College of Medicine Feb 2024

BT part 2A

University of Baghdad
College of Medicine
2023-2024

Title: BLOOD TRANSFUSION – Part 2A

Grade: 4

Module: PATHOLOGY (Hematology)

Speaker: Professor Dr. Haithem Ahmed Al-Rubaie

MBChB (1985)

FICMS-Hematopathology (1998)

DEPARTMENT OF PATHOLOGY AND FORENSIC MEDICINE

Feb 2023

Blood Transfusion (Part 2A)

Learning Objectives: at the end of this lecture, the student will be able to:

1. Recognize the sources of errors.
2. Describe the effects of RBC sensitization.
3. Describe the pathogenesis of the immediate hemolytic transfusion reaction.
4. Manage immediate HTRs
5. Diagnose the causes of febrile reactions, purpura and urticaria.
6. Diagnose and manage the fatal complications (anaphylactic reactions and TRALI)

CONTENTS:

Sources of errors causing complications of BT

Immunological complications:

- Sensitization to Red Cells Antigens
- Hemolytic Transfusion Reactions (HTR)
- Febrile Reactions due to WBC and Platelets Antigens
- Post-Transfusion Purpura (PTP)
- Reactions due to Plasma Protein Antibodies
- Transfusion-Related Acute Lung Injury (TRALI)

Complications of Blood transfusion

- The incidence of transfusion reactions is about 2-5%.
- It is mostly of mild degree.
- **Most of the cases are due to:**

Clerical or **Administrative errors** in:

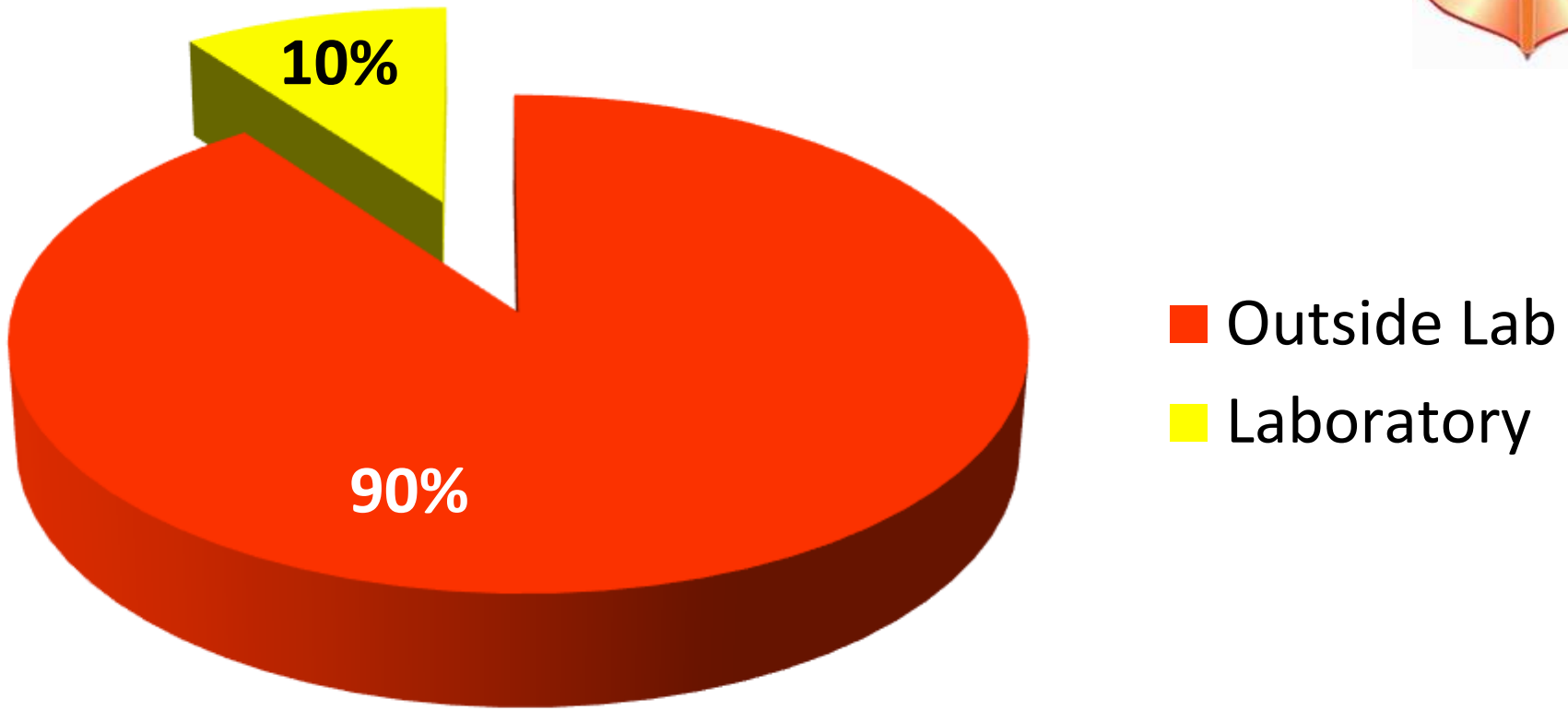
➢ Laboratory errors, **30%**

➢ Nursing service,

➢ Anesthesia service, and

➢ Clinical staff errors

ABO Incompatibilities Laboratory Errors account for:



- Fatal complications are uncommon:

  1 in 100,000 to 1 in 500,000 patients transfused, mainly due to **improper patient identification** (the major cause of transfusion deaths).

Complications can be divided broadly into:

1. **Immunological complications.**
2. **Non-immunological complications.**

Immunological Complications

1. Sensitization to red cells antigens

- Because the ABO & Rh antigens are the only antigens matched between donor & recipient, there is a possibility of sensitization to other red cells antigens.
- Alloimmunization is more likely in multitransfused patients. This sensitization could lead to:

A. HDFN if the recipient is a female.

B. Hemolytic transfusion reaction.

C. Difficulties in compatibility testing if the recipient requires further transfusion.

2. Hemolytic transfusion reactions

- This reaction is caused by premature RBC destruction, **almost always** of the donor cells by antibodies present in the recipient plasma.
- The hemolytic transfusion reaction (HTR) could be:
  - **Immediate HTR** is the most dangerous
  - **Delayed HTR** :

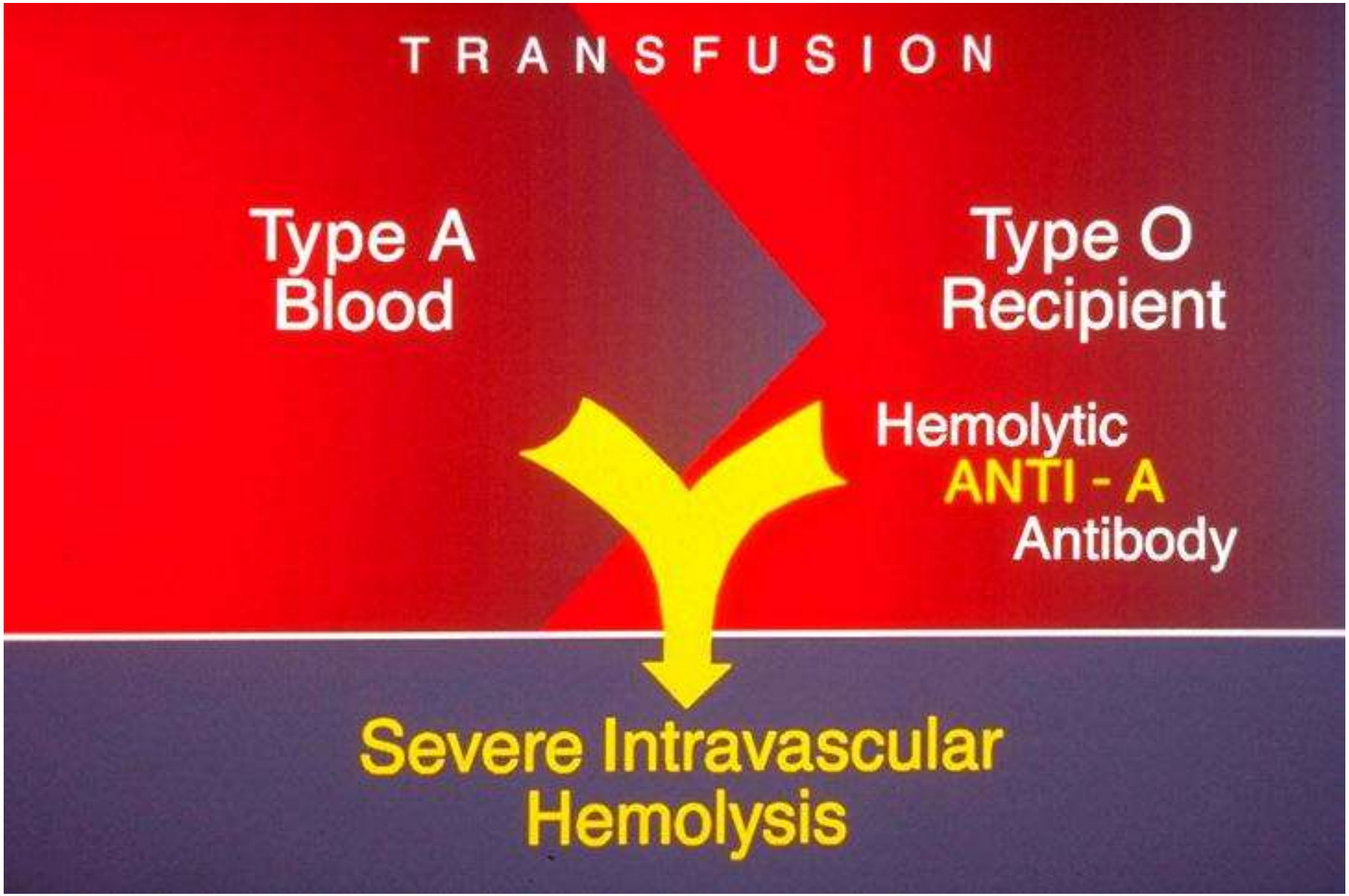
Pathogenesis of immediate HTR:

- Usually is caused by **ABO incompatibility.**
- The **antibodies are IgM** in type that bind to the red cells and cause complement activation leading to **intravascular lysis** of the red cells with production of the anaphylatoxins the **C3a & C5a** liberated during complement activation.
- Renal failure is common.

The C3a & C5a will cause:

- Smooth muscle contraction,
- Platelets aggregation,
- Increased capillary permeability,
- Release of vasoactive amines and hydrolases from mast cells and granulocytes.
- Hypotension

- Less commonly the hemolysis is **extra-vascular** caused by removal of C3b & IgG coated red cells by the macrophages in the liver and spleen.
- Symptoms are usually less rapid in onset and occur usually after 1 hour with fever, jaundice and unexplained decrease in Hb.
- Renal failure is rare.


TRANSFUSION
Type A Blood
Type O Recipient
Hemolytic
ANTI - A
Antibody
Severe Intravascular Hemolysis

Signs & Symptoms of immediate HTR usually occur within minutes to 1 hour from the start of BT

- Heat in the vein.
- Throbbing headache.
- Flushing of the face.
- Chest tightness.
- Nausea and vomiting.
- Lumber or loin pain.
- Hypotension & tachycardia.
- DIC, Hemoglobinemia, Hemoglobinuria, acute renal failure, collapse & death in severe cases.

Management of Immediate HTRs:

- Stop transfusion immediately.
- Keep the IV line open:
- In severe cases:

- Give normal saline (initially 20-30 ml/ Kg body weight) to:

  Maintain the systolic blood pressure > 100 mg Hg

- Give Diuretics: e.g. Frusemide up to 1 mg/Kg body weight intravenously to:

  Restore urinary outflow > 100 ml/ hour.

Collect blood samples from the vein opposite the infusion site in 3 tubes:

1. EDTA sample ➡ CBP.
2. Citrated sample ➡ Coagulation studies.
3. Clotted sample ➡ Serological studies.

- Collect the next urine sample and 24-hour urine post-transfusion and check for Hemoglobinuria.
- Check the label and the number on the blood unit.
- Check the crossmatch form for any errors.

Tests and measures to be done in the lab:

- Check the donor unit for hemolysis.
- Examine the post-transfusion blood sample for hemolysis.
- Do Coomb's test on the recipient post-transfusion sample.
- Check the ABO & Rh group of the recipient and the donor samples again.
- Screen the patient's pre- & post-transfusion samples and donor plasma for antibodies.
- Repeat crossmatch with both pre- & post-transfusion samples.

- Check the Hb level.
- Coagulation screening test for the possibility of DIC.
- Bacteriological evaluation: inspect the donor unit hemolysis or clot. (Blood from the giving set and the blood unit should be cultured).
- Biochemical studies: test for hemoglobinemia and for raised serum bilirubin.
- Check the urine for hemoglobinuria.

Case Scenario

A 30-year-old male had acute blood loss due to a car accident, his Hb was 7 g/dL, and he was given 3 units of blood. On discharge, his Hb level was 10 g/dL.

After 8 days he presented with fever and jaundice, his Hb was 7.8 g/dL, and serum bilirubin was 3.5 mg/dL.

Explain these findings and what is the diagnosis.

Delayed HTR

- This is manifested usually 7-10 days after transfusion and is caused by antibodies, which are present in low titer and are not detected at time of cross matching.
- So this reaction is **neither predictable nor preventable**.
- The antibodies are caused by sensitization due to previous pregnancy or transfusion.

Signs & Symptoms of Delayed HTR:

- Fever
- Jaundice and
- Lowering of Hb.

3. Febrile reactions due to WBC and platelets antigens

- Most common immunological reaction.
- Seen in patients having multiple blood transfusions or pregnancy.
- Caused by Ab to WBC & platelets HLA antigens.
- The onset of the reaction is delayed 30-90 minutes after the start of the transfusion.
- The main symptom is fever.

Management

- Slow the transfusion.
- Give antipyretic.
- No need to terminate the transfusion.
- If symptoms recur in patients requiring repeated transfusions we should check the patient for WBC or Platelets Abs & if these are present we should use **WBC-depleted blood** (by using a WBC filter).

4. Reactions to platelets antigens (Post-transfusion Purpura)

- PTP may be seen in women with a history of multiple pregnancies or in those with a history of multiple transfusions.
- Caused by Abs to platelets antigens.
- The reaction occurs 7-10 days after transfusion.
- The main feature is purpura due to thrombocytopenia (caused by the destruction of the platelets by the Abs)

The mechanism includes:

1. **Binding of immune complexes from donor plasma to the patient's platelets**

2. Demonstration of the presence of Abs in the patient's plasma against HPAs and the absence of the implicated antigen specificity in the patient's platelets.

The **Ag most commonly implicated** is **HPA-1a** (60%)

Up to a 13% **mortality** related to intracranial hemorrhage.

Treatment:

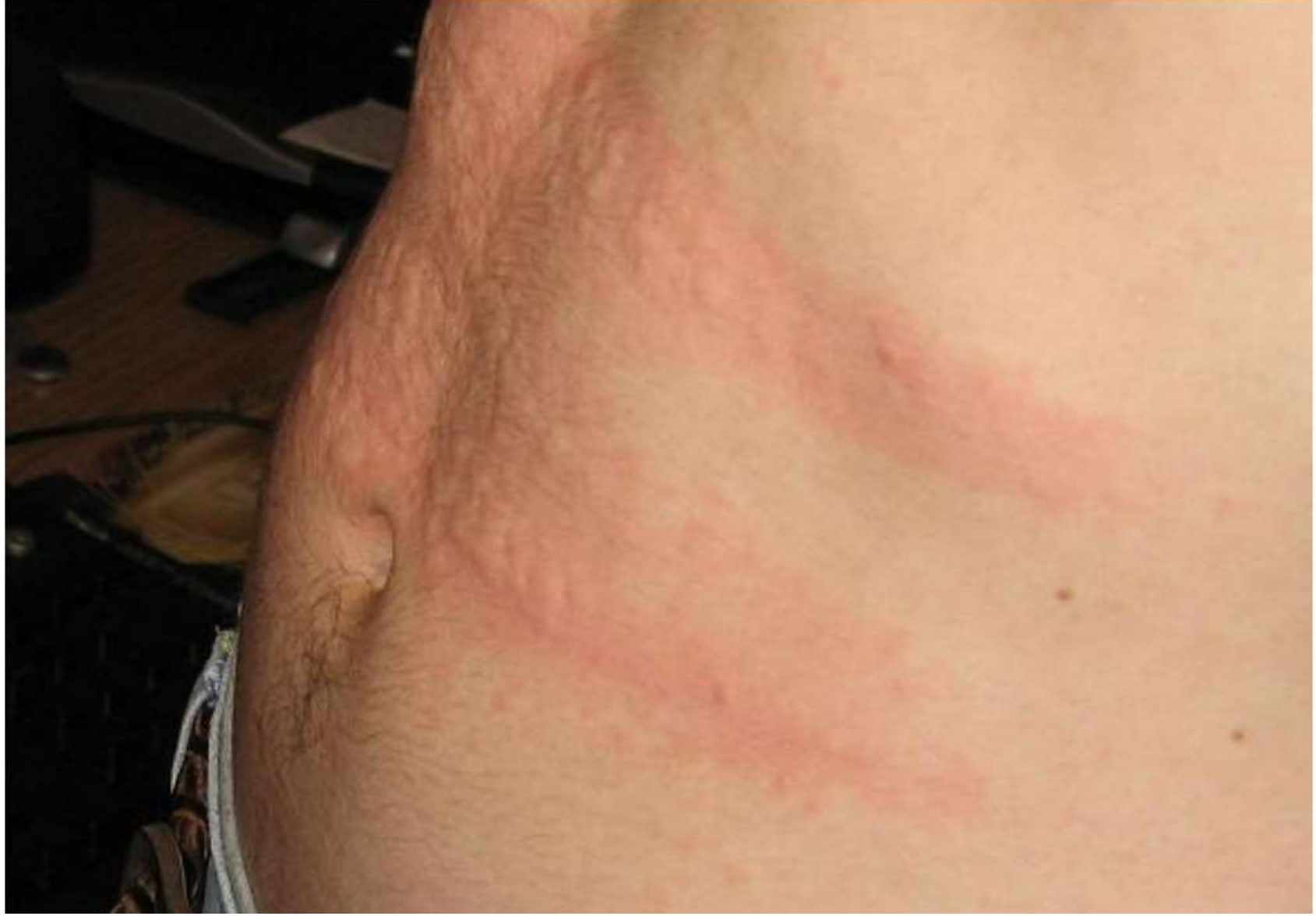
- Self-limiting and platelet count usually returns to normal within 2 weeks.
- Infusion of IVIG
- Ag-negative blood

5. Reactions due to plasma protein antibodies

- **IgE-mediated:** Usually pruritus, urticaria and angioedema
- **IgA-mediated:** Rarely more severe anaphylactic reactions are attributed to an interaction between transfused **IgA and anti-IgA** in IgA deficient individuals, **(immediate fatality of 1: 100,000.)**

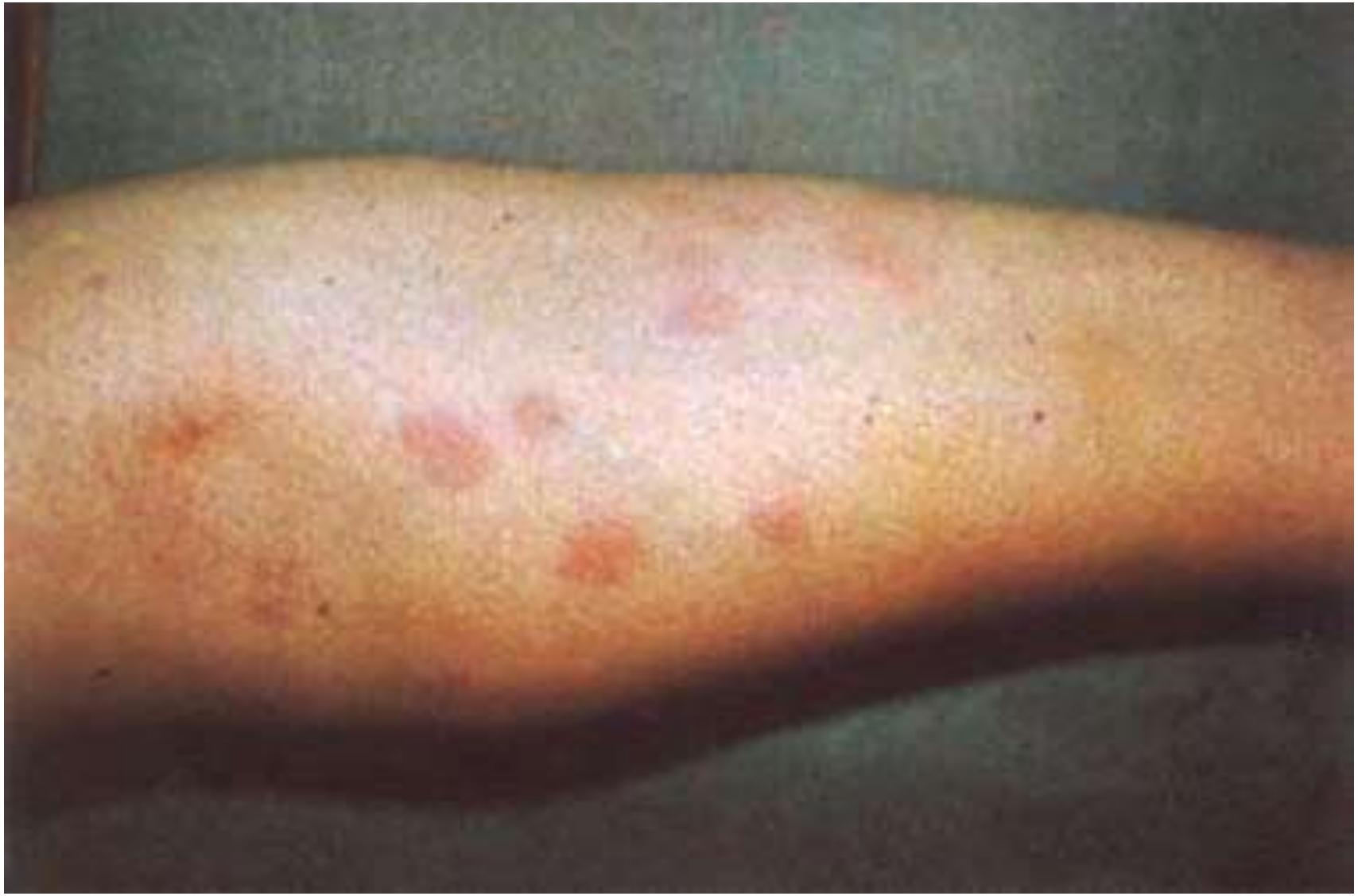
❑Treatment is by:

- Antihistamine.
- Anaphylactic reactions should be treated urgently with adrenaline and any next transfusion should be IgA-deficient blood.



University of Baghdad/ College of Medicine Feb 2024

Urticaria is a skin condition caused by an allergic reaction and is characterized by a raised red patches on the skin accompanied by itching and hives.



Urticaria is one of the commonest immunological complications of BT.

6. Transfusion- related acute lung injury (TRALI)

- There is a significant mortality.
- As little as 2 ml of plasma seems to be sufficient to cause respiratory distress.
- Symptoms develop very rapidly, usually within 1-2 hours, ideally 6 hours or up to 24 hours after infusion.
- TRALI consists of **non-cardiogenic** pulmonary oedema, accompanied by chills, fever, cough and dyspnoea with low oxygen saturation and low or normal central venous pressure.

Criteria for the Diagnosis of TRALI

Onset

Within 6 hours of transfusion

Oxygenation

$PaO_2/FiO_2 \leq 300$ mm Hg regardless of positive end-expiratory pressure level

or

Oxygenation saturation of $\leq 90\%$ on room air.

Chest X-ray

Bilateral infiltrates on frontal chest radiography

Blood Pressure

Pulmonary artery occlusion pressure ≤ 18 mm Hg when measured

or

No evidence of left atrial hypertension

FiO_2 = fraction of inspired oxygen; mm Hg = millimeters of mercury; PaO_2 = partial pressure of arterial oxygen; TRALI = transfusion-related acute lung injury

Data from Popovsky, MA: Transfusion associated circulatory overload: The plot thickens. Transfusion 49:2–4, 2009.

Pathogenesis:

The reaction is due in most cases to the passive transfer of **leuko-agglutinins** (mostly **anti-HLA** class I or class II or granulocyte antibodies, i.e. **anti-HNA-3a**) in donor plasma, leading to endothelial and epithelial injury, alveolar damage and inflammatory changes, mediated by cytokines and other inflammatory mediators.

Prevention:

- The donors are usually multiparous women. Such donors should be removed from the panel.
- Introduction of the policy to produce FFP and use plasma to suspend platelet pools mainly from **male** donors.

IMPORTANT NOTE

Severe reactions most commonly manifest during the first 15 minutes of a transfusion.

All patients and, in particular, unconscious patients should be monitored during this period and for the first 15 minutes of each subsequent unit.

Summary

- Alloimmunization of a pregnant woman may be associated with clinical impact on fetal life.
- Immediate HTR is the most dangerous complication of blood transfusion and may start within a few minutes.
- Fever is the most common immunological reaction.
- PTP is usually self-limiting but may be associated with intracranial hemorrhage.
- IgA deficient individuals may develop anaphylactic reactions during a blood transfusion.
- TRALI is a serious complication and may be prevented by using plasma products from males.

End of BT part 2A