ACUTE TRANSFUSION REACTIONS

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CLASSIFICATION

Transfusion reaction

acute

delayed

Immunologic   Nonimmunologic

Immunologic   Nonimmunologic

تعريف : هر نوع نشانه يا علامت ناخواسته يا نامساعدي كه درحين و يا به فاصله ۲۴ساعت از انتقال يك واحد خون يا فرآورده رخ ميدهد، ناشي از تزريق خون است مگر خلافش ثابت شود.

نشانه هاي يك واكنش مرگ آفرين(مثل واكنش هموليتيك حاد) و يك واكنش نسبتاً خفيف ممكن است در ابتداي امر كاملا شبيه به هم باشند (تب و لرز).
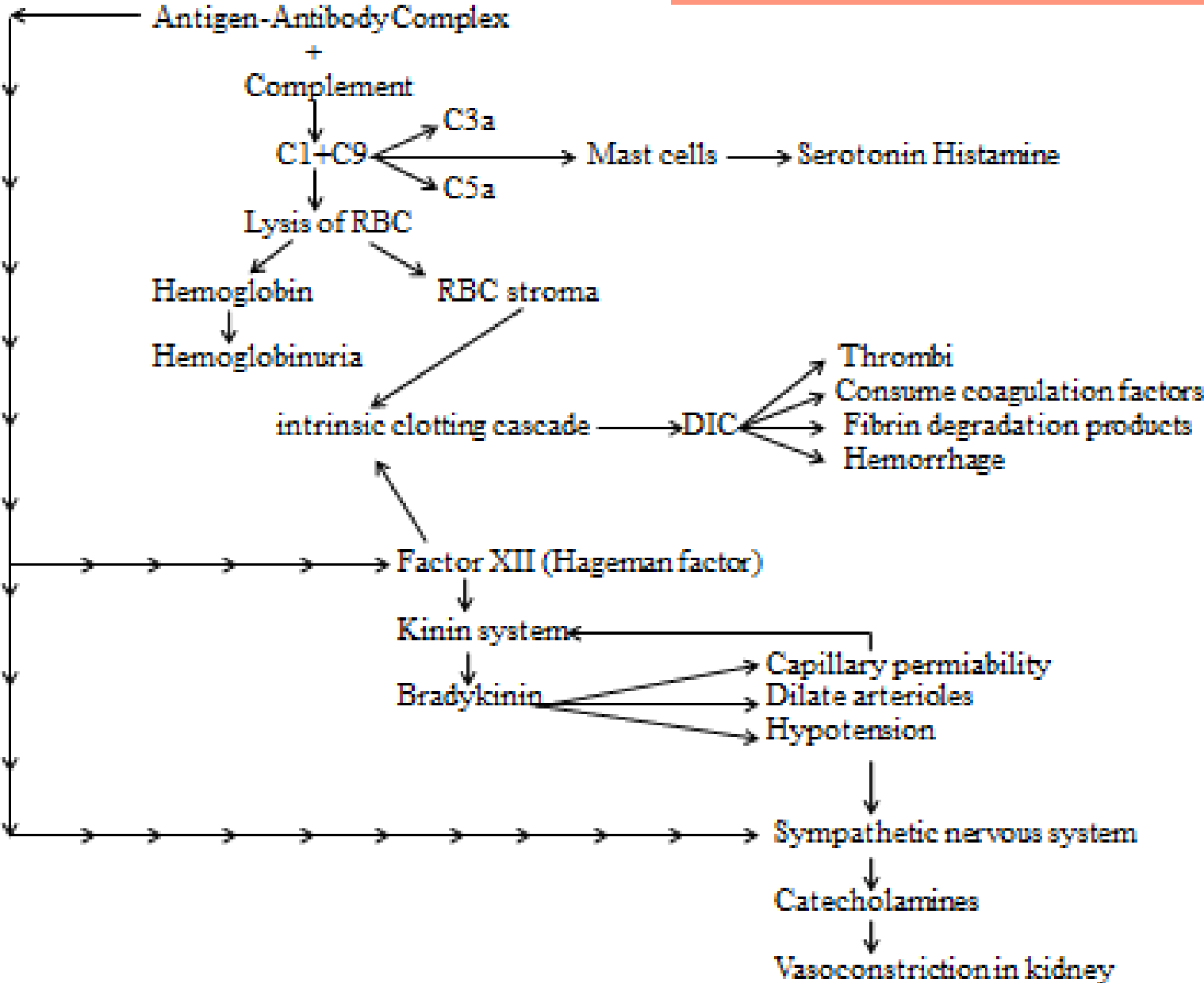
Acute Hemolytic Transfusion Reaction

- Incidence: 1:38,000 – 1:70,000
- Etiology: Red cell incompatibility
  - Most severe reactions are seen following ABO incompatible transfusions
  - As little as 5 – 20 ml of red cells can precipitate severe reactions
- Deaths due to ABO incompatibility
  - 1:500,000 to 1:600,000 transfusions
  - Approx. 24 fatalities reported to FDA each year in US
- 70% of errors occur outside of the lab (e.g. at time of sample collection and at the bedside)

Acute Hemolytic Transfusion Reaction

- Occur within minutes to hours after transfusion
  - Intravascular
  - Extravascular
- Signs & Symptoms
  - Chills
  - Fever
  - Hemoglobinuria
  - Hypotension
  - Renal failure with oliguria
  - DIC (oozing from IV sites)
  - Back Pain
  - Pain at infusion site
  - Anxiety

Antigen-Antibody Complex
+
Complement

C1→C9 → C3a → Mast cells → Serotonin Histamine
→ C5a

Lysis of RBC

Hemoglobin   RBC stroma

Hemoglobinuria

intrinsic clotting cascade → DIC → Thrombi
→ Consume coagulation factors
→ Fibrin degradation products
→ Hemorrhage

Factor XII (Hageman factor)

Kinin system

Bradykinin → Capillary permiability
→ Dilate arterioles
→ Hypotension

Sympathetic nervous system

Catecholamines

Vasoconstriction in kidney

Acute Hemolytic Transfusion Reaction

- Clinical Approach/Assessment
  - Stop transfusion – maintain venous access
  - Initiate a transfusion reaction work-up
    - Notify the blood bank
    - Return remaining product or empty bag and all attached tubing and IV fluid bags to the blood bank
    - Send new patient sample to blood bank
    - Send urine sample

LAB INDICATORS OF IHTR

- Early indicators
  - Decreased haptoglobin levels (binds free Hg)
  - Hemoglobinemia
  - Hemoglobinuria
- Delayed indicators
  - Serum bilirubin – 6 or more hours post reaction
  - Methemalbumin (heme combines with albumin)– 5 to 24 hrs post
  - Hemosiderinuria – several days post
  - Fecal urobilinogen – several days post
  - Abnormal coagulation tests (if DIC occurs)– several hours post

Freshly Hemolyzed Plasma (Actual Case from an OR)

Dr. DeChristopher's gloved fingers

Investigation of suspected AHTRs

**Send the following lab investigations:**

Immediate post transfusion blood samples (clotted and EDTA) for:

- Repeat ABO & Rh (D) grouping
- Repeat antibody screen and crossmatch
- Direct antiglobulin test
- Complete blood count (CBC)
- Plasma hemoglobin
- Coagulation screen
- Renal function test (urea, creatinine and electrolytes)
- Liver function tests (bilirubin, ALT and AST)

Blood culture in special blood culture bottles

Blood unit alongwith BT set

Specimen of patient's first urine following reactio
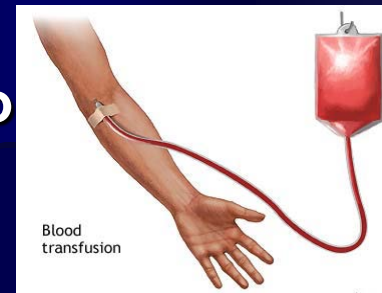
Blood transfusion

Acute Hemolytic Transfusion Reaction

- **Management**
  - Maintain urine output >1cc/kg/hr with fluids and diuretics
  - Analgesics
  - Pressors for hypotension (low dose Dopamine)
  - Hemostatic components (FFP, cryo, platelets) for bleeding/coagulopathy
  - Follow-up labs (total/indirect bilirubin, creatinine, LDH, haptoglobin, CBC, PT/PTT)
- **Prevention**
  - Adequate training
  - Follow specified procedures and policies
  - Reliable patient and sample identification

FEBRILE REACTIONS

- Fairly common, rarely fatal
- <u>Fever</u> (1ºC or more over baseline) and chills
- Caused by presence of <u>leukocyte Abs</u> in recipient
- Routine X-match protocols will not detect
- If patient has 2 or more FTR, measures taken to prevent subsequent reactions:
  - Use of antipyretics during transfusions
  - Use of leukoreducing filters

Febrile Non-hemolytic Transfusion Reaction

- Incidence:
  - RBCs: 1:200 – 1:17 (0.5% - 6%)
  - Platelets: 1:100 – 1:3 (1% – 38%)
- Etiology
  - Antibody to donor WBCs
  - Accumulated cytokines in bag
- Signs & Symptoms
  - Chills/rigors
  - Fever (generally defined as a 1C (2F) increase)
  - Headache
  - May be accompanied by changes in BP and HR, dyspnea, nausea or vomiting

Febrile Non-hemolytic Transfusion Reaction

- **Laboratory testing**
  - Rule out hemolysis (DAT, inspect for Hb)
- **Therapeutic/Prophylactic Approach**
  - Antipyretic premedication
  - Leukocyte-reduced blood products

Allergic (Urticarial) Transfusion Reactions

- Incidence: 1:100 – 1:33 (1% - 3%)
- Etiology: Antibody (IgE) to donor plasma proteins (found in platelets, FFP, Cryo, RBCs)
- Signs & Symptoms
  - Urticaria
  - Pruritis
  - Flushing
- Therapeutic/Prophylactic Approach
  - Antihistamine, treatment or premedication
  - May restart unit slowly after antihistamine if symptoms resolve

ALLERGIC REACTIONS

- Fairly common, rarely fatal
- Urticaria (hives)
- Caused by soluble agent (protein) in donor plasma to which R has Abs
- Histamine the key mediator of response (released from mast cells when allergen binds IgE that is on surface of mast cells)
- Routine X-match will not detect
- Treat with antihistamines or, if more severe or persistent, use washed cells subsequently

Allergic Transfusion Reactions: Hives and Itching

Anaphylactic Transfusion Reaction

- Incidence: 1:20,000 – 1:50,000
- Etiology: Ab to donor plasma proteins (IgE, IgA, C4)
- Pathophysiology: Immediate generalized reaction caused by release of histamine and other mediators
- Signs & Symptoms
  - Hypotension
  - Urticaria
  - Bronchospasm (respiratory distress, wheezing)
  - Local edema
  - Anxiety

ANAPHYLACTIC REACTIONS

- Respiratory distress, nausea/vomiting, abdominal cramps, diarrhea, shock, low b.p., collapse
- Caused by R Anti-IgA (congenital lack of IgA) which reacts with D IgA
- Occurs before 10 mL blood infused
- Routine X-match will not detect
- Treat by terminating transfusion and giving epinephrine
- If suspected, test R blood for IgA; give only washed cells subsequently

Anaphylactic Transfusion Reaction

- Laboratory testing
  - Rule out hemolysis (DAT, inspect for Hb)
  - Anti-IgA
  - IgA quantitative
- Therapeutic/Prophylactic Approach
  - Trendelenberg position
  - Fluids
  - Epinephrine, antihistamine, corticosteroids, ß2 agonists
  - IgA-deficient blood components

Transfusion-Related Acute Lung Injury (TRALI)

- Incidence:
  - 1:5,000 – 1:190,000
  - True incidence remains unknown
    - Recent increase with increased awareness
    - Pulmonary symptoms often attributed to circulatory overload or unknown cause
- Mechanism:
  - Anti-WBC (neutrophil, HLA) antibodies in donor which bind to granulocytes or monocytes leading to complement activation and neutrophil aggregation in the pulmonary vasculature
  - Activated neutrophils release inflammatory enzymes and biologic response mediators that result in endothelial injury and leakage of protein-rich fluid into the lungs
  - Rarely due to patient antibodies

TRALI

Pathogenesis

Two current working model hypothesis –

Both models are directed against increase in pulmonary – microvascular permeability

Leukocyte Antibody ←————————→ Bioactive Lipids

"Two-Hit" Model

↑ Pulmonary Microvascular Permeability

Pulmonary Edema

Transfusion-Related Acute Lung Injury (TRALI)

- Signs & Symptoms
  - Acute respiratory distress
  - Severe bilateral pulmonary edema
  - Severe hypoxia
  - Tachycardia
  - Fever
  - Hypotension
  - Cyanosis
- Usually arises within 1-6 hours of transfusion of plasma-containing blood components

Pre-Operative CXR

Post-Operative CXR

Transfusion-Related Acute Lung Injury (TRALI)

- Laboratory testing
  - WBC antibody (HLA, granulocyte) screen in donor and recipient
- Consequences
  - Mild to moderate cases
    - Lung injury and prolonged ventilator time
    - Predispose patient to pulmonary infection
  - Severe cases
    - Fatal outcomes (3rd most common cause of transfusion-related death)
- Therapeutic/Prophylactic Approach
  - Supportive care until recovery
  - Defer implicated donors

Canadian Consensus Conference Panel on TRALI

- Acute onset

- Hypoxemia
  - Research setting
    - PaO$_2$ / FiO$_2$ ratio $\leq$ 300mm Hg or
    - SpO$_2$ < 90% on room air
  - Non-research setting
    - As above or other clinical evidence of **hypoxemia**

- Bilateral infiltrates on frontal CXR

- No evidence of left atrial hypertension (circulatory overload)

Kleinman S, *et al.*, Transfusion 2004;44:1774-89.

E. BACTERIAL CONTAMINATION

Most common microbiological complication of transfusion

Higher incidence after platelet transfusion

Apparent infrequency of clinical events of bacterial contamination

Non pathogenic bacteria

- Insufficient no. of bacteria

- Premedication with steroides

- Pts already on antibiotics

- Immunosuppressed pts underinvestigated

Clinical features

- usually appear immediately during transfusion

- S/t symptoms delayed until after the end of transfusion

- - fever (inc > $2\,^{\circ}C$)

- - chills / rigors

- Hypotension, collapse, shock

- Nausea, vomitting

- DIC, intravascular hemolysis, renal failure

Management

- Stop transfusion. Retain unit for investigation

- Give general supportive Tt (iv fluids , inotropic agents , diuretics to maintain urine output)

- Broad spectrum antibiotics until blood culture report comes

- Assess need for intensive care bed

NON-IMMUNE REACTIONS

- TACO
  - Seen in pts with cardiac or pulmonary disease, extremely anemic pts, or infants
  - Caused by sudden increase in blood volume
  - Dyspnea, coughing, pulmonary edema, cyanosis
  - Administer units slowly but within 4 hours/unit

Circulatory Overload

- Signs & Symptoms
  - Dyspnea
  - Orthopnea
  - Cough
  - Tachycardia
  - Hypertension
  - Headache
- Therapeutic/Prophylactic Approach
  - Upright posture
  - Oxygen
  - IV diuretic
  - Transfuse split units

NON-IMMUNE REACTIONS

- Physical damage to donor RBCs ("artificial" hemolysis)
  - Accidental freezing
  - Overheating
  - Addition of hypo- or hypertonic solution to same limb
  - Use of pressure cuff on unit to force flow
- Dilution of coagulation factors and/or platelets (with many transfusions)
- Citrate toxicity (with many transfusions)
- Iron overload (with many transfusions in pts with thalassemias)

Metabolic Disturbances

- Hypothermia

- Hyperkalemia

- Acidosis

- Hypocalcemia

Nurses' Actions

- In patient's room:
  - Stop transfusion, notify physician
  - Keep IV line open with saline
  - Record vital signs and observe symptoms
  - Recheck ID or pt. and hospital #; compare with tag on donor unit
  - Collect clot and EDTA tubes immediately
  - Collect 1st urine passed
  - Collect clot and EDTA at 6 to 8 hours post
  - Unit, infusion set, and all forms and labels sent to lab

Blood Bank:

- Recheck the records for clerical error

- check for identification error

- Visual check for hemolysis, appearance of returned unit
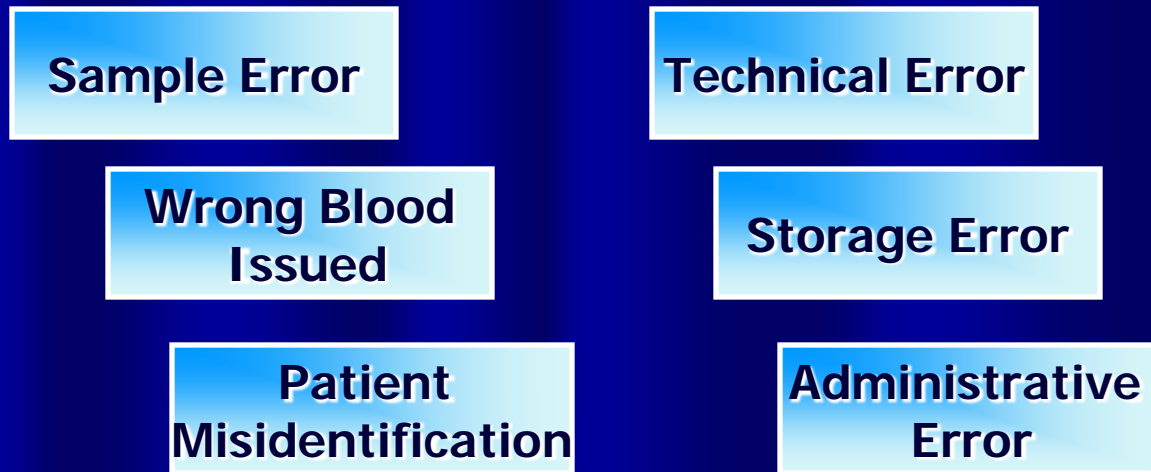
- Evidence of blood group incomparability

	Pre Tx sample	Post Tx sample
ABO,Rh group		
DCT		
ICT		
Repeat CxM		

- Gram stain, culture

- HLA, Plt, Granulocyte specific Abs in recipient

How to Prevent Errors in the Transfusion Chain

❖ Where in the process do errors occur?

| Sample Error | Technical Error |

| Wrong Blood Issued | Storage Error |

| Patient Misidentification | Administrative Error |

❖ Who is making the errors?

❖ Why are the errors occuring – which elements of good transfusion practice are failing

Error Prevention in the Transfusion Services

❖ Adherence to Standard Operating Procedures (SOPs) for pre-transfusion testing

❖ Antibody screen in patients at risk of alloimmunization; preferably universal screen

❖ Antibody identification when required

❖ Appropriate storage and transfusion instructions on labels

❖ Clerical checks prior to issue

Prevention of transfusion reaction

- Education and training of nurses health care assistants, doctors at every level

- Proper communication at all level should be appropriate, timely and effective.

- Promoting the knowledge in hospital, raising awareness by having more educational sessions and poster available to hospital