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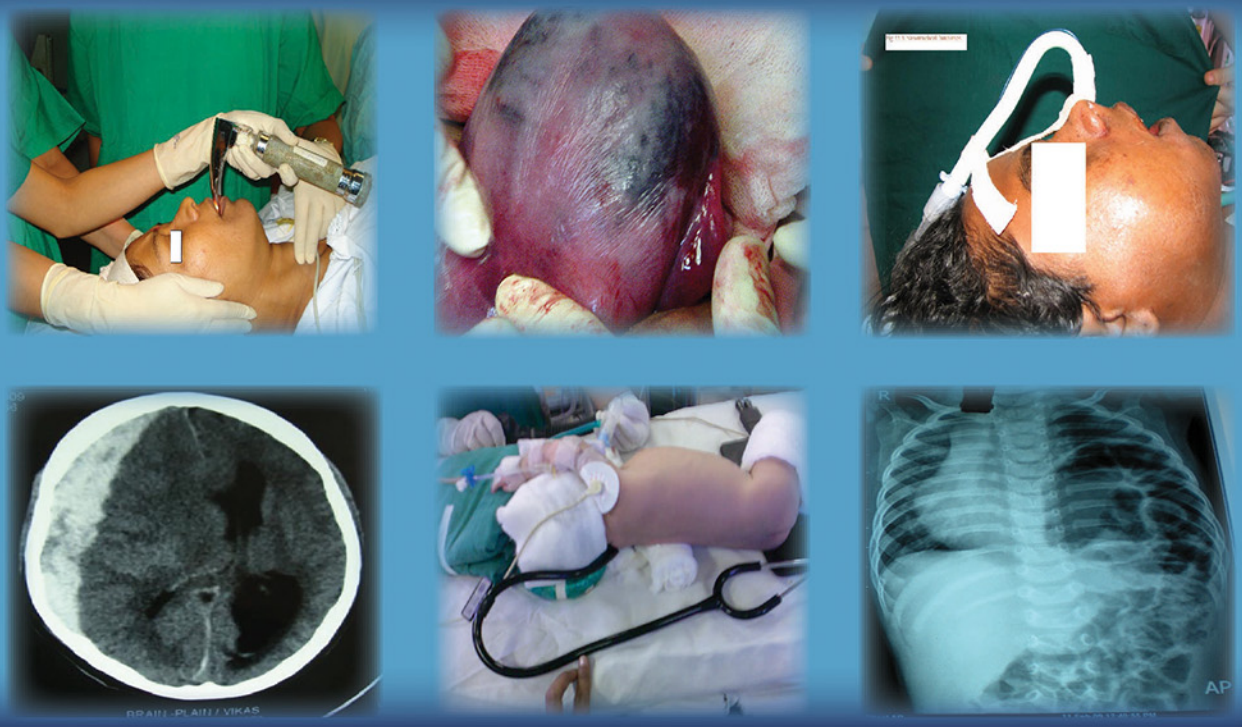
A Practical Approach to Anesthesia for Emergency Surgery



Forewords
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4 Blood and Blood Component Therapy in Emergency Anesthesia

Aparna A Nerurkar, Manish B Kotwani

KEY POINTS

- Blood management has been defined by Society for Advancement of Blood Management (SABM) as "the appropriate use of blood and blood components with a goal of minimizing their use."
- Hemoglobin triggers for transfusion are not to be taken as absolute indications. Patients should be transfused if signs or symptoms of inadequate myocardial oxygenation or organ insufficiency are present.
- All blood components including platelets should be transfused through a blood transfusion set with an integral mesh filter (170-200 micron).
- A new syringe and administration set should be used when administering different components.
- Aseptic technique must be employed during preparation and administration. If the container is entered in a manner that violates the integrity of the system, the component expires 4 hours after entry if maintained at room temperature (20-24°C), or 24 hours after entry if refrigerated (1-6°C).
- All unused components should be returned to the blood bank as soon as possible with information regarding the circumstances of return.
- If red cell units are out of temperature controlled storage for more than 30 minutes they should not be put back into storage for re-issue.
- The ideal solution to manage hypovolemia and anemia due to major blood loss is administration of fresh whole blood. However logistic and testing issues make it difficult for the blood bank to provide fresh whole blood.
- In an extreme situation where blood is required immediately and the patient's blood group is unknown, either type-specific or type O uncrossmatched red cells can be administered while awaiting a crossmatch.
- Type O Rh-negative, uncrossmatched packed RBCs should be used in preference to type O Rh-negative whole blood because packed erythrocytes have smaller volumes of plasma and are almost free of hemolytic anti-A and anti-B antibodies.
- When more than two units of type O Rh-negative, uncrossmatched whole blood have been administered, the patient probably cannot be immediately switched back to his or her blood type (A, B, or AB). Switching could cause major intravascular hemolysis of donor RBCs by increasing transfused anti-A and anti-B antibodies.
- The patient must not be transfused with his or her correct blood type until the transfused anti-A and anti-B has decreased to levels that permit safe transfusion of type-specific blood.
- Prophylactic administration of alkalinizing agents such as sodium bicarbonate or tris-hydroxymethyl aminomethane (THAM) is unnecessary and may cause serious alkalosis and hypernatremia.
- Hyperkalemia may occur, due to the high extracellular potassium concentration in stored red cell units. Treatment includes calcium gluconate, glucose insulin regimens (10 units of insulin with 50cc 50% dextrose over 20-30 mins) and beta-2 agonists together with bicarbonate to correct acidosis.
- Prophylactic platelet transfusion is rarely required for counts $\geq 100 \times 10^9$/L and always indicated at counts $\leq 50 \times 10^9$/L with massive bleeding. A platelet count increment of approximately 7 to10,000/mm^3 for each RDP (random donor platelet) given, or 30 to 60,000/mm^3 for each SDP (single donor platelet) given to an adult is expected.
- Treatment of microvascular bleeding due to congenital and acquired coagulopathies including massive blood loss, disseminated intravascular coagulation with depletion of clotting factors may require 10 to 20 ml/kg of fresh frozen plasma (FFP).

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- FFP is contraindicated for increasing plasma volume or albumin concentration.
- One cryoprecipitate unit per 7 to 10 kg of body weight can be used in massive hemorrhage or disseminated intravascular coagulopathy (DIC) to raise plasma fibrinogen concentration by ~ 50 to 70 mg/dl.
- As an off-label use in massive hemorrhage, recombinant factor VIIa (rfVIIa) 90μg/kg as a slow intravenous bolus can be considered if all possible hemostatic measures like surgical control of bleeding, temperature correction and blood product administration have been carried out.
- Transfusion-Associated Circulatory Overload (TACO) resulting in pulmonary edema can accompany transfusion of any component at a rate more rapid than the recipient's cardiac output can accommodate.
- Transfusion-Related Acute Lung Injury (TRALI), indistinguishable from adult respiratory distress syndrome (ARDS) and having a mortality rate of approximately 5 to 10%, may develop within 6 hours of a transfusion. Supportive therapy in the form of high FiO_2, endotracheal intubation with ventilatory support, volume resuscitation and vasopressor support is needed.
- A checklist for checking blood and blood components must be developed for each institute and the final check should always be by the patient's bedside.
- The responsibility of implementing the Guidelines is a shared one and requires the support of health departments, clinicians and laboratory staff.

INTRODUCTION

Anesthesiologists in their role as perioperative physicians play a major role in the utilization of blood and blood components. Life-threatening hemorrhage, especially in an emergency scenario, mandates quick and careful decisions about transfusion of blood and blood components. Pre-existing hematological derangements require rational and effective use of blood component therapy to optimize outcome in emergency surgeries.

Patients with massive blood loss and patients with deficiency of blood components pose a major challenge for hematological and blood transfusion services. The imbalance in the demand and supply of blood makes voluntarily donated allogenic blood a limited and a valuable resource. Blood and blood products must be used carefully, rationally, safely and on the basis of evidence based guidelines.

Triaging of blood and blood components to prioritize supply to patients whose transfusion cannot be deferred is one strategy for optimizing the balance between available blood inventory and clinical use during critical shortages. Such triaging is integral to many disaster management plans. Effective triaging requires precise information regarding the clinical setting of transfusion, its urgency, and its potential deferability. Also one needs to address the possibility of using anesthetic and surgical techniques, volume expanders, etc. to reduce the need for blood.

Blood management has thus been defined by Society for Advancement of Blood Management (SABM) as "the appropriate use of blood and blood components with a goal of minimizing their use."

Technological advances in blood collection, separation, anticoagulation, and preservation have resulted in component preparation of red blood cells, platelets, white blood cells and plasma which are superior to whole blood used in the past. Blood component separation also augments the meager supply of blood by making available the exact component needed for the patient's hematological condition.

However, there are substantial differences in the clinical use of blood and blood components across the globe. This reflects a lack of consensus among clinicians about specific criteria for the appropriate use. Several studies have found that the amount of blood used and the percentage of admissions involving the use of blood components vary across different types of hospitals, even for the same procedure or diagnosis, and that the rate of use that can be classified as inappropriate is unacceptably high.[1,2,3,4,5]

Various strategies have now been developed to reduce the inappropriate use of blood. These include guidelines (ASA[6,7], BSH[8,9,10], AAGBI[11], ARC[12], GOI[13]), circulars (AABB[14]), handbooks (WHO[15,16]), and consensus conferences, as well as monitoring of transfusion practice (retrospective and prospective), education and self-audit[17] by clinicians. Physicians prescribing blood components should have a basic understanding of indications and contraindications of their use. They should be cognizant of methods of preparation, proper storage conditions, indications, contraindications, dosages and methods of proper transfusion of blood products to prevent potential adverse effects. The following tables of blood component use have been compiled from the above

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mentioned learning material along with material in standard textbooks[18,19] (Tables 4.1 to 4.4).

TECHNICAL ASPECTS OF BLOOD COMPONENT ADMINISTRATION

Venous Access

- Blood components can be administered through peripheral intravenous cannula or most central venous access devices as per manufacturer's specifications.
- The size of the peripheral cannula depends on the size and integrity of the vein and the speed at which the blood component is to be transfused. In pediatric patients, special care must be taken to ensure blood transfusion through largest available venous access, to avoid hemolysis and consequent hyperkalemia.
- Peripherally inserted long central catheters (PICC lines) with narrow lumen diameter may lead to slower flow rates.
- When multi-lumen central venous access devices are used it is generally safe to coadminister other therapeutic solutions through a different lumen as rapid dilution occurs in the bloodstream.

Administration Equipment

Adult Administration

- All blood components should be transfused through a blood transfusion set with an integral mesh filter (170–200 micron).
- It is not essential to use the specially available platelet administration set that contains the same integral mesh filter (170–200 micron) as a blood administration set, but has a smaller lumen and thus a smaller priming volume.
- Platelets should be transfused through a fresh blood transfusion set. Blood sets utilized for other blood components should not be used.
- The administration set should be changed at least every 12 hours (or in accordance with manufacturer's instructions). This is intended to reduce the risk of bacterial growth.
- A new administration set should be used if another infusion is to continue after the transfusion. This is intended to reduce the risk of incompatible fluids or drugs causing hemolysis of residual red cells in the administration set or drip chamber.
- Leukodepletion filters can be used in special situations like cardiac surgery, oncology, etc.

Table 4.1: Packed red blood cells

Description	Packed Red Blood Cells consist of erythrocytes concentrated from whole blood donations by centrifugation or collected by apheresis method. 300–350 ml of RBCs in additive solution collected from 450 ml of whole blood Depending on the preservative-anticoagulant system used, the hematocrit of Red Blood Cells ranges from about 50–65% (e.g. AS-1, AS-3, AS-5) to about 65–80% (e.g. CPDA-1, CPD)
Storage	2–6°C in designated temperature controlled refrigerator.
Shelf Life	35 days (CPDA), 42 days (when Adsol® is added to CPDA)
Dosage/Yield	• One unit of PRBCs will increase the hematocrit by approximately 3% and the hemoglobin by about 1g/dl in the average adult. • In neonates, a dose of 5 ml/kg of packed red cells with a hematocrit of approximately 60% will increase the hemoglobin by about 1g/dl • In the case of a lower than expected transfusion yield, conditions causing the loss, sequestration or destruction of RBCs should be looked for. Such as occult bleeding; repeated blood sampling (particularly in children); fever; hypersplenism; primary and secondary immunological causes; mechanical or other type of hemolysis.
Indications	• Patients with values above 10 g/dl rarely require transfusion • Evidence supports transfusion in absence of physiologic signs with hemoglobin levels below 6 mg/dl in general patient population, below 7 mg/dl in patients > 80 years old or in febrile/ hypermetabolic patients, and below 8 mg/dl in patients with coronary artery disease or CHF. • The determination of whether intermediate hemoglobin concentrations (i.e. 6–10 g/dl) justify or require RBC transfusion should be based on any ongoing indication of organ ischemia, potential or actual ongoing bleeding, the patient's intravascular volume status, and the patient's risk factors for complications of inadequate oxygenation. • Cardiac patients should be transfused if signs or symptoms of inadequate myocardial oxygenation are present. Currently, red cell transfusion should be considered in following clinical scenario: – Anemic patients with relative hypotension/ tachycardia – New ST-segment depression > 0.1 mV or new ST-segment elevation > 0.2 mV – New wall motion abnormality – Mixed venous oxygen partial pressure less than 25 mmHg – Oxygen extraction rate more than 50% – Mixed venous oxygen saturation less than 50% and more than 10% decrease in oxygen consumption
Need for crossmatch	• A crossmatch is performed to ensure compatibility between the donor's RBCs and the recipient's plasma.

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Table 4.2: Plasma (≈ 250 ml)

Description	• FFP contains normal levels of the stable clotting factors, albumin and immunoglobulins. It contains at least 70% of the original coagulant factor VIII and at least similar quantities of the other labile clotting factors and natural inhibitors of coagulation.
Storage	• Frozen at –18°C or colder in a designated temperature controlled freezer within 6–8 h of collection
Shelf Life	• 24 months (frozen)
Dosage	• When FFP is indicated, it should be administered in a dose calculated to achieve a minimum of 30% of plasma factor concentration. • Usually 10–20 ml/kg of FFP will generally result in a rise of most coagulation proteins by 25–30% (or increases in 0.25–0.3 U/ml) though more may be required depending upon the clinical situation. • A dose of 5–8 ml/kg may be adequate to urgently reverse warfarin anticoagulation.
Indications	• Frozen plasma is indicated for patients on warfarin only if there is serious bleeding or urgent reversal of warfarin effect is necessary. • Treatment of microvascular bleeding due to congenital and acquired coagulopathies including massive blood loss, disseminated intravascular coagulation with depletion of clotting factors resulting in a prolongation of either the activated partial thromboplastin time (aPTT) or prothrombin time (PT) greater than 1.5 times normal or a coagulation factor assay of less than 25 percent or empirically for more than 1 blood volume blood loss.
Comments	• Prior to the administration of FFP, the plasma must be thawed in a waterbath at 37ºC, which takes approximately 30 minutes. • Once thawed, FFP must not be re-frozen and should be transfused as soon as possible. Post-thaw storage will result in a decline in the content of labile coagulation factors • If stored at 1–6ºC post thawing, the FFP should be transfused within 24 hours. • FFP which has been thawed but not used within 24 hours can be relabelled as "Thawed Plasma" (TP) and stored at 1–6ºC for an additional 4 days. • 'Thawed plasma' can be used as a source of all stable coagulation factors except factor V which falls to 80% of normal and factor VIII which falls to 60% of normal. • FFP is contraindicated for increasing plasma volume or albumin concentration.
Need for crossmatch	• Because of anti-ABO antibodies in units of plasma, only ABO-compatible units can be used. Rh compatibility is not required. Thus, the recipient's ABO type is needed for plasma transfusion. Because plasma from donors with type AB blood does not contain anti-ABO antibodies, it can be given to any patient and is used for emergency transfusion in patients with unknown blood types. Crossmatching of plasma is not required, since there are no RBCs in these products.

Table 4.3: Platelets

Description	• Platelet concentrate (random donor): Volume 50–70 ml Each unit contains approximately 5.5 × 10 platelets in 50 to 70 ml of plasma. • Pooled platelets: 5 to 10 units of random donor platelets may be pooled together in a single component bag. • Apheresis platelets (single donor): Volume 200 to 400 ml obtained by performing apheresis on volunteer donors. Each unit contains 15-50 × 10^{10} platelets, equivalent to 3–10 units of platelet concentrates.
Storage	• Room temperature (20°–24°C) with continuous gentle agitation to prevent platelet aggregation • Must not be refrigerated as it reduces platelet function
Shelf Life	• 5 days (7 days—in certain controlled circumstances)
Dosage/Yield	• Measure platelet count from 10 minutes to 3 hours after transfusion. • Generally, expect an adult platelet count increment of approximately 7–10,000/ mm^3 for each RDP given, or 30–60,000/ mm^3 for each SDP given. • In neonates and infants, a dose of 5–10 ml/kg of platelets (RDP or SDP) should result in a 50–100,000/mm^3 increment.
Indications	• Prophylactic preoperative transfusion is rarely required for counts ≥ 100 × 10^9/L, is usually required for counts < 50 × 10^9/L with bleeding • Factors to consider for the transfusion of platelets for counts between 50–100 × 10^9/L are the type of surgery, extent of actual blood loss or microvascular bleeding, presence of potent antiplatelet medications (e.g. clopidogrel, IIb/IIIa antagonists, etc.) and disorders like uremia known to affect platelet function and coagulation. Specific Procedures: • Procedures with insignificant blood loss or vaginal deliveries can be performed at counts <50 × 10^9/L without prophylactic transfusion. • Neurologic or ophthalmologic procedures require platelets near 100 × 10^9/L • In the absence of other coagulopathy, major invasive procedures require platelet counts of at least 40 to 50 × 10^9/L (including CVP placement, paracentesis/thoracentesis, respiratory tract/GI biopsies, closed liver biopsy, lumbar puncture, sinus aspiration and dental extraction). • A threshold of 80 × 10^9/L has been proposed for spinal epidural anesthesia. • Fiberoptic bronchoscopy without biopsy by an experienced operator may be safely performed in the presence of a platelet count ≈ 20 × 10^9/L • GI endoscopy without biopsy may be safely performed at platelet counts ≈ 20 × 10^9/L.[6] • Transfusion may be required with apparently adequate counts when known or suspected

Contd.

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	platelet dysfunction results in microvascular bleeding
Comments	• All platelet products should be tested for bacterial contamination prior to transfusion. • Platelet concentrates should not be transfused through administration sets which have already been used to administer other blood components • The infusion should be commenced as soon as possible after the component arrives in the clinical area • Typically administered over 30–60 minutes per dose. • Qualitative coagulation tests, such as bleeding time have been shown to have poor reproducibility and limited value.
Need for crossmatch	• ABO compatibility for platelet transfusion is desirable but not required because of the small amount of plasma present in a standard dose of platelets (each unit contains about 60 mL of plasma, and 5 or 6 units make up a standard dose)

Pediatric Administration

- Pediatric blood administration sets (with a smaller prime volume) are appropriate for small volume transfusions. Neonatal blood administration systems are also available which allow blood components to be delivered via a syringe driver. These systems should incorporate an integral three-way system allowing the blood component bag to remain attached throughout the transfusion.
- All administration systems should incorporate a 170 to 200 micron filter.
- A new syringe and administration set should be used when administering different components.
- Blood components from more than one donation should not be mixed in a syringe. Instead, it should be given sequentially using a new syringe in order to be able to identify the relevant donation in case of a reaction.

Infusion Devices

- Infusion devices should be used only by individuals competent in their use.
- Compatibility should be ensured between the blood component administration set and the infusion device as per manufacturers' recommendations.
- Administration sets used with infusion devices should incorporate an integral mesh filter (170-200 micron).
- The pre-administration checking procedure should include a check of the device and device settings.

Table 4.4: Cryoprecipitate

Description	• Cryoprecipitated antihemophilic factor or a cryoprecipitate unit is prepared by thawing one unit of FFP between 1–6°C and recovering the cold insoluble white precipitate which is removed following centrifugation and immediately refrozen • Each unit of cryoprecipitate contains 80 to 150 units of Factor VIII, 150 to 250 mg of fibrinogen, von Willebrand's factor, Factor XIII, and fibronectin in a volume of 5 to 15 ml • "Pooled Cryoprecipitate". Several units of cryoprecipitate are pooled into one bag and the volume of the pool is indicated on the label.
Storage/shelf Life	• Frozen at –18°C for 24 months
Dosage	• A typical dose for the treatment of hypofibrinogenemia is one cryoprecipitate unit per 7–10 kg of body weight. • One unit of cryoprecipitate per 10 kg of body weight raises plasma fibrinogen concentration by ~ 50 to 70 mg/dl in the absence of continued consumption or massive bleeding (assuming minimum fibrinogen content per bag of cryoprecipitate).
Indications	• Cryoprecipitate is used primarily to augment fibrinogen levels depleted because of massive hemorrhage or disseminated intravascular coagulopathy (DIC). • Rarely, it is used for the treatment of congenital or acquired Factor XIII deficiency. • Cryoprecipitate can also be administered prophylactically for non bleeding perioperative or peripartum patients with congenital fibrinogen deficiencies or von Willebrand's disease (deficient or abnormal von Willebrand's molecule) unresponsive to desmopressin.
Comments	• CMV testing and leukoreduction are not required. • Frozen cryoprecipitate is thawed in a protective plastic overwrap in a waterbath at 30–37°C up to 15 minutes. Thawed cryoprecipitate should be kept at room temperature and transfused as soon as possible or within four to six hours. • Should be infused through a 170 to 260 micron component filter • Because cryoprecipitate does not contain Factor V, it should not be the sole replacement therapy for disseminated intravascular coagulopathy (DIC), which is almost always associated with a variety of factor deficiencies and thrombocytopenia. Hence, FFP also needs to be administered along with platelet concentrates in those settings where a coagulopathy secondary to DIC is likely occurring.
Need for crossmatch	• Each unit of cryoprecipitate contains a small amount of plasma (15 mL/unit) and thus does not require ABO compatibility. Rh type need not be considered. It is preferable to use cryoprecipitate that is ABO-compatible with the recipient's red cells

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- Infusion devices should be regularly maintained in accordance with manufacturers and/or organizational guidelines.
- Any adverse outcome as a result of using an infusion device to transfuse red cells should be reported to the appropriate authorities.

Infusion Rate Devices

- Precise infusion rate controlled, gravity-based or electronic infusion devices may be used for the administration of blood and blood components.
- Rapid infusion devices may be used when large volumes have to be infused quickly, as in massive hemorrhage. These typically have a range of 6 to 30 liters/hour and usually incorporate a blood warming device.
- Infusion devices should only be used if the manufacturer verifies them as safe for this purpose and they are CE marked.
- The volume delivered should be monitored regularly throughout the infusion to ensure that the expected volume is delivered at the required rate.

Pressure Devices

- External pressure devices make it possible to administer a unit of red cells within a few minutes. They should only be used in an emergency situation together with a large gauge venous access cannula or device.
- External pressure devices should exert even pressure over the entire bag, have a gauge to measure the pressure which should not exceed 300 mm Hg pressure and be monitored at all times when in use.

Blood Warmers

- Most published guidelines[20,13,15] only recommend the routine use of blood warmers in adult patients undergoing rapid or high volume transfusion of red cells in the context of major hemorrhage. Blood transfusion at a rate of > 50 ml/kg/hr in adults and >15 ml/kg/hr in pediatrics, exchange transfusion in infants or patients with clinically significant "cold" antibodies are some of the indications for use of blood warmers.
- In most other clinical situations where there is concern, it is sufficient to allow blood to come up to ambient temperature before transfusion.
- Special consideration should be given when rapidly transfusing large volumes to neonates, children, elderly patients, and patients susceptible to cardiac dysfunction.
- Platelet warming to 37°C was earlier recommended but there is no evidence that warming platelets before infusion improves postinfusion platelet viability[21].
- Blood should only be warmed using approved, specifically designed and regularly maintained blood-warming equipment with a visible thermometer and audible warning. Settings should be monitored regularly throughout the transfusion. Some blood warmers operate up to 43°C but are safe provided they are used and serviced according to manufacturers' instructions.
- Blood components should never be warmed using improvisations, such as putting the pack in warm water, in a microwave or on a radiator. These may increase the chances of hemolysis and infection.

Compatible Intravenous Fluids

- It is generally advised that no other intravenous fluids should be coadministered via an infusion line that is being used for a blood component (when multi-lumen central venous access devices are used, it is generally safe to coadminister other therapeutic solutions through a different lumen as rapid dilution occurs in the blood stream).
- Intravenous solutions which contain calcium, such as Ringer Lactate, and calcium-containing colloids, such as Hemaccel™ or Gelofusine™ may antagonize citrate anticoagulant and allow clots to form in the blood component.
- Hypotonic intravenous solutions, such as 5% dextrose in water, may cause hemolysis of red cells.
- The practice of priming or flushing administration sets used for the transfusion of blood components with isotonic (0.9%) saline is not evidence-based and is unnecessary. No other intravenous fluids should be used for this purpose.

Coadministration of Drugs with Blood Components

- The addition of a drug to an intravenous line containing blood or blood components raises concerns about compatibility of the drug and its carrier with the blood component and any preservatives or additives.
- A break in the integrity of the infusion line may also increase the risk of bacterial contamination of the component.

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- Recent studies show that standard concentrations of morphine, hydromorphone or meperidine given by continuous infusion or single or multiple boluses have no significant deleterious effects on co-administered red cells [22,23]
- For the administration of any other drugs, wherever possible drugs should be timed to be administered between transfusions, or administered via a second venous access device.
- There is insufficient evidence to guide a policy change on the coadministration of drugs and red blood cells due to the lack of clinical applicability of *in vitro* experiments and diversity of clinical outcome measures used.
- Under no circumstances should drugs be directly added to a blood component bag.

Disposal of Equipment

- If there is any suspicion of a transfusion reaction, the component pack should be returned to the transfusion laboratory with full clinical details.
- If a transfusion is completed uneventfully, the empty blood component pack and administration set should be discarded according to the organization's policy for disposing of clinical waste. Generally the set is cut so as prevent misuse.
- If, in accordance with local policy, any paperwork is required for the traceability of blood components this must be done before disposal of the unit.

Return of Blood Components

- If a blood component is returned from a clinical area to a designated blood refrigerator/ storage location, the following information should be recorded for each individual unit:
- Identity of the person returning the component
- Date and time component placed in the blood refrigerator/storage location
- All unused components should be returned as soon as possible and the clinical areas should inform the laboratory of the circumstances of the return.
- If red cell units are out of temperature controlled storage for more than 30 minutes, they should not be put back into storage for reissue.

MASSIVE BLOOD TRANSFUSION

Definition

Massive blood transfusion is the replacement of blood loss equivalent to or greater than the patient's total blood volume in less than 24 hours which amounts to approximately 70 ml/kg in adults and 80 to 90 ml/kg in children or infants. Alternative definitions include 50% of the blood volume loss within 3 hours or the rate of blood loss >150 ml/min.

A dynamic definition of massive transfusion, such as the transfusion of four or more red cell concentrates within one hour when on going need is foreseeable, or the replacement of 50% of the total blood volume within three hours, may be more appropriate in the acute clinical setting.

Such definitions emphasize the importance of the early recognition of major blood loss and the need for effective action to prevent shock and its consequences. Massive blood transfusion is one of the main prognostic factor for mortality in trauma.[24]

Early consultation with surgical and hematology colleagues is advisable, and the importance of good communication and cooperation in this situation cannot be overemphasized.

The most common clinical situation leading to massive transfusion is extensive trauma; however, it also may occur in nontrauma settings during surgical procedures causing large blood loss especially after cardiothoracic and emergency obstetric surgery. In such situations, the ideal solution to manage hypovolemia and anemia due to major blood loss, involves administration of fresh whole blood since this approach restores not only oxygen carrying capacity and oxygen delivery but also hemostasis via maintenance of normal levels of coagulation factor and platelets. However due to logistic and testing issues, it is difficult for the blood bank to provide fresh whole blood every time. It may often be necessary to make a pragmatic decision regarding the relative risks of delaying transfusion or giving components that are not of the appropriate specification.

PRACTICAL APPROACH TO MASSIVE BLOOD TRANSFUSION

Priorities for treatment should be

- Maintenance of tissue perfusion and oxygenation by restoration of blood volume and hemoglobin.
- Achieving hemostasis by treating any surgical, obstetrical or traumatic source of bleeding and correcting coagulopathy by the judicious use of blood component therapy.

A successful outcome requires prompt action and good communication between clinical specialties, diagnostic laboratories, blood-bank staff and the local blood center. Blood component support takes time to organize and sometimes the blood center may be away from the hospital.

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Table 4.5: Goal directed management of massive blood loss

Goal	*Approach*	*Comments*
Volume Resuscitation	Secure wide bore peripheral venous access or central single lumen or multi-lumen devices Administer warm intravenous fluids—crystalloid or colloid as needed Avoid hypotension or urine output <0.5 ml/kg/h	Preferably 14-gauge cannulae monitor CVP Keep patient warm Account for concealed blood loss
Clear communication with concerned personnel	Surgeon, Physician, in-charge Consultant anesthesiologist, Blood Bank Officer or Hematologist, Relatives/Caregivers	Early communication facilitates availability of blood, blood products, control of bleeding and postoperative intensive care support if required Communication with relatives and documentation is essential for medico-legal purposes
Control bleeding	Early surgical or obstetric intervention Interventional radiology Use of anesthetic techniques to reduce bleeding	
Obtain laboratory investigations	Blood group/crossmatch CBC including platelets PT, APTT, Thrombin time, Fibrinogen, FDP BS, RFT, LFT, Electrolytes Blood gases TEG, if available Repeat tests after blood component infusion	Ensure correct patient and sample identification Results may be affected by colloid infusion. May need to give components before results available
Maintain Hb >8 g/dl	Employ techniques to reduce bleeding and use blood salvage to minimize allogenic blood use Give Group O Rh D negative packed red blood cells in extreme emergency until ABO and Rh D groups known. If blood group is known use ABO group specific packed RBCs Fully compatible blood should be used if time permits Use blood warmer and/or rapid infusion device if flow rate >50 ml/kg/h in adult	Use cell savers if available. O positive is acceptable in males and postmenopausal females Further serological crossmatch not required after 1 BV replacement. Do not switch back to patient's group, after O group administration, till antibody titers confirmed to be low.Transfusion laboratory will complete crossmatch after issue.
Maintain platelet count >7.5 × 10^{10}/L	Allow for delivery time from blood center Anticipate platelet count <50 × 10^{9}/l. After 2 × blood volume replacement	Allows margin of safety to ensure platelet count >5.0 × 10^{10}/L Keep platelet count >10.0 × 10^{10}/L if multi-organ or CNS trauma or if platelet function is abnormal
Maintain PT and APTT <1.5 × mean control	Give FFP 12–15 ml/kg (Four units for an adult) guided by tests Anticipate need for FFP after 1–1.5 × BV replacement.	PT/APTT >1.5 × mean normal value correlates with increased microvascular bleeding Keep ionized Ca^{2+} >1.13 mmol/l
Maintain Fibrinogen >1.0 g/l	If not corrected by FFP give cryoprecipitate (2 packs of pooled cryoprecipitate for an adult)	Rarely needed except in DIC
Avoid DIC	Treat underlying cause (shock, hypothermia, acidosis)	Although rare, mortality is high

CVP, central venous pressure; CBC, complete blood count; PT, prothrombin time; APTT, activated partial thromboplastin time; FDP-Fibrin degradation products; BS-Blood Sugar, RFT-Renal function tests, LFT-Liver Function Tests, FFP, fresh frozen plasma; DIC, disseminated intravascular coagulation; BV, blood volume

The blood bank must be informed of a massive transfusion situation at the earliest possible opportunity. This will provide an opportunity to check stock, reschedule nonurgent work and call in additional staff if required out of hours.

Clear local protocols for management of massive blood loss should be accessible in all relevant clinical and laboratory areas and understood by all involved staff (Table 4.5).

Volume Resuscitation

The overriding first requirement is maintenance of tissue perfusion and oxygenation. This is critical in preventing the development of hypovolemic shock and consequent high mortality from multiorgan failure. Restoration of circulating volume is initially achieved by rapid infusion of crystalloid or colloid through large bore (up to 14 gauge) peripheral cannulae. The 2007 Cochrane review[25] stated that there is no evidence from

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Table 4.6: Synthetic colloid solutions

Generic Name	*Contents*	*Intravascular Half Life*
Dextran 40	10% polysaccharide (MW 40,000) with normal saline	4–6 hrs
Dextran 60–70	6–7% polysaccharide (MW 70,000) with normal saline	6–8 hrs
Hydroxyethyl starch	6% hydroxyethyl starch solution in 0.9% saline (MW 45,000) or Ringer's lactate	24 hrs
Hydroxyethyl starch 0.4 molar substitution	6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride injection	5–6 hrs
Gelatin	3.5% gelatin polypeptide (MW 35,000) with Ringer's solution	3–5 hrs
Succinated Gelatin	4% succinylated (or modified fluid) gelatin, sodiumhydroxide	4–5 hrs

RCTs that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. Larger bore central access devices can be used depending on local skills and availability. Similarly, crystalloids and colloids can be chosen as per availability, intravascular half-life (Table 4.6), hemodynamic conditions and time for arrival of cross-matched blood and components.

Blood Component Therapy

Red cells: The function of red cells is oxygen delivery to tissues; they should not be used as a volume expander. Red cells also contribute to hemostasis by their effect on platelet margination and function.

The optimal hematocrit to prevent coagulopathy is unknown, but experimental evidence suggests that a relatively high hematocrit, possibly ≈35% may be required to sustain hemostasis in patients with massive blood loss. Red cell transfusion is likely to be required when 30 to 40% blood volume is lost; over 40% blood volume loss is immediately life-threatening.

Blood replacement should be guided by clinical estimation of blood loss in conjunction with the patient's response to volume replacement. Hemoglobin and hematocrit levels should be measured frequently, with the knowledge that the hemoglobin level is a poor indicator of blood loss in the acute situation.

Red cells are rarely indicated when the hemoglobin concentration is >10 g/dl but almost always indicated when it is <6 g/dl.[1] Decisions on red cell transfusion at intermediate hemoglobin concentrations should be based on the patient's risk factors for complications of inadequate oxygenation, such as rate of blood loss, cardio-respiratory reserve, oxygen consumption and atherosclerotic disease. Measured physiological variables, such as heart rate, arterial pressure, pulmonary capillary wedge pressure and cardiac output may assist the decision-making process, but it should be emphasized that silent tissue or organ ischemia may occur in the presence of stable vital signs[26]

The requisition form for blood should indicate the time scale within which blood is needed at the theater, (i.e. immediately, within 20 minutes, within an hour) in order that the blood bank personnel to know how much time is available for ABO and D grouping and pre-transfusion testing. The number and type of blood components needed, the area where it is needed and reason for transfusion should be clearly communicated.

Which fluids should be administered while awaiting crossmatched blood?

While waiting for crossmatched blood to be available, emergency transfusion needs can be met in various ways, depending on the clinical status of the patient, the available resuscitation fluids and equipment and the anticipated delay in obtaining blood.

Most patients can tolerate an acute decrease in hemoglobin and oxygen-carrying capacity providing circulating volume is maintained. Crystalloid or colloid solutions may be infused for volume resuscitation and maintaining hemodynamic stability. Resuscitation with colloids does not reduce the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery.[25] The Cochrane reviews[27,28] also suggest that there is no evidence that one colloid solution is more effective or safe than any other. Other studies state that trauma patients should continue to be resuscitated with crystalloids.[29] However, administration of crystalloid to normalize blood pressure should be titrated to the clinical condition. Penetrating torso injuries, head injuries may require careful crystalloid administration. In fact, studies have shown that attempting to achieve normal blood pressure in the setting of active bleeding through extensive fluid therapy is associated with disruption of haemostatic mechanisms, dilution of clotting factors, increased blood loss and decreased survival.[30] Therefore, maintaining blood pressure below normal (systolic 80 mmHg; mean 50–60 mmHg) and heart rate under 120 while closely monitoring indicators of organ ischemia are the suggested goals for early resuscitation in otherwise healthy patients.

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In an extreme situation where blood is required immediately and the patient's blood group is unknown or if the patient has cardiac disease, pulmonary disease or cerebrovascular disease and acute anemia will pose increased risk, then either type-specific or type O uncrossmatched red cells can be administered while waiting for a crossmatch to be performed. Type O Rh-positive Red Blood Cells for males or postmenopausal females can be transfused in this setting as well. Administration of Group O uncrossmatched blood is safe provided that the patient is not already alloimmunized to any non-ABO red cell antigens.[18,31,32,33]

However, it should be remembered, that some type O donors produce high titers of hemolytic IgG, IgM, anti-A, and anti-B antibodies. High titers of these hemolysins in donor units are capable of causing destruction of A or B RBCs of a non-type O recipient. Type O Rh-negative, uncrossmatched packed RBCs should be used in preference to type O Rh-negative whole blood because packed erythrocytes have smaller volumes of plasma and are almost free of hemolytic anti-A and anti-B antibodies. Females of reproductive age (i.e. under 50 years) whose blood group is unknown must be given group O Rh D negative red cells in order to avoid sensitization and the risk of hemolytic disease of the newborn in subsequent pregnancy[18]

During emergency transfusion of more than two units of type O Rh-negative, uncrossmatched whole blood, the patient probably cannot be switched to his or her blood type (A, B, or AB) as soon as the blood bank determines the correct blood type. Switching could cause major intravascular hemolysis of donor RBCs by increasing titers of transfused anti-A and anti-B. Continued use of O Rh-negative whole blood results only in minor hemolysis of recipient RBCs, with hyperbilirubinemia as the only complication. The patient must not be transfused with his or her correct blood type until the blood bank determines that the transfused anti-A and anti-B has decreased to levels that permit safe transfusion of type-specific blood.[18]

If type specific crossmatched blood is not available then alternative blood group that is available in the blood bank can be given as per following guidelines[13] (Table 4.7).

Development of artificial oxygen-carrying agents (so-called blood substitutes) that can be easily stored and readily given to patients with no crossmatching is expected to revolutionize resuscitation in emergency setting. These products are not currently approved for use by the FDA.

Table 4.7: Choice of alternative blood (in absence of patient's blood group)

Recipient's ABO type	*Alternative Blood Ist Choice (Given as Packed Cells)*	*Alternative Blood IInd Choice (Given as Packed Cells)*
O	None	None
A	O	None
A_2 with anti A_1	O	None
B	O	None
A_1B*	A or B	O
A_2B*	A or B	O

*In Group AB patients, Group A Blood as an alternate source is preferred over Group B blood, as anti-B in Group A is weaker than anti-A in Group B.

Are prophylactic platelets and fresh frozen plasma indicated in massive transfusion?

Recent studies[34,35,36,37,38] have stated that the ratio of plasma, platelets, cryoprecipitates to red blood cells may influence survival, though further studies are recommended for establishing guidelines for the optimal transfusion ratios.

The role of platelets during massive transfusion is under review. Earlier guidelines stated that platelets are not indicated in massive transfusion.[39] While thrombocytopenia may develop in massively transfused patients, administration of platelets should be reserved for the patient exhibiting microvascular bleeding, and a platelet count less than 50×10^9/L. Platelet transfusion may be necessary for patients with intermediate platelet counts ($50–100 \times 10^9$/L) if more bleeding is anticipated.[6,19] However, platelet counts ≥100,000/mm^3 for those with multiple trauma or CNS injury has been recommended as also when >1.5 to 2 blood volumes have been replaced with red cells. In the presence of microvascular bleeding, transfusion may be appropriate when counts are known or suspected to be <100,000/mm^3.[12]

Similarly role of FFP is under review. FFP also should not be administered prophylactically for massive transfusion.[6] In the massively transfused patient, clinical bleeding associated with coagulation factor deficiencies is unlikely until factor levels fall below 20 percent of normal. In the clinical setting, this usually does not occur until greater than one to one-half blood volume has been replaced and the PT and PTT are greater than 1.5 to 1.8 times control values based on studies performed in the trauma and cardiac surgical settings. FFP to be used when PT is 1.5 times control value, INR or APTT 1.8.[19]

It should be noted that however, prophylactic administration of platelets and FFP is not warranted but

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Table 4.8: Compatible blood products for transfusion according to recipient's ABO Type

Recipient's ABO type	*Compatible plasma*	*Compatible RBCs*	*Compatible platelets First choice*	*Compatible platelets Second choice*
A	A, AB	A, O	A, AB	B, O
B	B, AB	B, O	B, AB	A, O
O	O, A, B, AB	O	O*	A, B, AB
AB	AB	AB, A, B, O	AB	A, B, O

*Although type O red blood cells (RBCs) do not have A or B antigens, the recipient's plasma contains anti-A and anti-B antibodies, which could reduce the recovery of transfused platelets bearing A or B antigens.

rather "pre-emptive" use is advocated. For example, if a patient is massively bleeding one does not wait until the platelet count drops to less than 50000/mm^3 or until the INR is greater than 2 to infuse the blood components as it can take 30 to 45 minutes to thaw FFP. Also, in a trauma patient with massive bleeding, a rise in the PT may be a "late" sign that the patient is developing a severe dilutional coagulopathy. In the event that the PT and PTT tests cannot be obtained in time, FFP 10 to 15 ml/kg may be administered empirically for correction of microvascular bleeding in patients transfused with more than one blood volume.[6]

If compatible blood products are not available other alternative compatible groups may be used as above (Table 4.8).

Another thing to consider is that the practice of administering packed RBCs and FFP to the same patient adds to the cost and doubles the infection exposure. Hence, when conditions are appropriate, whole blood should be given.[18]

It has to be emphasized that once bleeding is controlled and the patient is hemodynamically stable, the transfusion of blood and blood components should be guided by bedside and laboratory tests as well as the clinical status of the patient.

What are the causes of coagulopathy during massive transfusion?

Coagulopathy during massive transfusion is of multifactorial origin. Dilutional coagulopathy due to crystalloid, colloid and red blood cells administration, hypothermia, tissue hypoperfusion with resultant lactic acidosis and disseminated intravascular coagulopathy due to tissue trauma contribute to coagulation abnormalities. Coagulopathy associated with massive transfusion is clinically characterized by the presence of microvascular bleeding or oozing from the mucosa, wound, and puncture sites. The development of acidosis, DIC, hypothermia and, rarely, a hemolytic transfusion reaction may accompany massive transfusion and complicate the ability to effectively manage the coagulopathy. Thus, empiric formulas using ratios of various components to volume lost or administered are inadequate to treat or prevent coagulopathy related to massive transfusion. Treatment of the coagulopathy should include restoration of systemic perfusion, maintenance of normal temperature, resolution of acid-base abnormalities and blood component therapy when supported by abnormal laboratory tests in the setting of active bleeding.

How should coagulation be monitored during massive transfusion?

There is no single coagulation test that will give complete information on coagulation function during massive transfusion. The use of routine coagulation tests to evaluate coagulation factor deficiencies such as PT, PTT and thrombin time, have not reliably predicted perioperative bleeding, but they can identify patients with deficiencies of coagulation factors. These standard laboratory tests along with platelet count and fibrinogen level should guide the component therapy. The bleeding time is not predictive of perioperative bleeding and is rarely accessible in the operating room setting. The activated clotting time (ACT) is influenced by hypofibrinogenemia, hypothermia, use of anti-fibrinolytic agents and coagulation factor deficiencies and this lack of specificity limits ACT as a useful test during massive transfusion.

Whole blood clotting analysis, as assessed with the Thromboelastograph® (TEG) and Sonoclot®, measure the viscoelastic properties of blood as it clots. Although the clinical utility of use of a TEG during liver transplantation and cardiac surgery to guide component therapy has been demonstrated their usefulness during massive transfusion has not been established.

Is it necessary to utilize blood warmers during massive transfusion?

Warming of red cells or blood components should be limited to patients receiving massive transfusions (i.e. adults at rates > 50 ml/kg/hr, children at rates > 15 ml/kg/hr), or patients with clinically significant "cold" antibodies.[13,15] Intravenous fluids (500 ml or more) and

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blood products should be warmed to 37°C using a fluid warming device.[40] Warming blood also enhances the intracellular transfer of potassium. Keeping the patient warm is usually more important than use of a blood warmer.

Only specially designed and regulated blood warmers with a visible thermometer and audible warning must be used. Blood must not be warmed by any other method, such as immersion in warm water, because of the risk of contamination through minute holes in the bag and lack of control of the temperature which may lead to dangerous hemolysis.

When massive blood transfusion is administered, hypothermia (temperatures below 35°C) is likely to occur. Low ambient temperature, large open wounds, use of irrigating fluids as in hemoperitoneum, initial infusion of room temperature fluids, and blood stored at 4°C contribute to hypothermia. The potential effects of hypothermia include ventricular dysrhythmias, shivering, increased oxygen consumption, cardiac arrest and citrate toxicity secondary to reduced metabolism of citrate and lactate. Hypothermia contributes to coagulopathy in the operating room by causing reversible platelet dysfunction, altering coagulation, and enhancing fibrinolysis.

What are the alternatives to minimize Allogenic Blood Transfusion during emergency? [41]

In theater: The best way to avoid the need for transfusion is by minimizing blood loss. A number of simple anesthetic and surgical techniques may be used to achieve this objective. They include:

Anesthetic Techniques

- Avoid hypertension and tachycardia due to sympathetic overactivity by ensuring adequate levels of anesthesia and analgesia.
- Avoid coughing, straining and patient maneuvres, which increase venous blood pressure.
- Avoid hypercarbia causing vasodilatation which will increase operative blood loss.
- Use regional anesthesia, such as epidural and spinal anesthesia where appropriate.
- Avoid hypothermia in the perioperative period.
- Controlled hypotension in experienced hands.

Surgical Techniques

- Training, experience and care of the surgeon are the most crucial factors.
- Meticulous attention to bleeding points—use of diathermy.
- Posture: The level of the operative site should be a little above the level of the heart, e.g. Trendelenberg position for lower limb, pelvic and abdominal procedures. Head-up posture for head and neck surgery. Avoid air embolism if a large vein above heart level is opened during surgery.
- Tourniquets wherever applicable: The inflation pressure of the tourniquet should be approximately 100 to 150 mmHg above systolic blood pressure of the patient. Tourniquet should not normally be used in patients with sickle cell disease or trait.
- Vasoconstrictors : Infiltration of the incision site with adrenaline (with or without local anesthetic agent).
- Postoperative period: Give adequate analgesia because the postoperative pain can cause hypertension and restlessness, which can aggravate bleeding, e.g. following limb surgery, postoperative elevation will reduce swelling, control venous blood loss and reduce pain. Give iron supplements (ferrous sulphate 200 mg tds) to restore hemoglobin level.

Intraoperative Blood Salvage

- Blood salvage is the collection of blood shed from the wound or body cavity and its subsequent infusion into the same patient. Contraindications to salvage include blood contaminated with bowel contents, bacteria, fat, amniotic fluid, urine, malignant cells and irrigation fluids. One should not reinfuse salvaged blood more than 6 hours old, since hemolysis of red cells is likely to be complete.
- Intraoperative blood salvage usually becomes cost-effective when 1,500 ml or more of blood is collected. It is also indicated if the patient has a rare blood type and adequate amounts of allogenic blood cannot be found. Intraoperative blood salvage is often acceptable to Jehovah's Witnesses, provided the salvaged blood remains in continuity with the patient's circulation.
- Methods of blood salvage:
  - Gauze filtration: Using aseptic technique, blood is collected with a ladle or small bowl and filtered through a gauze into a bottle containing anticoagulant.
  - Simple suction collection systems: Suction pressure should be as low as possible to avoid hemolysis of red cells.
  - Automated suction collection systems (cell savers): These are commercially available and are routinely used for many operation associated with substantial blood loss in some countries. They collect, anticoagulate, wash, filter and

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Salient Features

- A Practical Approach to Anesthesia for Emergency Surgery is a compilation, by four editors, of cumulative experience of 30 contributors of Lokmanya Tilak, Municipal Medical College and General Hospital, Sion, Mumbai, Maharashtra, India.
- A whole section written on general principles of management of emergencies including choice of anesthetics and transfusion therapy. A chapter devoted to challenges in patients with medical disorders coming for emergency surgeries. Separate chapters cover special considerations in obstetric and pediatric patients.
- Elaborates in great detail the anesthetic management of all routinely encountered general surgical, obstetric, ENT and ophthalmic emergencies.
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