

Massive Transfusion

دکتر تایماز امیراصلائی

استادیار بیهوشی دانشگاه علوم پزشکی ایران

MASSIVE TRANSFUSION

- The transition from administration of whole blood to component therapy in the 1970s created new challenges in transfusion medicine
- FFP was not usually required as a separate component with the administration of whole blood, and significant thrombocytopenia usually occurred only after 15 to 20 units of blood
- With the change from whole blood to PRBCs, the incidence of coagulopathies increased
- Kornblith and associates concluded that the laboratory clotting profile of 1:1:1 plasma/platelets/RBC was significantly more hemostatic when compared with a 1:1:2 ratio. Results of the Prospective Observational Multicenter Major Trauma Transfusion (PROMMTT) study supported this idea.

-
- These aggressive uses of FFP, platelets, and other blood products have only been shown to be beneficial in response to coagulopathies from massive blood transfusions. Aggressive plasma administration to other transfused patients was associated with an increased rate of serious complications, including acute respiratory distress syndrome (ARDS) and organ dysfunction.
 - A retrospective study showed that a higher FFP-PRBC ratio was associated with the need for advanced interventional procedures in patients with postpartum hemorrhage.

TYPE-SPECIFIC, PARTIALLY CROSSMATCHED BLOOD

- When using uncrossmatched blood, it is best to obtain at least an ABO-Rh typing and an immediate-phase crossmatch. This incomplete crossmatch is accomplished by adding the patient's serum to donor RBCs at room temperature, centrifuging it, and then reading it for macroscopic agglutination. This takes 1 to 5 minutes and eliminates serious hemolytic reactions resulting from errors that may occur in ABO typing.
- few unexpected antibodies outside the ABO systems most of which are not clinically significant.

TYPE O RH-NEGATIVE (UNIVERSAL DONOR), UNCROSSMATCHED BLOOD

- Type O blood lacks A and B antigens and consequently cannot be hemolyzed by anti-A or anti-B antibodies in the recipient's plasma
- when typing or crossmatching is not available.
- If emergency transfusion of more than 2 units of type O Rh-negative, uncrossmatched whole blood is used, the patient cannot be switched to his or her blood type (A, B, or AB) once that is determined 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.

Fresh Whole Blood

- fresh blood as blood stored at 1°C to 6°C within 8 hours after collection and used within 24 hours
- Whole blood stored for 24 hours at 4°C has less hemostatic effects than blood stored for less than 6 hours because of decreased platelet aggregability
- typed and crossmatched warm whole blood was extremely effective in treating the coagulopathy from massive transfusions

Complications

COAGULATION ABNORMALITIES :

- consumptive coagulopathy from tissue hypoperfusion
- manifested increased protein C levels
- most important cause are the dilution of coagulation factors by volume administration (e.g., crystalloid, colloid, PRBC), and the duration of hypotension and hypoperfusion.
- Patients who have adequate perfusion and are not hypotensive for a long period tolerate administration of multiple units of blood without developing a coagulopathy.
- hypotensive and has received many units of RBCs will develop a coagulopathy that resembles DIC
- differential diagnosis is dilutional thrombocytopenia, deficiency of factors V and VIII, a DIC-like syndrome, or a transfusion reaction
- signs include oozing into the surgical field, hematuria, gingival bleeding, petechia, bleeding from venipuncture sites, and ecchymosis.

THROMBOCYTOPENIA

- platelet count less than $150 \times 10^9/L$ or more than 50% decrease
- Clinical bleeding
- during surgery $50 \times 10^9/L$
- spontaneous bleeding $10 \times 10^9/L$
- Independent of whether whole blood or PRBCs, few viable platelets exist in a unit of blood stored for more than 24 hours.
- Thrombocytopenia can trigger a hemorrhagic diathesis in a patient who has received multiple units of bank blood.
- Platelet counts decreased to less than $100 \times 10^9/L$ when 10 to 15 units of blood were given
- bleeding problem from dilutional thrombocytopenia $75 \times 10^9/L$
- patients with an acute induced thrombocytopenia develop a hemorrhagic diathesis at a much higher platelet count than chronic thrombocytopenia
- Growing use of point-of-care viscoelastic tests is becoming more common.

LOW LEVELS OF FIBRINOGEN AND FACTORS V AND VIII

- fibrinogen is critical for effective clot formation, and its monitoring and supplementation as the treatment of major bleeding should be recognized.
- Many prospective studies of fibrinogen supplementation in acquired bleeding report that it is the most effective method of supplementation
- Factors V and VIII may also be affected during storage and significant transfusion. These factors decrease to 50% and 30% of normal, respectively, in whole blood after 21 days of storage and are not present in PRBCs. By 35 days of storage, factor V and factor VIII fall further to approximately 20% activity of normal.
- FFP, which contains all the factors, has been recommended
- this practice is of questionable benefit because only 5% to 20% of factor V and 30% of factor VIII are needed for adequate hemostasis during surgery, and even during massive blood transfusion, factors V and VIII rarely decrease below those levels.

DISSEMINATED INTRAVASCULAR COAGULATION–LIKE SYNDROME

- The coagulation system consists of clotting and fibrinolytic mechanisms
- With this DIC-like syndrome, the clotting system is deranged, leading to disseminated fibrin deposition, which renders the blood unclottable. The deposited fibrin may severely alter the microcirculation and lead to ischemic necrosis in various organs, particularly the kidney.
- Reason: hypoxic acidotic tissues release tissue thromboplastin directly or through the protein C pathway. may cause fibrinolysis. The coagulation system is activated by tumor necrosis factor and endotoxins, resulting in consumption of factors I, II, V, and VIII, and platelets. In an attempt to counteract the hypercoagulable state, the fibrinolytic system is activated to lyse the excessive fibrin. the result is massive focal necrosis or more generalized activation of the coagulation system.

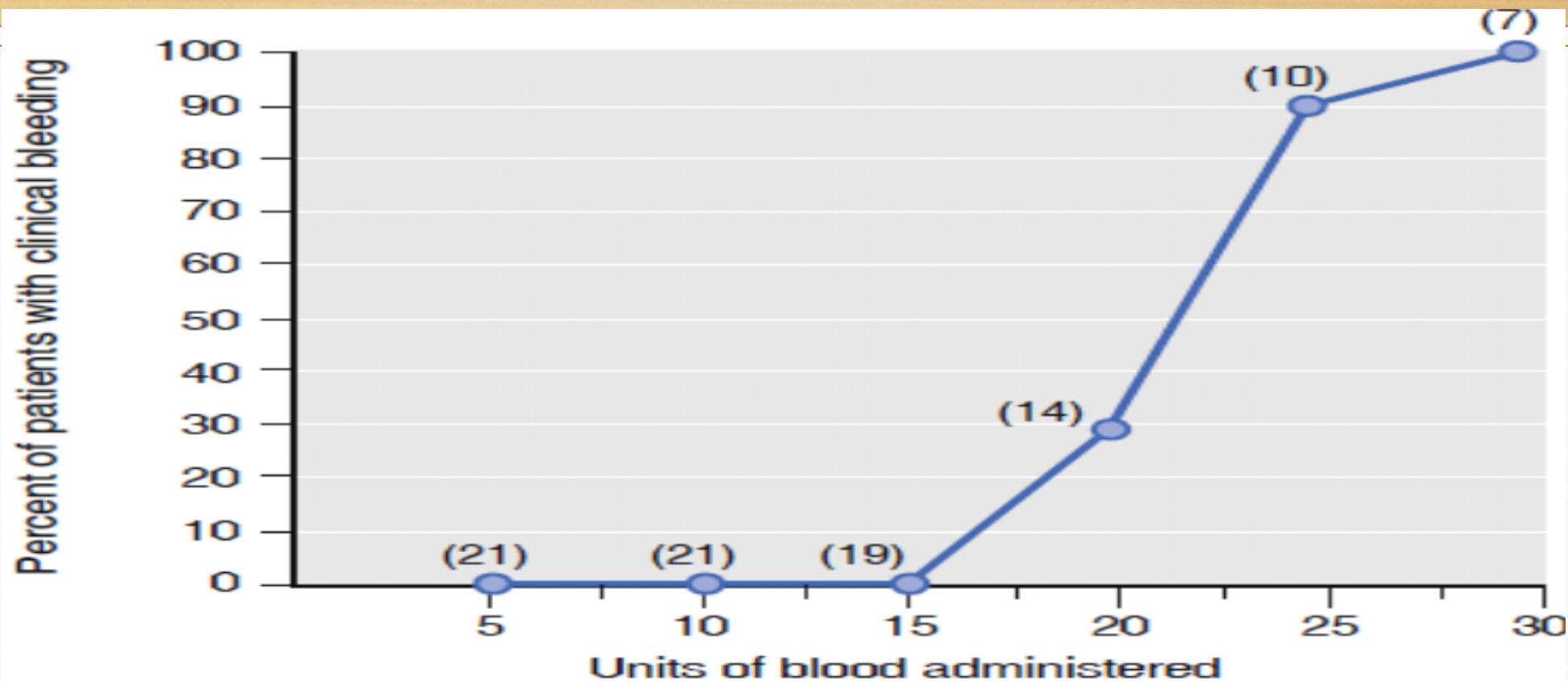


Fig. 49.9 Correlation between units of blood administered and percent of patients who had a hemorrhagic diathesis. The numbers in parentheses represent the number of patients at each data point. (From Miller RD. Transfusion therapy and associated problems. *Reg Refresher Courses Anesthesiol.* 1973;1:101.)

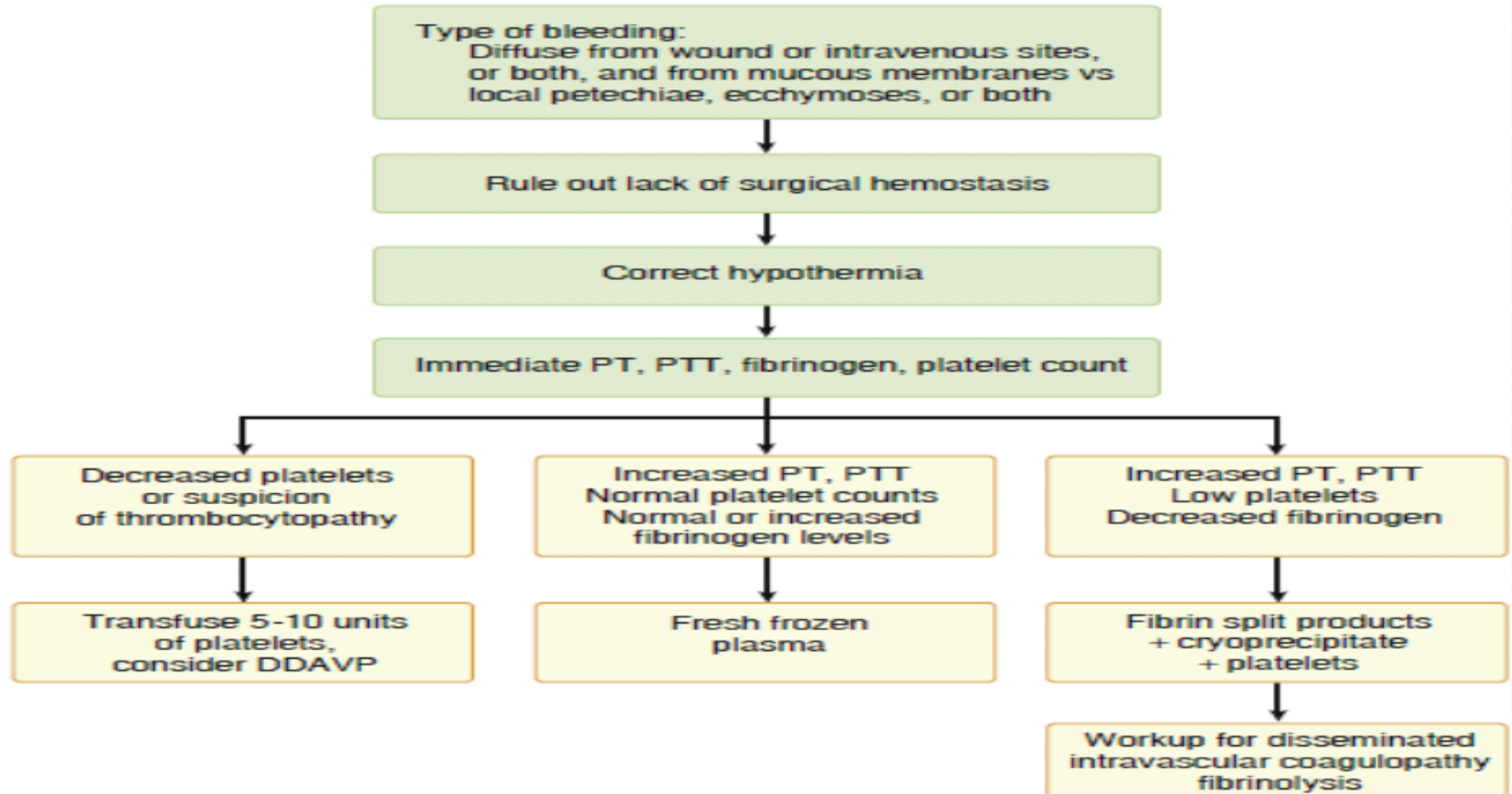
DIAGNOSIS&TREATMENT HEMORRHAGIC DIATHESIS AFTER BLOOD TRANSFUSIONS

- diagnosis is often difficult. In addition to clinical examination of the patient, various coagulation laboratory tests may be helpful.
- One traditional approach has been to obtain a blood sample for platelet count, PTT, and plasma fibrinogen level; observation of a clot for size, stability, and lysis; and observation of the plasma for evidence of hemolysis.
- If the PTT is 1.5 times normal or more and other tests are normal, the bleeding is probably a result of very low levels of factors V and VIII. This can be treated with FFP or with cryoprecipitate
- Platelet concentrates are contained in a 50-mL unit and provide approximately 70% of the platelets in a unit of blood.

DIAGNOSIS&TREATMENT HEMORRHAGIC DIATHESIS AFTER BLOOD TRANSFUSIONS

- fresh blood is extremely effective in treating transfusion-induced coagulopathies. Lavee and associates²³² found that 1 unit of fresh whole blood was as effective as, if not superior to, 8 to 10 platelet units.
- DIC is likely with thrombocytopenia, hypofibrinogenemia, and lysis of clot.
- dilution of certain coagulation values may be more profound with the use of PRBCs rather than whole blood.
- With use of PRBCs, fibrinogen levels decreased significantly in contrast to use of whole blood, in which fibrinogen levels remained unchanged unless DIC is present

Workup and Initial Therapy for Coagulopathy



Citrate Intoxication and Hyperkalemia

- Citrate intoxication leads to hypocalcemia, dysrhythmia, and hypotension due to the sequestration of ionized calcium by citrate
- Infusion of more than 1 unit of blood every 10 minutes can lead to decreasing ionized Ca^{2+} levels. Even at these rates of infusion, ionized calcium levels do not decrease enough to cause bleeding.
- Citrate reactions in the setting of apheresis for donation of blood components, however, are more common and in one study occurred in more than 5% of donations.
- hyperkalemia as a result of transfusion is relatively rare
- For clinically significant hyperkalemia to occur, banked blood must be given at a rate of 120 mL/ minute or more. Although still rare, hyperkalemia can occur more frequently in patients with impaired renal function

Temperature

- Administration of blood that has been stored at 4°C can decrease the recipient's temperature and should be avoided if possible due to complications from hypothermia
- Hypothermia can interfere with the coagulation process. Even small decreases in body temperature can significantly impair coagulation factors and platelet function.
- If the temperature decreases to less than 30°C, ventricular irritability and cardiac arrest may occur. Shivering from even mild hypothermia increases metabolic demands and is counterproductive to tissue perfusion, especially in settings where anemia or hypoperfusion is contributing to tissue ischemia
- Decreases in body temperature can be prevented by warming the blood to body temperature before transfusing. Perhaps the safest and most common method of warming blood is to pass it through plastic coils or plastic cassettes in a warm water (37°C-38°C) bath or warming plates. These heat exchangers should have upper (e.g., 43°C) and lower (e.g., 33°C) temperature limits

Acid-Base Abnormalities

- When this solution is added to a unit of freshly drawn blood, the pH of the blood immediately decreases from 7.4 to 7.1.
- As a result of accumulation of lactic and pyruvic acids by RBC metabolism and glycolysis, the pH of bank blood continues to decrease to approximately 6.9 after 21 days of storage.
- The empirical administration of sodium bicarbonate is not indicated administration should be guided by analyses of arterial blood gases.
- Blood transfusions provide citrate, which can lead to the endogenous generation of bicarbonate. In some patients, this leads to a significant incidence of metabolic alkalosis after blood transfusions

TABLE 49.18 Noninfectious Hazards of Transfusion

| Transfusion Reaction | Incidence (per 10 ⁵ Transfusions) | Etiology | Therapy | Prevention |
|-------------------------|---|--|--|--|
| Febrile | All components: 70-6800 | Storage-generated proinflammatory cytokines Patient antileukocyte antibodies bind to donor leukocytes | Stop transfusing Give antipyretics Supportive care | Prestorage leukoreduction |
| TACO | All components: 16.8-8000 Practice-dependent | Circulatory overload Patients with cardiac or renal disease, infants, and the critically ill are at increased risk | Stop transfusing Give diuretics Oxygen | Identify patients at high risk Transfuse slowly |
| TRALI | Erythrocytes: 10-20 Platelets/plasma: 50-100 | Passive transfusion of donor antibodies Storage-generated toxic lipids | Supportive care | Remove high-risk donors from the donor pool |
| Allergic | All components: 3000 mild, 2 anaphylactic | Mild reactions: Transfusion of soluble antigens in donor plasma Anaphylaxis: IgA deficiency or other recipient protein deficiency | Stop transfusing ASA monitors Large-bore IV access Epinephrine Antihistamines Supportive care | Pretransfusion antihistamine use remains common practice despite limited evidence |
| Hemolytic | Erythrocytes: 1.1-9.0 | Donor antibodies bind to patient erythrocytes Patient antibodies bind to donor erythrocytes | Stop transfusing Repeat matching Supportive care Treat DIC | Standard operating procedures |
| TRIM | Unknown | The mechanism is unknown but may depend on the presence of donor leukocytes | Treat complications (e.g., infection, malignancy) | Prestorage leukocyte reduction may be beneficial, but this approach is controversial |
| Microchimerism | All components: 5000-10,000 massive transfusion | Permanent residence of donor cells in recipient | Unknown | Unknown |
| Posttransfusion purpura | All components: 2 | Recipient alloantibodies attack donor platelet antigens | IVIg | Avoid units positive for implicated HPA antigens in patients with a history of PTP |
| Hypotensive | Unknown | Production of kinins by the activation of the contact system Patients on ACE inhibitors are at increased risk | Stop transfusing ASA monitors Large-bore IV access Supportive care | Avoid the use of negatively charged leukocyte reduction filters |
| Graft-versus-host | Varies by patient population | Transfusion into immunocompromised host Transfusion of donor cells closely matching HLA type | No consensus exists Consider bone marrow transplant | Gamma irradiation of cellular products |

