

Hemorrhage and blood transfusion

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Hemorrhage

Hemorrhage must be recognized and managed aggressively to reduce the severity and duration of shock and avoid death and/ or multiple organ failure. Hemorrhage is treated by arresting the bleeding – not by fluid resuscitation or blood transfusion. Although necessary as supportive measures to maintain organ perfusion, attempting to resuscitate patients who have ongoing hemorrhage will lead to physiological exhaustion (coagulopathy, acidosis and hypothermia) which is known as (LETHAL TRIAD) and subsequently

Pathophysiology

- Haemorrhage leads to a state of hypovolemic shock.
- The combination of tissue trauma and hypovolaemic shock leads to the development of an endogenous coagulopathy called acute traumatic coagulopathy (ATC). Up to 25 per cent of trauma Haemorrhage patients develop ATC within minutes of injury and it is associated with a four-fold increase in mortality. It is likely that ATC exists whenever there is the combination of shock and tissue trauma (e.g. major surgery). ATC is the component of trauma- induced coagulopathy (TIC) which is ultimately multifactorial
- Ongoing bleeding with fluid and red blood cell resuscitation leads to a dilution of coagulation factors which worsens the coagulopathy.
- In addition, the acidosis induced by the hypoperfused state leads to decreased function of the coagulation proteases, resulting in coagulopathy and further haemorrhage.
- The reduced tissue perfusion includes reduced blood supply to muscle beds. Underperfused muscle is unable to generate heat and hypothermia ensues.
- Coagulation functions poorly at low temperatures and there is further haemorrhage, further hypoperfusion and worsening acidosis and hypothermia. These three factors result in a downward spiral leading to physiological exhaustion and death

Medical therapy has a tendency to worsen this effect.

1. Intravenous blood and fluids are cold and exacerbate hypothermia.
2. Further heat is lost by opening body cavities during surgery.
3. Surgery usually leads to further bleeding and many crystalloid fluids are themselves acidic (e.g. normal saline has a pH of 6.7).

Every effort must therefore be made to rapidly identify and stop haemorrhage, and to avoid (preferably) or limit physiological exhaustion from **coagulopathy, acidosis and hypothermia** which is called (**LETHAL TRIAD**)

Definitions

Revealed and concealed haemorrhage

1. **Revealed haemorrhage** is obvious external haemorrhage, such as exsanguination from an open arterial wound or from massive hematemesis from a duodenal ulcer.
2. **Concealed haemorrhage** is contained within the body cavity and must be suspected, actively investigated and controlled. In trauma, haemorrhage may be concealed within the chest, abdomen, pelvis, retroperitoneum or in the limbs with contained vascular injury or associated with long-bone fractures. Examples of nontraumatic concealed hemorrhage include occult gastrointestinal bleeding or ruptured aortic aneurysm.

primary, reactionary and secondary haemorrhage

1. **Primary haemorrhage** is haemorrhage occurring immediately due to an injury (or surgery).
2. **Reactionary haemorrhage** is delayed haemorrhage (within **24 hours**) and is usually due to dislodgement of clot by resuscitation, normalisation of blood pressure and vasodilatation. Reactionary haemorrhage may also be due to technical failure, such as slippage of a ligature.
3. **Secondary haemorrhage** is due to sloughing of the wall of a vessel. It usually occurs **7–14 days** after injury and is precipitated by factors such as infection, pressure necrosis (such as from a drain) or malignancy.

Surgical and non-surgical haemorrhage

1. **Surgical haemorrhage** is due to a direct injury and is amenable to surgical control (or other techniques such as angioembolisation).
2. **Non-surgical haemorrhage** is the general ooze from all raw surfaces due to coagulopathy and cannot be stopped by surgical means (except packing). Treatment requires correction of the coagulation abnormalities.

Degree and classification

- The adult human has approximately **5 litres** of blood (**70 mL/ kg children and adults, 80 mL/kg neonates**). Estimation of the amount of blood that has been lost is difficult, inaccurate and usually underestimates the actual value.
- External haemorrhage is obvious, but it may be difficult to estimate the actual volume lost. In the operating room, blood collected in suction apparatus can be measured and swabs soaked in blood weighed.
- The haemoglobin level is a poor indicator of the degree of haemorrhage as it represents a concentration and not an absolute amount. In the early stages of rapid haemorrhage, the haemoglobin concentration is unchanged (as whole blood is lost). Later, as fluid shifts from the intracellular and interstitial spaces into the vascular compartment, the haemoglobin and haematocrit levels will fall.
- The amount of haemorrhage can be classified into classes 1–4 based on the estimated blood loss required to produce certain physiological compensatory changes. Although conceptually useful, there is variation across ages (the young compensate well, the old compensate very poorly), variation between individuals (athletes versus the obese) and variation due to confounding factors (e.g. concomitant medications, pain).
- Treatment should therefore be based upon the degree of hypovolaemic shock according to ***1.vital signs, 2.preload assessment, 3.base deficit and, 4.most importantly, the dynamic response to fluid therapy.***

Classification of Hemorrhagic Shock

	CLASS I	CLASS II	CLASS III	CLASS IV
Blood Loss (ml) %	<750 15%	750-1500 15%-30%	1500-2000 30-40%	>2000 >40%
HR	<100	>100	>120	>140
BP	normal	normal	decrease	decrease
PP	normal	decrease	decrease	decrease
RR	15-20	20-30	30-40	>35
UOP	>30	20-30	5-15	negligible
CNS	Normal	mildly anxious	anxious confused	confused lethargic

Management

1. Identify haemorrhage

External haemorrhage may be obvious, but the diagnosis of concealed haemorrhage may be more difficult. Any shock should be assumed to be hypovolaemic until proved otherwise, and similarly, hypovolaemia should be assumed to be due to haemorrhage until this has been excluded.

2. Immediate resuscitative manoeuvres

Direct pressure should be placed over the site of external haemorrhage. Airway and breathing should be assessed and controlled as necessary. Large-bore intravenous access should be instituted and blood drawn for cross-matching (see Cross-matching below). Emergency blood should be requested if the degree of shock and ongoing haemorrhage warrants this.

3. Identify the site of haemorrhage

Once haemorrhage has been considered, the site of haemorrhage must be rapidly identified. Note this is not to definitively identify the exact location, but rather to define the next step in haemorrhage control (operation, angioembolisation, endoscopic control). Clues may be in the history (previous episodes, known aneurysm, non-steroidal therapy for gastrointestinal (GI) bleeding) or examination (nature of blood – fresh, melaena; abdominal tenderness, etc.). For shocked trauma patients, the external signs of injury may suggest internal haemorrhage, but haemorrhage into a body cavity (thorax, abdomen) must be excluded with rapid investigations (chest and pelvis x-ray, abdominal ultrasound or diagnostic peritoneal aspiration).

4. Haemorrhage control

The bleeding, shocked patient must be moved rapidly to a place of haemorrhage control. This will usually be in the operating room but may be the angiography or endoscopy suites. These patients require surgical and anaesthetic support and full monitoring and equipment must be available

TRANSFUSION of blood and blood products

The transfusion of blood and blood products has become commonplace since the first successful transfusion in 1818

Blood and blood products

In the UK, up to 450 mL of blood is drawn, a maximum of three times each year. Each unit is tested for evidence of hepatitis B, hepatitis C, HIV-1, HIV-2 and syphilis. Donations are leukodepleted as a precaution against variant Creutzfeldt–Jakob disease (this may also reduce the immunogenicity of the transfusion). The ABO and rhesus D blood group is determined, as well as the presence of irregular red cell antibodies. The blood is then processed into subcomponents.

Whole blood

Whole blood is now rarely available in civilian practice as it is an inefficient use of the limited resource. However, whole blood transfusion has significant advantages over packed cells as it is

1. coagulation factor rich
2. if fresh, more metabolically active than stored blood.

Packed red blood

cells are spun-down and concentrated packs of red blood cells. Each unit is approximately **330 mL** and has a haematocrit of **50–70 per cent**. Packed cells are stored in a

SAG-M solution (saline–adenine–glucose–mannitol) to increase shelf life to **5 weeks at 2–6°C**.

(Older storage regimens included storage in CPD – citrate–phosphate–dextrose solutions which have a shelf life of 2–3 weeks.)

Fresh-frozen plasma

Fresh-frozen plasma (FFP) is rich in coagulation factors and is removed from fresh blood and stored at -40 to -50°C with a two-year shelf life. It is the first-line therapy in the treatment of coagulopathy hemorrhage

Cryoprecipitate

Cryoprecipitate is a supernatant precipitate of FFP and is rich in factor VIII and fibrinogen. It is stored at -30°C with a two-year shelf life. It is given in

- low fibrinogen states
- factor VIII deficiency.
- Massive blood transfusion
- Hemophilia
- DIC
- Uremic bleeding tendency

Platelets

Platelets are supplied as a pooled platelet concentrate and contain about $250 \times 10^9/\text{L}$. Platelets are stored on a special agitator at $20-24^\circ\text{C}$ and have a shelf life of only 5 days. Indications of Platelet transfusions

- thrombocytopenia
- Patients with platelet dysfunction who are bleeding or undergoing surgery.
- Rapid reversal of antiplatelet for patients undergoing emergency surgery
- Massive blood transfusion
- DIC

Prothrombin complex concentrates

Prothrombin complex concentrates (PCC) are highly purified concentrates prepared from pooled plasma. They contain factors **II, IX and X. Factor VII** may be included or produced separately. It is indicated for the

emergency reversal of anticoagulant (warfarin) therapy in uncontrolled haemorrhage.

Indications for blood transfusion

Blood transfusions should be avoided if possible, and many previous uses of blood and blood products are now no longer considered appropriate use. The indications for blood transfusion are as follows:

- ***acute blood loss*** to replace circulating volume and maintain oxygen delivery
- ***Perioperative anaemia*** to ensure adequate oxygen delivery during the perioperative phase
- ***symptomatic chronic anaemia***, without hemorrhage or impending surgery.

How to transfuse the blood

- Hb < 8g/dl
- At least over 4 hours
- Sensible time of the day (*avoid transfusion at night*)
- Consider loop diuretics (*elderly, children, heart failure*)
- Prepare for complications (*antihistamines*)
- A day before surgery (to allow 2,3 diphosphoglycerate to recover)

Transfusion trigger

Historically, patients were transfused to achieve a ***haemoglobin >10 g/dL***. This has now been shown to not only be unnecessary but also to be associated with an increased morbidity and mortality compared to lower target values. A ***haemoglobin level of 6 g/ dL*** is acceptable in patients who are

- not actively bleeding,
- not about to undergo major surgery
- are not symptomatic.

Complications of blood transfusion

Complications from a single transfusion

- Complications from a single transfusion include:
- incompatibility haemolytic transfusion reaction
- febrile transfusion reaction
- allergic reaction
- infection
 - *bacterial infection (usually due to faulty storage)*
 - *hepatitis*
 - *HIV*
 - *malaria*
- air embolism
- thrombophlebitis
- transfusion-related acute lung injury (usually from FFP).

Complications from massive transfusion

- Complications from massive transfusion include:
- coagulopathy hypocalcaemia hyperkalaemia hypokalaemia hypothermia.

In addition, patients who receive repeated transfusions over long periods of time (e.g. patients with thalassaemia) may develop iron overload. (Each transfused unit of red blood cells contains approximately 250 mg of elemental iron.)

MASSIVE BLOOD TRANSFUSION

Massive blood transfusion is defined as follow

1. Whole blood replacement in 24 hours
2. >50% of blood volume is transfused in 4 hours
3. 10 units of blood transfused in 6 hours