1. Basal pathogenetic mechanisms of circulatory shock

Definition of circulatory shock: An acute dysbalance between delivery and consumption of oxygen in all (or all vital at least) organs, which cannot be compensated for (or only transitorily)

Dynamics: generalization, self-maintainance, refractoriness

Tissue ischemia could be produced by:
- decline of circulating volume (haemorrhagic shock)
- failure of cardiac performance (cardiogenic shock)
- failure of regulation of peripheral resistance → relative lack of volume and/or of exchange area of capillaries (anaphylactic shock, septic shock)

Hypotension is typical, however, normotonic phases may be present
- regulatory reaction (sympathoadrenal system, glucocorticoids, vasopressine, endorphins)
- endotoxin → „hyperdynamic shock syndrome“

2. Changes in macro- and microcirculation

Excessive activity of sympathoadrenal system

↑ catecholamine concentration → tachycardia, ↑ contractility of myocardium, vasoconstriction, tonisation of capacitance vessels → ↑ venous return → centralisation of circulation (for the benefit of heart and brain) → long-term organ dysfunction (kidneys!)

Specific microcirculatory and vasomotoric disturbance

Fig. 1 Vasomotorics and fluid exchange in shock:

1 - normal
2 - sympathetic
   → precapillary vasoconstriction → ↓ tissue perfusion → sucking of fluids → ↓ hematocrit, ↓ blood viscosity,
   ↓ plasma oncotic pressure → dissociation of capillary regions with:
   - stasis
     - fast streaming plasma poor in cells
   → unbalanced capillary perfusion → ↓ perfusion per unit area
3 - tissue acidosis → dilation of precapillary sphincters → extravasation → hemoconcentration (+ edema) → ↓ perfusion
3. Shock mediators

Kallikrein-kinin system:

Kininogens in plasma (HMWKG and LMWKG) → cleaved by kallikrein (plasma and tissue) → bradykinin (=kinin 9) and kallidin (= kinin 8) → ↓BP, contraction of extravascular smooth musculature, ↑vasodilation and ↑permeability, pain

Contact activation:

Complex of prekallikrein + HMW-kininogen + Hageman factor (XII) present in plasma → affinity to negatively charged surfaces → addition to them → mutual activation of Hageman factor and prekallikrein → → rise of kinin → ↑permeability etc. 
→ rise of plasmin → fibrinolysis 
→ activation of the intrinsic pathway of blood clotting (coagulation)

In shock the following systems are activated (Fig. 2):

- blood clotting ← stasis, acidosis, effusion of tissue factor (in traumas)
- complement ← immunocomplexes, plasmin, thrombin etc.
- kallikrein-kinin ← Hageman factor; effects as above
- arachidonic acid

Endo+ exotoxins of bacteriaars → role in septic shock syndrome

In all forms of shock, releasing of cytokines and other mediators influencing the vasculatory tonus is of basal importance:

- Aggregated platelets → thromboxan A2, serotonin, leucotriens, reactive oxygen species
- Adhering and activated leucocytes → thromboxan A2, PGE2, PAF, ROS, proteases
- Damages endothelial cells → PGI2, thromboxan, PAF, HETE, interleukin-1, ROS
- Macrophages → TNF ↓vascular resistance and ↓BP
Reperfusion damage
Shock therapy $\rightarrow$ (xanthine dehydrogenase $\rightarrow$ xanthinoxidase) $\rightarrow$ rise of ROS $\rightarrow$ lipid peroxidation $\rightarrow$ rise of AA metabolites and denaturation of cellular (incl. membrane) proteins $\rightarrow$ endothelial lesions, intracellular edema, inflow of calcium ions into cells $\rightarrow$ cellular necrosis
Hyopoperfusion $\rightarrow$ ↑ production and ↓ metabolism of lactic acid $\rightarrow$ tissue acidosis

4. Types of shock syndrome

Hypovolemic shock
Definition: A shock caused by decline of intravascular volume (acute loss of 20-30% of volume) $\rightarrow$ insufficient preload $\rightarrow$ ↓ cardiac output: $\frac{Q'}{P} = \frac{P}{R}$ (Fig. 3).
Administration of fluids $\rightarrow$ restoration of CO
Traumatic shock: extensive tissue lesions, ↓↓↓ of volume.
Early stimulation of humoral cascades, nociceptors $\rightarrow$ ↑ sympathetic reaction

Cardiogenic shock
Definition: A shock caused by all types of cardiac failure, inclusive by cardiac tamponade, pneumo- and hemothorax and pulmonary embolism. Preload is adequate, in spite of this, CO is insufficient: $\frac{Q'}{P} = \frac{P}{R}$ (Fig. 4)
Diagnosis must prove the adequate preload

Distributive = vasodilatory = vasogenic = hyperdynamic shock
Definition: Shock produced by loss of regulation of peripheral resistance $\rightarrow$ relative lack of volume + decline of exchange area of capillary bed (Fig. 5)
Inappropriate vasodilation $\rightarrow$ peripheral amassing of blood $\rightarrow$ ↓ preload $\rightarrow$ compensatory rise of contractility (hyperdynamic circulation$^*$); CO may be high, normal or decreased
Etiology: sepsis, anaphylaxis, CNS depression
Combined shock syndromes are common
5. Disturbances of organ functions – multiple organ failure (MOF)

Focal ischemia, activation of humoral systems (esp. of complement s.), interaction of leucocytes with endothelial cells → progressing disturbance of perfusion and function of organs. Cytokines (esp. IL-1 α TNF) stimulate granulocytes → ROS → adhesion to endothelial cells, cytotoxicity. MOF could be invoked by sole cytokine infusion. It appears after lag of hours to days

Pulmonary failure („shock lung“)

Pulmonary permeability edema:
- Initial phase: ↓intrapulmonary blood volume (not in cardiogenic shock!), collaps of alveoli in dependent regions → ↓ventilation-perfusion ratio (functional shunt)
- Adult respiratory distress syndrome:
  - Exsudative phase
  - Early proliferative phase: fibrin and leucocytes in interstitial and alveolar spaces
  - Late proliferative phase: fibroblasts and histiocytes, thickening of alveolar septa

Pulmonary functions: progressing hypoxemia, ↓pulmonary compliance, ↑dynamic pulmonary resistencies, ↑mechanical work

Renal failure
Ischemic damage and/or compensatory mechanism → ↓diuresis. Sympatoadrenal stimulation → ↓renal perfusion. Prerenal azotemia, later acute tubular necrosis

Hepatic failure
Lowering of syntheses in the liver (clotting factors!), lowering of the trapping liver capacity for some metabolites (lactate!)
Storage of glycogen exhausted soon → therapeutic delivering of energy
↓“cleaning” function of the system of mononuclear phagocytes → accumulation of vasoactive and clotting promoting metabolites → disseminated intravascular coagulation → „spill-over“ of bacteria and endotoxins into systemic circulation

Gastrointestinal failure
Disturbances if microcirculation and focal ischemia → ↓permeability of gut vessels → leakage of fluid rich in proteins into interstitium → loss of circulating volume into gut lumen and peritoneal cavity → accentuation of hypovolemia. Corruption of mucosal barrier → bacteriemia, sepsis

6. Shock dynamics

Stages of shock (Fig. 6 : I. early, „latent“ stage, „compensated“ shock; II. „progressive“, „decompensated“ shock; III. „irreversible“, „refractory“ shock

[Image of shock dynamics diagram]
Compensated shock: blood pressure and CO may be normal. Extremely labile stage, weight of the situation may go unnoticed. Progressive (decompensated) stage: positive feedbacks → "spontaneous" deepening of shock. ↓BP, ↓CO, ARDS and oliguria, metabolic acidosis (!)


7. Shock therapy

Fig. 10 Normal pressures in cardiac chambers