Circulatory shock (hypoperfusion) syndrome

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1. Basal pathogenetic mechanisms of 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 (sympatoadrenal system, glucocorticoids, vasopressine, endorphins)**
- **endotoxin ® „hyperdynamic shock syndrome“**

2.Changes in macro- and microcirculation

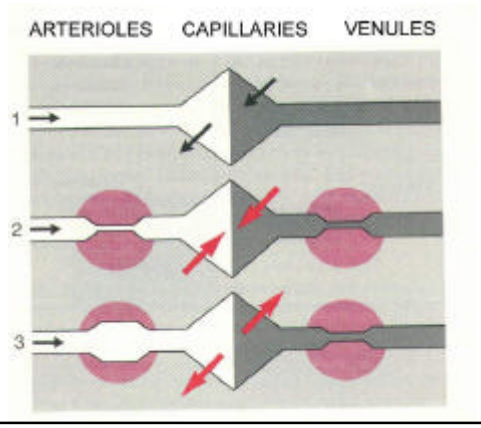
Excessive activity of sympatoadrenal system

- **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 - ↑sympaticus
→ 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



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3. Shock mediators

Kallikrein-kinin systeme:

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:

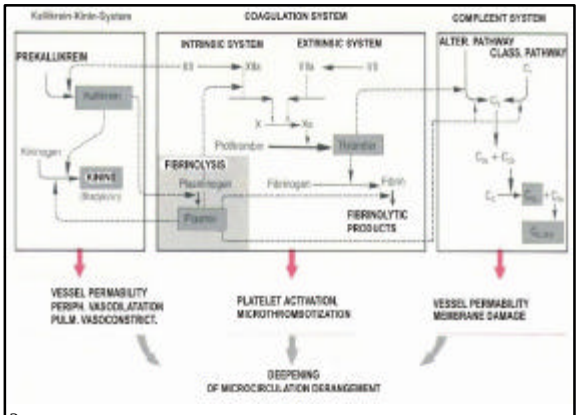
Complex of prekallikrein + HMW-kininogen + Hageman factor (XII) present in plasma ® affinity to negatively charged surfaces ® addition to them ® mutual activation of Hageman factor and prekallikrein ®

® 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 bacterias ® role in septic shock syndrome



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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 resistence and ¯BP

Reperfusion damage

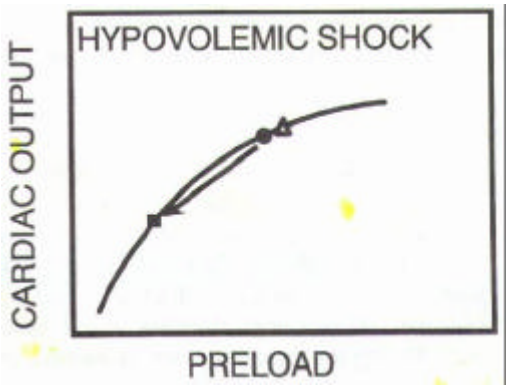
Shock therapy ® (xanthindehydrogenase ® xanthioxidase) ® rise of ROS ® lipid peroxidation ® rise of AA metabolites and denaturation of cellular (incl. membrane) proteins ® endothelial lesions, intracellular edema, inflow of calcium ions into cells ® cellular necrosis

Hypoperfusion ® -production and ¯metabolism of lactic acid ® 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) ®** ***insufficient preload*** **® ¯cardiac output: ¯ Q' = ¯ P/ -R (Fig. 3).**
Administration of fluids (Ù) ® restauration of CO
Traumatic shock: extensive tissue lesions, ¯¯ of volume.
Early stimulation of humoral cascades, nociceptors ® - - sympatoadrenal reaction



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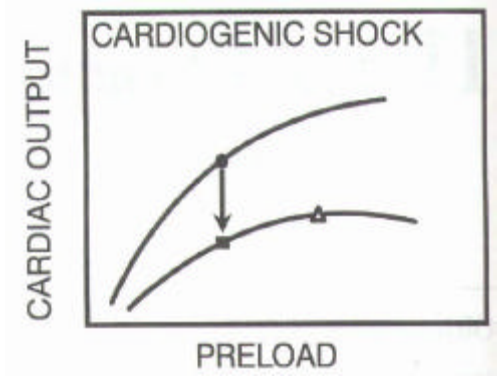
Cardiogenic shock

Definition: **A shock caused by all types of cardiac failure, inclusive by cardiac tamponade, pneumo- and hemothorax and pulmonary embolism. Preload is adaequate, in spite of this, CO is insufficient: ß Q' = ¯ P/-R (Fig. 4)**
Diagnosis must prove the adaquate preload



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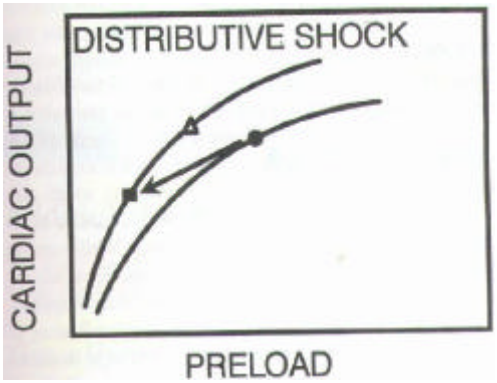
Distributive = vasodilatory = vasogenic = hyperdynamic shock

Definition: **Shock produced by loss of regulation of peripheral resistance ® relative lack of volume + decline of exchange area of capillary bed (Fig. 5)**
Inappropriate vasodilation ® peripheral amassing of blood ® ¯preload ® compensatory rise of contractility („hyperdynamic circulation"); CO may be high, normal od decreased

Etiology: sepsis, anaphylaxis, CNS depression

Combined shock syndromes are common



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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 a 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 volumen (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

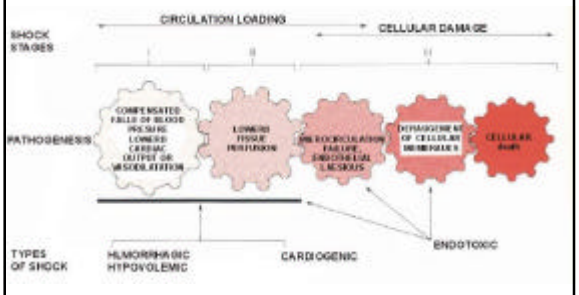
Lowering of syntheses in the liver (clotting factors!), lowering of the trapping liver capacity for some metabolites (lactate!)
Storage of glycogen exhausted soon ® therapetic delivering of energy
¯“cleaning“ function of the system of mononuclear phagocytes ®
® accumulation of vasoactive and clotting promoting metabolites ® disseminated intravascular coagulation
® „spill-over“ of bacterias 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 intu 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



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Compensated shock: **blood pressure and CO may be normal. Extremely labile stage, weight of the situation may go unnoticed**
Progressive (decompensated) stage: **positive feebacks ® „spontaneous“ deepening of shock. ¯BP, ¯CO, ARDS and oliguria, <u>metabolic acidosis</u> (!)**
Irreversible (refractory) shock: **no therapeutic measure can avoid progressive worsening. Steady decline of CO, ¯¯BP, - - acidosis. Koma and reanal failure with uremia.**

Fig 7 Positive feedback in a progressive shock

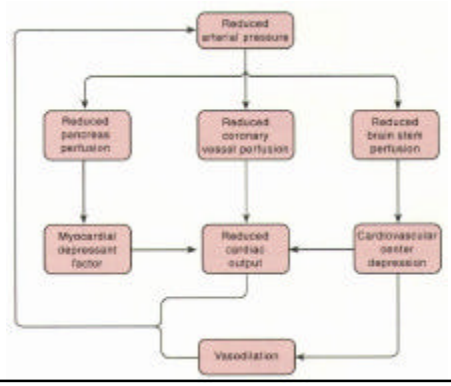


Fig. 8 Synopsis of pregressive shock

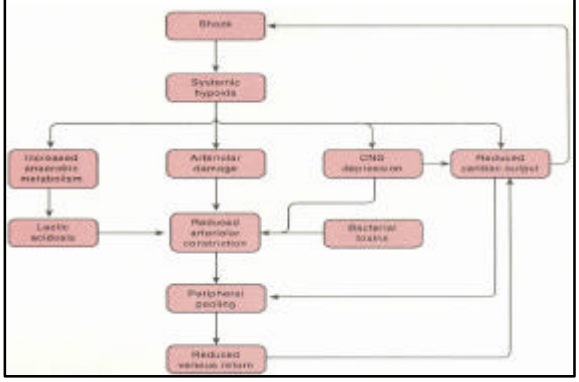
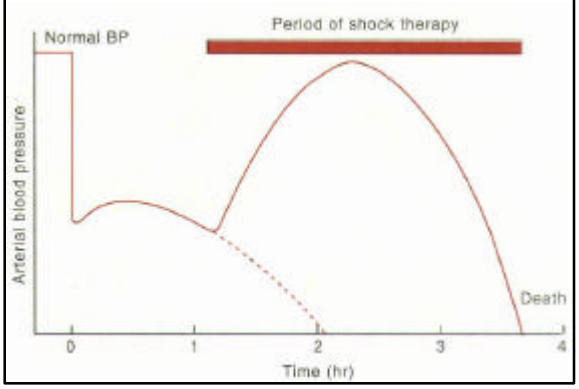


Fig. 9 Irreversible shock



7. Shock therapy

Fig. 10 Normal pressures in cardiac chambers