

Whole blood - the current update

Since late 1960s component therapy has increasingly been used in the developed world, rapidly replacing the whole blood usage. However, in developing countries like India, whole blood is still used in many centres, mostly due to the lack of availability of blood components. Barring few studies (primarily in combat settings) done on small number of patients, there are still no randomized clinical trials or studies on large patient groups to validate the usefulness and safety of whole blood use. Hence, blood component therapy with a proven track record in terms of safety, efficacy, efficiency and usefulness is still the benchmark and whole blood use has to be discouraged in routine clinical practice.

b. Packed Red Blood Cells

Annually more than 80 million units of red cells are transfused globally and a wide variation in transfusion threshold and practices is seen for this particular blood component.

<i>Approximate Volume:</i>	Minimum 250 ml \pm 10% from 450 ml bag Minimum 150 ml \pm 10% from 350 ml bag. (This volume is exclusive of any additive solution added to the PRBC)
<i>Hematocrit:</i>	65-70% when stored in CPDA1 solution 50-60% when stored in additive (SAGM/Adsol/etc) solution
<i>Storage Conditions:</i>	2-6°C in a monitored blood refrigerator
<i>Special Treatment:</i>	Leukocyte depletion: Leucocytes in the final PRBC should be less than 5×10^8 when intended to prevent febrile reactions and less than 5×10^6 when required to prevent alloimmunization or cytomegalovirus infection. For achieving a level of less than 5×10^6 , use of leucocyte filters is usually necessary. Saline washing: Red cells are washed with sterile Normal Saline by centrifugation at 2 to 8 degrees centigrade to remove residual plasma and other additives/ preservatives suspected of causing allergic/ anaphylactic reaction in select patients. Irradiation: Done using gamma rays or x-ray irradiation at 25 Gray to prevent graft versus host disease due to proliferation of lymphocytes Freezing: Cryoprotective substance is added to the PRBCs for extended storage between minus 80 to minus 196 degrees centigrade.
<i>Crossmatch:</i>	Required.

Transfusion triggers for Therapeutic platelet transfusion (BJH guidelines 2017)²⁴

Clinical condition	Platelet transfusion trigger for therapeutic transfusion.
Severe bleeding (Massive transfusion)	50,000/ μ l
Multiple trauma, traumatic brain injury or spontaneous intracerebral haemorrhage	1 lac/ μ l
Non severe bleeding	30,000/ μ l
DIC in presence of bleeding	30,000/ μ l

Use in cardiopulmonary bypass surgery:

Platelet function defects and thrombocytopenia often occur after cardiac bypass surgery.

Platelet transfusion is recommended for patients with bleeding not due to surgically correctable causes (closure time done by Platelet Function Analyzer – PFA-100/Innovance PFA-200/ Sonoclot-provides global indication of platelet function). Prophylactic platelet transfusions are not required for all bypass procedures.

e. Cryoprecipitate

Cryoprecipitate is a blood component which is derived from FFP. It has relatively higher concentration per milliliter for fibrinogen, factor VIII, Von Willebrand factor (vWF), factor XIII and fibronectin

<i>Approximate Volume:</i>	10 – 20 ml
<i>Storage Conditions:</i>	Below minus 30°C in a blood centre freezer. It should be immediately transfused after thawing however, it can be stored at 2 - 6°C for a maximum duration of 6 hours post thawing, if not immediately transfused.
<i>Special Treatment:</i>	nil

All the blood components can be volume reduced to suit the patient requirement. If done in a sterile manner (e.g. using sterile connecting device), there is no change in the original expiry and remaining aliquots can be used till the expiry of the original blood component. This is particularly useful in decreasing donor exposure in neonates and infants.

c. **Fresh Frozen plasma (FFP)**

FFP is conventionally transfused to patient with active bleeding or prophylactically to patients with modest to severe abnormality in the various coagulations tests like Prothrombin time, International normalized ratio (INR) and activated partial thromboplastin time (aPTT).

Indications of FFP transfusion (British Journal of Haematology guidelines 2018)²²

1. **Therapeutic Indications with Active bleeding :**

- Patient with massive bleed like trauma or obstetric cases may develop multiple coagulation factor deficiency require FFP transfusion along with other blood components for maintaining the hemostatic and hemodynamic stability. details regarding massive transfusion are covered in chapter on massive transfusion
- Disseminated Intravascular Coagulation or consumptive coagulopathy with active bleeding.
- Immediate correction of Vitamin K deficiency and warfarin reversal
- Thrombotic thrombocytopenic Purpura
- Patient with congenital factor deficiency like factor V deficiency when no alternative therapies are available

2. **Prophylactic Indications abnormal coagulation tests (INR >1.5) in the absence of bleeding:**

- FFP transfusion before an invasive procedure : Abnormal coagulation test are poor predictors of bleeding risks in non-bleeding patients prior to an invasive procedure (2C). Various studies have shown that mild to moderate abnormalities in the coagulations tests is not associated with bleeding and prophylactic plasma transfusion in these patients does not affect bleeding outcomes (AABB). BCSH recommends that coagulations tests should be considered in patients undergoing procedures with a moderate or high bleeding risk, any patient on anticoagulant , or those who have a personal/family bleeding history (1B).
- Patients on anticoagulants like warfarin to correct the INR prior to an invasive procedure.

3. **Other Indications:**

- As replacement fluid during therapeutic plasma exchange procedures for TTP and HUS
- In patients with liver disease, abnormal coagulation tests should be interpreted with caution as some of the patient may have prothrombotic tendency with elevated prothrombin time. Fresh frozen plasma transfusion is recommended only if active bleeding is present or prophylactically for high bleeding risk invasive procedures.

- Since sickle red cells are poorly deformable, simple red cell transfusions that increase the Hb levels to >10-11 g/dl may cause hyperviscosity in patients not receiving chronic transfusions and should be avoided.
- Partial exchange transfusion, generally by erythrocytapheresis (using apheresis technology), may be needed for severe life-threatening illness or in situations where a relatively high baseline Hb precludes a simple transfusion that would lead to the risk of hyperviscosity.
- Partial exchange transfusion or erythrocytapheresis to achieve Hb 10 g/dl and keep Hb Sickle (patient's RBC) <30%. Remove femoral or central venous catheter as soon as possible after exchange transfusion to reduce risk of thrombosis.
- Simple transfusion with PRBCs to achieve post-transfusion Hb approximately 10 g/dl may be considered as an alternative to partial exchange transfusion for stable patients with Hb 6-7 g/dl (do not transfuse acutely to Hb >10 g/dl, Hct >30%)

NICE guidelines published in 2015 recommend that individual thresholds and Hb targets should be set for each patient who needs regular blood transfusions for chronic anemia as seen in Hemoglobinopathies¹².

Modification of PRBC – leukodepletion, irradiation, volume reduction.

Leukodepletion, irradiation and volume reduction are one of the most common blood unit manipulations done in a blood centre to enhance blood safety for select category of patients.

Leukocyte depletion or leukodepletion (LD) is the process of removing leukocytes (mostly before storage of blood) from whole blood or platelets to prevent:

- Transfusion transmitted cytomegalovirus transmission
- HLA immunization
- Febrile non-hemolytic transfusion reactions
- Platelet refractoriness (failure to increase platelet count in a patient after repeated platelet transfusions)

Blood centre supplying the blood units can be asked about the availability of LD blood units.

Irradiation is done on the cellular blood components like RBC, platelets and granulocytes to prevent a fatal blood transfusion reaction called TA-GVHD (transfusion associated graft versus host disease) in at risk patients. When the blood donor/ unit is a blood relative of the transfusion recipient or the product is HLA matched, the recipient is at high risk for TA-GVHD. Acellular blood components like plasma and cryoprecipitate do not require irradiation treatment.

Volume reduction is preparing smaller aliquots for blood transfusion. This is most commonly done for the neonates and infants and may be required in the patients at risk of transfusion associated circulatory overload.

- Platelet function defects.
- Prevention of bleeding due to thrombocytopenia as in bone marrow failure.

- **Contraindications:**

- **Absolute :** Thrombotic thrombocytopenic purpura (TTP). British Journal of Haematology recommends platelet transfusion in cases of TTP only during life threatening bleeds.
- **Relative :**
 - Idiopathic autoimmune thrombocytopenic purpura (ITP).
 - Untreated DIC.
 - Thrombocytopenia associated with septicaemia, or in cases of hypersplenism.

Transfusion triggers (Platelet count below which platelet transfusion is indicated) for prophylactic platelet transfusion (BJH guidelines 2017)²⁴

Clinical condition	Platelet transfusion triggers for prophylactic transfusion
Reversible bone marrow failure where recovery is anticipated	<ul style="list-style-type: none"> • 10,000/μl in non-bleeding, non-infected patient • Threshold for patient with increased risk of bleeding can be increased to 10-20,000/μl
Chronic bone marrow failure where recovery is not anticipated	<ul style="list-style-type: none"> • No prophylactic platelet is recommended • Manage patient according to severity of their sign and symptoms.
Critical illness with no bleeding	10,000/ μ l in non-bleeding, non-infected patient
venous central lines	10,000/ μ l
Lumbar Puncture	40,000/ μ l
Insertion removal of epidural catheter	40,000/ μ l
Major surgery	40,000/ μ l
Neurosurgery/ophthalmic surgeries	1 lac/ μ l
Percutaneous liver biopsy	50,000/ μ l
Renal Biopsy	<ul style="list-style-type: none"> • Avoid platelet transfusion because infused platelet will acquire a dysfunction similar to patient own platelets • consider desmopressin
Bone marrow aspirate, trephine biopsy, peripheral catheter insertion and cataract surgery	No prophylactic platelet required

Compatible alternate blood groups

See table in below.

Indications and dosage^{11,12}: [References: Clinical Practice Guidelines From the AABB (2016) & National institute for health and care excellence (NICE 2015) guidelines on blood transfusion]

- PRBC transfusion is not indicated until the Hb level is **7 g/dL (restrictive transfusion threshold)** and is recommended for hospitalized adult patients who are **hemodynamically stable, including critically ill patients** (strong recommendation, moderate quality evidence).
- A restrictive RBC transfusion threshold of **8 g/dL** is recommended for patients undergoing orthopedic surgery, cardiac surgery and those **with preexisting cardiovascular disease** (strong recommendation, moderate quality evidence).
- Above recommendations do not apply to the patients with acute coronary syndrome, severe thrombocytopenia and chronic transfusion-dependent anemia.**
- Patients, including neonates, should receive PRBC units, irrespective of duration of storage in blood centre, rather than limiting patients to transfusion of only fresh PRBC units (strong recommendation, moderate quality evidence).
- Adults without any active bleeding should be transfused single-unit red blood cell transfusions (or equivalent volumes calculated on the body weight basis for children or low body weight adults). In these patients, clinical reassessment and Hb levels should be done before further transfusions are given.

Compatible blood groups for PRBC transfusion

The below grid is for the **PACKED RED BLOOD CELLS transfusion ONLY** as there is no alternate choice of blood groups for the whole blood transfusion.

Patient's Blood Group	1 st choice for PRBC	2 nd choice for PRBC	3 rd choice for PRBC	4 th choice for PRBC
"A pos"	"A pos/ neg"	"O pos/ neg"		
"B pos"	"B pos/ neg"			
"O pos"	"O pos/ neg"			
"AB pos"	"AB pos/ neg"	"B pos/ neg"	"A pos/ neg"	"O pos/ neg"
"A neg"*	"A neg"	"O neg"		
"B neg" *	"B neg"			
"O neg" *	"O neg"			
"AB neg" *	"AB neg"	"B neg"	"A neg"	"O neg"

[pos = Rh(D) positive; neg = Rh(D) negative]

* Rh positive Packed RBCs can be transfused to Rh negative patients (post menopausal females, elderly men) when antibody screen is negative and only as a life saving measure. Informed consent from the patients/ relatives should be taken by the treating doctor/ transfusion medicine physician.

- Improved appetite.
- Suppressed over active erythropoiesis leading to bone deformities.

Red cell transfusions should be given at an interval of 2-5 weeks. This interval is optimized based on:

- The amount of red cells transfused so that pre-transfusion Hb remains >9 g/dl but post-transfusion Hb does not go above 12 g/dl
- There is no fluid overload.
- Transfusion process is over within a reasonable time (within 4 hours).
- Frequency of transfusions is not such that it interferes with patient's normal activities.
- Reducing the number of venipuncture (as lifelong transfusion is needed, peripheral veins need to be preserved well).

Suitable blood components for transfusion:

- Red cell concentrates (hematocrit around 0.65) is suitable
- Leucodepleted (prestorage) blood is desirable.

Amount of PRBC to be transfused:

- Pretransfusion Hb is to be estimated along with the weight of the patient and recorded.
- If the hematocrit of the red cell concentrate used is 0.65, then 3-4 ml/kg will raise the Hb by 1 g/dl in the absence of hypersplenism.
- Generally in a single transfusion an attempt is made to raise the Hb by 4 g/dl if transfusions are scheduled at 3- to 5 weekly intervals.
- Below mentioned grid can be used to guide the volume of transfusion based on the desired Hb increase in the patient and the hematocrit of the blood bag²¹:

Target increase in Hb level	Hematocrit of the blood bag			
	50%	60%	75%	80%
1 g/dl	4.2 ml/kg	3.5 ml/kg	2.8 ml/kg	2.6 ml/kg
2 g/dl	8.4 ml/kg	7.0 ml/kg	5.6 ml/kg	5.2 ml/kg
3 g/dl	12.6 ml/kg	10.5 ml/kg	8.4 ml/kg	7.8 ml/kg
4 g/dl	16.8 ml/kg	14.0 ml/kg	11.2 ml/kg	10.4 ml/kg

Pre-transfusion testing should be done before starting chronic transfusion therapy as follows:

- Irregular antibody screening at regular intervals in necessary and should be done during pre-transfusion testing. Once an alloantibody is detected, it should be identified and antibody negative blood should be crossmatched.

- Transfuse if symptomatic anemia, e.g. chest pain, tachycardia unresponsive to fluid resuscitation, orthostatic hypotension or congestive heart failure is present.
- The same thresholds can be safely applied to the patients with stable cardiovascular disease.
- Patients who are not actively bleeding should be transfused with a single unit of red cells and then reassessed before further blood is given.

It is commonly believed, that the surgeons and orthopedics prefer liberal blood transfusion strategy over a restricted one. However, there is now ample evidence that adhering to restrictive transfusion strategies and lower Hb thresholds (7-8 g/dl) is safe, effective as well as cheaper.

4. Rationale PRBC use in Cardiac surgery

Cardiac surgeries have traditionally been considered as big consumers of blood and blood components with incidence of peri-operative blood transfusion ranging from 40-90%¹⁵. However, with increased awareness of adverse outcomes associated with BT and additional cost, it is now realized that transfusions should be done optimally. Indian professional bodies like ICCA and IACTA have not yet officially endorsed (till Jan 2020) any guidelines for blood use in cardiac surgery in India.

Pre-operative transfusion (EACTS & EACTA 2017 guidelines) -Preoperative erythrocyte transfusion is not routinely recommended in preoperative anemic patients to prevent postoperative AKI¹⁶. However, in the case of emergency surgery and life-threatening anemia, it is legitimate to use preoperative blood transfusions to increase the Hb levels.

Oral or intravenous iron alone may be considered in mildly anemic patients (women, Hb 10-12 g/dl; men, Hb 10-13 g/dl) or in severely anemic patients (both genders, Hb \leq 10 g/dl) to improve erythropoiesis prior to cardiac surgery. Erythropoietin with iron supplementation should be considered to reduce postoperative transfusions in patients with noniron deficiency (e.g. EPO, vitamin D or folate acid deficiency) anemia, undergoing elective surgery.

Pre-operative autologous blood donation - In patients posted for elective surgery with Hb > 11 gm/dl and without severe aortic stenosis or an acute coronary syndrome within 4 weeks, PABD may decrease the number of postoperative BT. Acute normovolemic hemodilution (ANH) has not shown much advantage in cardiac surgery patients.

Quality of blood - The use of PRBCs of all ages is recommended, because the storage time of the PRBCs does not affect the outcomes (Class I, level A evidence). The use of leucocyte-depleted PRBCs is recommended to reduce infectious complications (Class I, level B evidence).

Hemoglobin trigger – The Society of Thoracic Surgeons and Society of Cardiovascular Anesthesiologists 2011 guidelines recommended RBC transfusion for Hb <6 g/dL during cardiopulmonary bypass and <7 g/dL post-operatively, except in patients at risk for decreased cerebral oxygen delivery, for whom a higher Hb level was recommended¹⁷. However, 2017 EACTS & EACTA guidelines recommend that instead of a fixed Hb threshold, BT should be based on the clinical condition of the patient (Class I, level B evidence). A restrictive Hb of 7-8 gm/dl (Hct 21-24%) with patient maintaining adequate DO_2 (> 273 ml O_2 /min/ m^2) level can be considered during cardiopulmonary bypass (Class IIb, level B evidence). Most cardiac anesthesiologists now agree that it is reasonable to transfuse blood with Hb <7 g/dl and transfusion is unnecessary when Hb is >10 g/dl¹⁸. The individualized approach used in between these two triggers (Hb between 7-10 g/dl) should be based on a restrictive strategy, with a focus on the improved clinical outcome along with the additional cost and risk of a BT.

5. Rationale PRBC use in neonates and pediatric patients [Source: Technical Manual. 19th ed. Bethesda, Maryland: AABB; 2017. p. 505 – 26]¹⁹

Age appropriate hemoglobin levels, the ability to tolerate blood volume loss and total blood volume differs in pediatric patients as compared to adults. Following are the indications of RBC transfusion in pediatric patients:

Infants less than 4 months of age:

Category	Recommendation for RBC transfusion @10-15ml/ kg
Symptomatic anemia (tachycardia, tachypnea, poor feeding)	Maintain Hb above 7 gm/dl
On oxygen (cannula/ hood) or mechanical ventilation, significant tachycardia (>180 beats/ min) or tachypnea (>80 breaths/ min) or apnea or bradycardia	Keep Hb > 10 gm/dl
On >35% oxygen by hood or on CPAP/ IMV* with mean airway pressure \geq 6-8cm of water	Keep Hb > 12gm/ dl
Congenital cyanotic heart disease or on ECMO	Keep Hb > 15 gm/ dl

* CPAP continuous positive airway pressure IMV intermittent mandatory ventilation

- Extended phenotyping of patient's red cells is desirable. If possible, an extended phenotype of the patient should be done and record kept for any future need.
- If the family is interested in stem cell transplantation, then counseling and early referral to such a centre should be done.
- Serum ferritin level is not needed if the child is <2 years
- Serum ferritin levels should be recorded at regular intervals (3 months) after first 10 units of red cells have been transfused and iron chelation should be started and the dose should be adjusted so as to maintain serum ferritin between 500 and 1000 ng/ml.
- Before starting chronic red cell transfusions, hepatitis B vaccination should be completed.
- Every 3 months, virus serology should be done to detect viral infection at the earliest.
- Patient should receive NAT tested blood components as far as possible.
- Detailed record of red cell transfusions, complication, management, etc should be kept.
- Close relative's blood should not be transfused.

Blood transfusion in Sickle cell disease

- PRBC transfusions play an important role in the treatment of some acute illnesses in patients with sickle cell disease. Timely BT may be lifesaving in severe complications.
- PRBC should be transfused if the Hb is $\geq 1-2$ g/dl, below baseline and the patient shows any signs of cardiovascular compromise.
- Indications for red cell transfusions include acute exacerbation of the patient's baseline anemia (e.g. hyperhemolysis, hepatic sequestration, splenic sequestration, aplastic crisis) that requires increased oxygen carrying capacity, acute life or organ-threatening vaso-occlusive episodes (e.g. stroke, acute chest syndrome, severe infection, multiorgan failure, etc.) and preparation for surgical or radiographic procedures.
- Leukocyte-depleted, packed RBCs are recommended and where available Rh, Kell antigen matched, sickle-negative cells are preferred.
- Slow correction of the anemia, for example, 4-5 ml/kg PRBC over 4 h often with furosemide or isovolemic partial exchange transfusion may be needed to prevent precipitation of heart failure.
- Simple transfusion with 10 ml/kg of PRBC typically raises the Hb by about 2 g/dl.
- PRBC transfusion in a dose of 10 ml/kg for Hb <4-5 g/dl and signs of cardio vascular compromise should be done. Transfusion may be needed for Hb <7-8 g/dl for patients with relatively high baseline Hb Sickle levels. In severe cases, urgent initiation of transfusion prior to inpatient admission may be life-saving. A post-transfusion Hb level <8-9 g/dl is generally recommended to avoid the risk of hyperviscosity that may occur several days later when RBCs sequestered in the spleen may return to the circulation and increase the Hb 1-2 g/dl above the post-transfusion levels.

a. Whole blood

<i>Approximate Volume:</i>	365 to 560 ml (including the anticoagulant-preservative and acceptable variation of $\pm 10\%$ during collection of 350 – 450 ml whole blood from the donors)
<i>Hematocrit:</i>	30 – 40%
<i>Storage Conditions:</i>	2-6°C in a monitored blood refrigerator
<i>Special Treatment:</i>	Leukocyte reduction, washing, irradiation,
<i>Crossmatch:</i>	REQUIRED.
<i>Compatible alternate blood groups</i>	NIL. Only patient's blood group can be used for whole blood. O negative whole blood CANNOT be used as a universal donor.
Indications: <ol style="list-style-type: none"> Exchange transfusion in neonates. When packed red blood cells are not available, whole blood can be used in acute bleeding conditions when there is also a need to correct hypovolemia, e.g. battle field injuries, road traffic injuries, etc. 	

Rationality of use



Rationale blood transfusion not only decreases the cost, it also affects the patient outcomes!

The appropriate use of blood and blood products means the transfusion of safe blood products, only to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means¹⁰. With red cell concentrate replacing the whole blood in most of the situations, there are very few clinical and practice circumstances where whole blood use can be justified as mentioned in the table above. Platelet function is rapidly lost during the whole blood storage and there is no useful platelet function left after 24 hours of cold storage. Routine use of whole blood should thus be discouraged, as better and more specific therapy in the form of component transfusion is available.

4. BLOOD COMPONENTS AND THEIR INDICATIONS

<p>Appropriate and rational blood use</p> <ul style="list-style-type: none"> - World Health Organization (WHO) 	<p>The appropriate use of blood and blood products means the transfusion of safe blood products only to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means.</p> <p>Rational use of blood and blood products is to reduce unnecessary transfusions and minimize the risks associated with transfusion, the use of alternatives to transfusion where possible, and safe and good clinical transfusion practices, including patient blood management.</p>
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Various blood components – contents, storage and indication^{7,10}

A blood component is a constituent of blood which is separated from whole blood for e.g. red cell concentrate, platelet concentrate, fresh frozen plasma, etc. Table given below gives a snapshot of most commonly used blood components:

Name of the component	Approximate volume (ml)	Shelf life	Storage temperature
PRBC	150 - 250 ($\pm 10\%$)	35 - 42 days	2 - 6°C
FFP	180 - 300	1 year	Below minus 30°C
RDP	50 - 70	5 days	20 - 24°C
SDP (single donor platelet)	200	5 days	20 - 24°C
Cryoprecipitate	10 - 20	1 year	Below minus 30°C
Whole Blood	365 to 560	21 - 35 days	2 - 6°C

- Cardiopulmonary bypass surgery – use in the presence of bleeding but where abnormal coagulation is not due to heparin. Routine perioperative use is not indicated
- Severe sepsis, particularly in neonates (independent of DIC).

Dosage of FFP²²

1. FFP are transfused using weight based dosing of 10-15 ml/kg of recipient weight.
2. During massive transfusion, FFP transfusion may be given in a fixed ratio with red cell transfusion as per the massive transfusion protocol
3. As per BCSH, Patients with high bleeding risk during a procedure, starting dose of 15ml/kg body weight can be considered, although this is not evidence based.

Inappropriate use of FFP²³

Plasma products are associated with the highest rate of inappropriate utilization (upto 50%) with evidence of inappropriate practice based on local audits. The main reason for this inappropriate use of FFP is non availability of national/local guidelines in various countries like India. Even in countries with national guidelines, the compliance is really poor as per the published studies or audits.

FFP transfusion is not indicated in the following conditions:

1. Use of FFP for volume replacement in patients who are not bleeding.
2. Use of FFP for nutritional purposes like hypoproteinemia.
3. Lack of evidence based local guidelines for FFP transfusion
4. Prophylactic FFP transfusion for invasive procedures with normal or mildly (INR <1.5) deranged coagulation tests.
5. FFP transfusion in patient with bleed with normal coagulation tests.

d. Platelet components

Platelet components are required for patients with bleeding due to thrombocytopenia. However, they are also given prophylactically in conditions with low platelet count with the potential to cause bleeding.

- **Dosage:**

1 unit of platelet concentrate/10 kg; for an adult of 60-70 kg, 4-6 single donor units containing at least 240×10^9 platelets should raise the platelet count by $20-40 \times 10^9/L$.

Increment will be less if there is splenomegaly, disseminated intravascular coagulation (DIC) or septicaemia.

- **Indications:**

Treatment of bleeding due to:

- Thrombocytopenia.

- The use of rFVIIa may be considered as a treatment for life-threatening postpartum hemorrhage (PPH), but should not delay or be considered a substitute for a life-saving procedure such as embolisation or surgery, or transfer to a referral centre.
- During major obstetric hemorrhage or with clinically diagnosed PPH, in addition to the standard care, early (within 3 hours of birth) use of intravenous Tranexamic acid is recommended (WHO 2017).

2. Rationale PRBC use in intensive care units[source: Red Blood Cell Transfusion: 2016 clinical practice guideline from AABB. Transfusion. 2016 Oct;56(10):2627-2630¹¹]

Sr. No	Clinical condition	Transfusion trigger	Strength of recommendation	Quality of evidence
1	Hemodynamically stable adult or pediatric patient	Hb \leq 7gm/ dl	Strong	High
2	Post-operative surgical patients	Hb \leq 8 gm/ dl Or symptoms like chest pain, orthostatic hypotension, tachycardia	Strong	High
3	Hemodynamically stable patients with pre-existing cardiovascular disease	unresponsive to fluid resuscitation or congestive heart failure	Weak	Moderate
4	Hemodynamically stable patients with acute coronary syndrome	No recommendation for or against a liberal or restrictive RBC transfusion threshold	Uncertain	Very low

3. Rationale PRBC use in Surgery & orthopedics

Effective and rationale BT involves pre-operative optimization of the patient, minimizing blood loss during surgery and avoiding unnecessary transfusions after the surgery. Clinical practice guidelines by AABB are relevant for BT in surgical and orthopedic patients (refer to the Rationale use in intensive care units section above). Additionally, the outcomes from the landmark FOCUS trial¹⁴ which included only the hip fracture patients with co-existing cardiovascular (CVS) disease or CVS disease risk factors, groups previously thought to require aggressive anemia management, made it amply clear that restrictive transfusion strategy is safe. Briefly:

- There was no difference in rates of mortality or mobility limitation at 60 days when patients with CV disease/ risk received BT at Hb of \leq 8 g/dl versus those who received BT at Hb of \leq 10 g/dl.

<i>Crossmatch:</i>	NOT REQUIRED.
<i>Compatible alternate blood groups</i>	Although blood group specificity is preferred it is not mandatory especially in adults. However in neonates or small children it is desirable to give blood group specific or neutral (AB) group cryoprecipitate. The Rh type can be ignored if there is no red cell contamination of the product.
<i>Indications:</i> <ol style="list-style-type: none"> Hemophilia A (when pathogen inactivated antihemophilic concentrate factors are not available) Von Willebrand's disease Congenital or acquired fibrinogen deficiency (when pathogen inactivated fibrinogen is not available or cannot be used) Acquired factor VIII deficiency (when pathogen inactivated antihemophilic concentrate factors are not available) Factor XIII deficiency As a source of fibrin glue for preparing topic hemostatic agent in surgical procedures when pathogen inactivated fibrinogen is not available or cannot be used. 	

There are many existing international guidelines recommending RBC transfusions for various category of patients. Although decision to transfuse should be individualized according to the patient's condition, below mentioned indications are based on the latest scientific evidence and shall help in standardizing the blood transfusion practices in patients. Hemoglobin level is one of the critical factor used daily by the doctors to make a decision to transfuse and thus below mentioned guidelines incorporate Hb as one of the triggers wherever feasible.

1. Rationale PRBC use in Obstetrics and Gynecology

The WHO guidelines for blood transfusion in Obstetric patients published more than 15 years back recommended that blood transfusion should not be based on the Hb levels alone. There were no specific recommendation regarding the trigger for blood transfusion in these patients. In view of absence of any specific recommendations/ guidelines from the Indian obstetrics and gynecology bodies/ societies (e.g. FOGSI, ICOG) till December 2019, the below mentioned practice points have been taken from the RCOG, UK guidelines (2018)¹³.

- For normocytic or microcytic anemia, a trial of oral iron should be considered as the first step and further tests should be undertaken if there is no demonstrable rise in Hb at 2 weeks and compliance has been checked.
- Pregnant women should be offered screening for anemia at booking and at 28 weeks. Women with multiple pregnancies should have an additional full blood count done at 20–24 weeks.
- Parenteral iron is indicated when oral iron is not tolerated or absorbed or patient compliance is in doubt or if the woman is approaching term and there is insufficient time for oral supplementation to be effective.
- All women should have their blood group and antibody status checked at booking and at 28 weeks of gestation.
- Pre-delivery autologous blood deposit is not recommended.
- There should be a clear local protocol on how to manage major obstetric hemorrhage.
- There are no firm criteria for initiating red cell transfusion. The decision to provide blood transfusion should be made on clinical and hematological grounds. FFP at a dose of 12–15 ml/kg should be administered for every 6 units of red cells during major obstetric hemorrhage. Subsequent FFP transfusion should be guided by the results of clotting tests. Aim to maintain the platelet count above 50,000/ microliter in the acutely bleeding patient. A platelet transfusion trigger of 75,000/ microliter is recommended to provide a margin of safety.
- Anemic women who are not actively bleeding intrapartum or immediate post-partum, an Hb less than 7gm/dl is an indication for PRBC transfusion. For actively bleeding patients, follow with major obstetric protocols or massive transfusion protocol developed locally by the Hospital Transfusion Committee.

Infants older than 4 months and children

Category	Recommendation for RBC transfusion
Intraoperative blood loss > 15% of blood volume, Perioperative anemia, chemotherapy, radiotherapy, chronic congenital or acquired symptomatic anemia	Maintain Hb above 8gm/ dl
Severe pulmonary disease, ECMO	Keep Hb > 13 gm/ dl
Sickle cell disease for surgery under general anesthesia	Keep Hb > 10gm/ dl
Acute blood loss with unresponsive hypovolemia	Any Hb level

6. **Rationale PRBC use in common Hemoglobinopathies in India**[Source: Guidelines for screening, diagnosis and management of Hemoglobinopathies. Indian J Hum Genet. 2014;20(2):101-19]²⁰ -

Thalassemia and Sickle cell diseases are two common Hemoglobinopathies in India that require long and specialized treatment. Despite many advancements in the diagnosis and management of these diseases, it is unfortunate that still most of the patients in India are dependent mainly upon repeated blood transfusions.

Blood transfusion in Thalassemia

In thalassemia, excess iron due to these repeated blood transfusions, needs to be removed by the use of the expensive chelation treatment.

Thalassemia intermedia and Hb E thalassemia patients may not need regular red cell transfusions. Even in thalassemia major patients, regular transfusions are not justified only on the basis of Hb levels. Clinical parameters should be assessed before advising a chronic transfusion therapy because of grave risks with chronic BT therapy²¹. Following parameters suggest that the patient will need chronic red cell transfusions.

- Hb level <7 g/dl on two successive occasions separated by at least 2 weeks (the patient should be on folic acid replacement and there should be no other aggravating cause, i.e. infection, bleeding, etc.)
- Patient's growth, activity, academic performance, zeal, etc., are hampered
- Unnatural bony growth due to marrow expansion
- Development of organ failure such as cardiac failure, edema.
- Even if Hb level is >7 g/dl and <10 g/dl, and above clinical features are present, the patient may need chronic transfusion therapy.

Objectives of chronic red cell transfusions is to ensure adequate Hb level so that O₂ delivery to the tissue is not hampered. This will be indicated by:

- Normal growth spurt.
- Increased zeal, energy, enthusiasm, and improved academic performance.