

Pathophysiology

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Cellular As perfusion to the tissues is reduced, cells are deprived of oxygen and must switch from aerobic to anaerobic metabolism. The product of anaerobic respiration is not carbon dioxide but lactic acid. When enough tissue is underperfused the accumulation of lactic acid in the blood produces a systemic metabolic acidosis. As glucose within cells is exhausted, anaerobic respiration ceases and there is failure of sodium/potassium pumps in the cell membrane and intracellular organelles. Intracellular lysosomes release autodigestive enzymes and cell lysis ensues. Intracellular contents, including potassium, are released into the bloodstream. Microvascular As tissue ischaemia progresses, changes in the local milieu result in activation of the immune and coagulation systems. Hypoxia and acidosis activate complement and prime leukocytes, resulting in the generation of oxygen free radicals and cytokine release. These mechanisms lead to injury of the capillary endothelial cells. These, in turn, further activate the immune and coagulation systems. Damaged endothelium loses its integrity and becomes 'leaky'. Spaces between endothelial cells allow fluid to leak out and tissue oedema ensues, exacerbating cellular hypoxia. Ischaemic cell death releases potassium into the circulation, leading to systemic hyperkalaemia and acidosis, as well as further damage to molecules that systemically activate the immune system. - Systemic Cardiovascular As preload and afterload decrease, there is a compensatory baroreceptor response, resulting in increased sympathetic activity and release of catecholamines into the circulation. This results in tachycardia and systemic vasoconstriction (except in sepsis - see Distributive shock). Respiratory The metabolic acidosis and increased sympathetic response result in an increased respiratory rate and minute ventilation to increase the excretion of carbon dioxide (and so produce a compensatory respiratory alkalosis). Renal Decreased perfusion pressure in the kidney leads to reduced filtration at the glomerulus and a decreased urine output. The renin-angiotensin-aldosterone axis is stimulated, resulting in further vasoconstriction and increased sodium and water reabsorption by the kidney. Endocrine As well as activation of the adrenal and renin-angiotensin systems, vasopressin (antidiuretic hormone) is released in -

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and resorption of water in the renal collecting system. Cortisol is also released from the adrenal cortex, contributing to the sodium and water resorption and sensitising cells to catecholamines. Pathophysiology

In trauma and surgery, the combination of tissue trauma and hypovolaemic shock leads to the development of an endogenous coagulopathy called acute traumatic coagulopathy (ATC). Up to 25% of all trauma patients develop ATC within minutes of injury and it is associated with a fourfold increase in mortality. ATC is characterised by systemic hyperfibrinolysis, low fibrinogen levels and platelet dysfunction. ATC evolves into a more complex, multifactorial 'trauma-induced

coagulopathy' owing to further derangements induced by resuscitation (Figure 2.1). Fluid and red blood cell transfusions lead to dilution of coagulation factors, which worsens the pre-existing coagulopathy . Underperfused muscle is unable to generate heat and hypothermia ensues, again worsened by cold fluid or blood transfusion. Further heat is lost by opening Figure 2.1 body cavities during surgery . Severe acidosis and hypothermia both inhibit coagulation proteases and reduce coagulation function. These then lead to further bleeding and a downward spiral, leading to physiological exhaustion and death.

ATC Haemorrhage Acidaemia Hypothermia Inflammation Fibrinolysis Genetics Loss, dilution
TRAUMA-INDUCED COAGULOPATHY (TIC) Trauma-induced coagulopathy. ATC, acute traumatic coagulopathy.

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