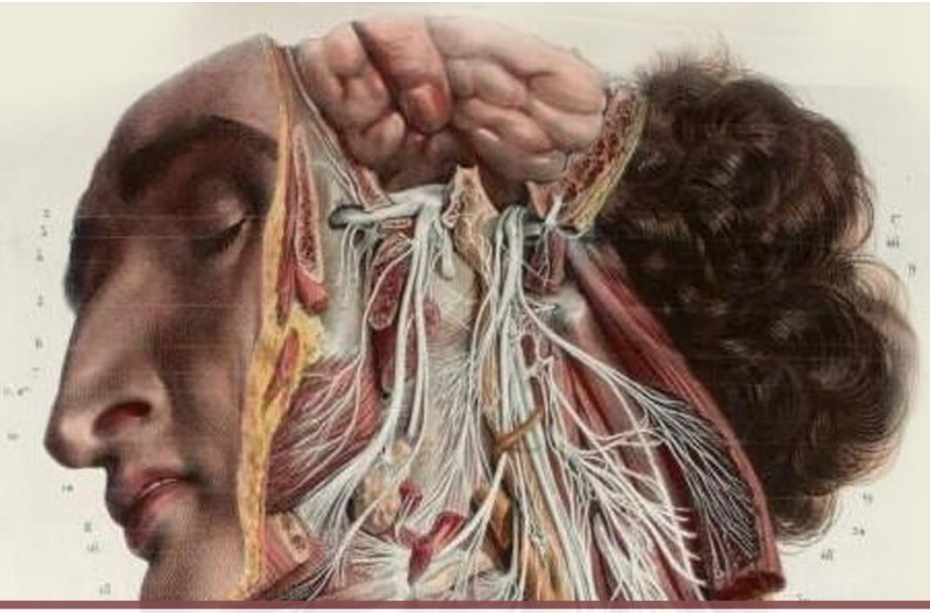

433 SURGERY TEAM

Transfusion of Blood and Blood Products

Done By:

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Team Leader :

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Blood transfusion

(60% of it occur perioperativly and it is the anesthesiologist's responsibility).

❖ Why?

- Increase oxygen carrying capacity
- Restoration of red cell mass
- Correction of bleeding caused by platelet dysfunction
- Correction of bleeding caused by factor deficiencies

When it is necessary?

(Up to 30% of blood volume loss can be treated with crystalloids)

Transfusion Trigger: Hemoglobin (Hb) level at which transfusion should be given varies with patients and procedures.

Tolerance of acute anemia depends on:

- Maintenance of intravascular volume
- Ability to increase cardiac output
- Increases in 2,3-DPG to deliver more of the carried oxygen to tissues (i.e. shifting the Hb association curve to the right)

Oxygen delivery (DO_2)

$DO_2 = CO \times CaO_2$

CO: cardiac output
CaO_2: Oxygen content in arterial blood

Since: CO = Stroke volume (SV) x Heart rate (HR)
Then: DO_2 = SV x HR x CaO_2

- If HR or SV are unable to compensate, then **Hb is the major determinant factor in O2 delivery**
- Healthy patients can tolerate Hb levels of 7 gm/dL.
- Compromised patients may require Hb levels above 10 gm/dL.

Oxygen content (CaO_2)

$CaO_2 = (Hb \times 1.34) \times O_2$ saturation + PaO2x(0.003)

- **Hemoglobin is the main determinant of oxygen content in the blood**

Hb = 14 gm /dl	Hb = 10 gm/dl	Hb = 7 gm/dl
14x 1.34 x 0.99+ (100X0.003	10 X 1.34 x 0.99 +(100X 0.003)	7 X 1.34 x 0.99 + (100X0.003)
18.87 ml/dl	13.56 ml/dl	9.58 ml/dl

**The above examples show that hemoglobin is the main determinant of oxygen content in the blood because as hemoglobin decrease, oxygen content decreases directly.

Blood groups

Blood group	Antigen on RBCs	Antibodies in plasma	Incidence	
			White	African America
A	A	Anti B	40 %	27 %
B	B	Anti A	11 %	20 %
AB	A & B	None	4 %	4 %
O	None	Anti A & Anti B	45 %	49 %
Rh	Rh	-	42 %	17 %

Cross match

Major	Minor	Agglutination	Type-specific
Donor's erythrocytes incubated with recipients serum	Donor's serum incubated with recipients erythrocytes	Occurs if either is incompatible	Only ABO-Rh determined; chance of hemolytic reaction is 1:10,000 with TS blood (Both have same group we only determine ABO-Rh)

Type and Screen

- Donated blood that has been tested for ABO/Rh antigens and screened for common antibodies (not mixed with recipient blood).
- Used when usage of blood is unlikely, but needs to be available (hysterectomy).
- Allows blood to available for other patients.
- Chance of hemolytic reaction: 1:10,000.

Component Therapy

A unit of whole blood is divided into components; Allows prolonged storage and specific treatment of underlying problem with increased efficiency: these components are as follow:

1. **Packed red blood cells (pRBC's)**
2. **Platelet concentrate**
3. **Fresh frozen plasma (contains all clotting factors)**
4. **Cryoprecipitate** (**contains factors VIII and fibrinogen; used in Von Willebrand's disease**)
5. **Albumin**
6. **Plasma protein fraction**
7. **Leukocyte poor blood**
8. **Factor VIII**
9. **Antibody concentrates**

Component	Storage	Indications	Consideration	Notes
Whole blood	**4^0 for up to 35 days**	**1- Massive Blood Loss 2- Trauma 3- Exchange Transfusion**	**- Use filter as platelets and coagulation factors will not be active after 3-5 days - Donor and recipient must be ABO identical**	**-**
Packed RBCs (pRBCs)	**-**	**-**	**- Mixed with saline: LR has Calcium which may cause clotting if mixed with pRBC's. - Do NOT mix with medications**	**- 1 unit = 250 ml - Hct = 70-80%. - 1 unit pRBC's raises Hgb 1 gm/dL.**
Platelet concentrate	**Up to 5 days at 20-24°**	**1- Thrombocytopenia and platelet count is <15,000 2- Bleeding and platelet count is <50,000 3- Invasive procedure and platelet count is <50,000**	**- Contain Leukocytes and cytokines - 1 unit/10 kg of body weight increases PLT count by 50,000 - Donor and Recipient must be ABO identical**	**-**
Fresh frozen plasma: (FFP) Plasma from whole blood frozen within 6 hours of collection.	**for 12 months at (– 25C) or colder**	**1- Reversal of Coumadin effect, TTP, etc. 2- when PT and PTT are >1.5 normal 3- Coagulation Factor deficiency 4- Fibrinogen replacement 5- DIC 6- liver disease 7- Exchange transfusion 8- Massive transfusion**	**- Plasma should be recipient ABO compatible - In children, should also be Rh compatible - Usual dose is 20 cc/kg to raise coagulation factors approx 20%**	**Contains coagulation factors (1 unit/ml)**
Cryoprecipitate		• **Rich in Fibrinogen and Factor VIII and XIII** • **Dose 10-20 ml/kg Or 0.2 X wt. in Kg or one bag per 5 Kg** • **Will increase fibrinogen level by 1 gm/L**		

Blood transfusion complication

- Hemolytic transfusion reaction
  - Acute
  - Delayed
- Disseminated intravascular coagulation
- Physical
  - Circulatory overload
  - Embolism (air, micro aggregate)
  - Hypothermia

- Immunological
- Pyrogenic
- Type 1 Hypersensitivity (Anaphylactic reaction)
- Graft versus host reactions
- Infective
- Biochemical
  - Acid base disturbances
  - Hyperkalemia
  - Citrate toxicity
  - Impaired oxygen release

Transfusion reactions:

Hemolytic Reactions (Acute or delayed):

Wrong blood type administered cause activation of complement system which leads to intravascular hemolysis and spontaneous hemorrhage.

Signs:

- Hypotension, fever, chills, dyspnoea, skin flushing, substernal pain.
- *Signs are easily masked by general anaesthesia.*
- Free Hb in plasma or urine
- Acute renal failure
- Disseminated Intravascular Coagulation (DIC)

What to do to manage acute haemolytic transfusion reaction (AHTR)?

- **STOP TRANSFUSION**
- ABC's
- Maintain IV access and run IVF (NS or LR)
- Monitor and maintain BP/pulse
- Give diuretic
- Obtain blood and urine for transfusion reaction workup
- Send remaining blood back to Blood Bank

What blood bank work-up should be done?

- Check paperwork to assure no errors
- Check plasma for free hemoglobin
- Repeat crossmatch
- Repeat Blood group typing
- Blood culture

What to monitor in AHTR?

- Patient clinical status and vital signs
- Renal status (BUN, creatinine)
- Coagulation status (DIC panel– PT/PTT, fibrinogen, D-dimer/FDP, platelets, Anti-thrombin-III)
- Signs of hemolysis (LDH, bilirubin, haptoglobin)

Other Complications:

- Decreased 2,3-DPG storage *(i.e. shifting the Hb dissociation curve to the left, which decreases O2 release from Hb, inducing tissue hypoxia. However this is theoretical and not significant practically)*
- Citrate: metabolism to bicarbonate; Calcium binding
- Microaggregates (platelets, leukocytes) pass through micropore filters causing small vessels thromboses.
- Hypothermia: warmers used to prevent
- Coagulation disorders: massive transfusion (>10 units) may lead to dilution of platelets and factor V and VIII

Here the concept of 1:1:1 comes, it's recommended when >10 units of pRBCs are needed to be transfused, to add 1 unit of FFP and 1 unit of platelets for each 1 unit of pRBCs. This is done to prevent blood dilution and occurrence of coagulopathy.

- DIC

DIC: uncontrolled activation of coagulation system

- Diagnosis of DIC

- Increased APTT, PT, and fibrin degradation product
- Decreased platelet count and fibrinogen concentration

- Treatment

- 4 units of FFP
- 6-8 units of platelets
- Cryoprecipitate if fibrinogen level less than 1 g/l
- PH less than 7.2 administrate 50 mmol bicarbonate
- Recombinant activated factor VIIa if bleeding continue in spite of use FFP platelets and cryoprecipitate

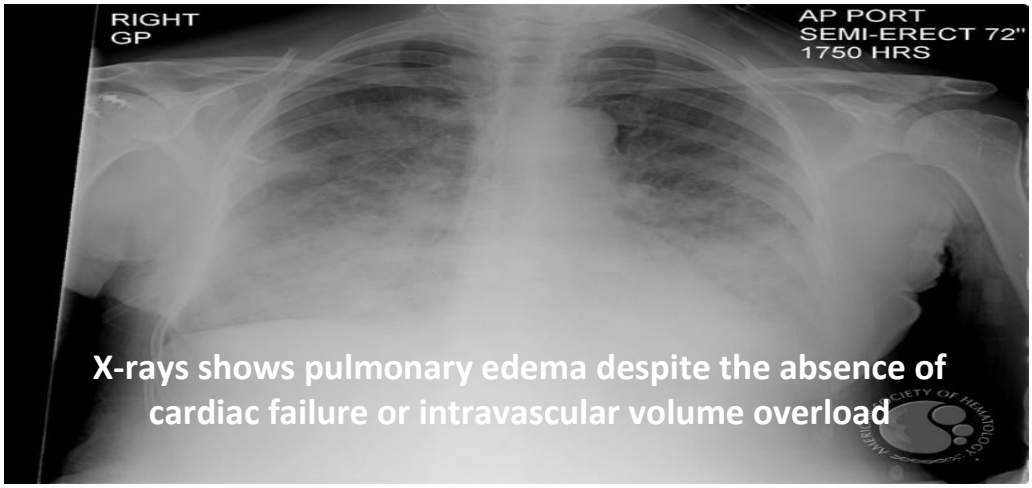
- Transmission of viral diseases

E.g.

- Hepatitis C (1:30,000 per unit)
- Hepatitis B (1:200,000 per unit)
- HIV (1:450,000-1:600,000 per unit), 22 day window for HIV infection and test detection.
- CMV may be the most common agent transmitted, but only affects immunocompromised patients.
- Parasitic and bacterial transmission very low.

➢ TRANSFUSION RELATED ACUTE LUNG INJURY

(Pathophysiology) Transfused leuko-agglutinating antibodies bind to recipients' neutrophils localized to pulmonary endothelium resulting in activation and release of oxidases and other damaging modifiers that cause capillary leak

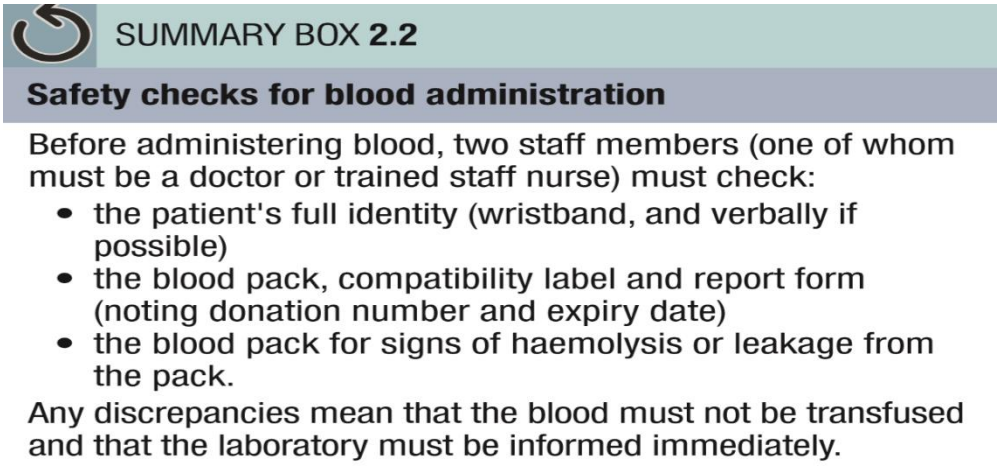


X-rays shows pulmonary edema despite the absence of cardiac failure or intravascular volume overload

Administering blood products

What are the pre-requisites of blood products administration?

- Consent necessary for elective transfusion
- Unit is checked by 2 people for Unit number, patient ID, expiration date, physical appearance.
- pRBCs are mixed with saline solution (not LR)
- Products are warmed mechanically and given slowly if condition permits
- Close observation of patient for signs of complications
- If complications suspected, infusion discontinued, blood bank notified, proper steps taken.


SUMMARY BOX **2.2**

Safety checks for blood administration

Before administering blood, two staff members (one of whom must be a doctor or trained staff nurse) must check:

- the patient's full identity (wristband, and verbally if possible)
- the blood pack, compatibility label and report form (noting donation number and expiry date)
- the blood pack for signs of haemolysis or leakage from the pack.

Any discrepancies mean that the blood must not be transfused and that the laboratory must be informed immediately.

What is the estimated blood volume for each age/sex?

Neonate	2 years old infant	Adult male	Adult female
90 ml/kg	80 ml/kg	70 ml/kg	60 ml/kg

Massive blood transfusion

- ❖ It is the replacement of patients' blood volume by stored bank blood in less than 24 hours (in another word, >10 pRBCs units/24 hours)

- ❖ **Basic screening test after six-unit transfusion:**

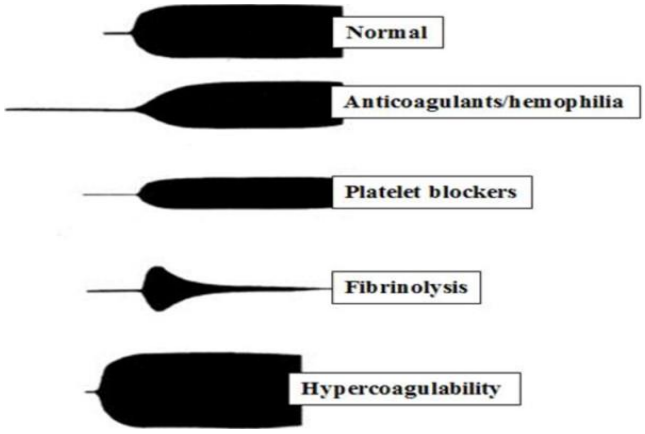
- Hemoglobin and platelets count
- Coagulation profile (PT & APTT)
- Plasma fibrinogen concentration
- Fibrin degradation products
- PH from arterial blood gas analysis
- Plasma Electrolyte

- ❖ **Complications of massive transfusion**

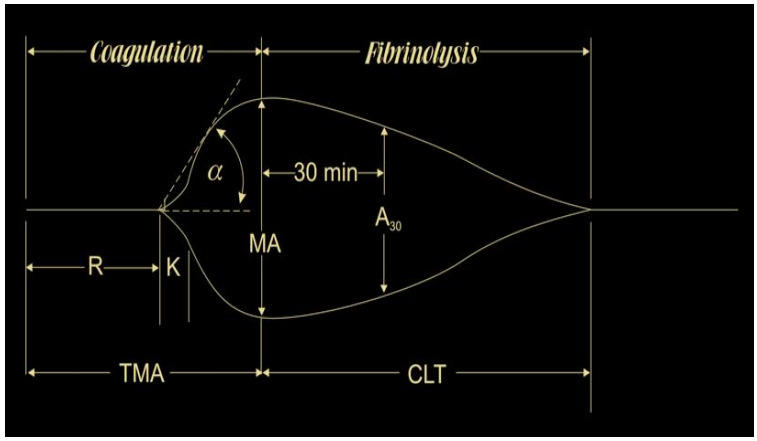
Coagulopathy	- Due to dilutional thrombocytopenia and dilution of the coagulation factors
Citrate toxicity	- Does not occur in most normal patients unless the transfusion rate exceeds 1 U every 5 min
Hypothermia	-
Acid-base changes	- The most consistent acid–base abnormality after massive blood transfusion is postoperative metabolic alkalosis
Serum K changes	- The extracellular concentration of potassium in stored blood steadily increases with time. - The amount of extra-cellular potassium transfused with each unit less than 4 mEq per unit. - Hyperkalemia can develop regardless of the age of the blood when transfusion rates exceed 100 mL/min.

Thromboelastography

- Hemorrhage is responsible for 30% to 40% of trauma mortality
- On admission, 25% to 35% of trauma patients present with coagulopathy, which is associated with a sevenfold increase in morbidity and mortality.
- *The literature supports that routine plasma based routine coagulation tests, such as prothrombin time, activated partial thromboplastin time, and international normalized ratio, are inadequate for monitoring coagulopathy and guided transfusion therapy in trauma patients.*
- TEG assesses both thrombosis and fibrinolysis
- Conventional tests are performed in plasma without platelets and tissue bearing cells (the cellular component) while TEG requires whole blood.
- It measures viscoelastic changes of entire clotting process, its formation, first fibrin strands. It evaluates clot formation strength and platelet function until clot lysis (A complete analysis of clot formation/lysis)
- *There is growing interest in its clinical use in trauma resuscitation, particularly for managing acute coagulopathy of trauma and assisting decision making concerning transfusion.*



How TEG appears in different situation



Full analysis of clotting/lysing cascade

Alternatives to Blood Products

<table>
<tr><td rowspan="3">Auto-transfusion</td><td>Pre-donation or pre-deposit</td><td>- Pre-donation of patient’s own blood prior to elective surgery.
- 1 unit donated every 4 days (up to 3 units).
- Last unit donated at least 72 hrs prior to surgery.
- Reduces chance of hemolytic reactions and transmission of blood-borne diseases.
- Not desirable for compromised patients.</td></tr>
<tr><td>Intra-operative acute normovolemic hemodilution</td><td>- 1-1.5L can be collected with volume replacement.
- Blood stored in OR Re-infused during or after surgery
- Cheaper than pre-deposit.
- Little risk of clerical error.
- Suitable for elective surgery.</td></tr>
<tr><td>Intra-operative cell salvage</td><td>- Commonly known as “Cell-saver”
- Allows collection of blood during surgery for re-administration.
- Shed blood is collected from surgical field
-Heparin added.
- RBCs washed with saline and concentrated by centrifugation.
- Effective when > 1000ml are collected.
- Large volume could be used.
- Platelets and clotting factors are consumed.
- Suitable for cardiac surgery.
- Contraindicated in contaminated surgical field.</td></tr>
<tr><td rowspan="3">Blood Substitutes</td><td colspan="2">- Experimental oxygen-carrying solutions, developed to decrease dependence on human blood products.
- Military battlefield usage is the initial goal
- Multiple approaches:
1/Outdated human Hb reconstituted in solution
2/Genetically engineered/bovine Hb in solution
3/Liposome-encapsulated Hb
4/Perfluorocarbons</td></tr>
<tr><td>Advantages</td><td>Disadvantages</td></tr>
<tr><td>- No cross-match requirements
- Long-term shelf storage
- No blood-borne transmission
- Rapid restoration of oxygen delivery in traumatized patients
- Easy access to product (available on ambulances, field hospitals, hospital ships)</td><td>- Undesirable hemodynamic effects:
e.g. Mean arterial pressure and pulmonary artery pressure increases
- Short half-life in bloodstream (24 hrs)
- Still in clinical trials, unproven efficacy
- High cost</td></tr>
</table>

Additional tables from Davidson

Table 2.3 Acute transfusion reactions

	Cause	Implicated components	Clinical features
Immunological			
Acute haemolytic transfusion reaction	ABO-incompatible transfusion resulting in acute intravascular haemolysis	RCC Platelets FFP Cryo	Develops within minutes. Chills, fevers, rigors, chest tightness, infusion site pain, hypotension, shock, DIC and acute renal failure. May be fatal.
Transfusion-associated acute lung injury	HLA or neutrophil Abs in donor plasma react with recipient leucocytes	Any plasma-containing component (RCC, FFP, cryo, platelets)	Develops within 4 hours of transfusion. Dyspnoea, cough, fever, hypoxia, pulmonary infiltrates (ARDS). With supportive care, improvement over 2–4 days in 80% of patients.
Febrile non-haemolytic transfusion reaction	Neutrophil Ab in recipient plasma reacts with donor leucocytes	RCC Platelets FFP Cryo	Develops late in course of transfusion. Usually mild. Full recovery expected.
Allergic reactions	Reaction to plasma proteins	Any plasma-containing component	Urticaria/itch within minutes of start of transfusion. Occasionally severe with anaphylaxis. Usually full recovery with appropriate management.
Non-Immunological			
Bacterial contamination	Contamination during collection or storage. Rarely, bacteraemic donor	Platelets most commonly RCC	Symptoms/signs of sepsis develop early in course of transfusion. May be fatal.
Transfusion–associated circulatory overload	Over-transfusion	Any	Symptoms/signs of acute left ventricular failure. Resolves with appropriate management.

(Ab = antibody; Ag = antigen; ARDS = acute respiratory distress syndrome; Cryo = cryoprecipitate; DIC = disseminated intravascular coagulation; FFP = fresh frozen plasma; HLA = human leucocyte antigen; RCC = red cell concentrate)

Table 2.4 Delayed transfusion reactions

	Cause	Implicated components	Clinical features
Immunological			
Delayed haemolytic transfusion reaction	Patient has red cell Ab at undetectable level. Re-exposure to Ag results in secondary immune response and extravascular haemolysis	Red cells Platelets	May be asymptomatic or develop jaundice, fever and haemoglobinuria with a fall in haemoglobin. Seldom fatal but can result in significant morbidity if the patient is already unwell
Alloimmunization	Recipient forms Ab in response to donor Ag	Red cells	Usually not detected until subsequently grouped and saved or cross-matched
Post-transfusion purpura	Recipient has a platelet-specific Ab and develops secondary immune response on re-exposure, resulting in destruction of donor platelets and, through an unknown mechanism, recipient platelets	Platelets Red cells	Sudden development of severe thrombocytopenia associated with bleeding 5–12 days following transfusion. Complications are related to bleeding. Platelet count usually recovers with appropriate management, which includes i.v. immunoglobulin
Transfusion-associated graft-versus-host disease	Viable T lymphocytes transfused into immunocompromised recipient	Any cellular product	Fever, desquamating rash, abnormal LFTs and pancytopenia develop 1–4 weeks following transfusion. Mortality rate > 90%. Prevent by irradiation of cellular components in patients at high risk
Non-Immunological			
Transfusion-transmitted infection: Risks shown in Table 2.5 **Iron overload**: Chronic red cell transfusion leads to accumulation of iron in tissues, e.g. liver, heart, pancreas			

(Ag = antigen; Ab = antibody)

Table 2.6 **Complications of massive transfusion**

Complication	Mechanism	Management
Thrombocytopenia	Consumption/DIC Dilutional after 1.5–2.0 blood volumes replaced	In patients with acute bleeding, transfuse platelets to maintain count > 50×10^9/l (> 100×10^9/l if acute trauma or CNS injury)
Coagulopathy	Consumption/DIC Dilutional after 1.0 blood volume replaced	If continued blood loss and PT or APTT ratio > 1.5 × control levels, give FFP 10–15 ml/kg. If fibrinogen < 1.0 g/l, cryoprecipitate is also indicated
Hypocalcaemia	Citrate anticoagulant binds to ionized Ca, lowering plasma levels (only problematic in neonates and liver disease)	If ECG shows signs of hypocalcaemia, give 5 ml Ca gluconate (or equivalent paediatric dose) over 5 mins. Repeat if ECG remains abnormal
Hyper- or hypokalaemia	Red cell degeneration during storage increases plasma K^+. Following transfusion, red cells rapidly normalize Na/K equilibrium, which may lead to ↑ K^+	Careful monitoring of K^+ levels in massive transfusion
Hypothermia	Transfusion of blood at 4°C lowers core temperature	Prevent by use of blood warmer when transfusion rate > 50 ml/kg/h in adults (15 ml/kg/h in children)
ARDS	Multifactorial	Minimize risk by maintaining tissue perfusion, correct hypotension and avoid over-transfusion

(APTT = activated partial thromboplastin time; ARDS = acute respiratory distress syndrome; DIC = disseminated intravascular coagulation; FFP = fresh frozen plasma; PT = prothrombin time)