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

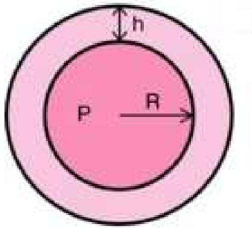
Preload and afterload in heart

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

  P….pressure inside the sphere

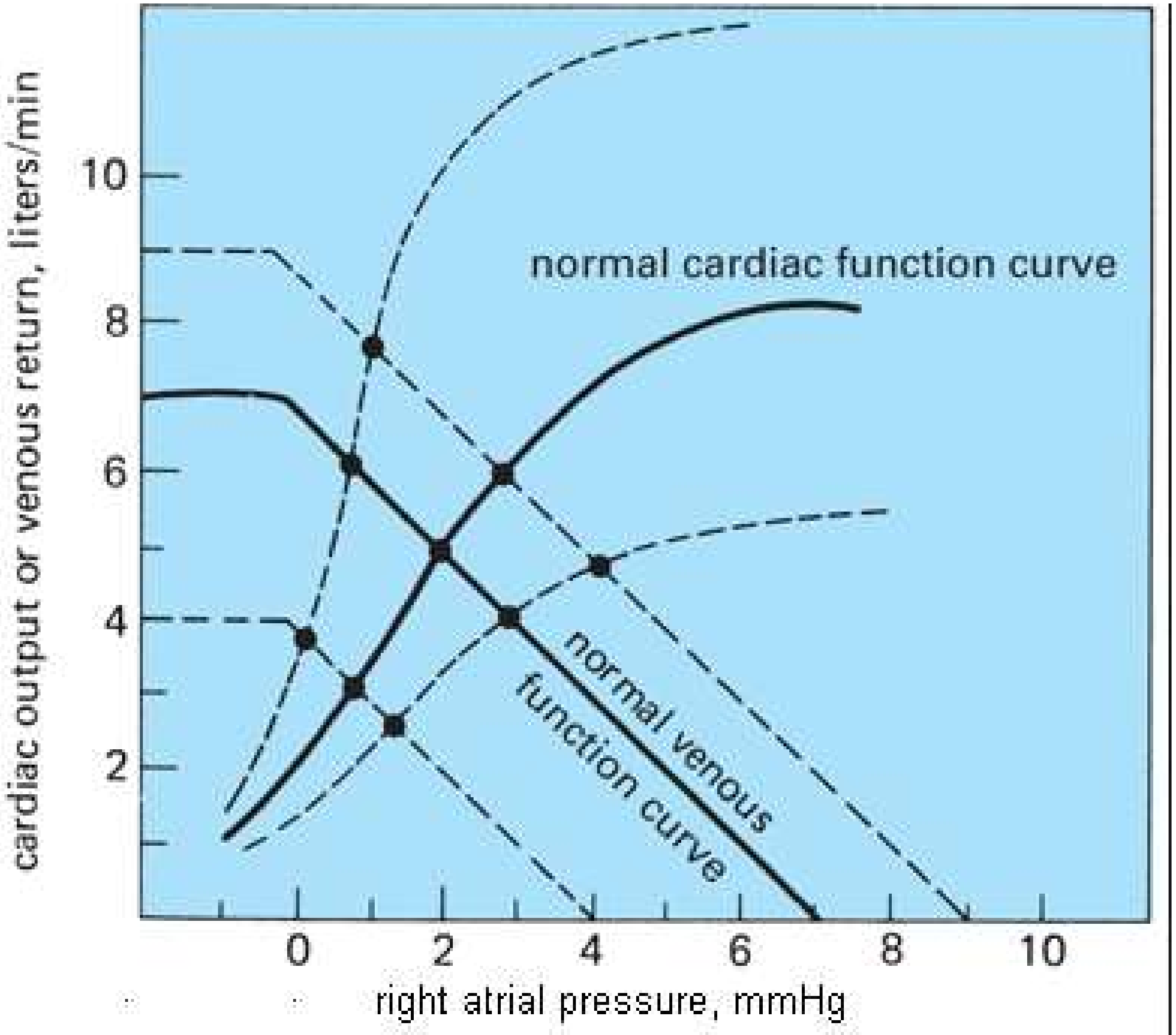
  r….inner radius

  h….wall thickness



- Preload – wall tension ($N.m^{-2}$ = 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 resistence in a case of the right ventricle
- Preload is higher in the right ventrikle, afterload is higher in the left one

Cardiac function and venous function

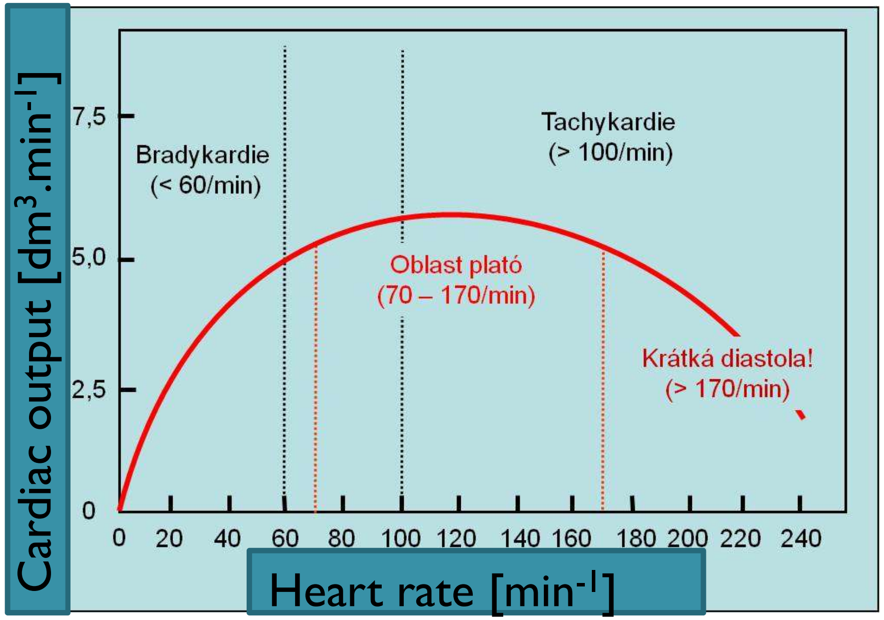


Phases of shock

- 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

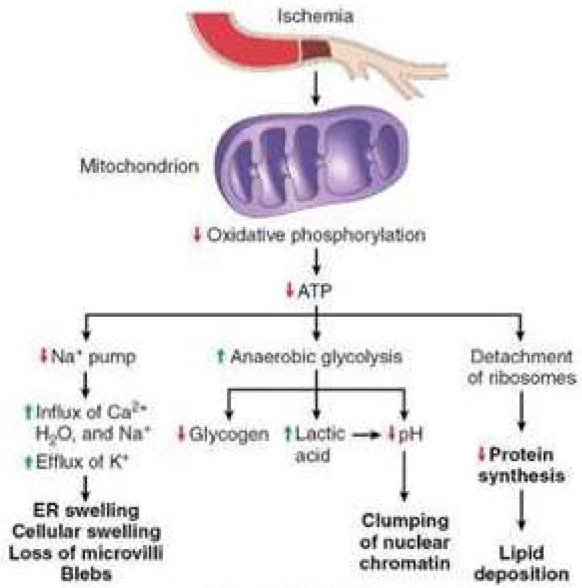


Decompensated shock

- ↓ BP
- ↓ diuresis
- Brain hypoperfusion – involvment 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 →↑intracelular Ca^{2+})
- Activation of Ca^{2+} -dependent proteases
- Lysosomal abnormalities – release of lysosomal proteases
- ↓ intracelular 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)

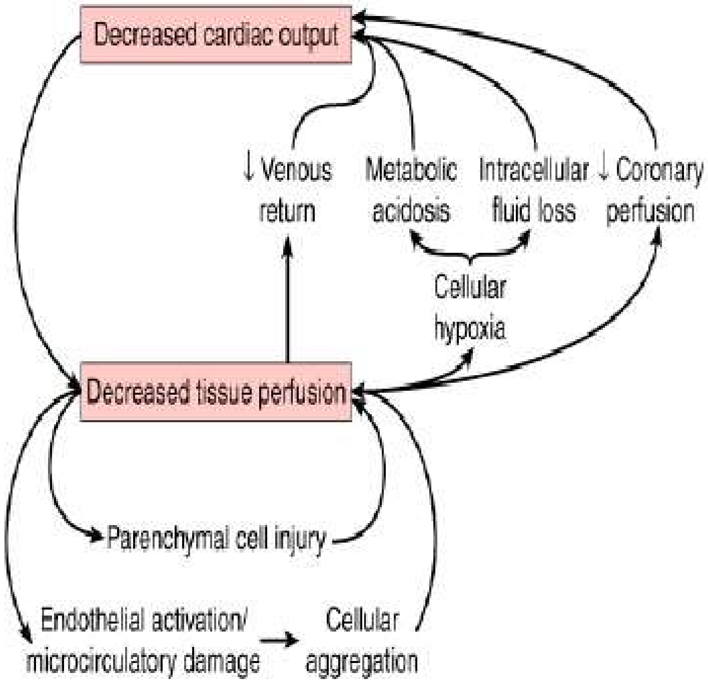
  2) Myocardial hypoxia ↔ lower contractility
  - Lower myocardial perfusion leads into ↓CO, which further reduces coronary flow
  - Myocardium does not benefit from the shift of Hb saturation curve – efficiency of O_2 extraction is already at its maximum

  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)



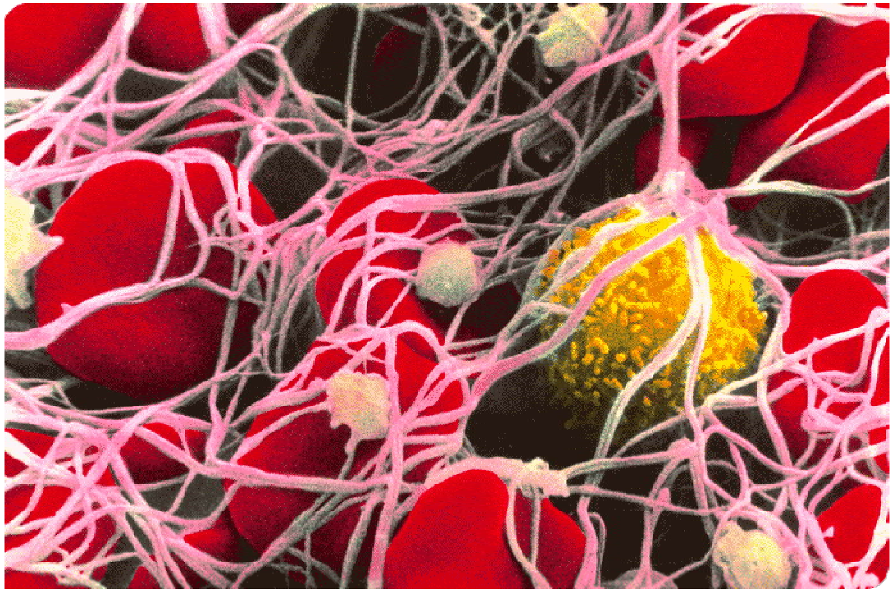
Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition*: http://www.accessmedicine.com

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



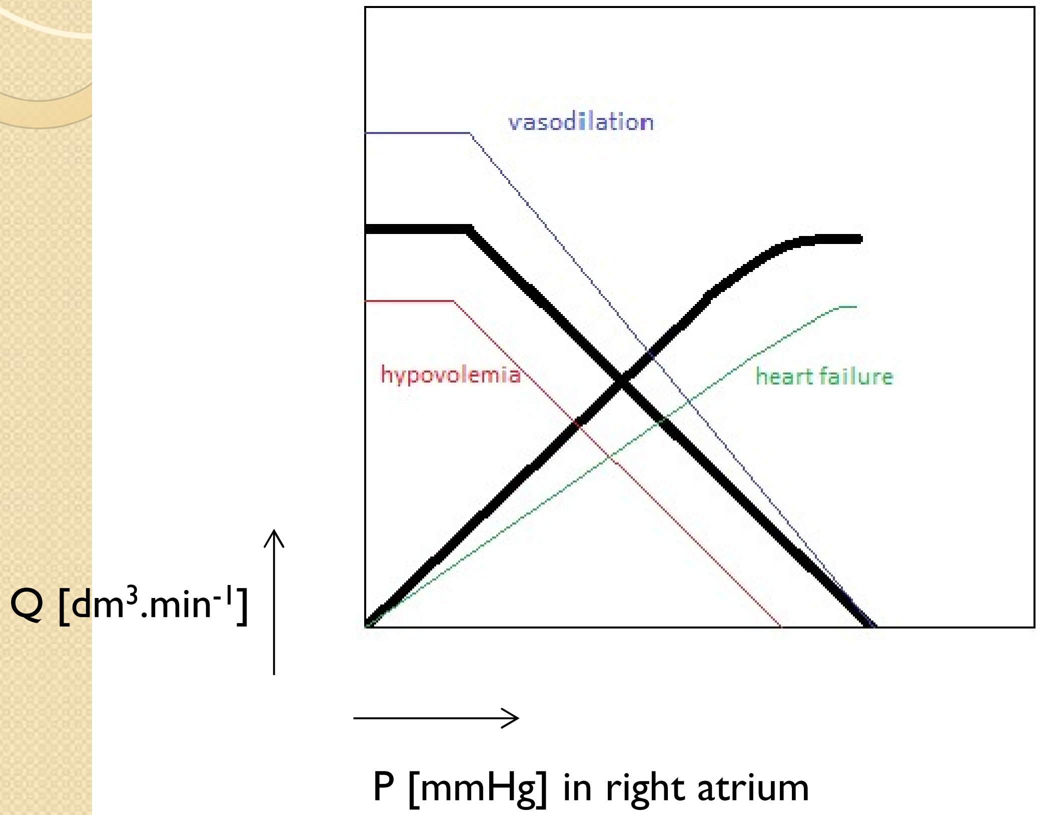
Signs of shock (benchmark)

- 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) Cardiogennic (“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 cardiogennic shock (but congestion occurs in one half of the circulation)

Cardiac and venous function in shock



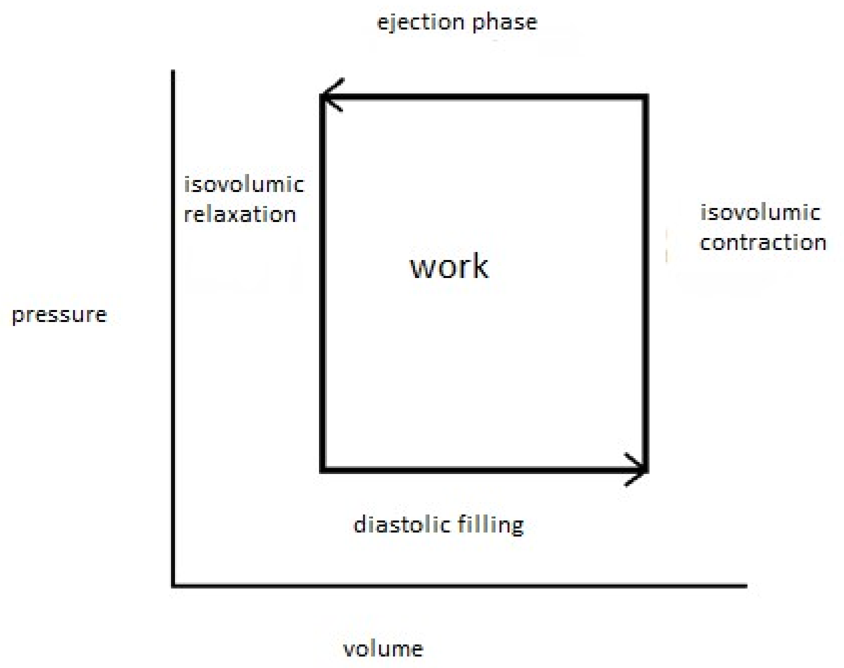
Type of shock	CO	SVR	PWP	CVP
Hypovolemic	↓	↑	↓	↓
Cardiogenic	↓	↑	↑	↑
Distributive	↑	↓↓	↓	↓

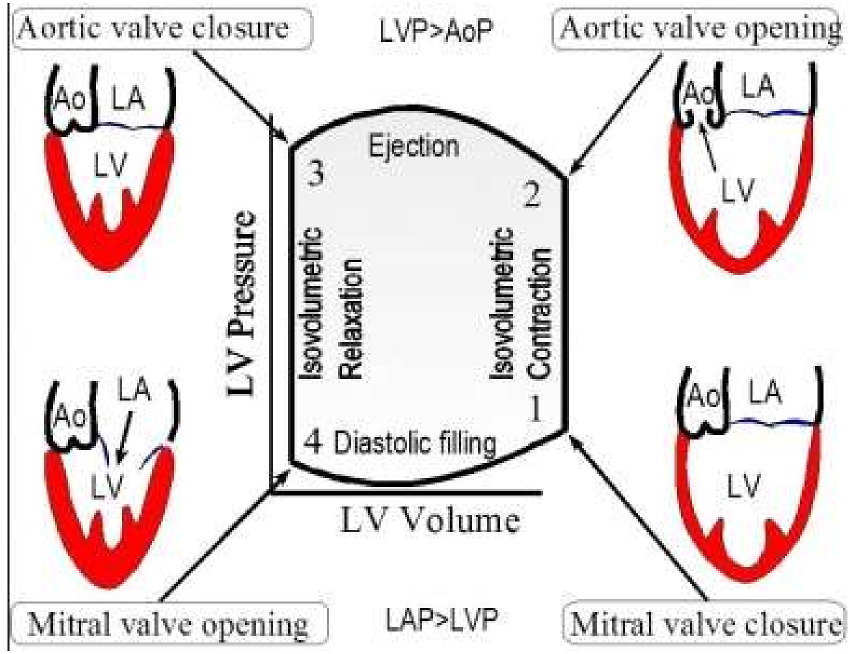
- Hypovolemic shock: compensation by the vasoconstriction and cardiac mechanisms
- Distributive shock: compensation by cardiac mechanisms (vasoconstriction is usually impossible)
- Cardiogennic (and obstructive) shock: compensation by vasoconstriction

„Interests“ of the heart and perfused tissues

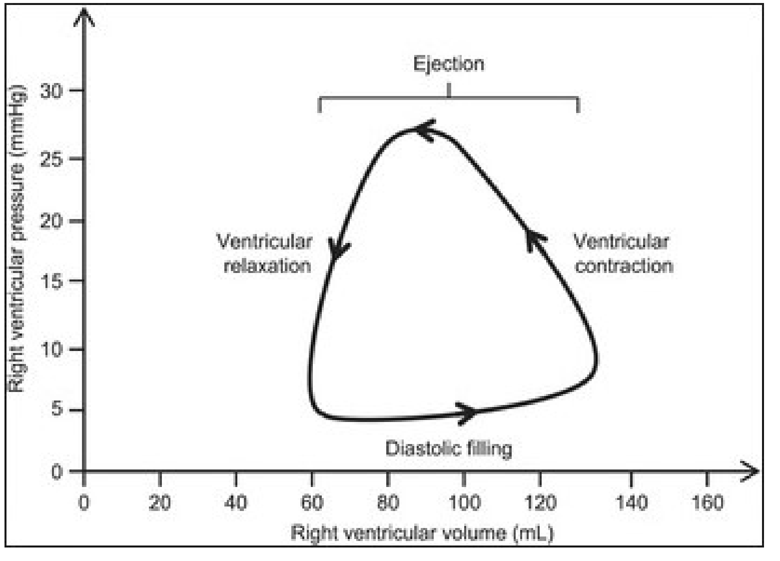
- Hypovolemic shock - ↓ preload
- Distributive shock - ↓ afterload
- From the heart‘s viewpoint, ↓ preload and ↓ afterload ere advantageous, regarding the blood supply to key organs they may be linked to circulatory failure (shock states) – the cause is, however, an extracardiac insult → ↓ preload or ↓ 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:





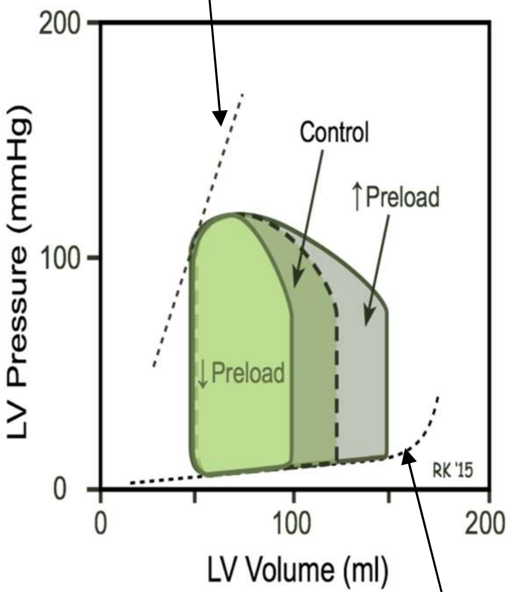
P-V diagram in the right ventricle

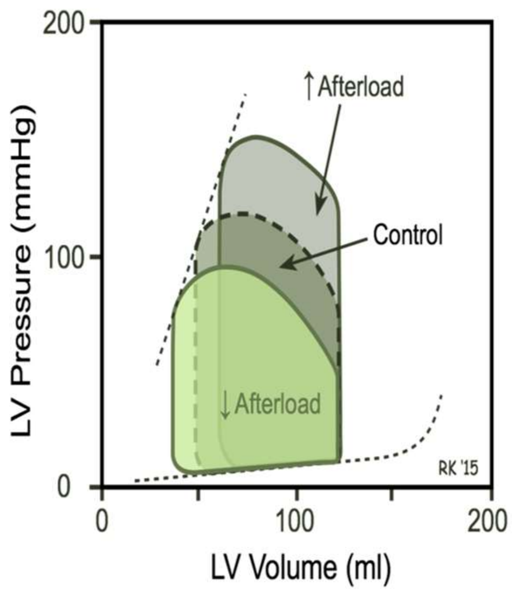


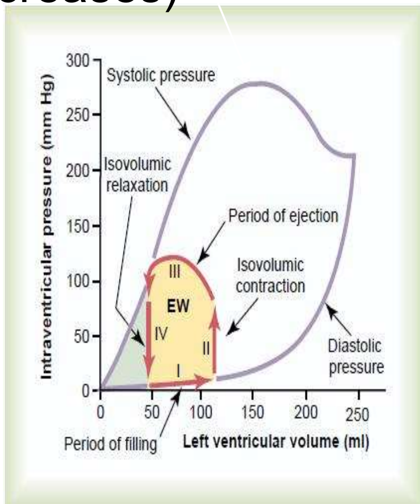
P-V diagram during changes of preload or afterload

Endsystolic P-V curve

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



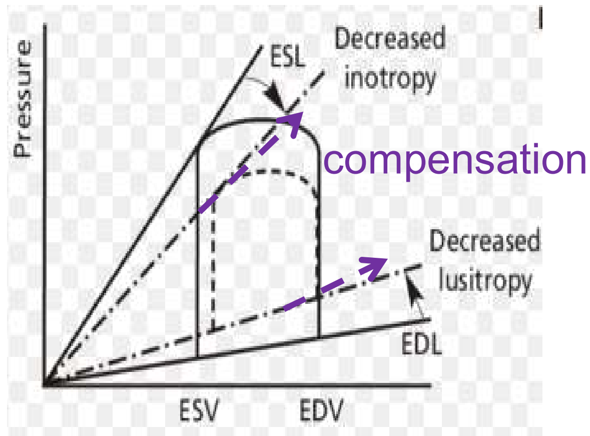




Enddiastolic P-V curve

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)



Hypovolemic shock - causes

- Acute bleeding
- Burns, trauma
- Rapid development of ascites
- Acute pancreatitis
- Severe dehydratation
  - 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 derivates (erythrocytes + plasma + thrombocytes)

Distributive shock - causes

- Anafylactic shock
- Anafylactoid 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 PGE_2 and NO
- Neurogennic shock
  - Vasodilatation as a result of vasomotoric centre (or its efferent pahways) impairment

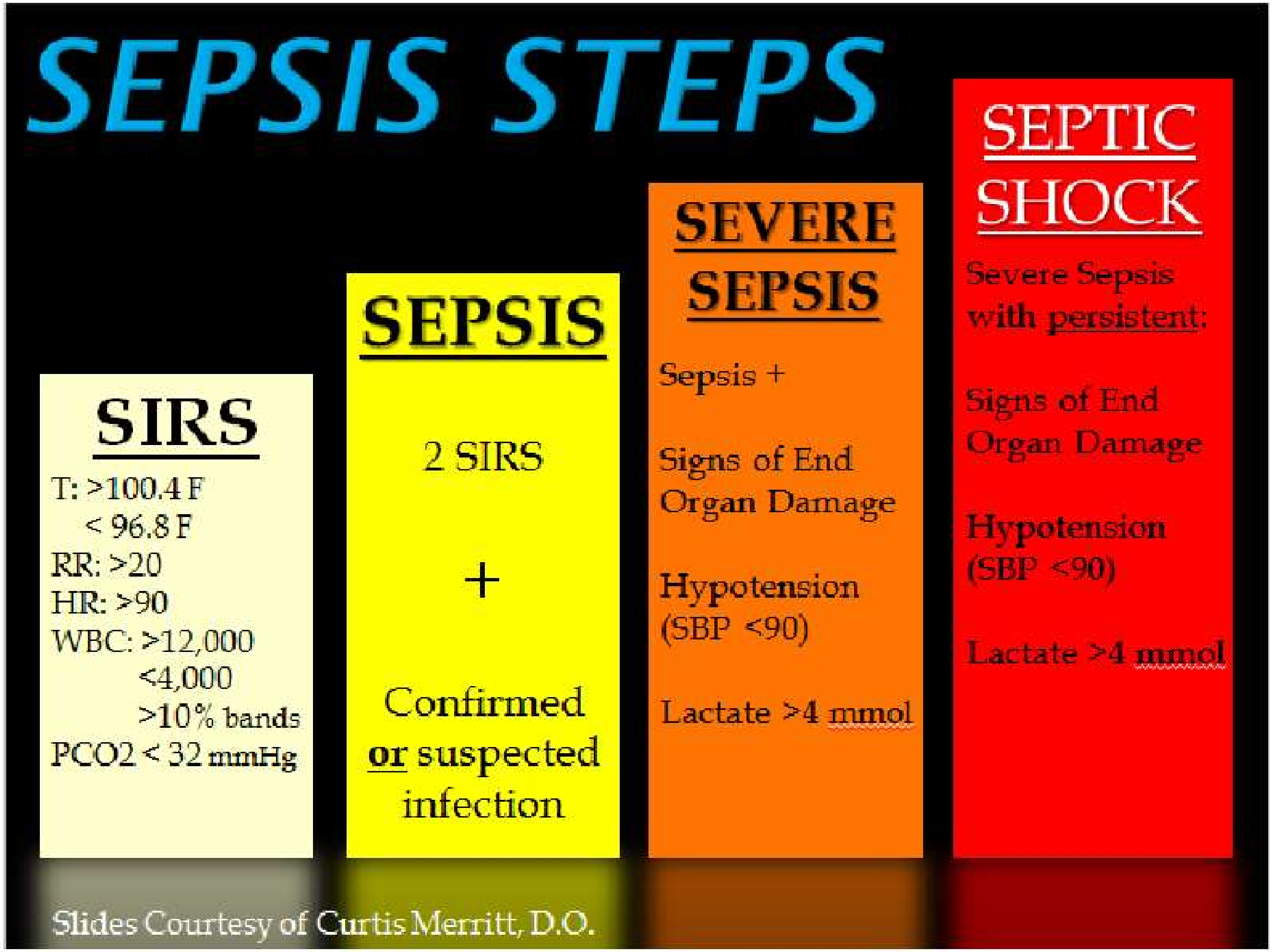
Development of anaphylactic reaction

- 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 H_1 receptors)
    - secondary (newly formed) – PG, LTA, PAF, bradykinin, cytokines, …
  - efects
    - vazodilatation, SMC contraction (incl. bronchoconstriction), ↑capillary permeability, chemotaxis, ↑mucus secretion, platelet aggregation

Anaphylactic and anaphylactoid reaction

- Anaphylaxis
  - závažná, systémová, potencionálně život ohrožující reakce zpravidla po parenterálním přestupu alergenu
  - léky, potraviny, hmyz, alergenové extrakty, latex
  - projevy
    - 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…

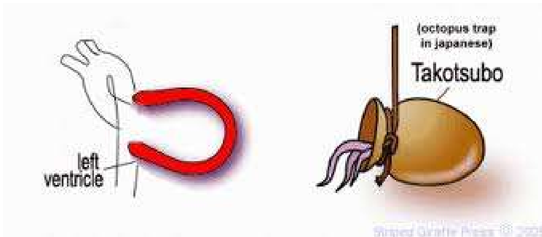
SIRS and sepsis



https://upload.wikimedia.org/wikipedia/commons/a/ad/Sepsis_Steps.png

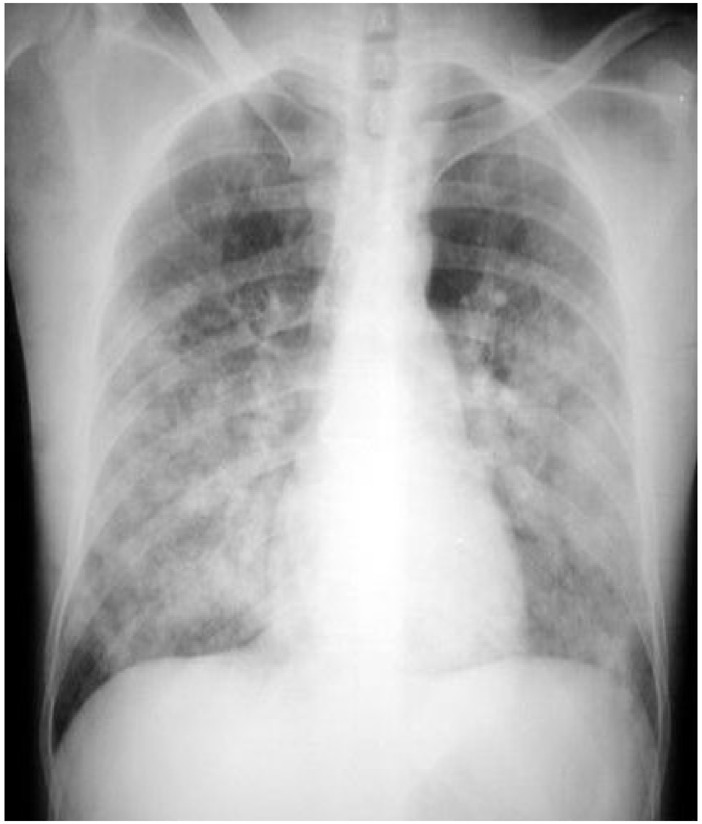
Cardiogennic shock - causes

- 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)

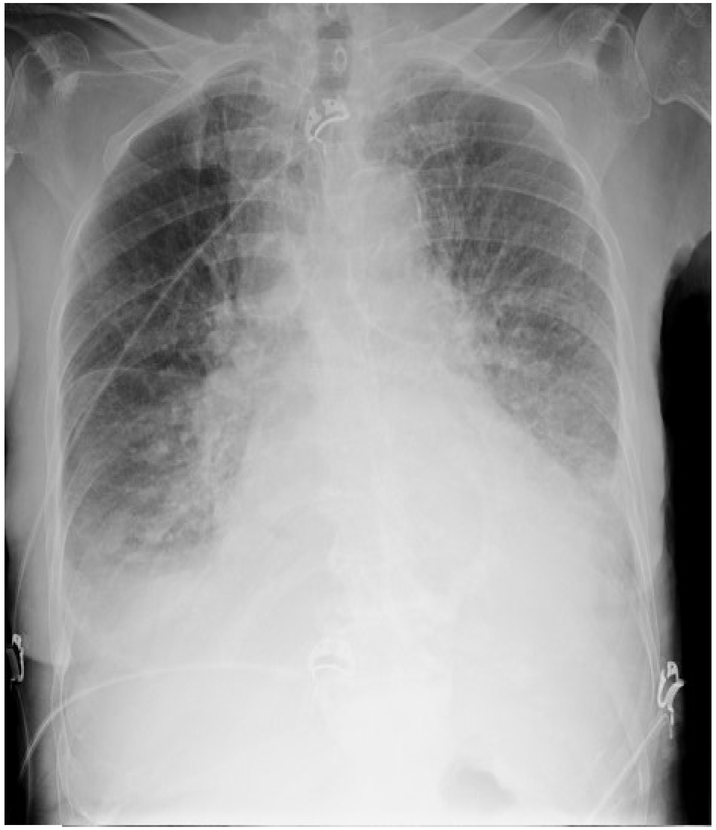


- Rupture of ventricular septum
- Obstructive shock – e.g. cardiac tamponade, massive pulmonary embolism, aortic dissection

„Backward“ acute heart failure – X-ray



Pulmonary oedema



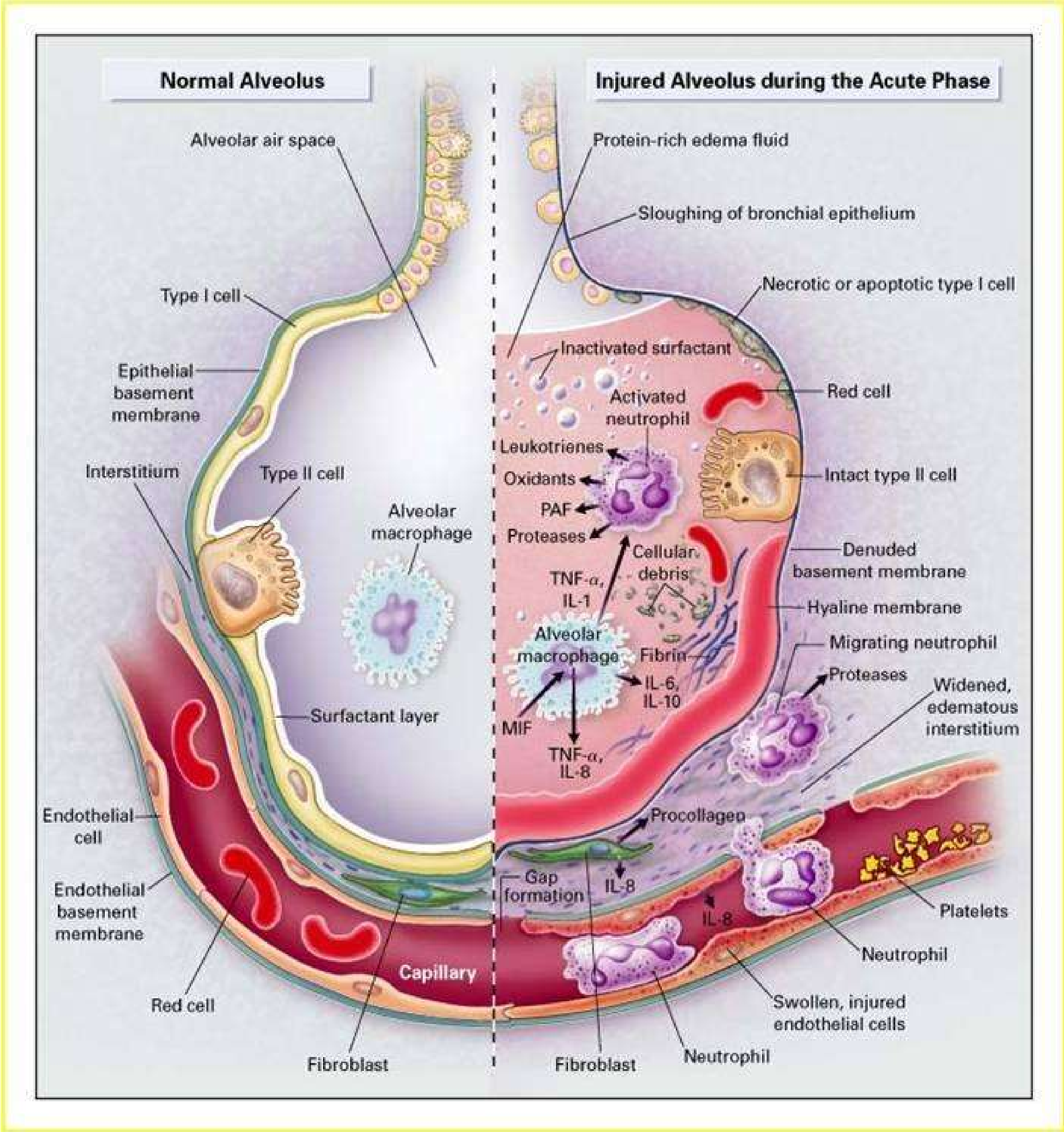
Bilateral pleural effusion

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 preceed or result from SIRS (primary vs. secondary MODS)
- Dysfunction → failure

Persistent MODS as an adaptation?

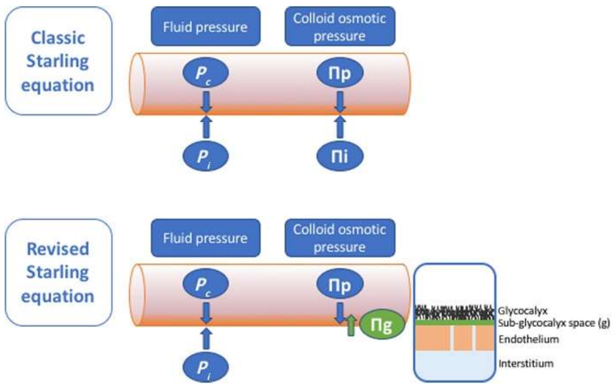
- ↓ mitochondria in tissues
- ↓ T3
- Analogy of hibernating myocardium (here, also ↓ of contractile apparatus and energy consumption)
- Gene expression similar to hibernating animals
- Later functional improvement is possible

General principles of treatment

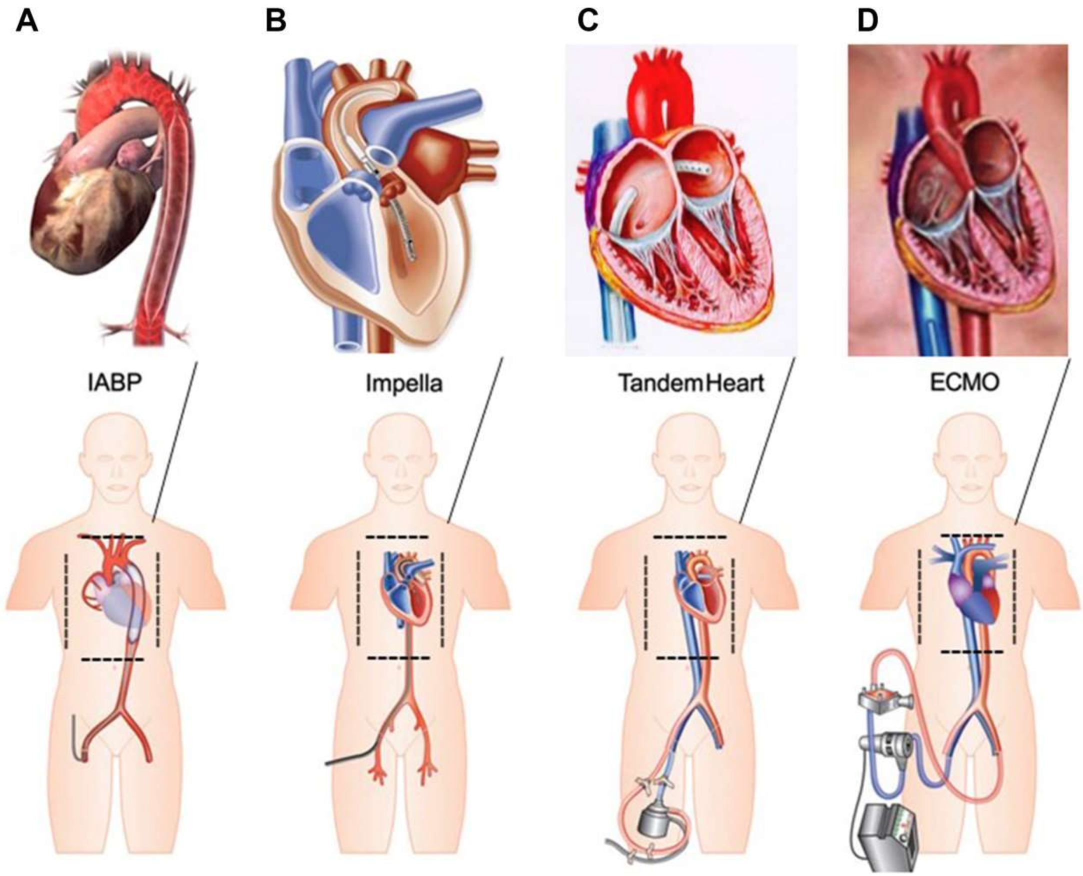
- Treatment of underlying cause
- Positively inotropic drugs, vasopressors (e.g. catecholamines – but: they can worsen the situation in obstructive shock)
- Colloid solutions, crystalloid solutions (but: there is a risk of oedema in cardiogenic shock)
- O_2
- i.v. corticoids (anaphylaxis, SIRS?)
- ATB (septic shock)
- Mechanic circulation support (cardiogenic shock)
- Anti-shock position (?)

Crystalloid x colloid solutions

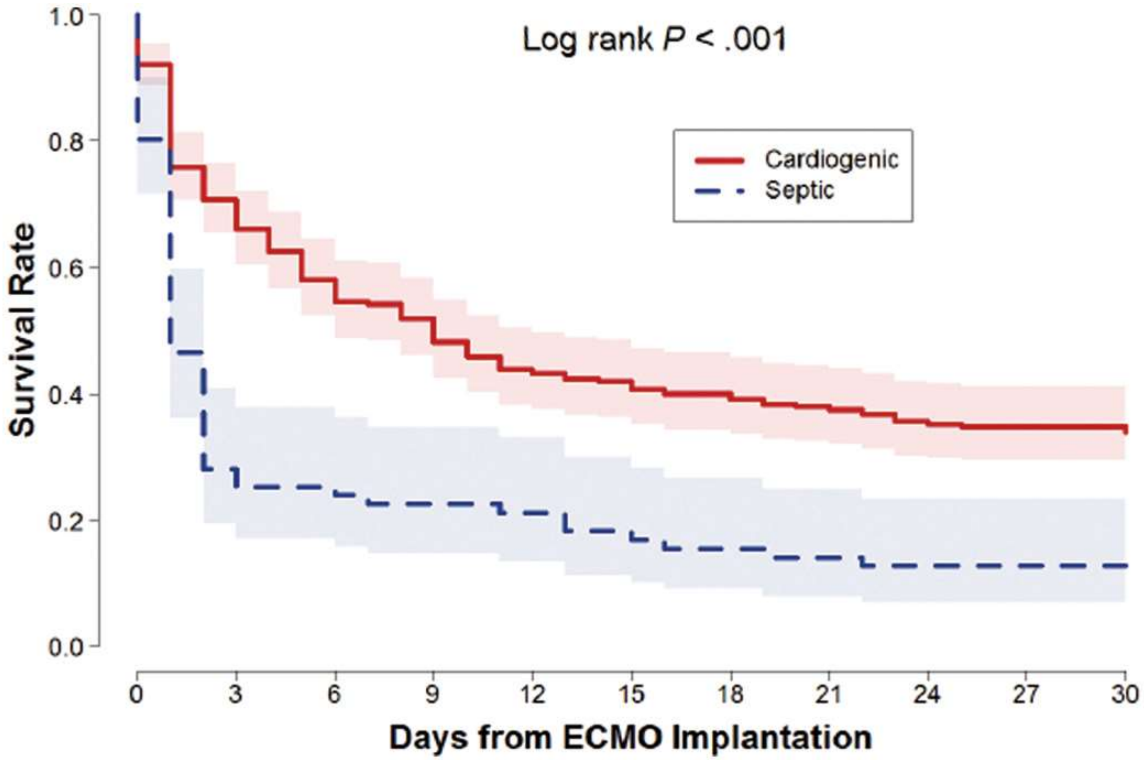
- Crystalloid – ionic solutions (best normochloremic)
  - They do not induce allergic reactions or alter coagulation
- Colloids – high molecular weight compounds (hydroxyethylstarch, gelatine, albumin)
  - Fluid distribution points more to intravascular compartment
    - But less than is expected theoretically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



Mechanical circulatory support



ECMO: Kaplan-Meier curves



www.jtcvs.org/article/S0022-5223(18)30906-1/fulltext

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