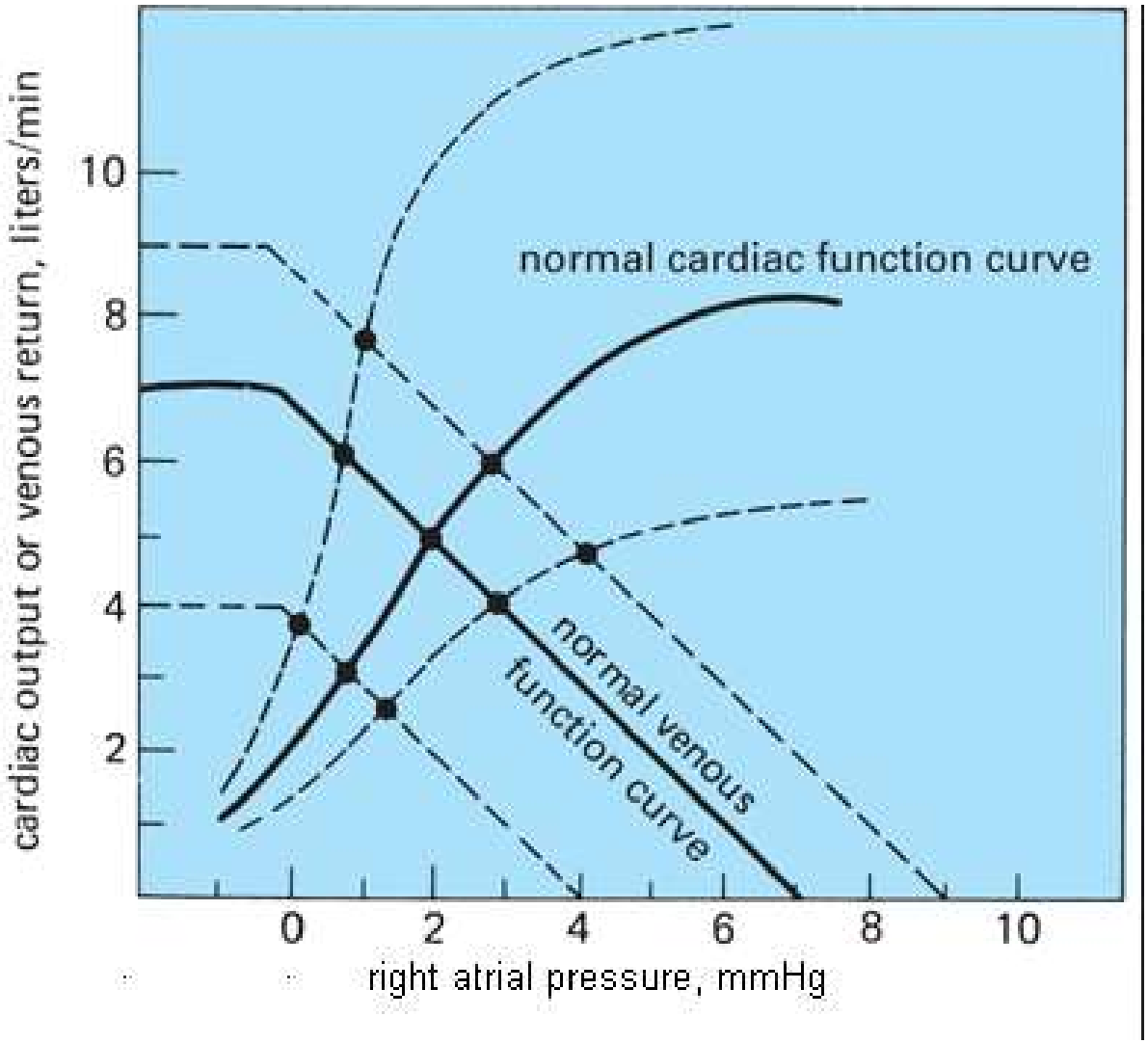
Pathophysiology of circulatory shock

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 (→preload)
- R – systemic resistance (mostly arterioles) - afterload

Cardiac function and venous function

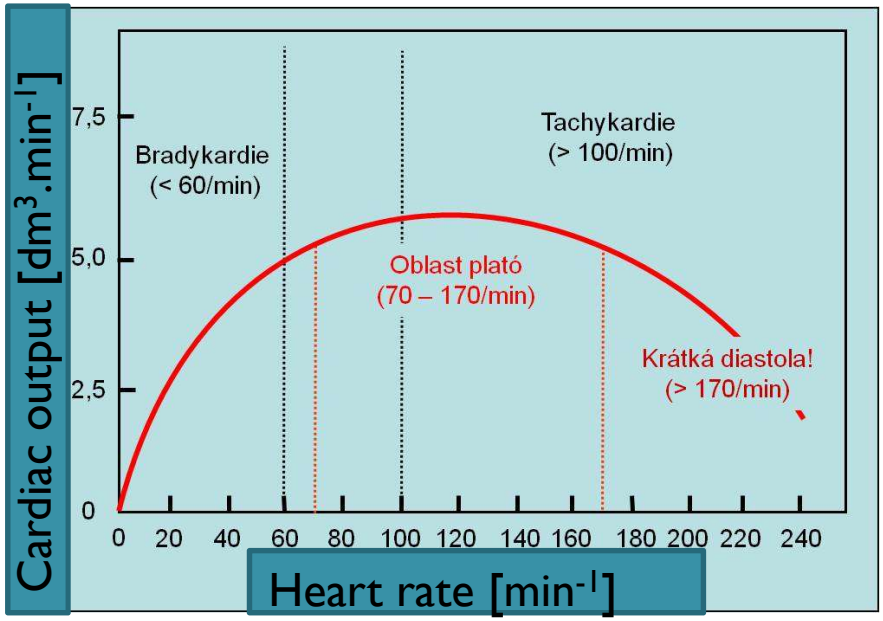


Phases of shock

- 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)
- Shift of saturation curve of hemoglobin to right (↑2,3-DPG)
- Hyperglycemia – but there is decreased utilization of Glc in the periphery

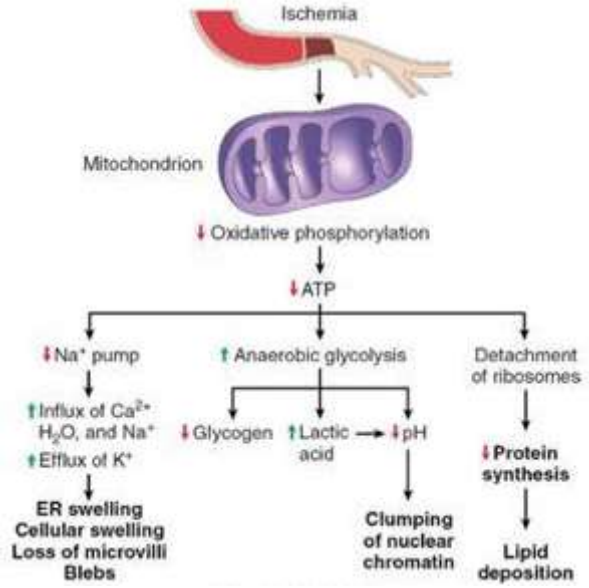


Decompensated shock

- ↓ BP
- ↓ diuresis
- Brain hypoperfusion – involvment of mental functions
- Acrocyanosis
- Tachypnoe

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

2) Myocardial hypoxia ↔ lower contractility

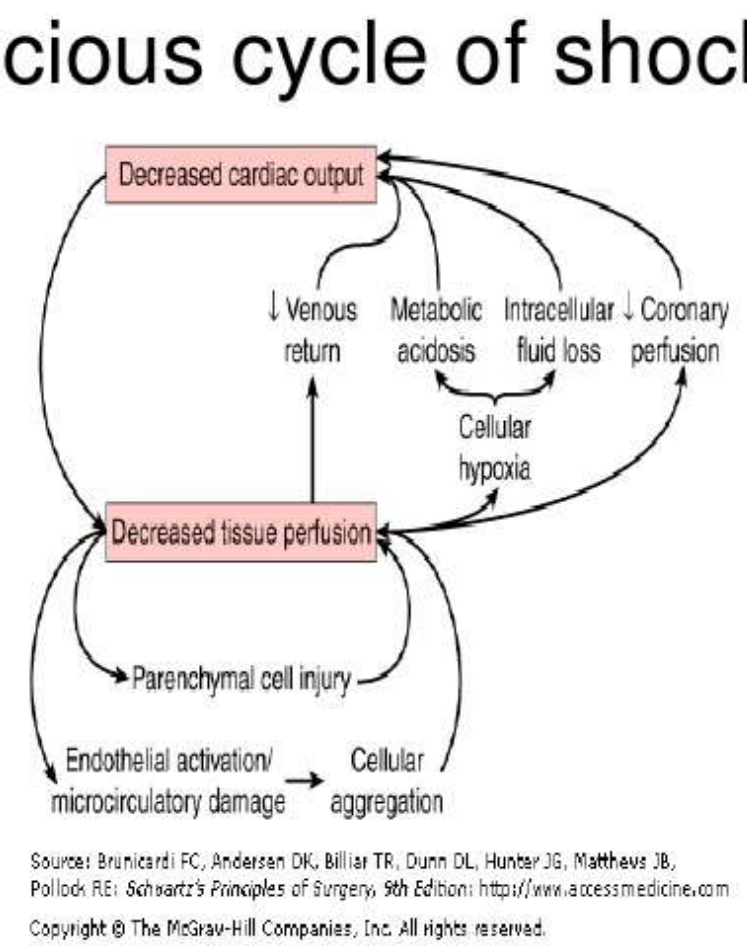
- Lower myocardial perfusion leads into ↓CO, which further reduces coronary flow
- Myocardium does not benefit from the shift of Hb saturation curve – efficiency of O_2 extraction is already at its maximum

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

* SIRS
* DIC

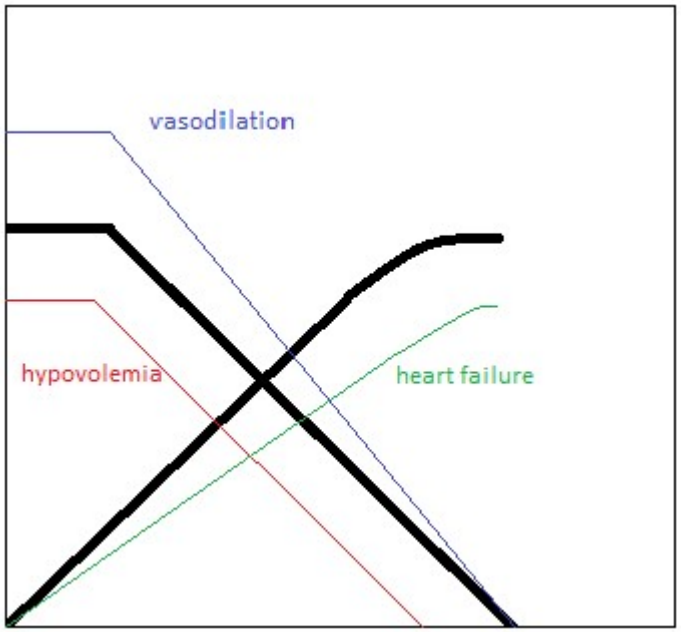


Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition*: http://www.accessmedicine.com

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

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

Hypovolemic shock - causes

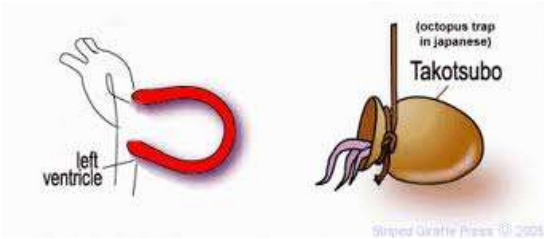
- Acute bleeding
- Burns, trauma
- Rapid development of ascites
- Acute pancreatitis
- Severe dehydratation
  - Vomiting, diarrhoea
  - Excessive diuresis (e.g. in diabetes insipidus)

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

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 cardiomyopathy" – apical akinesia + basal hyperkinesia)



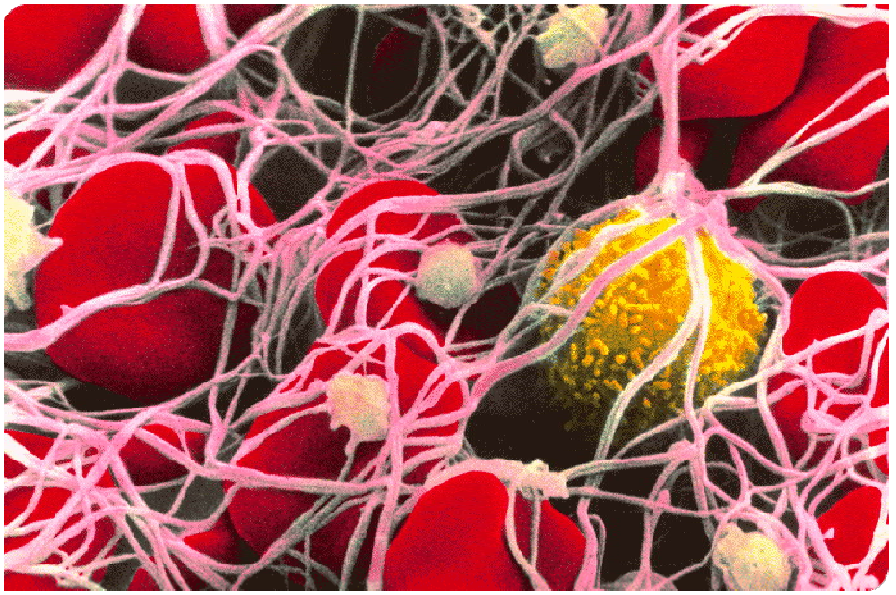
- Rupture of ventricular septum
- Obstructive shock – e.g. cardiac tamponade, massive pulmonary embolism, aortic dissection

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

Disseminated intravascular coagulopathy (DIC)

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

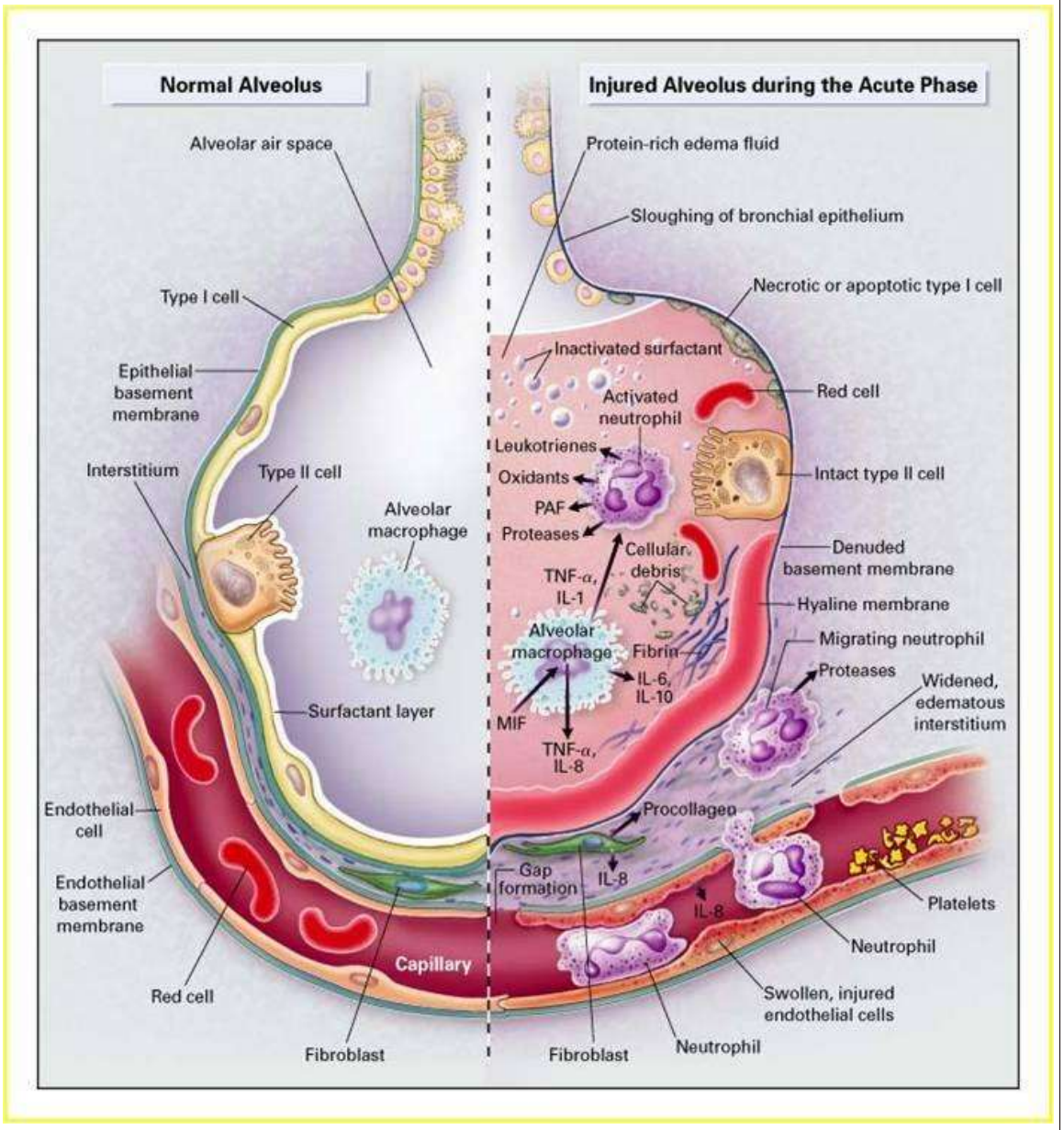


Systemic Inflammatory Response Syndrome(SIRS)

- 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)

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)

- Failure 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)

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, crystaloid solutions (but: there is a risk of edema in cardiogennic shock)
- O_2
- i.v. corticoids (anafylaxis, SIRS?)
- ATB (septic shock)
- Mechanic circulation support (cardiogennic shock)
- Anti-shock position