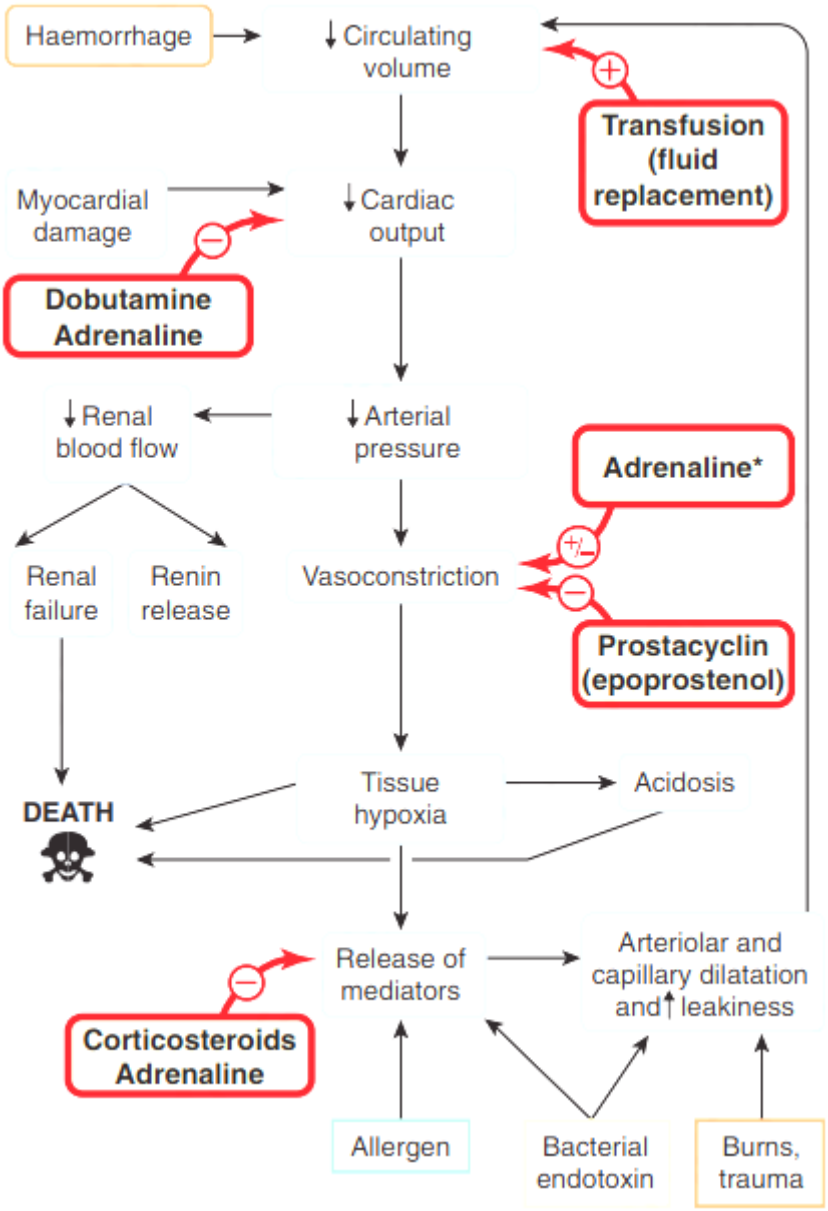
Pharmacotherapy of Shock

- Shock is a medical emergency with a very high mortality, even with optimal treatment in an intensive care unit
- Shock is characterised by complex acute systemic circulatory failure associated with hypoperfusion of tissues/vital organs. Tissue hypoxia damages intracellular structures.
- This leads to anaerobic metabolism and hence to increased lactate production, i.e. acidosis and liberation of substances such as histamine, kinins, prostaglandins and cardiodepressant peptides into the circulation.
- It may be initiated by trauma, acute blood loss, depletion of body fluids, burns, severe infection or acute myocardiac dysfunction; of these, hypovolemia is the most important.
- The common factor is reduced effective circulating blood volume (hypovolaemia) caused either directly by bleeding or by movement of fluid from the plasma to the gut lumen or extracellular fluid.
- The coronary filling is mainly diastolic and excessive fall in diastolic BP (together with cardiodepressant peptides) adds a cardiogenic element to any other variety of shock.
- Cardiogenic: This is due to failure of the heart as a pump as in acute myocardial infarction (MI). Rarely, in some cases, there is complete failure of the compensatory sympathoadrenal discharge.
- The septic shock is initiated by the toxins released by the micro-organisms: exotoxins (as in the case of Toxic Shock Syndrome (TSS) due to staphylococci or streptococci); or endotoxins (as with Gram-negative bacilli). These toxins cause the release of tumour necrosis factor alpha (TNF alpha) and a variety of interleukins especially IL-1β, and the platelet activating factor (PAF) from the mononuclear phagocytes and the endothelial cells. These cytokines cause a further cascade of synthesis and release of substances such as leukotrienes, PGs and thromboxane A2 . They injure the vascular endothelium, increase its permeability, and cause fluid loss from the circulation leading to hypovolemia. They also depress the myocardium.

Clinical picture of shock:

- Sweating, cold extremities, rapid and thready pulse and air hunger.
- Cyanosis of the extremities may be present.
- Oliguria (urine output less than 25 ml per hour for 4 hours or less than 500 ml/24 hours in adults)
- Mental changes (somnolence, confusion, restlessness)
- Acidosis and a marked difference in the temperature between the rectum and the skin

Survival depends on a balance between vasoconstriction in non-essential vascular beds and vasodilatation in vital ones. The dividing line between the normal physiological response to blood loss and clinical shock is that in shock tissue hypoxia produces secondary effects that magnify rather than correct the primary disturbance.



Pathogenesis of hypovolaemic shock.