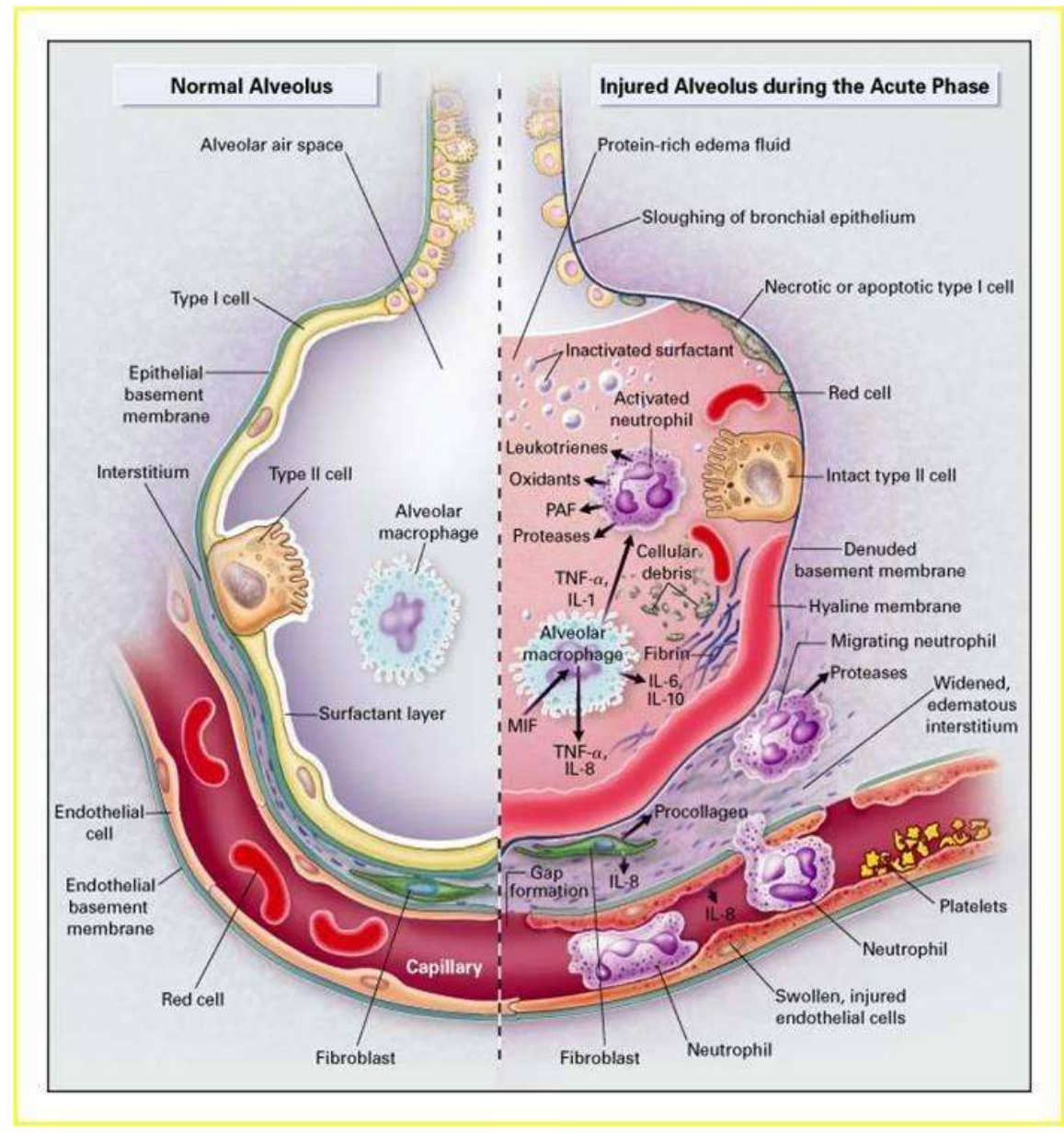
Bilateral pleural effusion

Organ complications in shock

- Lungs
 - ARDS
- Liver
 - necrosis of hepatocytes
- GIT
 - stress ulcer
 - Damage of intestinal mucosa by ischemic necrosis → sepsis
- Kidneys
 - Acute renal failure in vasoconstriction of a. afferens
 - Acute tubular necrosis during ischemia

Adult Respiratory Distress Syndrome (ARDS – „shock lung“)

- Result of lung inflammation in SIRS, pulmonary infections, aspiration of gastric juice, drowning
- Exsudative phase (hours): cytokine release, leukocyte infiltration, pulmonary edema, destruction of type I pneumocytes
- Proliferative phase: fibrosis, dead space, proliferation of type II pneumocytes
- Reparative phase: ↓ inflammation, ↓ edema, continuing fibrosis, in most cases permanent restrictive diseases





Multiorgan dysfunction syndrome (MODS)

- Functional disorder of more organs at once (lungs, liver, GIT, kidneys, brain, heart)
- It can develop after initial insult (days or weeks)
- Hypermetabolism, catabolic stress
- Can both precede or result from SIRS (primary vs. secondary MODS)
- Dysfunction → failure



Persistent MODS as an adaptation?

- ↓ mitochondria in tissues
- ↓ T3
- Analogy of hibernating myocardium (here, also ↓ of contractile apparatus and energy consumption)
- Gene expression similar to hibernating animals
- Later functional improvement is possible

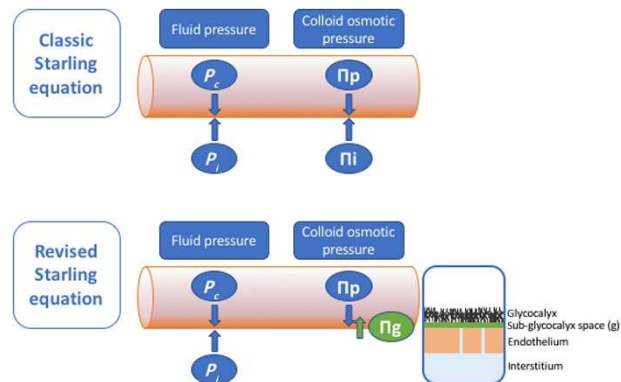


General principles of treatment

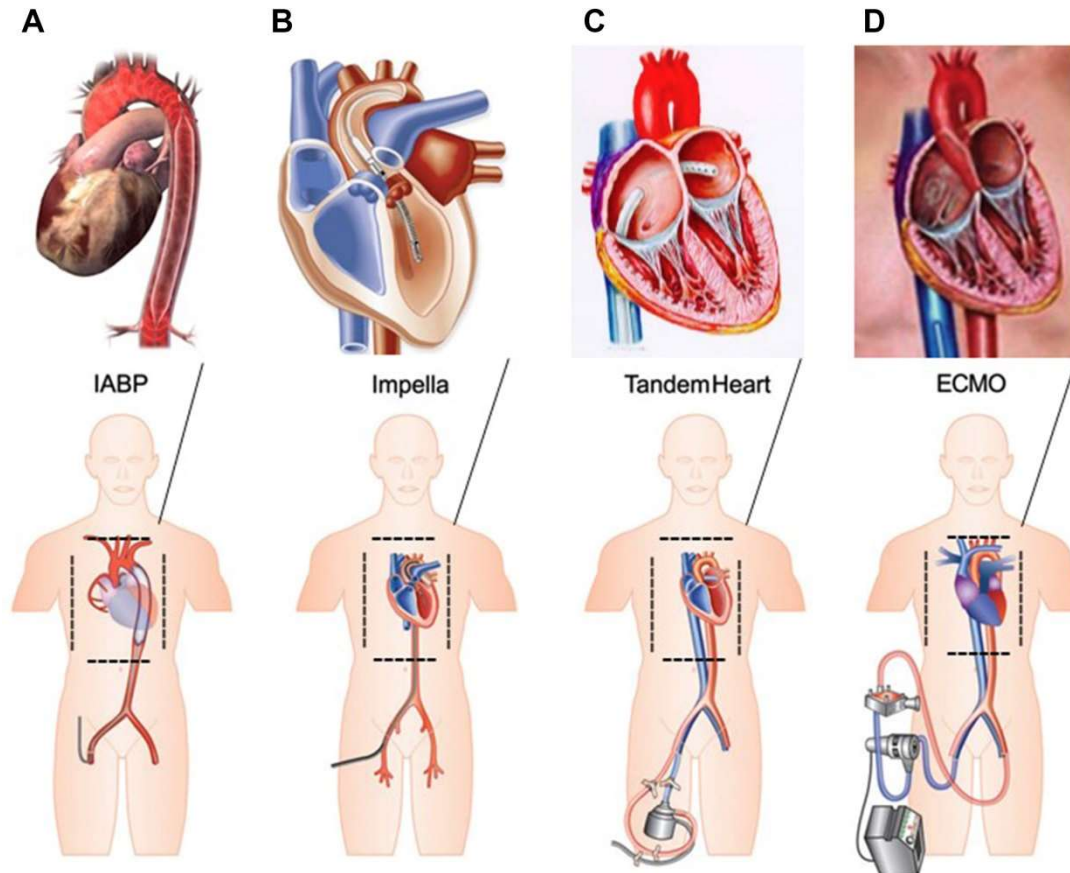
- Treatment of underlying cause
- Positively inotropic drugs, vasopressors (e.g. catecholamines – but: they can worsen the situation in obstructive shock)
- Colloid solutions, crystalloid solutions (but: there is a risk of oedema in cardiogenic shock)
- O₂
- i.v. corticoids (anaphylaxis, SIRS?)
- ATB (septic shock)
- Mechanic circulation support (cardiogenic shock)
- Anti-shock position (?)

Crystalloid x colloid solutions

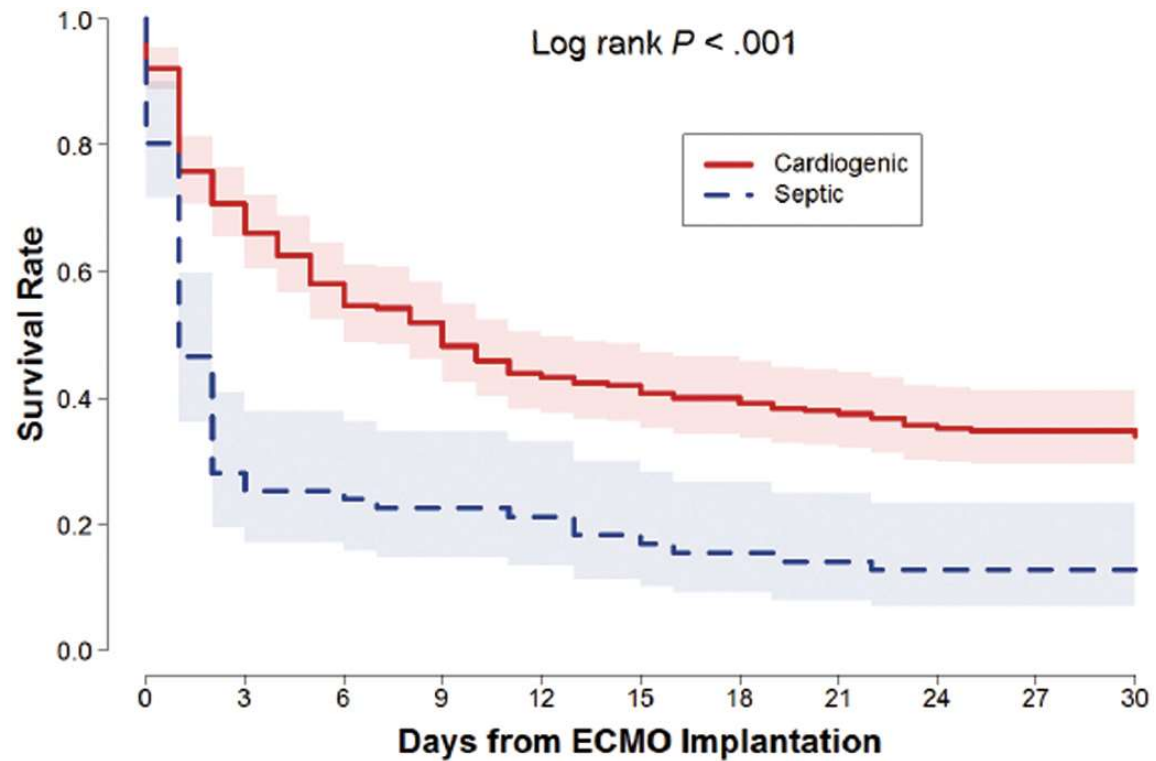
- Crystalloid – ionic solutions (best normochloremic)
 - They do not induce allergic reactions or alter coagulation
- Colloids – high molecular weight compounds (hydroxyethylstarch, gelatine, albumin)
 - Fluid distribution points more to intravascular compartment
 - But less than is expected theoretically – damaged glycocalyx – defines water reabsorption



Mechanical circulatory support



ECMO: Kaplan-Meier curves



[www.jtcvs.org/article/S0022-5223\(18\)30906-1/fulltext](http://www.jtcvs.org/article/S0022-5223(18)30906-1/fulltext)

Trendelenburg („anti-shock“) position

- 15-30°
- ↑ Venous return
- After collapse
- Inefficient in the long term
- Central venous catheter insertion (circulatory support administration)
- Worsens pulmonary ventilation
- Cave cardiogenic shock, bleeding, ↑ ICP

