Physiology of shock and volume resuscitation

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Abstract

Haemorrhagic and severe hypovolaemic shock can be rapidly fatal unless identified and resuscitated quickly. Monitoring of haemodynamic and cellular end points is crucial in guiding treatment and improving outcomes. This article therefore focuses on the pathophysiology of hypovolaemic shock, volume resuscitation, haemostasis and approaches to management. Fluid resuscitation saves lives but considerable debate remains regarding the ideal fluid type and strategy to use. Blood transfusion is also a critical therapy in the shocked, bleeding patient with a lower threshold for transfusion being appropriate in the elderly patient with less physiological reserve. Reversal of anticoagulant medications and the administration of coagulation products should support both fluid and red cell therapy to counteract the multifactorial coagulopathy that can accompany severe trauma, haemorrhage and shock. The aim is to stabilize the patient such that any interventional strategies (both percutaneous and surgical) can be considered for uncontrolled bleeding.

Keywords Coagulation; fluid balance; frank–starling; haemorrhage; haemostasis; hypovolaemia; transfusion

A significant reduction in blood pressure is life-threatening and associated with a state of shock. Shock is a clinical condition that is defined by the presence of:

- hypotension with a systolic blood pressure less than 90 mmHg or a mean arterial pressure (MAP) less than 60 mmHg or reduced by greater than 30%, for at least 30 minutes
- oliguria (urine output less than 0.3 ml/kg/hour for two consecutive hours)
- poor peripheral perfusion.

The aetiology of shock can be classified as hypovolaemic, cardiogenic, obstructive or distributive. Hypovolaemic shock caused by haemorrhage remains the most common preventable cause of death after major trauma, therefore this article will focus on the pathophysiology of hypovolaemic shock, volume resuscitation, haemostasis and approaches in the management of this critically ill group of patients.

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Pathophysiology

Frank–Starling curves and pressure–volume loops

An understanding of cardiac haemodynamic physiology is critical in correcting the altered physiological state that accompanies shock. This can be explored using the Frank–Starling relationship of preload to ventricular stroke volume and analysing the pressure–volume loop of ventricular function.

Figure 1a demonstrates the relationship of preload to stroke volume across a range of cardiac contractile function but assumes afterload remains constant. A more complete physiological approach, which complements the Frank–Starling curve, is the pressure–volume loop as shown in Figure 1b. The loop begins at the end-diastolic volume (EDV) and the pressure increases with no change in volume (isovolumetric contraction). Opening of the ventricular outflow valves follows this as the pressure exceeds aortic and pulmonary root pressure. Systole ends with closure of the outflow valves and a rapid decrease in ventricular pressure (isovolumetric relaxation) reaching the end-systolic volume (ESV). Stroke volume is the difference between the EDV and ESV. Opening of the atrioventricular valves and return to EDV follows this phase. The relationship between diastolic and systolic function is described by the end-systolic pressure–volume relationship (ESPVR) and the end-diastolic pressure–volume relationship (EDPVR). The slope of the ESPVR reflects changes in contractility (which is analogous to the Frank–Starling relationship), while that of the EDPVR represents diastolic function and elasticity of the heart.

The role of afterload can now be considered using this model. Afterload describes the impedance to ventricular ejection and comprises the whole of the systolic phase unlike preload, which is only equivalent to the EDV. The primary contribution to afterload is vascular resistance. The pressure–volume loop allows incorporation of the acute effects of afterload and can be used to explore the influence of changes in afterload on ventricular performance (Figure 1c).

In hypovolaemic shock, intravascular volume is reduced resulting in decreased venous return, EDV and cardiac output. Figure 2 explores these changes using the Starling and pressure–volume relationships. Loss of intravascular volume will result in vasoconstriction in order to maintain systemic pressure with consequent reduction in cardiac output. This reduction in stroke volume is described by the pressure–volume loop, where EDV is shifted leftwards on the EDPVR curve, afterload is increased (vasoconstriction) and contractility (ESPVR) is unchanged.

Cellular responses to hypovolaemic shock

The haemodynamic collapse associated with hypovolaemic shock results in decreased oxygen and nutrient delivery to tissues. A brief discussion on the processes of oxygen delivery also adds to the cellular understanding of the pathophysiology of shock. Total oxygen delivery (DO_2; mlO_2/minute/m^2) is the product of cardiac index (litres/minute/m^2) and the arterial oxygen content (CaO_2; mlO_2/litre blood). In the resting state, systemic oxygen consumption ($\dot{V}O_2$) is proportional to the body's energy needs and can be calculated by Fick's principle (Box 1).

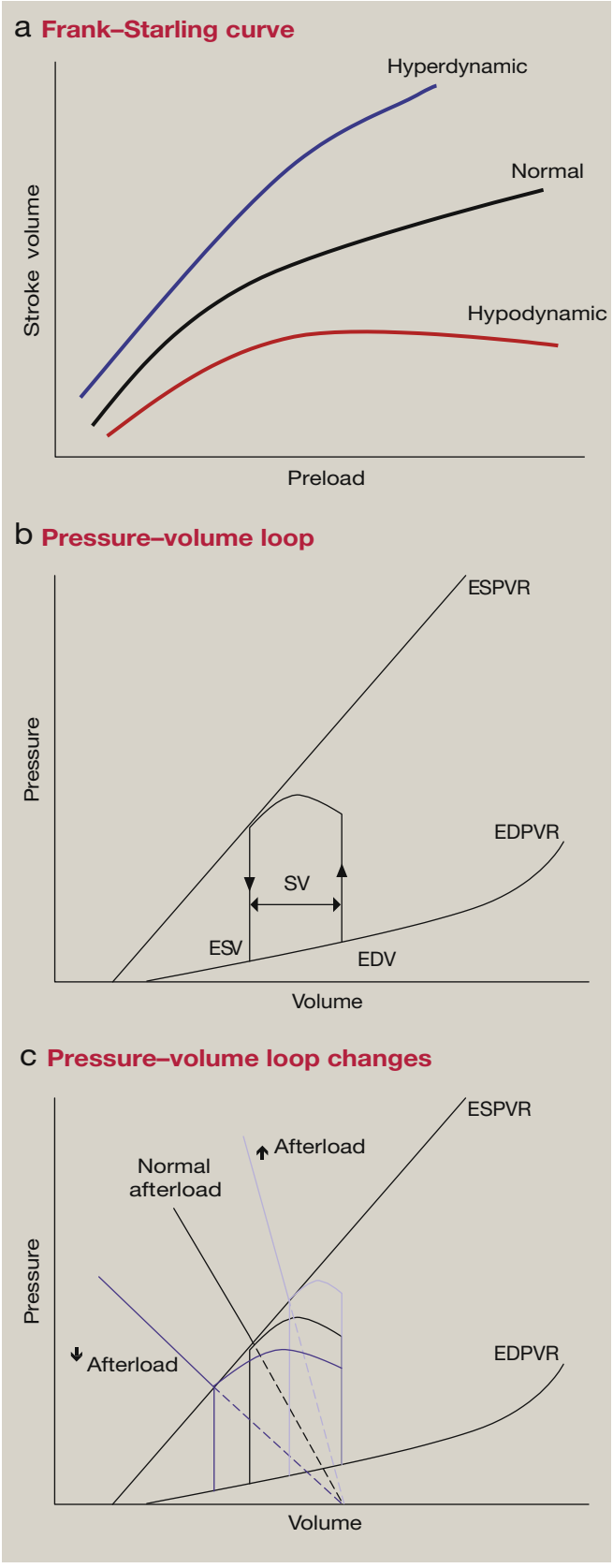


Figure 1 (a) Frank–Starling curves demonstrating the link between ventricular filling (preload or end-diastolic volume) and ventricular stroke volume across a range of contractile states at constant afterload. **(b)** Pressure–volume loop integrating the relationship between contractility (end-systolic pressure–volume relationship, ESPVR), compliance (end-diastolic pressure–volume relationship, EDPVR), preload and stroke volume (SV). This model does not take into account the influence of afterload on cardiac function. ESV, end-systolic volume; EDV, end-diastolic volume. **(c)** Pressure–volume loop changes with varying afterload conditions as defined by afterload. With increasing afterload, ventricular developed pressure increases but stroke volume is reduced, and the converse occurs when afterload is reduced.

Rapid haemorrhage results in decreased cardiac output and DO_2 with little change in $\dot{V}O_2$ due to redistribution of blood flow to the critical organs. Oxygenation is also maintained by a favourable shift in the oxygen dissociation curve and a regional metabolic vasodilatation. The hypoxia caused by severe haemorrhage increases capillary recruitment, raising the surface area for oxygen diffusion and therefore reducing diffusion distance. These adaptive microvascular changes are eventually overwhelmed leading to a shift from aerobic to anaerobic metabolism, and the rate of DO_2 where this occurs defined as the critical DO_2 (DO_{2crit}).

The transition from aerobic to anaerobic metabolism below the DO_{2crit} marks a state known as compensated shock. Cellular function is maintained while the production of adenosine triphosphate (ATP) from all sources is sufficient to maintain protein synthesis and contractile function. The resistance to hypoxic insults is also tissue specific, with muscle and hepatocytes able to resist irreversible damage for hours while the brain and intestinal mucosa can only withstand minutes of hypoxia.

When the supply of ATP cannot meet cellular need, uncompensated shock ensues. Irreversible cell damage now occurs through a variety of mechanisms including failure of membrane ion transporters, cell swelling, acidosis, increased free radicals and loss of adenine nucleotides from the cell. These changes are reflected clinically by an increase in plasma lactate levels.

Physiological responses to hypovolaemia

The loss of intravascular volume leads to a cascade of physiological responses that can be divided into immediate (neural), intermediate (intrinsic) and delayed (humoral).

The neural response occurs within minutes of onset of hypovolaemia. Atrial pressure is reduced activating low-pressure receptors in the atria, pulmonary arteries, cardiac veins and ventricles. Further reduction in circulating volume leads to a fall in cardiac output and blood pressure leading to activation of high-pressure receptors in the aortic arch and carotid sinus. When the MAP drops below 50 mmHg, chemoreceptors in the aortic and carotid bodies are activated followed by a central nervous system ischaemic response at MAP less than 40 mmHg. Afferent signals from these receptors are transmitted to the vasomotor centre in the medulla and pons that results in efferent sympathetic and parasympathetic outflow.

Sympathetic responses result in increased heart rate, myocardial contractility and vasoconstriction. Vagal tone is reduced, thereby accentuating the sympathetic response caused by increased catecholamine release.

Hours into sustained hypovolaemia, intermediate responses are engaged. Capillary pressure is reduced leading to fluid shift from the interstitium into the vasculature followed by protein

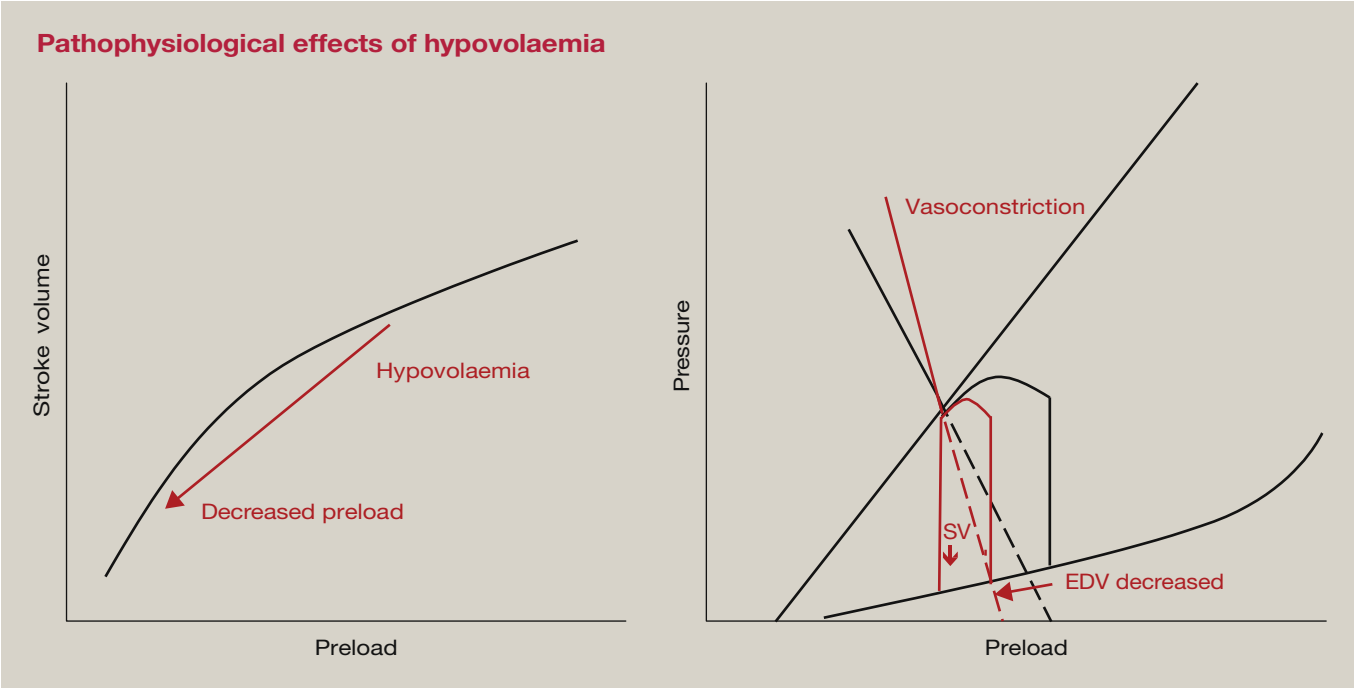


Figure 2 The pathophysiological effects of hypovolaemia explored via Frank–Starling and pressure–volume relationships. Loss of circulating volume reduced preload which directly leads to a fall in cardiac output as shown by the Starling curve. The pressure–volume loop panel also demonstrates this reduction in stroke volume and pressure. Hypovolaemia leads to a reduction in EDV with vasoconstriction as compensation (red lines), with the combined effect a reduction in stroke volume. SV, stroke volume; EDV, end-diastolic volume.

shift to plasma, which also draws in fluid to replace the intravascular losses. In the first 24–48 hours, up to 2 litres of fluid can shift to maintain the intravascular compartment. Blood glucose also rises with shock, which results in an osmotic effect that returns 17 ml of fluid per 1 mmol/litre rise in glucose to the vascular compartment.

Delayed responses occur within hours to days and are mediated by a variety of hormones. Antidiuretic hormones, renin, angiotensin and aldosterone secretion is activated to drive renal retention of fluid and maintain circulating volume.

Fick's principle for calculating $\dot{V}O_2$

$$\dot{V}O_2 = Q \times (CaO_2 - CvO_2)$$

$$CaO_2 = (1.34 \times \text{haemoglobin concentration} \times SaO_2) + (0.0031 \times PaO_2)$$

$$CvO_2 = (1.34 \times \text{haemoglobin concentration} \times SvO_2) + (0.0031 \times PvO_2)$$

Q is the cardiac output
PaO_2 is the partial pressure of oxygen in the arterial blood
SaO_2 is the arterial oxyhaemoglobin saturation
PvO_2 is the partial pressure of oxygen in the mixed venous blood
SvO_2 is the mixed venous oxyhaemoglobin saturation

Box 1

Clinical features and stages of shock

The haemodynamic and cellular changes described above now need to be integrated into the clinical presentation and assessment of hypovolaemic shock. Hypovolaemia may result as a loss of whole blood or plasma. Blood loss may be either from open wounds or often concealed within the abdominal, thoracic or retroperitoneal compartments. Concealed losses also occur in tissues surrounding bony fractures with pelvic fractures resulting in blood loss up to 2500 ml. Plasma losses leading to intravascular fluid depletion occur with any condition that results in loss of extracellular fluid with or without protein loss. Protein- and fluid-losing states include pancreatitis, peritonitis and burns, whereas diarrhoea, vomiting and sodium-losing nephropathy are examples of fluid loss with low protein loss.

The principal clinical features of hypovolaemic shock are hypotension, tachycardia and oliguria. Patients may also appear pale, agitated, dyspnoeic, diaphoretic and demonstrate pulsus paradoxus and faint heart sounds. Clinical assessment of these parameters and an estimation of blood loss allow shock to be classified into four stages that can be linked to the underlying cellular physiology as shown in Figure 3.

In summary, stage 1 is associated with minimal fluid/blood loss, normal clinical examination and preserved cellular ATP production. Stage 2 ensues with up to 30% loss of intravascular volume and heralds the onset of early clinical signs with preserved cellular function (compensated shock). Decompensation occurs at stage 3 with further volume depletion, clinical instability,

A summary of the four stages of shock as characterized by the physiological, neurological and cellular responses to the mismatch between falling oxygen delivery (eDO_2) and metabolic rate ($\dot{V}O_2$).

	Stage 1	Stage 2	Stage 3	Stage 4
Blood loss (ml)	<750 <15%	750–1500 15–30%	1500–2000 30–40%	>2000 >40%
Heart rate (bpm)	<100	>100	>120	>140
Blood pressure	Normal	Reduced	Reduced	Reduced
Respiratory rate (breaths/minute)	14–20	20–30	30–40	>35
Urine output (ml/hour)	Normal >30	Oliguria 20–30	Oliguria 5–15	Anuria
Neurological status	Normal	Agitated	Confused	Lethargic
ATP status	supply= demand	supply= demand	supply< demand	supply<< demand

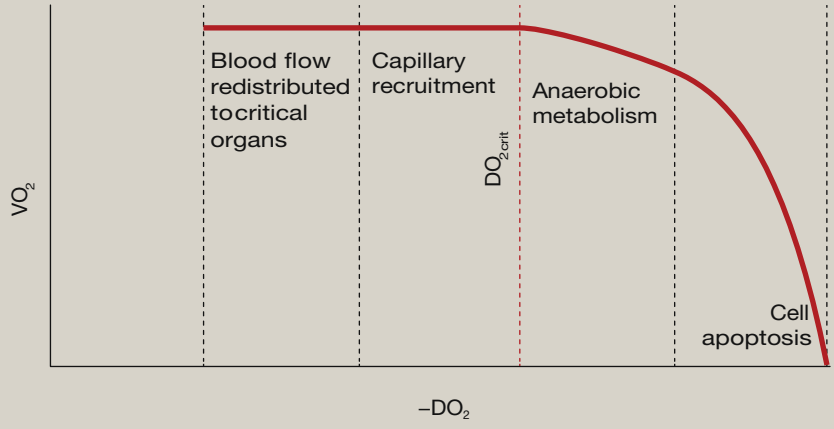


Figure 3

confusion and ATP supply not meeting demand. With greater than 2000 ml (or greater than 40%), stage 4 is reached which is associated with mortality greater than 50% if left untreated.

Clinical assessment, investigations and therapeutic end points

A rapid clinical assessment should focus on the parameters detailed in Figure 3 in order to gauge the extent of cardiovascular instability. Younger patients may display relatively minor reductions in blood pressure and heart rate, but compensatory mechanisms fail rapidly unless resuscitation is commenced. In contrast, older patients taking β-blockers may have little tachycardiac response and cardiovascular reserve in the presence of shock physiology. In cases of haemorrhagic shock, an estimation of blood loss is critical in planning treatment strategies. For example, intra-thoracic, intra-abdominal and large bone trauma may result in concealed blood loss and the history and examination should be tailored to exclude these pathologies.

Following conventional laboratory investigations, the shocked patient should be monitored for the basic parameters of cardiovascular stability — blood pressure, heart rate, capillary refill, urine output, and mental status. Additional clinical information may be gained by monitoring arterial pressure, arterial oxygen saturation (pulse oximetry and blood gas analysis) and central venous pressure (via central venous catheter). Assessment of lactate along with the blood gas and base deficit indicates the severity of shock and serial haemoglobin measurements provide indicators of on-going bleeding. Improvements in clinical, arterial blood gas, and lactate parameters can be used to determine the efficacy of resuscitation.

Defining therapeutic end points in these patients is extremely challenging. Conventional end points include blood pressure and urine output; however, up to 85% of patients are under-resuscitated when these variables are the only parameters monitored. We have defined the haemodynamic and cellular consequences of shock, and blood pressure and urine output will fail to identify cases in whom cellular recovery and perfusion is delayed despite restoration of baseline physiology. Therefore emerging therapeutic end points will address cellular as well and haemodynamic physiology. These indices and tests include current standards such as lactate and base deficit, but also newer technologies including skeletal muscle PO_2, fibreoptic gastric and

bladder mucosa pH and partial CO_2 tension. Future approaches also aim to assess the dysfunctional inflammatory response that is initiated by shock. Cytokines including tumour necrosis factor-α (TNF-α), interleukin-1 (IL-1) and IL-6 are elevated in plasma following major trauma and blood loss and correlate with prognosis. Measurement of these mediators is routinely possible but plasma levels do not accurately reflect tissue inflammation and organ damage. Despite this limitation, assessment of levels may provide insights into the cellular dysfunction in this group of patients. In the intensive care setting, measurement of variation of surrogates of stroke volume in response to respiratory variation can be used to assess fluid responsiveness. These include the use of trans-oesophageal ultrasonography of the superior vena cava and estimation of cardiac output by arterial waveform analysis (e.g. PiCCO (R) and LiDCO (R) systems.

Resuscitation

The main goal of resuscitation is to restore circulating blood volume and in cases of haemorrhage stop the source of bleeding. Patients with on-going bleeding should have their circulating volume restored as soon as possible, as tissue oxygenation will be maintained in the presence of low haemoglobin concentrations. Therapy should be guided by changes in haemodynamic parameters including blood pressure, heart rate, urine output and where invasive monitoring is indicated, central venous pressure, cardiac output, pulmonary wedge pressure and oxygen saturation.

Fluid resuscitation

Rapid restoration of circulating volume and haemodynamic status with isotonic crystalloid fluid has been the dogma of resuscitation strategies for decades, the so-called 'golden hour'. The key issues to address in approaching fluid resuscitation include the type of fluid, volume, rate and what end points to monitor. Early goal-directed therapy uses a specific protocol in patients with septic shock to measure physiological end-points and guide haemodynamic resuscitation. However, while a single-centre trial in 2011 suggested reduced mortality, subsequent multi-centre trials and a meta-analysis (PRISM trial) have not shown benefit over usual standard of care. The ideal fluid for resuscitation remains elusive; lactated Ringer's (Hartmanns) solution and normal saline are the most frequently used isotonic fluid. The debate regarding their efficacy compared to colloidal fluids and hypertonic fluids currently remains unresolved (see reference 1 for a detailed review).

Clinical and experiment evidence do not point to a favoured crystalloid fluid for resuscitation. Lactate Ringer's solution is preferred by some over normal saline due to reports of increased physiologic derangements with the latter, including hyperchloraemic acidosis and dilutional coagulopathy with large volumes. A unifying feature of the use of crystalloids in the treatment of haemorrhagic shock is the 'three to one' rule – 3 ml of crystalloid should be infused for every 1 ml of blood loss in order to account for losses into the interstitium and tissues (third space loss).

Colloidal solutions such as albumin and hetastarch are often used in clinical practice to increase circulating volume rapidly and are assumed to remain in the intravascular compartment for longer than crystalloids. Early, prospective randomized controlled trials attempted to compare these two fluids in critically ill patients. These trials were all small scale and heterogeneous in design, and the largest randomized trial to date (the CRISTAL trial) demonstrated no difference in mortality with either approach at 28 days.

This debate continues till today with large variances in clinical practice. Furthermore, these debates have led to alternative fluid strategies to be investigated including hypertonic saline, albumin, hetastarch and human serum albumin. These approaches are unified by the fact that available data do not demonstrate a benefit compared to conventional resuscitation with crystalloids.

Transfusion

Despite the significant interest in the crystalloid versus colloid debate, transfusion of red cells in the setting of haemorrhagic shock provides an alternative to decrease the need for infusing large volumes of isotonic fluids. Blood transfusion is indicated when estimated blood loss exceeds 30% (stage 3), but determining this is limited by the haemodilution from initial fluid resuscitation, and therefore its use remains guided by clinical and laboratory assessment. For example, a patient with probable blood loss and hypotensive unresponsive to 2 litres of fluids should be treated with transfusion (O negative until cross-matched blood is available). The threshold set by most professional bodies responsible for critical care is a haemoglobin concentration of 6–8 g/dl and they advocate against prophylactic transfusion above 10 g/dl. Up to a third of patients admitted to a critical care setting undergo transfusion for active bleeding, therefore restrictive (Hb kept 7–9 g/dl) versus liberal (Hb kept 10–12 g/dl) transfusion strategies in this group of patients has been examined by a large, multi-centre, randomized controlled trial. Mortality was equivalent in the two groups, but sub-group analysis showed reduced mortality in the restrictive group in patients under 55 years of age or less critically unwell.

Blood transfusion, particularly when extensive, is also associated with complications such as increased infection, risk of transmissible disease, metabolic complications (hyperkalaemia) and risk of erroneous administration. There are clinical scenarios where special consideration should be given to transfusion. The elderly patient is a particular example as tolerance of anaemia is dependent on the degree of physiological reserve. While young patients are able to increase their cardiac output in order to physiologically compensate in the setting of anaemia, the same level of anaemia may result in haemodynamic instability in the elderly. This is supported by evidence of patients presenting with myocardial infarction and anaemia, with patients over 65 and low haematocrit having increased 30-day mortality, which could be corrected by transfusion. In the surgical setting, intraoperative blood salvage (or cell salvage) can also be used to salvage patients' whole blood and allow autologous blood transfusion, using cell processors which wash and separate the red blood cells, before reinfusing them. In major haemorrhages requiring massive transfusion (eg. >50% of total blood volume within 3 hours), protocols have been developed to guide the transfusion of blood products and monitoring of response. These often make use of predefined ratios of red cells, FFP/cryoprecipitate and platelets (e.g. 1:1:1 or 2:1:1 ratio) for transfusion. Such protocols

are highlighted in guidelines such as those by the Task Force for Advanced Bleeding Care in Trauma.

Alternatives to red cell transfusion

Recent experimental approaches have considered if there are alternatives to red cell transfusion to improve tissue oxygen delivery. These artificial oxygen carriers are currently undergoing development or are in early phase clinical trials. Perfluorocarbons were developed to deliver near complete oxygen dissociation in the presence of high blood-tissue gradients but their entry into clinical practice has been limited by complex delivery requirements and complications including immunosuppression. Newer agents are based on haemoglobin and show promise in experimental models of shock, although none has as yet entered into clinical use.

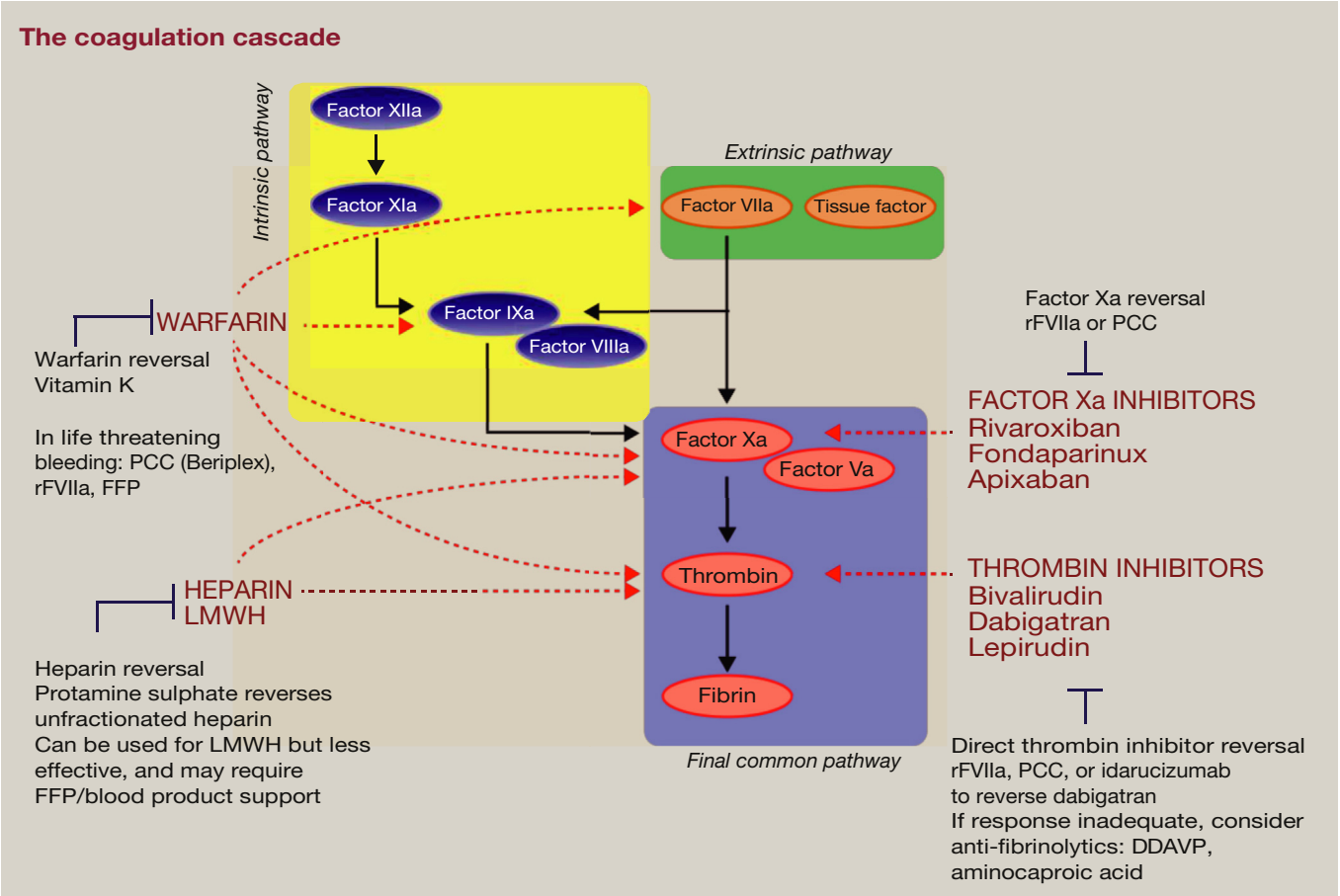
Vasopressor support

The early stages of resuscitation in haemorrhagic shock may require vasopressors and fluids to maintain blood pressure, but if bleeding continues or is uncontrolled, this strategy is no longer effective. This is thought to be due to paralysis of the vasculature caused by acidosis, hypoxia and ATP depletion. Tissue perfusion is regulated by arteriolar tone and regional changes act to maintain perfusion to critical organs during hypovolaemia. However, in advanced shock, demand from other organs cannot be met leading to a vicious cycle of organ failure. Vasopressin an endogenous stress hormone has been shown to be a potential therapy in this scenario. In patients with trauma and haemorrhagic shock, vasopressin administration reduced intravenous fluid volumes, improved haemodynamic parameters, and increased survival. Following these early case reports, multicentre trials are underway to clarify and support these findings, particularly as earlier trials reported increased mortality in patients with haemorrhagic shock treated with aggressive fluid resuscitation and vasopressors.

Coagulation and control of bleeding

Bleeding results in the initiation of a complex series of reactions with the ultimate aim of arresting bleeding at the source (Figure 4). This is a three-stage process involving:

- generation of a prothrombin activator
- the prothrombin activator catalyses the conversion of prothrombin to thrombin
- thrombin enzymatically converts fibrinogen to fibrin, which allows a mesh of platelets, red cells and plasma to form a clot at the site of bleeding.



A summarized description of the coagulation cascade and common anticoagulants and their targets within this system. Each anticoagulant is also accompanied by reversal strategies in the event of bleeding complications.

DDAVP, 1-deamino-8-D-arginine vasopressin; FFP, fresh frozen plasma; LMWH, low-molecular-weight heparin; PCC, prothrombin complex concentrate; rFVIIa, recombinant factor VIIa.

Figure 4

Step 1 is critical in initiating this response and is dependent upon the intrinsic and extrinsic coagulation pathways. These pathways occur in parallel and interact constantly. The extrinsic pathway is triggered by damage to the vascular wall and tissues while the intrinsic pathway begins in the blood itself.

Control of bleeding is a critical part of the resuscitation of the bleeding shocked patient alongside fluid replacement therapy. Contemporary approaches to bleeding control aim to target the site of bleeding, manage coagulopathy, maintain tissue perfusion and limit the inflammatory response. The clotting factors and downstream mediators in this cascade are targets for commonly used anticoagulants and therefore may contribute or be responsible for bleeding events leading to shock. Figure 4 summarizes the targets for these agents and lists the reversal agents that are discussed below. Reversal agents for the newer novel oral anticoagulant drugs were initially lacking although a reversal agent for dabigatran, the antibody fragment idarucizumab, has been shown to produce rapid reversal within minutes (REVERSE-AD trial). In addition, intravenous recombinant factor Xa (andexanet alpha) has recently been approved in the USA for reversal of Rivaroxaban and Apixaban and is expected to be approved for use in Europe soon.

Microcirculatory dysfunction mediates some of the pathophysiological response to haemorrhage, and experimental evidence has highlighted the failure of fluid resuscitation to reverse these changes. Resuscitation after haemorrhage leads to changes seen with ischaemia-reperfusion injury: reactive oxygen species, activation of inflammatory pathways and cell apoptosis. Prompt haemostasis and resuscitation can improve outcomes by preventing microcirculatory dysfunction.

Arresting bleeding in actively bleeding patients minimizes the extent of haemorrhage and inflammation. This is achieved most simply by external compression of open wounds, tourniquets and immobilization of long-bone fractures. Haemostatic agents come in multiple formulations, including sprays, liquids and absorbable pads and are all used widely in elective surgery but their use in trauma patients is untested.

Coagulation products

Management of coagulopathy that accompanies up to 25% of severely injured trauma patients is critical to reduce the associated increase in early and late mortality. Severe shock in the presence of physical trauma drives an endogenous coagulopathy, which occurs early and is driven by systemic anti-coagulation and fibrinolysis. This process was thought to be driven by loss or consumption of coagulation factors but recent clinical and experimental evidence points to dilutions of these factors following transfusion or massive fluid replacement without coagulation support perhaps being the dominant mechanism. Other potential contributors to this coagulopathy are systemic hypothermia, acidosis, inflammation, platelet dysfunction and underlying genetic variations. Assessment of this coagulopathy to guide treatment includes laboratory measurement of the prothrombin time (INR), activated partial thromboplastin time (APTT) and fibrinogen. In addition, thromboelastography (TEG) is a point of care test which gives a global assessment of blood coagulability by measuring the viscoelastic properties of a blood sample during clotting, and can be invaluable due to its rapid turnaround time compared to conventional testing.

Blood coagulation products therefore form the mainstay of haemorrhage control in parallel with surgical interventions and red cell therapy. These include plasma, platelets and cryoprecipitate. Current evidence suggests high doses of fresh frozen plasma (FFP) and red cell transfusion may be associated with improved outcomes, but concern remains regarding utilizing scarce plasma resources in this way. Forthcoming clinical trials will aim to discover the optimum strategy for this approach, while emerging options include freeze-dried or lyophilized plasma, which do not need thawing and maintain clotting factor activity.

Blood product therapy does have limitations beyond those of cost and logistics. A resuscitation protocol of red cells, platelets, FFP and cryoprecipitate in equal measures does not meet the coagulation profile of whole blood, and does not target systemic processes such as fibrinolysis. Therefore there is increasing evidence supporting the use of systemic treatments such as fibrinogen concentrate and procoagulants, particularly recombinant factor VIIa. Fibrinogen concentrate use is initiated when fibrin network formation is decreased but supporting evidence remains case series only. Recombinant factor VIIa (rFVIIa) is approved for the control of bleeding in haemophilia or as a complication of warfarin therapy. In animal studies, rFVIIa has been shown to be effective procoagulant in controlling bleeding. Case studies of its use in trauma have indicated that mortality is reduced, however a review of available data demonstrated no improvement in blood loss, transfusion requirements or death. Therefore further randomized controlled trials are needed, and current indications for rFVIIa are massive bleeding and failure of surgical and conventional therapies. Tranexamic acid is an antifibrinolytic drug which is used as an adjunct in major haemorrhage, and a recent meta-analysis has not only confirmed its benefits in terms of survival in acute severe bleeding, but showed that this benefit is greatest the earlier it is given, with a 10% reduction in survival benefit for every 15 minutes of treatment delay and no survival benefit beyond 3 hours.

Interventional approaches

Endovascular techniques are now utilized in the early management of severe bleeding. Vascular injury is amenable to angioembolization with balloon catheters or stent placement and may be associated with less bleeding and complications than conventional surgery. Abdominal injury leading to hepatic or splenic bleeding can also be arrested percutaneously with increased organ salvage and lower operation rates. The future of interventional control of severe and rapid bleeding is likely to be a combined surgical and percutaneous approach in a new type of operating theatre known as RAPTOR (resuscitation with angiography, percutaneous techniques and operative repair) suites.

Conclusions

Haemorrhagic and severe hypovolaemic shock can be rapidly fatal unless identified and resuscitated quickly. Fluid resuscitation saves lives but considerable debate remains regarding the ideal fluid type and strategy to use. Blood transfusion is a critical therapy in the shocked, bleeding patient with lower thresholds for transfusion appropriate in the elderly patient. However, coagulation products should support both fluid and red cell

therapy in order to manage the multifactorial coagulopathy that accompanies severe trauma, haemorrhage and shock with interventional strategies considered for uncontrolled bleeding. Monitoring haemodynamic and cellular end points is crucial in guiding treatment and improving outcomes in this critically ill group of patients. ◆

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