



TRANSFUSION REACTIONS

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● Non hemolytic

1. FNHTR (The febrile nonhemolytic transfusion reaction)
2. *Allergic* Reactions
3. Anaphylactic Reactions
4. *Bacterial* Contamination
5. *Circulatory Overload*
6. TRALI (*Transfusion-Related Acute Lung Injury*)
7. PTP (Post-transfusion Purpura)
8. *Hemosiderosis*
9. GVHD (Graft-versus-Host Disease)

● HTR (Hemolytic Transfusion Reactions)

The febrile nonhemolytic transfusion reaction (FNHTR)

- is defined by a temperature increase of greater than 1°C during up to two hours after a transfusion of blood and when other causes have been excluded.
- accompanied by chills, nausea, vomiting, malaise, and headache.
- FNHTRs are seen in 1 % to 3% of RBC transfusions
 - and in up to 30% of platelet transfusions.
- more frequently in patients who have been repeatedly transfused
 - or women who have had multiple pregnancies.
- mechanism : alloantibodies in the recipient reacting with HLA antigens
 - Cytokines generated by leukocytes during storage of blood components are now thought to play a major role, particularly during platelet transfusion.
 - This accumulation of TNF1, IL-1, IL-6

Allergic Reactions

- hives (urticaria) and itching, with or without wheezing and stridor.
- Patients who have only urticarial reactions rarely, if ever, progress to a systemic generalized reaction (see later under Anaphylactic Reactions).
- These allergic reactions are usually IgE mediated, and occur predominantly in plasma- containing products.
- Released histamine causes respiratory and gastrointestinal smooth muscle to contract and capillaries to dilate. The clinical response to generalized histamine release is headache, facial flushing, hypotension, dyspnea/wheezing, vomiting, and diarrhea.

Anaphylactic Reactions

- Anaphylaxis, a potentially lethal complication of blood transfusion, typically occurs suddenly, after transfusion of only a few milliliters of blood. It is characterized by acute respiratory distress, laryngeal edema, coughing and wheezing due to bronchospasm, and profound hypotension and shock. Other accompanying symptoms may include flushing of the skin, nausea, vomiting, and diarrhea

Bacterial Contamination

- in red cells is usually due to cold-growing, gram-negative, endotoxin-producing bacteria such as *Pseudomonas*, *Citrobacter freundii*, *E. coli*, *Yersinia enterocolitica*,
- in platelets the contaminating organisms can be either gram-positive or negative.
- The reaction to the transfusion of heavily contaminated blood is characterized by bright red malar (facial) flushing, high fever, a subjective feeling of heat, abdominal cramps, vomiting, diarrhea, and shock
- Sometimes DIC may also occur.
- Treatment consists of antibiotics and steroids.
- the presence of clots or clumping, dark color of the plasma due to hemolysis, or the presence of gas in the unit

Circulatory Overload

- more frequently seen in older patients, and those with compromised cardiac or pulmonary function.
- Patients with severe chronic anemia (Hb, 4 to 5 g/ dL) are at risk because they may have compensated high-output cardiac failure, which may decompensate with the added volume of transfusion.
- Symptoms include dyspnea and coughing from pulmonary edema and a sudden increase in systolic blood pressure

Transfusion-Related Acute Lung Injury **(TRALI)**

- occurs rarely (1 in 10,000 transfusion events)
- characterized by bilateral noncardiogenic pulmonary edema.
- It typically occurs within the first one to six hours after transfusion
- Severe hypoxemia and, on chest x-rays, bilateral pulmonary infiltrates are seen.
- It is caused by either (1) donor leukoagglutinins (neutrophil-specific antibodies) or HLA antibodies that react with the recipient's leukocytes to produce WBC aggregates that are trapped in the pulmonary capillaries resulting in capillary leakage
- (2) antibodies in the recipient reacting with donor leukocytes.
- TRALI has also been attributed to other substances, including lipid activators, causing activation of the complement components C3a or C5a, which subsequently induce release of mediators, producing capillary leak in lung tissue.

Post-transfusion Purpura(PTP)

- characterized by severe thrombocytopenia occurring about a week after a blood transfusion.
- In 80% of cases, platelet counts are below 10,000/ μ L. This condition is usually caused by antibodies to platelet-specific antigens (HPAs).
- Most cases are due to antibodies to HPA-1a (PIA1) but may be caused by other platelet-specific antibodies

Hemosiderosis

- Hemosiderosis is a condition caused by iron deposition in vital organs, such as the liver and heart, with their subsequent malfunctions.
- It occurs in patients who need chronic transfusions such as thalassemics.
- Each unit of blood contains about 200 mg of iron and after 100 red cell transfusions, total body iron deposition can be significant.
- One option to reduce the total iron transfused is to use neocytes, so that fewer transfusions are necessary
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- Treatment with desferrioxamine, an iron-chelating agent, is important in lowering the body iron stores in patients with thalassemia

Graft-versus-Host Disease (GVHD)

- When immunologically competent allogeneic T lymphocytes are transfused into an individual who is severely immunocompromised because of lymphocyte deficiency or malfunction, transplanted T lymphocytes may engraft in the host's lymphoid/hematopoietic tissue and become functional. These engrafted allogeneic T lymphocytes recognize the antigens on the host's cells as foreign and mount a cellular and/ or humoral immune response against the host, creating the syndrome of GVHD.
- Bone marrow transplant GVHD (BMT-GVHD)
- Transfusion-associated GVHD (TA-GVHD)

Bone marrow transplant GVHD (BMT-GVHD)

● Acute GVHD

- It is seen in up to 70% of allogeneic bone marrow transplant recipients,
- 20% of patients with this syndrome will die from its effects
- The first sign of acute GVHD is usually fever
- followed by a generalized maculopapular rash
- watery diarrhea and HSM, with elevated ALT-AST-BIL

● Chronic GVHD (40%)presents more than three months after HPC transplantation

- erythematous rash, most prominent in the malar and palmar areas
- progress to cutaneous atrophy and sclerosis;
- the sicca syndrome; esophageal fibrosis;
- elevated AST / ALT; restrictive and obstructive pulmonary disease;

Transfusion-Associated GVHD (TA-GVHD)

- A more aggressive form of acute GVHD is seen when severely immunosuppressed patients receive nonirradiated blood components.
- These individuals present rapidly with acute GVHD, in less than 30 days from the time they are exposed to transplanted lymphocytes.
- In addition to the usual symptoms of acute GVHD, they exhibit prominent **pancytopenia and bone marrow hypoplasia**.

Hemolytic Transfusion Reactions (HTR)

1. Nonimmune *Hemolysis*

2. immune *Hemolysis*

- Acute
 - Acute intravascular hemolysis
 - Acute extravascular hemolysis
- Delayed HTR

Nonimmune *Hemolysis*

- overheated in an improperly functioning blood warmer,
- frozen after being placed in an unmonitored refrigerator or
- placed on a windowsill during winter.
- Hemolysis can take place also when packed RBCs are diluted with a hypotonic solution such as DsW,
- RBCs are transfused through a small-bore needle
- using a blood pressure cuff.
- Calcium, found in Ringer's lactate, can cause clotting with subsequent hemolysis
- Bacterial contamination
- if a patient on quinine receives blood from a donor deficient in G6PD the donor RBCs

Immune Hemolysis

Acute intravascular hemolysis

- The most severe, life-threatening,
- almost always due to the transfusion of ABO- incompatible blood
- This ABO incompatibility causes intravascular hemolysis, shock, DIC, and subsequent renal failure.

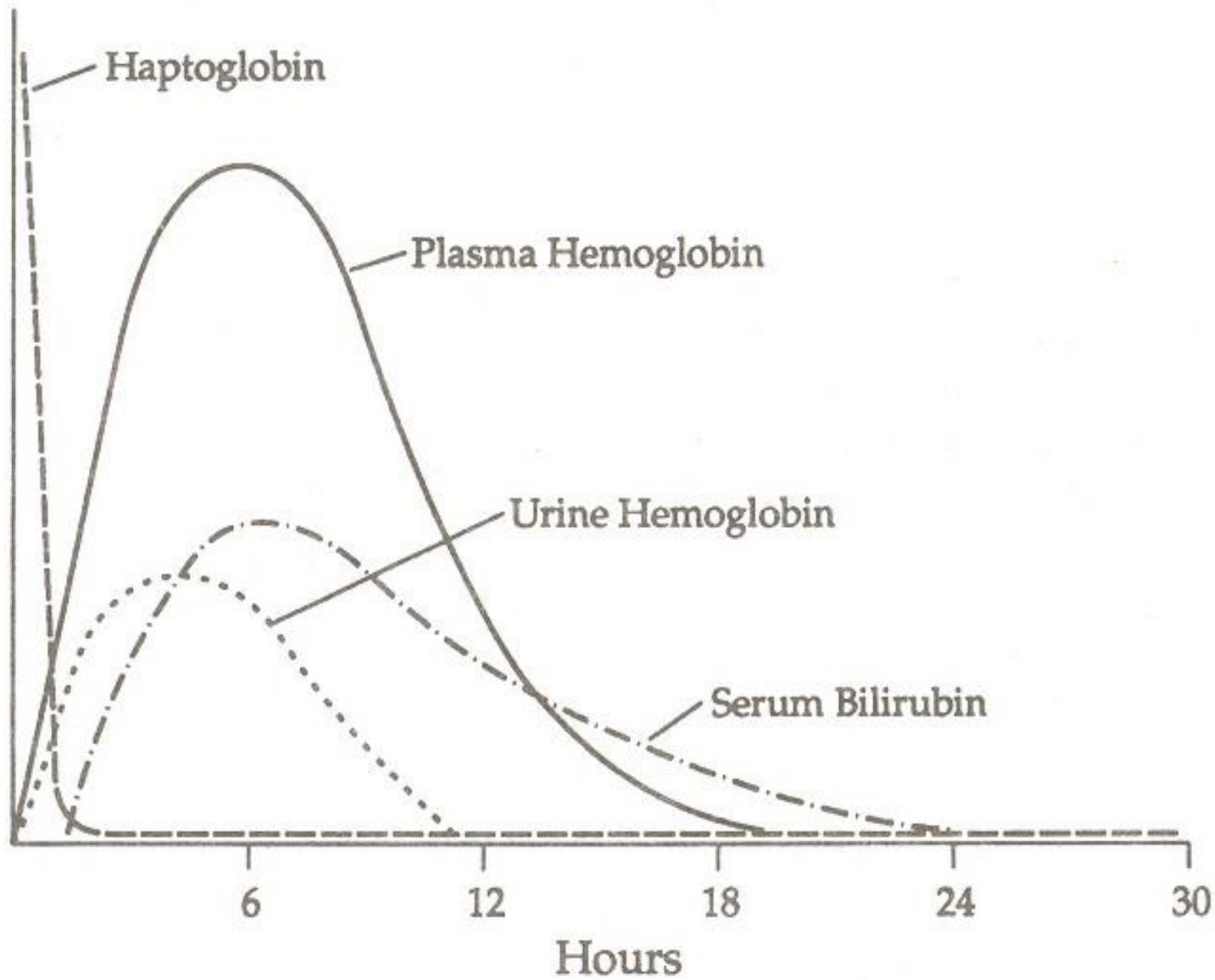
- The initial signs and symptoms include:
 - pain at the infusion site, fever, chills, chest pain, hypotension, shock, nausea, vomiting, flushing of the skin, dyspnea, hemoglobinuria, oliguria, back pain, and generalized bleeding from the severe thrombocytopenia due to DIC.
 - In the anesthetized, unconscious patient, the first signs will be hypotension and generalized bleeding at the venipuncture and surgical incision sites from thrombocytopenia

- Since severe acute hemolytic transfusion reactions are almost always due to a clerical error the transfusion reaction investigation should begin with an immediate comparison of the donor unit paperwork with the identifying information on the patient's wristband.
- It is important to try to prevent a second such reaction, in another patient, if it is found that the blood units were inadvertently switched

Acute extravascular hemolysis

- due to the non-ABO red cell systems.
- These can be serious, but are not as severe as for the ABO system
- because DIC and complement activation usually do not occur.
- Extravascular hemolysis is seen with IgG in the Rh, Kell, Kidd, and Duffy systems.
- Fever, anemia, increased bilirubin, and a positive DAT are the usual symptoms.
- Serum bilirubin may be increased four to six hours after the initiating event
- Treatment is supportive.

Incompatible Transfusion



Transfusion Reaction Investigation

- A clerical check of the compatibility tag on the blood bag, the blood bag label, and the patient identification (wrist- band) for discrepancies.
- Examination of the pretransfusion clotted blood specimen, an EDTA anticoagulated post-transfusion blood specimen, and the blood bag.
- a. Look for hemolysis in the post-transfusion specimen. If pink or red serum is present, compare to the pretransfu- sion specimen.
- b. Perform a DAT on the post-transfusion EDTA specimen. A mixed field reaction is strongly suspicious of an antibody-mediated transfusion reaction. If the DAT is negative and hemolysis has occurred but ABO incompat- ibility has been ruled out, there are several nonimmune mechanisms, mentioned earlier, that should be consid- ered as the cause of the intravascular hemolysis. Examine the unit for hemolysis, which may be due to bacterial overgrowth, or inadequate conditions of storage. If the DAT is negative and there is no evidence of hemolysis, an acute, immune, life- threatening hemolytic reaction will probably not occur

- c. Perform a Gram's stain on the blood in the bag and a culture, if necessary, to determine the presence of bacterial contamination, if indicated.
- d. Repeat the ABO /Rh typing, antibody screen, and the crossmatch to see if a patient antibody directed against donor cells is present. If an antibody is suspected, a red blood cell panel should be performed for identification of the antibody.
- 3. Examination of the post-transfusion urine. dark color (hemoglobinuria)
- 4. Determination, on a post-transfusion anticoagulated specimen for PT, PTT, platelet count, fibrinogen, and fibrin split,products, if DIC is suggested.
- 5. Measurement of Hct/Hb at frequent intervals if hemolysis is observed.

Delayed HTR

- Delayed hemolytic transfusion reactions occur as a result of an anamnestic response to renewed antigen exposure.
- A previously developed antibody may disappear and when re-exposure to the Ag occurs, a rapid Ab response usually takes place **within two weeks of transfusion**.
- These IgG antibodies are from the same antigenic systems as mentioned for extravascular hemolysis and produce the same symptoms, (JK-P1)
- but the sole manifestation of a delayed hemolytic transfusion reaction may only be a drop in hematocrit/hemoglobin

hyper- hemolysis

- An infrequent and life-threatening syndrome of "hyper- hemolysis" has been reported in patients with sickle cell disease or thalassemia, with fatality in some cases.
- The reaction may be triggered by the transfusion of RBC units to which the patient has preformed antibodies, initially undetected by antibody screening and crossmatch.
- Once the reaction starts, the patient will hemolyze all transfused units, including those appearing to be compatible.
- Increased rate of hemolysis of the patient's own red cells may also occur by "bystander immune cytotoxicity"
- Management of this reaction has included cessation of all transfusion, administration of prednisone, and in some cases intravenous immunoglobulin

