

The background of the slide is a dense field of red blood cells, depicted as biconcave discs in various shades of red. Some cells are in sharp focus in the foreground, while others are blurred in the background, creating a sense of depth. The overall color palette is monochromatic, dominated by different tones of red.

Massive Transfusion Complications

Reyhaneh Abri
Anesthesiologist

Tabriz University of Medical Sciences

Obstetric Massive Transfusion



Massive Transfusion (MT): Introduction

- **Obstetric Hemorrhage** is a common cause of **Massive Transfusion**

In adults, several definitions of MT exist based on:

- The **Volume** of the blood products transfused
 - The **Time** frames over which these transfusions occurred
1. Transfusion of ≥ 10 u PC within 24 h
 2. Replacement of **Total Blood Volume** (TBV) of adult within 24h
 3. Transfusion of ≥ 6 u PC within 12 h
 4. Transfusion of 4u PC in 1h with anticipation of continued need for blood product
 5. Replacement of 50% of the TBV by blood products within 3 h

Table 1 TBV estimation: TBV for adults based on Gilcher's rule of five for blood volume (in ml kg⁻¹ body weight)

Patient	Fat	Thin	Normal	Muscular
Male	60	65	70	75
Female	55	60	65	70

Massive Transfusion: Introduction

- The **Aim** of MT is to maintain:
 - ❑ **Adequate Circulation** (volume status, cardiac output, oxygen carrying capacity, tissue oxygenation)
 - ❑ **Hemostasis** (management of bleeding and coagulation abnormalities, changes in ionized calcium, potassium, and acid-base balance)
- Optimal management of MT requires coordination between clinical, laboratory, and hematology **Teams**.

Massive Transfusion Complications

- MT is a lifesaving treatment of hemorrhagic shock, but high volume and rapid transfusion episodes can be associated with significant **complications**.
- ⊗ The **lethal triad** associated with MT may result in **high mortality**:
 - ✓ **Acidosis**
 - ✓ **Hypothermia**
 - ✓ **Coagulopathy**
- Close monitoring of **Metabolic** and **Coagulation** function is essential to prevent the **lethal triad**.

Massive Transfusion Complications

❑ Transfusion reactions

- Allergic
- Hemolytic transfusion reaction
- Febrile non-hemolytic transfusion reaction

❑ Coagulopathy

- Acidosis, Hypothermia
- Dilutional

❑ Metabolic and Electrolyte Abnormalities

- Citrate toxicity
 - Hypocalcemia
 - Hypomagnesemia
 - Metabolic alkalosis
 - Hyperkalemia

❑ Transfusion-associated circulatory overload (TACO)

❑ Transfusion-associated acute lung injury (TRALI)

Alterations in hemostasis

Coagulopathy in Massive Transfusion

Coagulopathy may have two etiologies:

1. Acute traumatic coagulopathy

Shock and the associated physiologic changes

- **Acidosis** (hypoxia-induced)
- **Hypothermia**,
- **Factor consumption** during bleeding from the placental bed
- **Reduced activity** of coagulation factors
- **Fibrinolysis**
- **DIC**

2. Dilutional coagulopathy

- **Coagulation Factors**
- **Dilutional Thrombocytopenia**

Alterations in hemostasis

Coagulopathy in Massive Transfusion

Coagulopathy may have two etiologies:

1. Shock

- Acidosis
- Hypothermia

2. Dilutional coagulopathy

- Coagulation Factors
- Dilutional Thrombocytopenia

Coagulopathy in Massive Transfusion

➤ Acidosis

- The pH of a unit of blood at the time of collection is 7.10 due to citric acid and phosphate present in the anticoagulant/preservative in the collection bag.
 - The pH then falls 0.1 pH unit/week due to the production of lactic and pyruvic acids by the red cells.
- Acidosis does not develop in a massively bleeding patient even if "acidic" blood is infused as long as tissue perfusion is maintained.

Coagulopathy in Massive Transfusion

➤ Acidosis

- ✓ Lactate production in hypoperfused tissues
 - ✓ Interferes with assembly of coagulation factor complexes
 - As a result, the activity of the factor xa/va prothrombinase complex at a PH of 7.2, 7.0, and 6.8 is reduced by 50, 70, and 80 percent, respectively.
 - ✓ Decreases enzymatic activity of clotting factors
 - ✓ Impaired platelet aggregation
 - ✓ Delayed and reduced thrombin production lead to delayed fibrin production, altered fibrin structure, and fibrinolysis
-
- Monitor acid–base status
 - Use fresh blood
 - Bicarbonates.

Coagulopathy in Massive Transfusion

Coagulopathy may have two etiologies:

1. Shock

- Acidosis

- Hypothermia

2. Dilutional coagulopathy

- Coagulation Factors
- Dilutional Thrombocytopenia

Coagulopathy in Massive Transfusion

➤ Hypothermia

- Core temperature less than 36 degrees Centigrade.
- May be due to the environmental conditions, infusion of a large amount of inadequately warmed crystalloid and blood products, exposure of body cavities, and impaired thermal control.
- **10 units of cold** blood products and **an hour** of surgery can lead to a **3°C** drop in core temperature and **hypothermic coagulopathy**.

Deleterious effects on the **hemostatic mechanisms**:

- Reduces the **enzymatic activity** of plasma coagulation proteins
- Preventing the **activation of platelets** predisposing to **DIC**.

Coagulopathy in Massive Transfusion

- **Hypothermia** can cause
 - ✓ Impairment of **oxygen delivery** by the RBC
 - ✓ Decreased cardiac output
 - ✓ Increased risk of cardiac arrhythmias
 - ✓ Increased cardiac toxicity secondary to electrolyte derangement

➤ **Prevention of hypothermia:**

Blood warmer when more than three units are transfused.



Coagulopathy in Massive Transfusion

Coagulopathy may have two etiologies:

1. Shock

- Acidosis
- Hypothermia

2. Dilutional coagulopathy

- Coagulation Factors
- Dilutional Thrombocytopenia

Dilutional Coagulopathy in MT

1. Coagulation Proteins

- The transfusion of PC and a crystalloids will result in dilution of plasma **clotting proteins**, leading to prolongation of PT and PTT.
- There will be an approximate **10% decrease** in the concentration of clotting proteins for each **500 mL** of blood that is replaced.
- **Additional bleeding** based solely on dilution can occur when the level of individual coagulation proteins **falls to 25% of normal**. This usually requires 6 to 10 units of PC.

Coagulopathy in Massive Transfusion

Coagulopathy may have two etiologies:

1. Shock

- Acidosis
- Hypothermia

2. Dilutional coagulopathy

- Coagulation Factors
- Dilutional Thrombocytopenia

Dilutional Coagulopathy in MT

2. Dilutional Thrombocytopenia

- Each **10-12 u** of transfused PC are associated with a **50% fall** in the platelet count; thus, significant thrombocytopenia can happen.
- For replacement therapy in this setting, six units of platelets or one apheresis concentrate should be given; each unit should increase the platelet count by 5000/microL or 30,000/microL for a full six u adult dose.

Coagulopathy in Massive Transfusion

- **Colloids** such as hydroxyl ethyl starch can adversely affect the function of **VWD**. It is advisable to **limit** the administration of **colloids** as far as possible.

Coagulopathy Monitoring in MT:

- Measurement of the **PT, PTT, platelet** and **fibrinogen** or a **viscoelastic test (TEG)** after the administration of every **5 to 7 u of PC** may help to assess coagulation status serving as guide for further transfusion
- Replacement therapy should be based on these parameters rather than on any formula.

Metabolic Complications of MT

Citrate Toxicity:

- Large amounts of citrate are given with MT, since blood is anticoagulated with sodium citrate and citric acid.
- PC contains only traces of citrates whereas **platelets** and **FFP** transfusions contain **higher** concentration of citrate
- Complications of citrate infusion:
 - ✓ **Metabolic alkalosis**
 - ✓ **Hypocalcemia**
 - ✓ **Hypomagnesaemia**
- Measured plasma **electrolyte** levels at **baseline** and **every hour after initiation of MT**, with specific assessment for hyperkalemia, hypomagnesemia, hypocalcemia.

Metabolic Complications of MT: Citrate Toxicity

Hypocalcemia (Ionized Calcium level < 1.15 mmol/L)

- The first pass of citrate through the liver will lead to metabolic breakdown in less than **5 min**. A standard blood transfusion may hardly cause any alteration in the calcium levels.
- However in **MT** accompanied with **hypothermia** then the **liver function** gets altered, thereby **decreasing the clearance** of citrate from the blood leading to increased concentration of citrate in the circulation.
- This causes **binding of citrate to ionic calcium** leading to **hypocalcemia**.

➤ Clinical findings in hypocalcemia:

- Tetany, prolonged QT interval, decreased myocardial contractility, HOTTN, narrow pulse pressure and elevated central venous pressure.
- Hypocalcemia may also predispose to hyperkalemia induced arrhythmia, VF and pulseless electrical activity.

Metabolic Complications of MT: Hypocalcemia

- Monitor ionized calcium level and correct if necessary:
 - ❑ **Calcium Gluconate** 10%, 10ml (1gr) IV for each 5u of blood infused over 5-10min.
 - ❑ **Calcium Chloride** 10%, only 2 to 5 ml per 5u of blood over 5-10min.
- **Calcium Chloride** is preferable in the presence of **abnormal liver function**, since does not require normal liver function to release ionized calcium.
- In contrast, **Calcium Gluconate** metabolism is decreased in the setting of abnormal liver function, resulting in a slower release of ionized calcium.
- Care must be taken to avoid administering too much calcium and inducing hypercalcemia, ideally by monitoring the **ionized calcium concentration**.

Metabolic Complications of MT: Citrate Toxicity

Metabolic alkalosis

- In MT and **citrate toxicity**, the metabolism of each mmol of citrate generates 3 mEq of **bicarbonate** (for a total of 23 mEq of bicarbonate in each unit of blood).
- **Metabolic alkalosis** can occur if the renal ischemia or underlying **renal disease** prevents urine excretion of excess bicarbonate.
- ✓ Monitor acid–base status

Metabolic Complications of MT: Citrate Toxicity

Hypomagnesaemia

- In MT may be due to two reasons:
 - over administration of magnesium poor fluids
 - citrate toxicity and binding of magnesium to citrates.
- **Hypomagnesaemia** can lead to **prolonged QT** interval, **arrhythmia** as well as contribute to **coagulopathy**.

Metabolic Complications of MT

Hyperkalemia

- ✓ The **extracellular** K^+ increases with **time** in stored blood which is attributable to the inactivation of the RBC **membrane ATPase pump** or **hemolysis** of RBC or **irradiation**.
- ✓ In PC storage, K^+ increases by 1 mEq/day, increasing from 3 mEq/L at the time of donation to 45 mEq/L during 42 days of storage. **Irradiation** can increase this rate to 1.5 mEq/day.
- During MT through **central lines**, a large bolus of extra cellular K may reach the **right heart** leading to **dysrhythmias**
- **Pre-existing cardiac** and **renal** diseases are at risk for hyperkalaemia

Metabolic Complications of MT

Prevention of Hyperkalemia

In these patients, to minimize the risk:

- Select **Fresh** PC collected **less than 10 days** prior to transfusion.
- **Wash** any unit of PC immediately before infusion
- Transfuse the blood through an IV line which is **far** away from the right atrium
- Concomitant **correction of acidosis** is important in enhancing the intracellular uptake

Treatment:

Glucose Insulin drips, beta2 agonist, bicarbonates and furosemide, IV calcium

Massive Transfusion Complications

- Transfusion-related acute lung injury (TRALI) and Transfusion-associated circulatory overload (TACO) can occur with **Massive Transfusion**.

Complications of MT

Transfusion-Associated Circulatory Overload (TACO)

- Typically occurs in MT, especially in **underlying cardiovascular or renal disease**.
- **Incidence:** 1 % or more of transfused individuals
- New onset or exacerbation of the following **within 12h of the end** of a transfusion:
 - ✓ Respiratory distress: dyspnea, or tachypnea, hypoxia
 - ✓ Pulmonary edema due to volume excess, rales and/or wheezing
 - ✓ Elevated brain natriuretic protein (BNP) or N-terminal pro- BNP (NT-pro BNP)
 - ✓ Evidence of positive fluid balance (elevated central venous pressure)
 - ✓ Tachycardia, Increased BP
 - ✓ The cardiac examination may show an S3 heart sound

❑ **D/D:** TRALI

Complications of MT

Transfusion-Associated Circulatory Overload (TACO)

Management

Treatment is similar to of **cardiogenic** pulmonary edema from other causes.

Supportive care:

- Once the diagnosis is strongly suspected, stop the transfusion
- Oxygen and Ventilatory support
- Upright position
- Diuretics

Complications of MT

Transfusion Related Acute Lung Injury (TRALI)

- Incidence: **1/5000-1/190,000**
 - The incidence **increases** as **number** of blood products given increases.
 - TRALI can be seen with **any blood component** in any patient.
 - **Immune mediated** process where in the **donor antibodies** activate the receptors on the leucocytes causing pulmonary injury, endothelial damage and capillary leakage.
- **Acute onset** of hypoxemia during or **within 6 h** of transfusion, but could be delayed up to even 24 h
 - **Non-cardiogenic** pulmonary edema, PAO₂/FIO₂ less than 300 mmHg, bilateral fluffy infiltrates in CXR, cyanosis, and hypotension.
- **Mortality: 5-10%.**
 - D/D: TACO

Complications of MT

Transfusion Related Acute Lung Injury (TRALI)

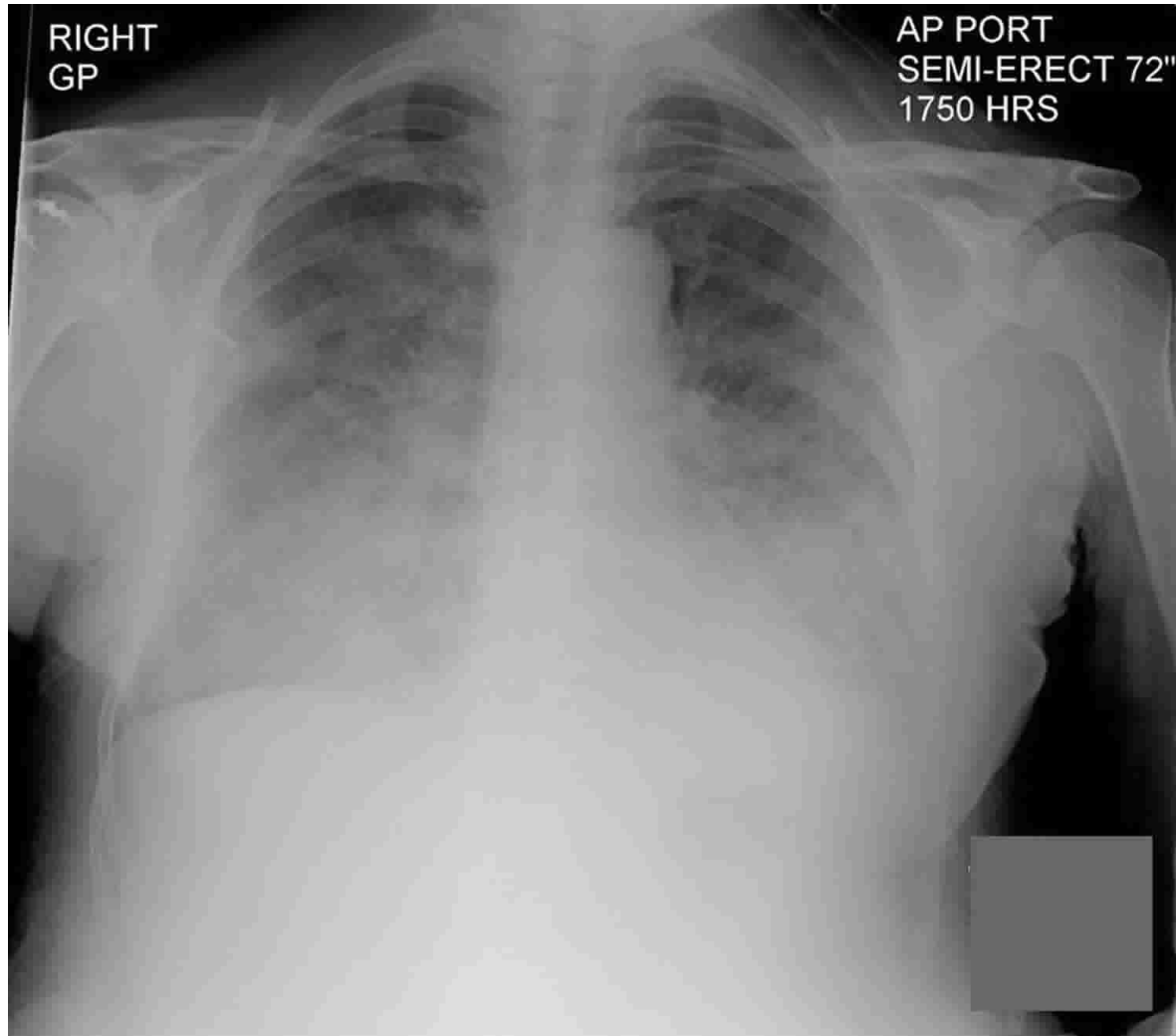
Management

- When TRALI is suspected, Stop transfusion immediately
- V/S and respiratory status should be assessed
- CXR
- The blood bank should be notified that TRALI is suspected.
- Therapy is **supportive** with supplemental oxygen and MV support

Prevention

- Donations from **multiparous women** are most likely to contain antileucocyte Ab.
- **High plasma-volume-containing** products from:
 - **Male** donors
 - Female donors with **no prior pregnancy**
 - Donors who test negative for **HLA-antibodies**
 - Washed blood products.

Transfusion Related Acute Lung Injury (TRALI)





Thank You