Transfusion Reactions

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Types of reactions

- Hemolytic transfusion reactions
- Febrile non-hemolytic transfusion reactions
- Allergic reactions/ Anaphylactic reactions
- Transfusion related acute lung injury (TRALI)
- Transfusion associated circulatory overload (TACO)
- Post transfusion purpura

Hemolytic Transfusion Reactions

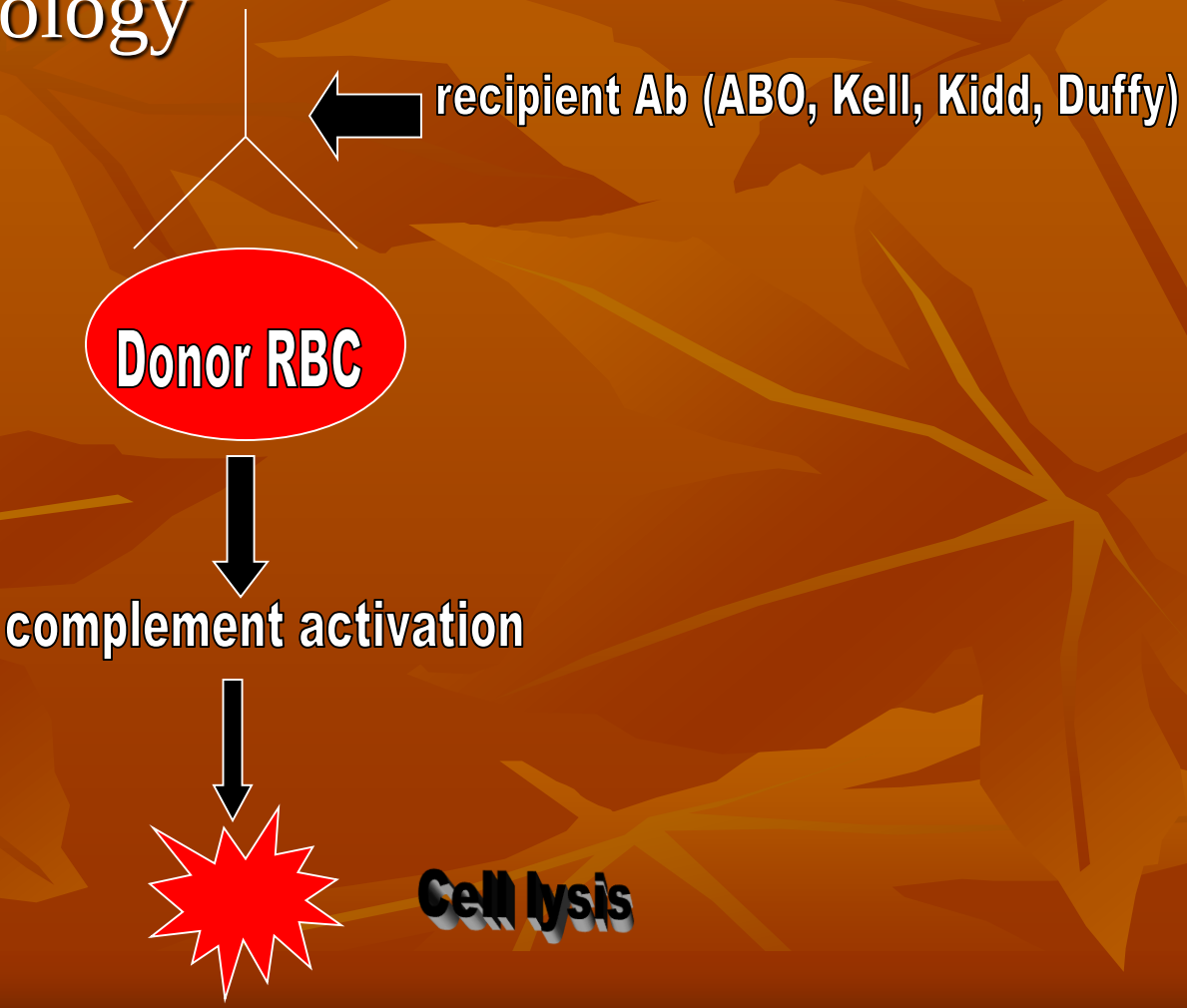
- They may be acute (occurring within 24 hours of transfusion) or delayed (when signs of red cell destruction do not occur until 4 to 10 days after transfusion).
- These patients usually have been exposed to the antigen through previous pregnancies or transfusions.

Acute Hemolytic Transfusion Reaction

- Definition: RBC destruction $\leq$ 24 hrs of transfusion
- Occurs mainly with RBCs and whole blood, but can occur with any plasma-derived products (plts, FFP, cryo, etc…)
- Fatal 1 in 100,000 – 600,000 units transfused
- Most common cause: incompatible RBCs leading to intravascular hemolysis

Acute Hemolytic Transfusion Reaction

- Pathophysiology



Acute Hemolytic Transfusion Reaction

- Complement activation leads to:
  - Hypotension (C3a and C5a anaphylotoxins)
  - Vasoconstriction and renal ischemia
  - Activation of plts and coag cascade leading to DIC

Acute Hemolytic Transfusion Reaction

- Clinical
  - Depends on antigen involved, quantity of RBCs infused, and titer of the Ab
  - Clinical presentation also varies depending on premorbidity factors, so use common sense when evaluating your pts., i.e., if pt is paralyzed then you won't see chills/rigors
  - AIHA with either warm or cold Abs may look like AHTR clinically AND these pts may also develop alloantibodies and that makes our job even harder…
  - TTP, HUS, DIC, Heart valves, congenital hemolytic anemias (hereditary spherocytosis, G6PD, sickle cell anemia) also mimic AHTRs

Acute Hemolytic Transfusion Reaction

- Signs and Sxs:
  - Fever
  - Chills/rigors
  - Anxiety
  - Flushing
  - Chest/ abdominal/ back pain
  - N/V/D
  - Dyspnea
  - Hypotension
  - Hemoglobinuria
  - Pallor
  - Icterus
  - Oliguria/anuria
  - Pain at transfusion site
  - Diffuse bleeding jaundice

Acute Hemolytic Transfusion Reaction

- Lab Dx:
  - 1. Make sure that the right patient got the right blood product
    - Reconfirm ABO/RH type and antibody screen results
  - 2. Direct and indirect Coombs test (usually yields mixed field reactions b/c of combination of pt and donor RBCs only one of which is sensitized)
  - 3. Direct evidence of hemolysis
    - Pretransfusion blood sample is compared with posttransfusion sample for visible evidence of hemolysis. Free serum hemoglobin appears as a pink color in the serum in a clotted centrifuged specimen. This may be observed with as little as 5-10 mL of hemolyzed blood.

Acute Hemolytic Transfusion Reaction

- Labs:

  CBC w/plts

  UA

  bilirubin, BUN/CREATININE

  Coags: PT/PTT/FSP/fibrinogen/haptoglobin

Hb/Hct
haptoglobin

unconjugated bilirubin
LDH

Acute Hemolytic Transfusion Reaction

- Serum bilirubin peaks in 3-6 hours as the free hemoglobin is metabolized.
- Haptoglobin binds to hemoglobin and the serum hemoglobin level falls, reaching its nadir in 1-2 days.
- Examine urine for hemoglobinuria.
- A repeat CBC fails to show the expected rise in hematocrit in patients developing intravascular or extravascular hemolysis.

Acute Hemolytic Transfusion Reaction

- Prevention:
  - Make sure that pt really needs transfusion (treat the patient and not the labs!)
  - Accurate clerical function (patient ID, sample collection, sample and unit labeling, unit ID, patient testing, component handling…)
  - Don’t add meds to blood
  - Blood is stored at proper temperature
  - Blood is not exposed >37°C

Acute Hemolytic Transfusion Reaction

- Management:
  - If suspected, STOP transfusion! And maintain IV access
  - Make initial rapid assessment of pt and requirements for basic and advanced support
  - Notify blood bank, collect transfused units (full or partial), tubing, etc. and return them to BB
  - Reconfirm identity of blood units & pt
  - Collect appropriate patient blood specimens

Acute Hemolytic Transfusion Reaction

- Supportive approaches:
  - IV fluid resuscitation for hypotension
  - Maintain IV fluids
  - Diuretics Make efforts to maintain urine output at 30-100 mL/h.
  - Low dose dopamine
  - Replace procoagulant factors and fibrinogen with FFP and cryo; also plts as needed

Acute Hemolytic Transfusion Reaction

- Non-immune mediated acute hemolysis:
  - Bacterial contamination
  - Mechanical trauma during infusion
  - Thermal hemolysis
  - Osmotic lysis from reconstitution of blood components with hypotonic solutions

Delayed Hemolytic Transfusion Reaction

- Pathophysiology same as acute EXCEPT:
  - Low titer of reactivity so undetected on initial screen
  - Repeat post-transfusion sample will show the Ab

Delayed Hemolytic Transfusion Reaction

- Symptoms:
  - Milder than in acute
  - Fever
  - Unexplained anemia
  - Jaundice
  - Hemoglobinuria
  - Rarely DIC and ARF

Delayed Hemolytic Transfusion Reaction

- Any antibody can cause it, but most common culprits:
  - Rh
  - Kidd

Delayed Hemolytic Transfusion Reaction

- Prevention:
  - More sensitive antibody screens
  - Medical records of Ab maintained for pts
  - Pts with multiple transfusion histories, i.e., sickle cell dz., should undergo extensive Phenotyping
- Treatment same as for acute

Delayed Hemolytic Transfusion Reaction

- 3-10 days after transfusion of blood that initially appeared to be serologically compatible
- Previously transfused or pregnant and Ab not detected on pretransfusion sample

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Incidence:
  - 0.5%- 1.4 % of nonleukoreduced red blood cell transfusions
  - 43-75% of all transfusion reactions

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Nonhemolytic febrile reactions are due to WBCs, WBC antibodies, or cytokines elaborated by either donor or recipient
- Granulocyte and human leukocyte antigen 5(HLA5) antibodies
- Cytokines accumulate during storage so to prevent this all samples are leukoreduced prior to storage

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Symptoms
  - Fever (increase of temp 1°C from baseline)
  - Chills

  In absence of other causes of fever

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Treatment
  - Discontinue transfusion
  - Antipyretics
  - Supportive care

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Prevention:
  - Antipyretics
  - Prestorage leukoreduced blood products
  - Of course…
    - Make sure to exclude a Hemolytic transfusion reaction

Uncomplicated Allergic Reactions

- Incidence:
  - 1-3% of transfusions
  - 45% of all transfusion reactions

Uncomplicated Allergic Reactions

- Pathophysiology:
  - IgE directed against soluble donor antigens

Uncomplicated Allergic Reactions

- Symptoms:
  - Local or diffuse urticaria

Uncomplicated Allergic Reactions

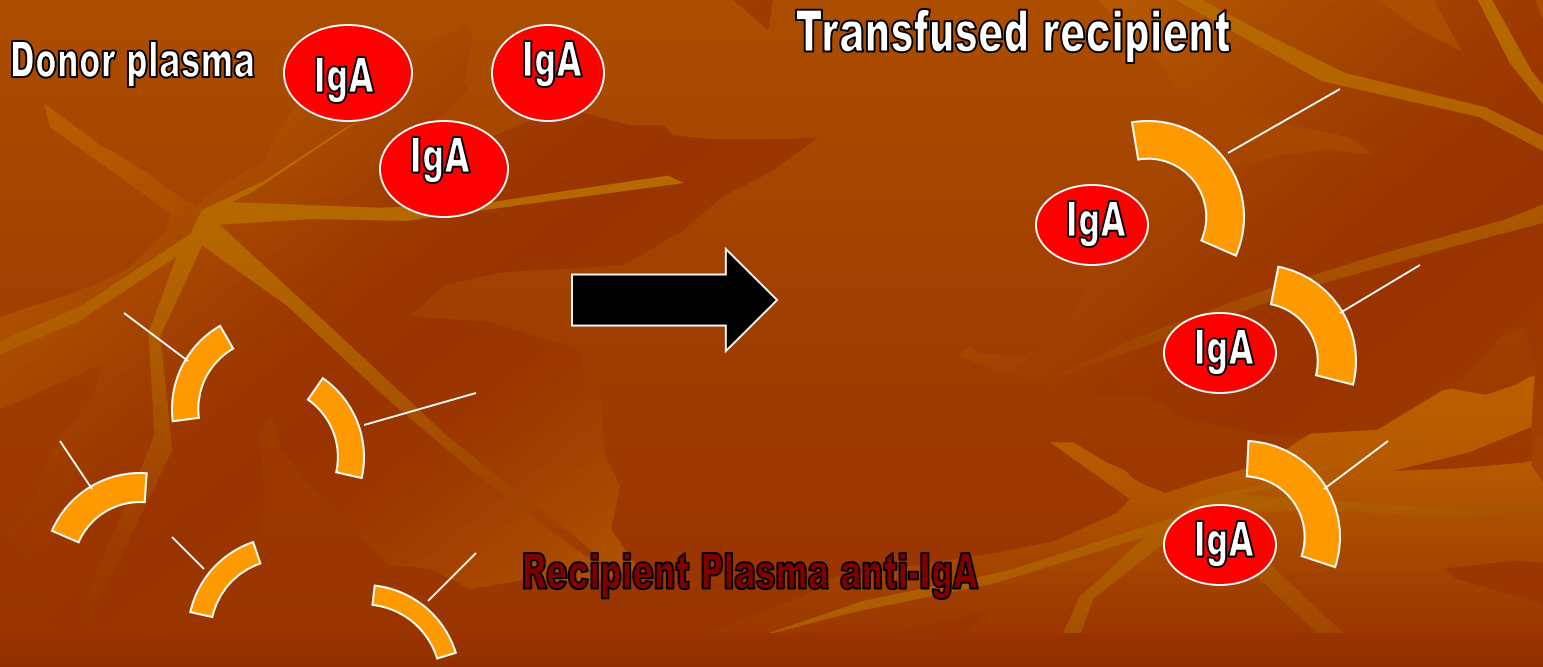
- Treatment
  - Discontinue transfusion
  - Antihistamines
  - If urticaria resolved, then can restart transfusion

Uncomplicated Allergic Reactions

- Prevention:
  - Antihistamines

Anaphylactic Reactions

- Incidence:
  - 1-3% of all transfusion reactions
- Pathophysiology:



Anaphylactic reactions

- Anaphylactic reactions most often are observed in those patients with a hereditary immunoglobulin A (IgA) deficiency.
- Some of these patients have developed complement-binding anti-IgA antibodies that cause anaphylaxis when exposed to donor IgA.

Anaphylactoid Reactions

- Subclass, allotypic or specific anti-IgA in patients who have demonstrable levels of IgA
- Donor products may also have anti-IgA
- Difficult to identify these patients b/c of an infinite number of specific IgA proteins

Anaphylactic Reactions

- Symptoms:
  - In anaphylactic reaction, symptoms usually occur with less than 10 mL of blood transfused and only rarely occur more insidiously.
  - Tachycardia
  - Flushing
  - Urticaria
  - In more severe cases, wheezing, laryngeal edema, and hypotension

Anaphylactic Reactions

- Treatment:
  - Stop transfusion immediately.
  - Support airway and circulation as necessary.
  - Administer epinephrine, diphenhydramine, and corticosteroids.
  - Maintain intravascular volume.

Anaphylactic Reactions

- Prevention
  - IgA deficient patients should avoid plasma-containing products or donations from other IgA deficient donors
  - Washed RBCs

Transfusion Related Acute Lung Injury (TRALI)

- Incidence:
  - rare

Transfusion Related Acute Lung Injury (TRALI)

- Noncardiogenic pulmonary edema associated w/
  - transfer of donor granulocyte Abs directed against the patient's WBCs
  - Agglutination of Ab-antigen complex within the pulmonary vasculature
- By-products of neutrophil activation result in:
  - Altered vascular permeability
  - Capillary leak syndrome and thus pulmonary edema
- Clinical picture resembling ARDS

TRALI

- Can occur with:
  - FFP
  - RBCs
  - Whole Blood
  - Platelets
  - Granulocytes
  - Cryoprecipitate
- Not reported with:
  - Albumin
  - IVIG
  - RhIg
  - Coagulation factor concentrates

TRALI

- Clinically similar to ARDS, but TRALI:
  - Better prognosis
  - Lower mortality (10%)
  - More rapid resolution (3-7days)
  - Lower likelihood of permanent pulmonary sequelae

TRALI

- Signs and symptoms
  - Acute onset of respiratory distress and hypoxemia with clinical and X-ray evidence of acute pulmonary edema
  - Hypotension
  - Fever
  - Chills
- Diagnosis of exclusion, fluid overload and cardiac failure must be ruled out

TRALI

- Treated with supportive care:
  - Ventilatory support
  - Supplemental oxygen
  - Pressors
- Important to recognize
  - Donor specific phenomenon
  - Donor will not be permitted to donate plasma-containing blood components
- Blood donor center will evaluate unit for:
  - HLA granuloyte-specific antibodies in the donor
  - HLA granulocyte-specific antibodies in the recipient
  - Reverse lymphocyte crossmatches (pt's lymphocytes with donor serum)

Transfusion Associated Circulatory Overload (TACO)

- Incidence:
  - 1 in 100 transfusions
- Pathophysiology:
  - High rates of infusion
  - High volume of infusion
  - Underlying cardiovascular of pulmonary pathology

TACO

- Symptoms:
  - Dyspnea
  - Orthopnea
  - Cough
  - Tachyacardia
  - Hypertension

TACO

- Treatment:
  - Stop or slow rate of infusion
  - Diuretics
  - Oxygen if necessary
  - Supportive care

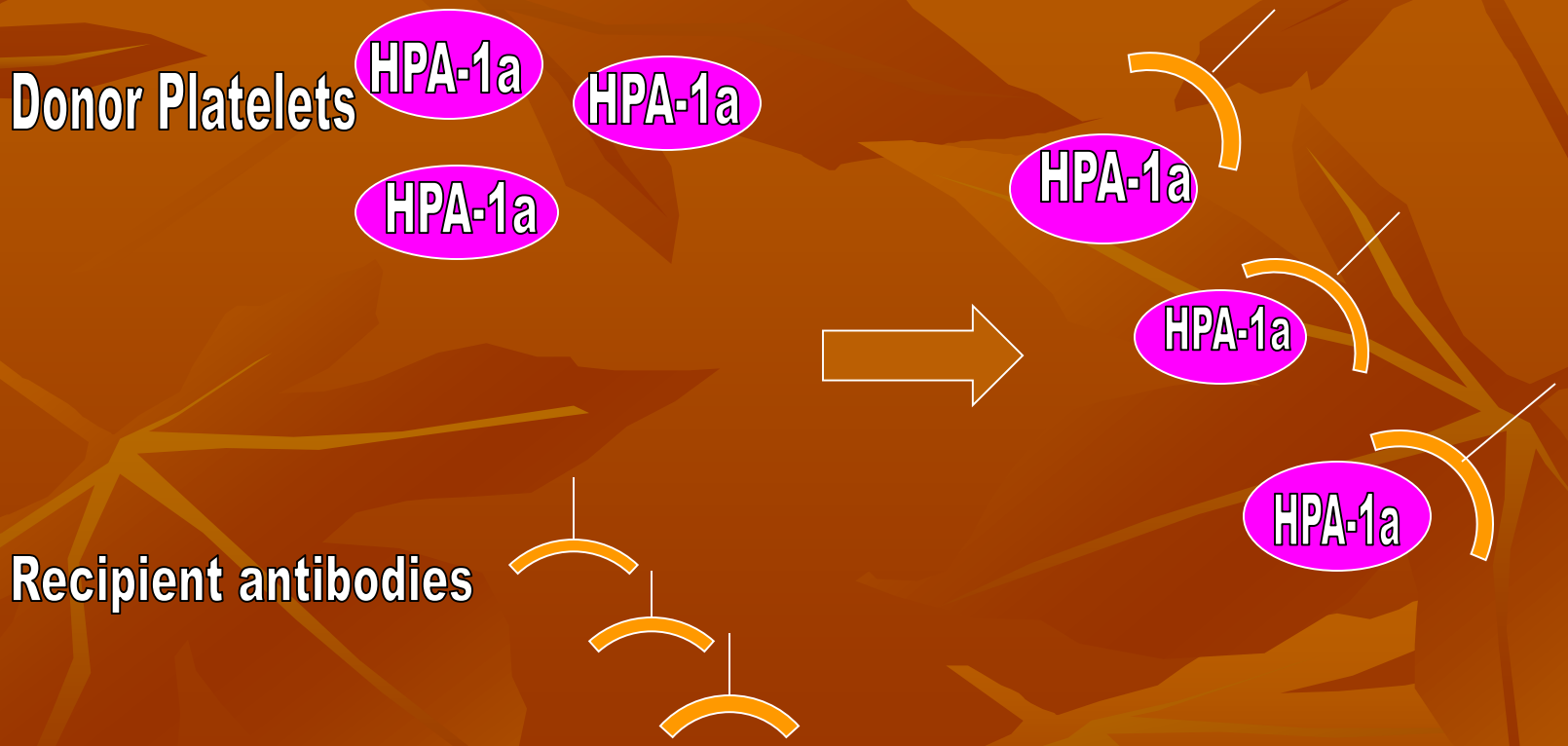
TACO

- Prevention:
  - Vigilant assessment of pt's ins/outs
  - Slow rates of infusion
  - Pretransfusion and/or intratransfusion diuretic administration

Post-transfusion purpura

- Incidence:
  - Rare
  - 200 cases reported
- Pathophysiology
  - Profound thrombocytopenia 1-2 wks post transfusion
  - Transfusion of donor platelets with a platelet antigen lacking in the recipient
  - Human platelet specific alloantigen 1a (HPA-1a)

Post-transfusion Purpura



Post-transfusion Purpura

- Treatment
  - IVIG (mechanism of action ?)
    - Reticuloendothelial blockade
    - Nonspecific adherence to target antigen blocking access by specific antibody
  - Plasmapheresis if poor response
  - If the pt doesn't die from hemorrhage, then it's self-limited with recovery within 4-5 days of therapy

Post-transfusion Purpura

- Prevention:
  - Avoid antigen positive platelet transfusion in pts in whom this has previously occurred