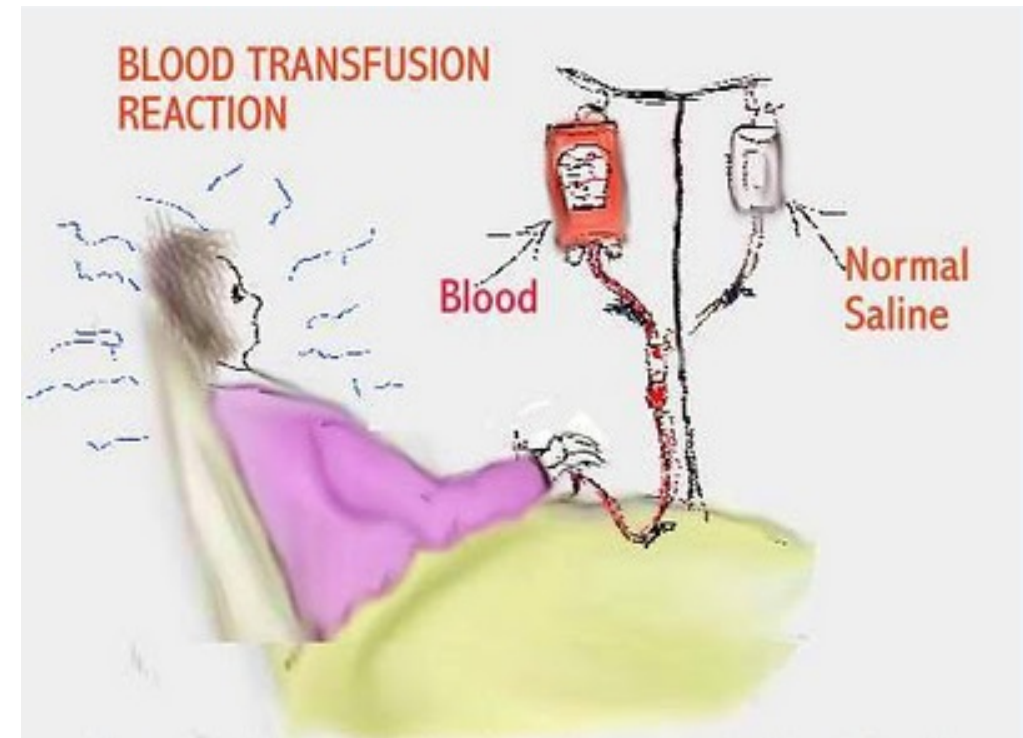


# Adverse Effects of Blood Transfusion



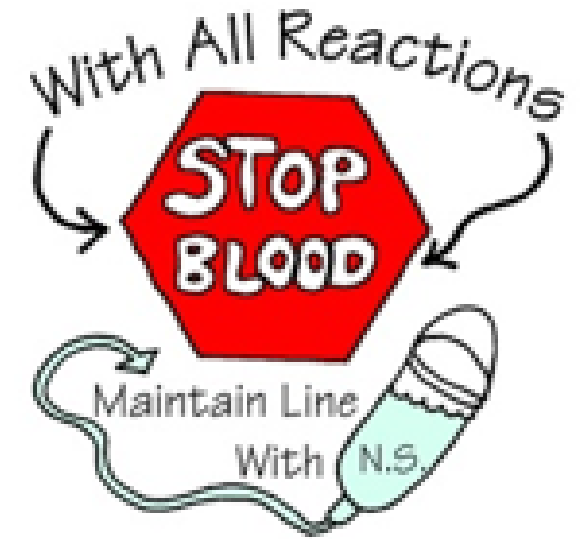
# Transfusion Reaction

- Any transfusion-related adverse event that occurs during or after the transfusion of blood components
- **Acute reaction:** signs and symptoms present within 24 hours of transfusion
- **Delayed reaction:** signs and symptoms present after 24 hours of transfusion



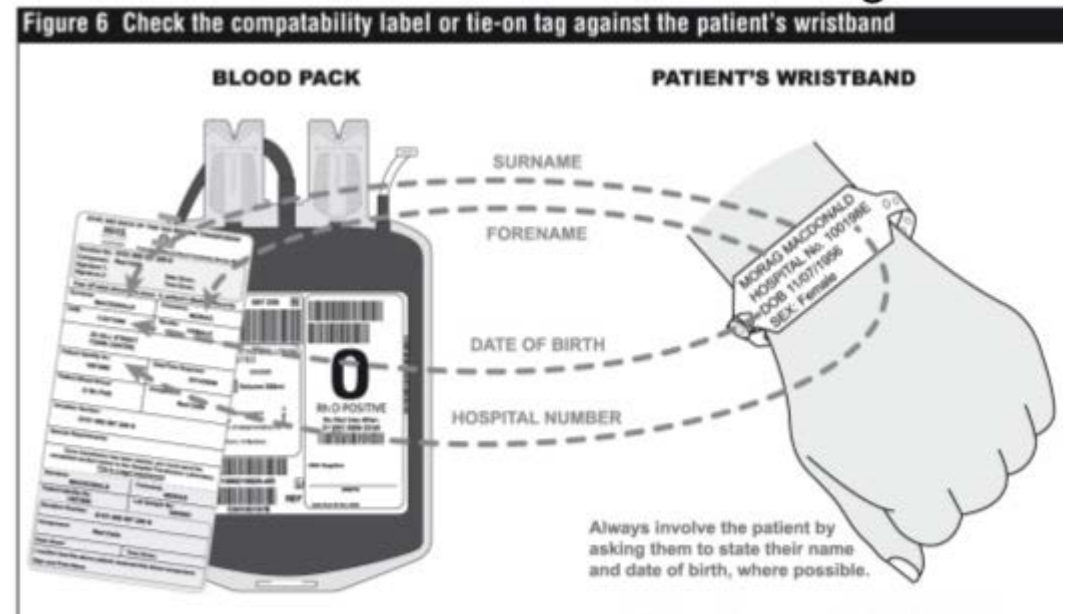
# Step One

- If a nurse suspects a transfusion they need to STOP THE TRANSFUSION.
- This should be the first thing you tell the nurse
- Leave line open with saline



# Step Two: Transfusion Reaction Work-up

- **Clerical Check:** check that all information matches
  - Bedside- check name on unit matches patient
  - Blood Bank- recheck all computer work with returned unit
    - Patient name, blood type, unit number, etc.



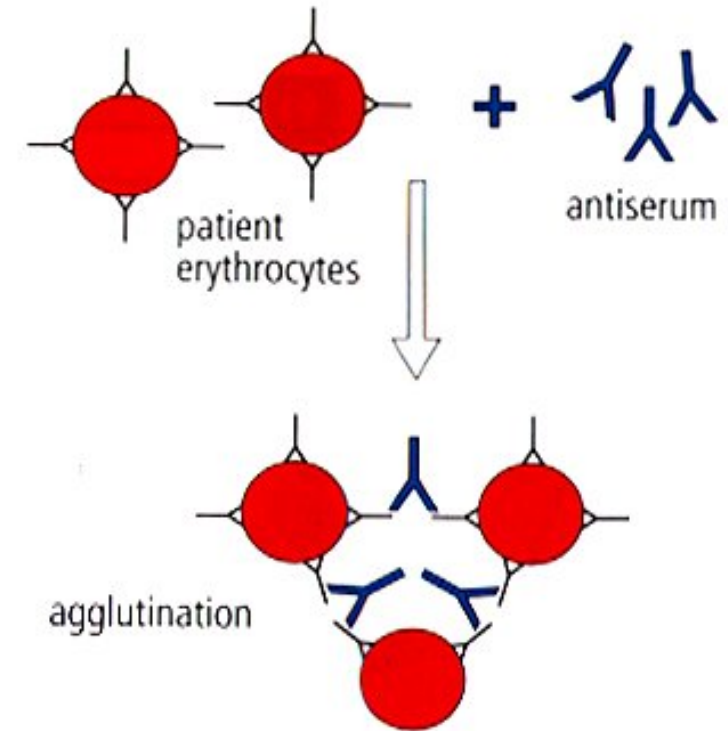
# Transfusion Reaction Work-up

- **Hemolysis Check:**
  - Free hemoglobin- causes patient plasma to be red/pink
  - Have a new tube drawn
  - Compare hemolysis of post-transfusion tube to pre-transfusion tube
  - If hemolyzed, request redraw to rule-out traumatic draw



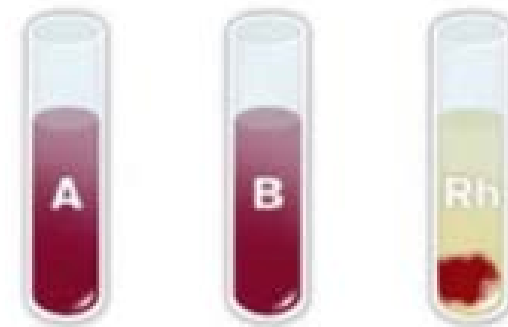
# Transfusion Reaction Work-up

- **DAT:**
  - Detects red cell sensitization with antibody or complement in-vivo
  - Perform DAT on post-transfusion sample
  - If positive, compare to DAT of pre-transfusion sample
  - If post is positive and pre is negative, perform elution to identify any antibodies
  - **Positive DAT does not prove acute hemolytic reaction**



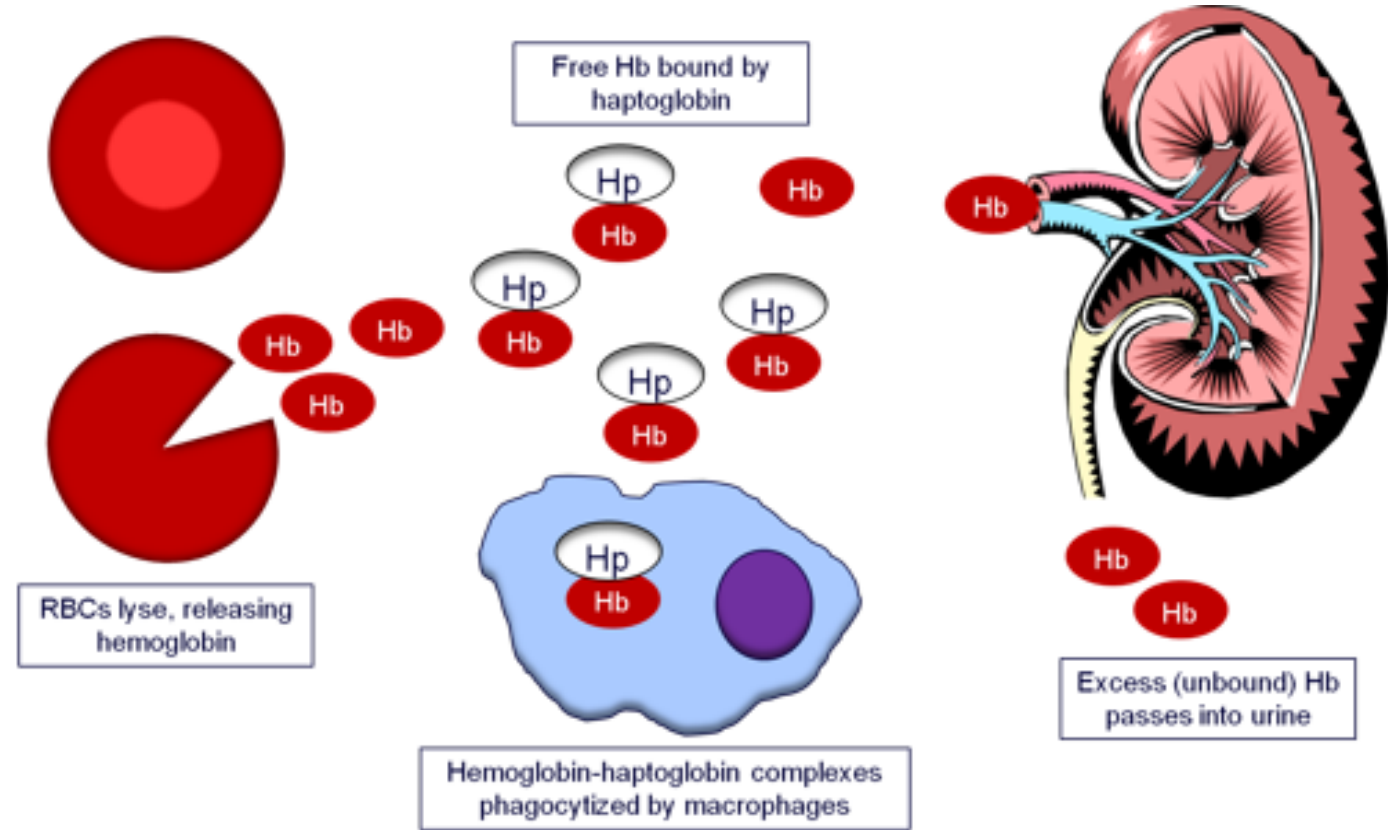
# Transfusion Reaction Work-up

- **Repeat ABO/Rh testing:**
  - Check pre and post samples
  - Verify patient's ABO typing is correct and sample was not misdrawn



# Other testing that may be performed

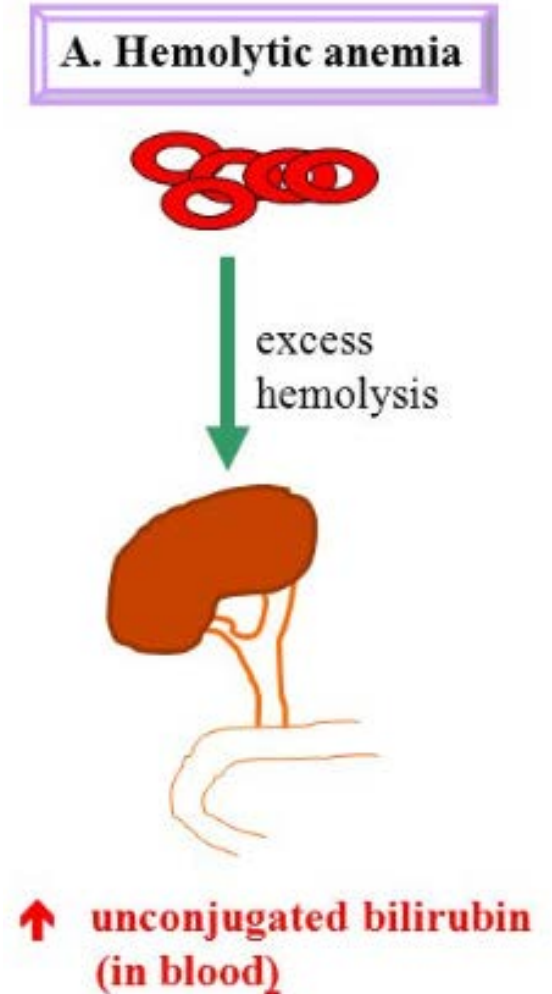
- Repeat antibody screen
- Repeat crossmatches
- Urine Hemoglobin
- Haptoglobin:
  - Haptoglobin binds free hemoglobin and removes from circulation
  - Decreased with hemolysis (being removed with free hemoglobin)





# Other Testing

- **Indirect and Direct Bilirubin**
  - Waste product produced by breakdown of heme
  - Increases during hemolytic reaction due to large amounts of heme being broken down
- **Lactate Dehydrogenase (LDH)**
  - Enzymes catalyzing lactate to pyruvate
  - When RBCs hemolyze it is released into the blood stream
  - Increased during hemolytic reactions



# Transfusion Reaction Classifications

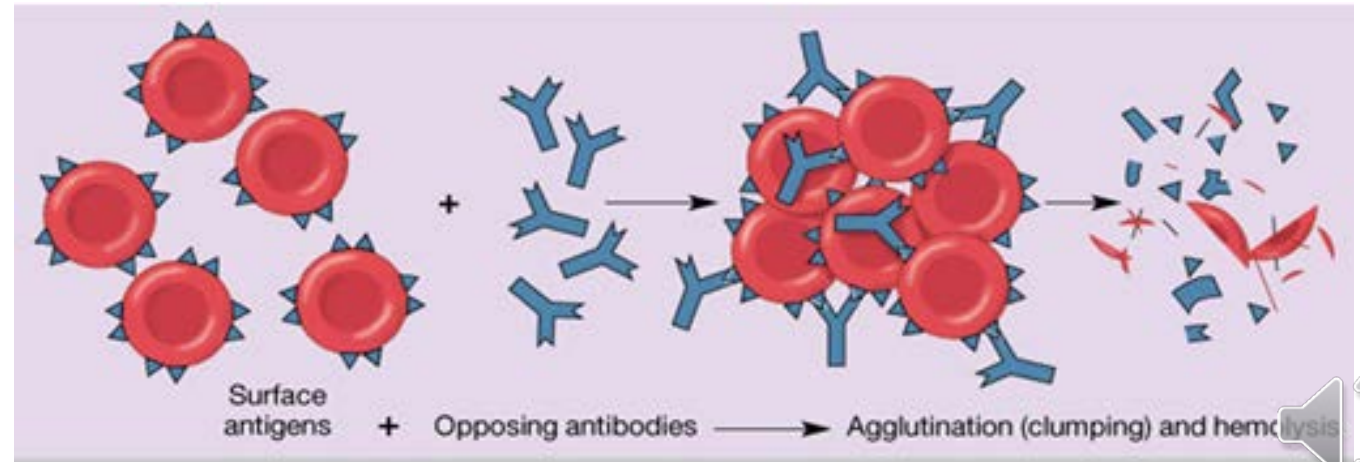
Acute	Delayed
Acute Hemolytic	Delayed Hemolytic
Febrile Non-hemolytic	Delayed Serologic
Transfusion-related Sepsis	TA-GVHD
TRALI	Post-transfusion purpura
Allergic	Iron Overload
TACO	

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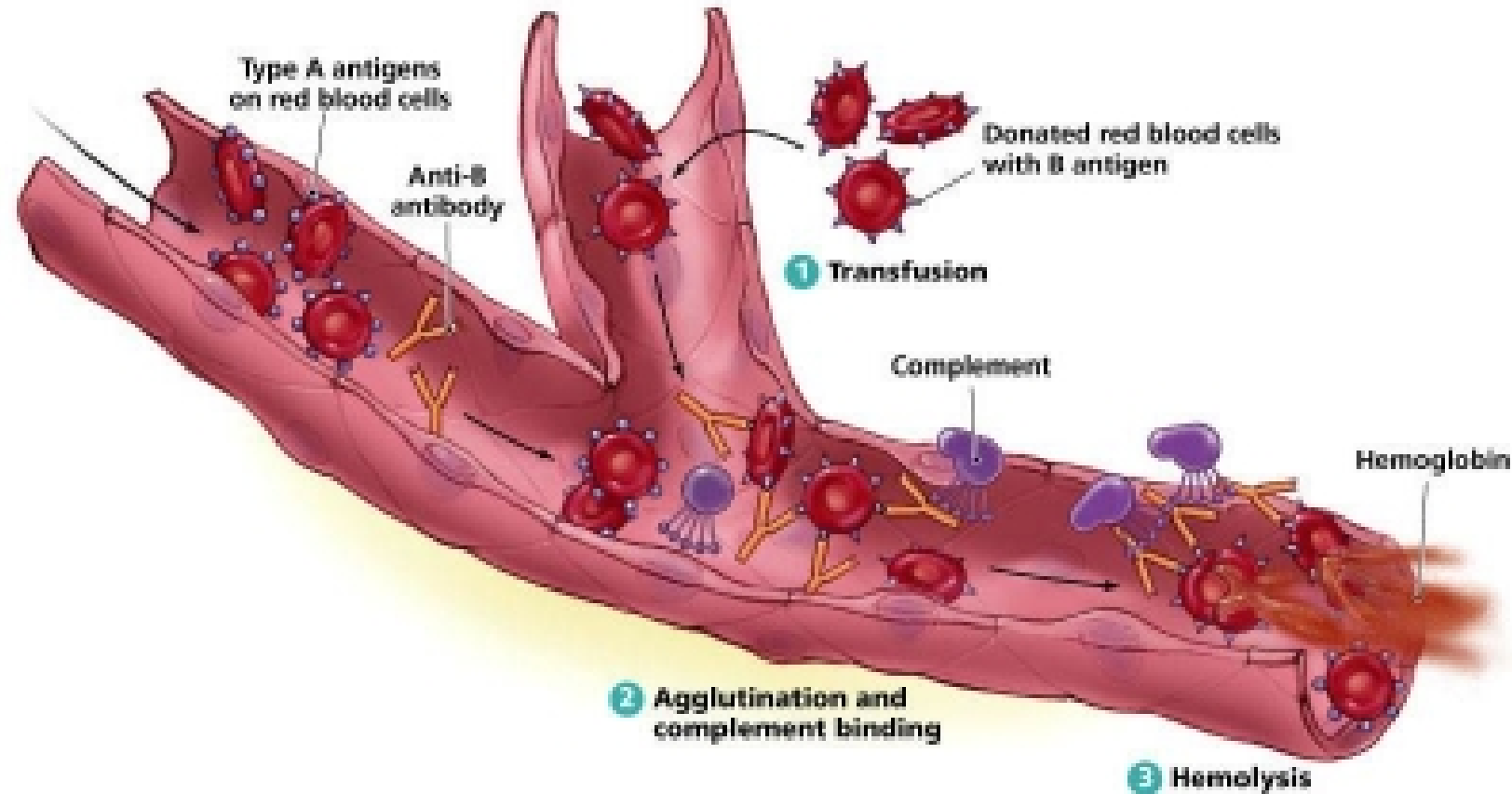


# Acute Hemolytic Transfusion Reactions (AHTR)

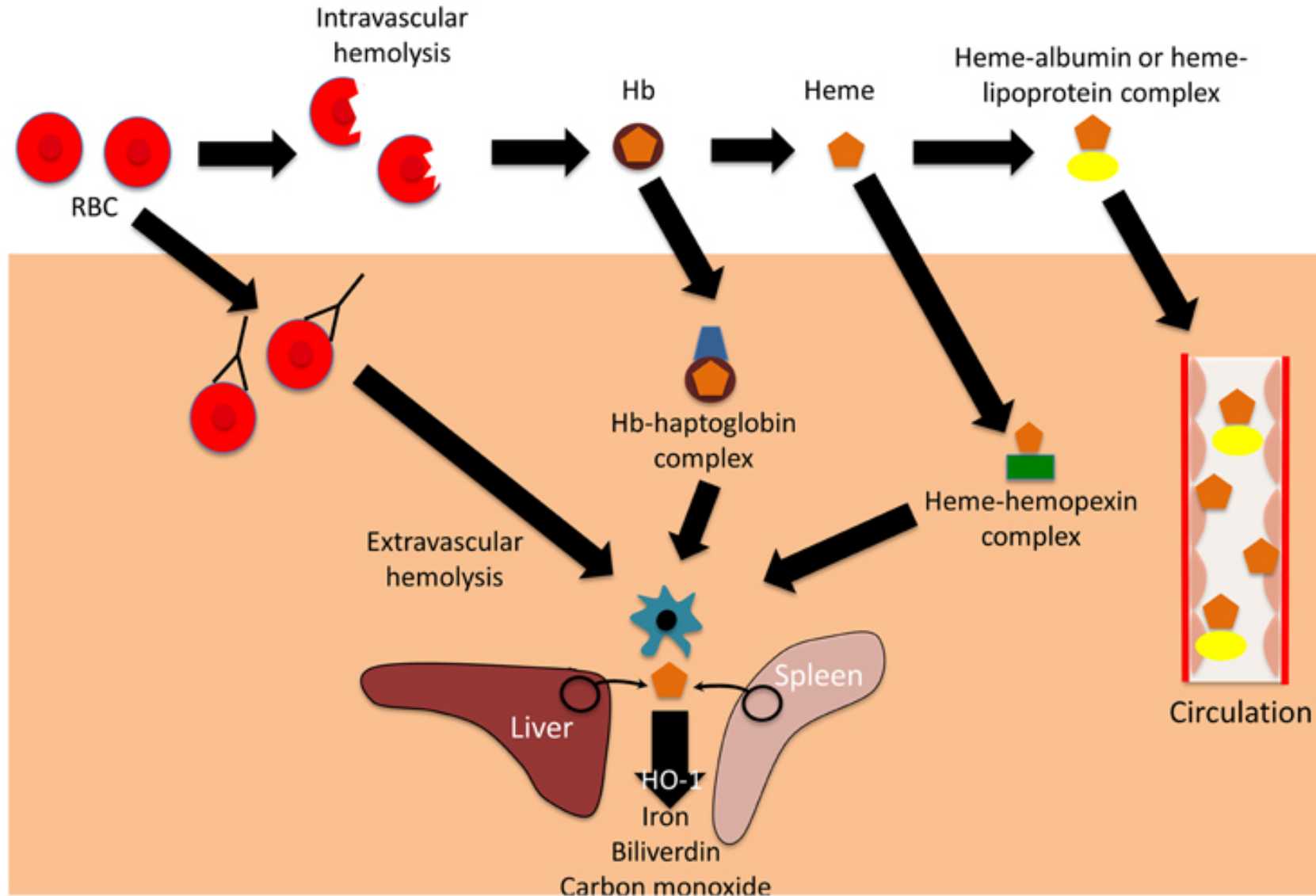
- 1:76,000 transfusions (1:1.8 million fatal)
- Antibodies in recipient react with donor red cell antigens
- Ex. ABO antibodies fix complement when wrong blood type is transfused causing hemolysis
- RBC destruction can be intravascular or extravascular
- Usually caused by clerical errors in blood bank or at bedside
- Reactions usually occur early in transfusion
- Most commonly to ABO antibodies



# Intravascular RBC Destruction

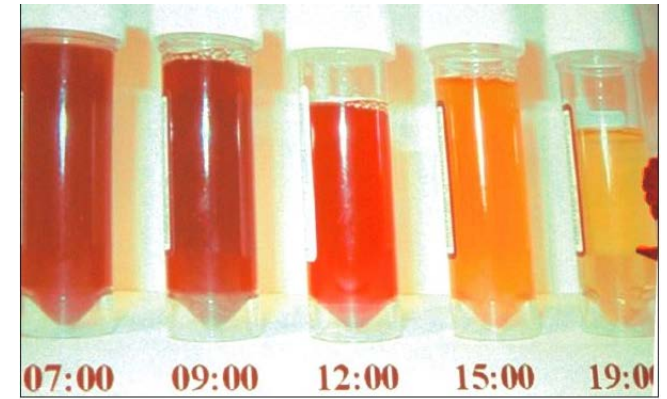
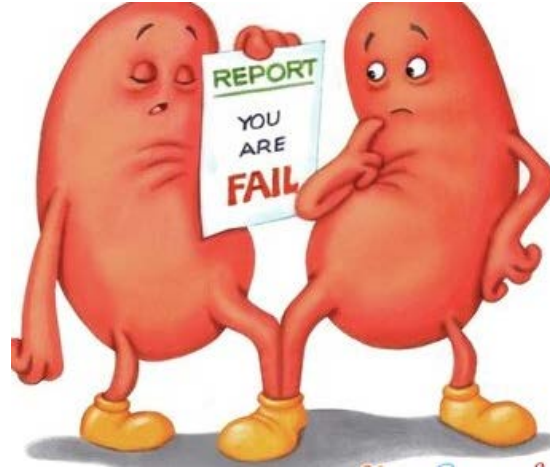


# Extravascular RBC Destruction



# AHTR Signs and Symptoms

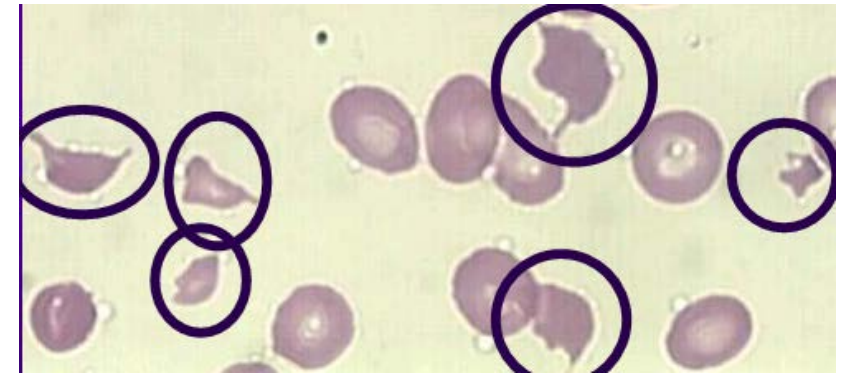
- Fever and chills
- Back pain
- Pain at infusion site
- Hypotension/shock
- Hemoglobinuria
- Hemoglobinemia
- DIC/increased bleeding
- Feeling of “impending doom”
- Renal failure



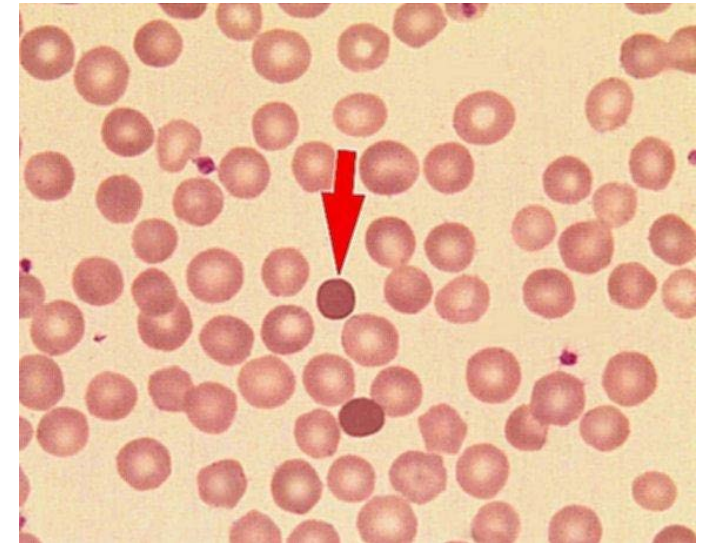


# AHTR Lab Findings

- Hemoglobinemia
- Hemoglobinuria
- Positive DAT on postreaction sample
- Increased bilirubin
- Decreased hemoglobin
- Decreased haptoglobin
- Increased LDH
- Schistocytes: intravascular hemolysis
- Spherocytes: extravascular hemolysis



Schistocytes: fragmented RBCs



Spherocytes: sphere-shaped instead of bi-concave disk



# Preventing AHTR

- Training and careful attention during:
  - Phlebotomy (draw right patient)
  - Issue (label blood for correct patient)
  - Administration (transfuse blood to correct patient)
- Draw two tubes for blood typing before issuing blood
- Obtain accurate patient history



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# Non-immune Acute Hemolytic Transfusion Reactions

- Chemical damage of transfused product
  - Incomplete deglycerolization
  - Bacterial contamination
- Mechanical damage of transfused product
  - Needle with inappropriate bore size
  - Improper shipping/storage temps
  - Improper use of blood warmers
  - Rapid pressure infuser
  - Infusion of unapproved fluids (instead of saline)



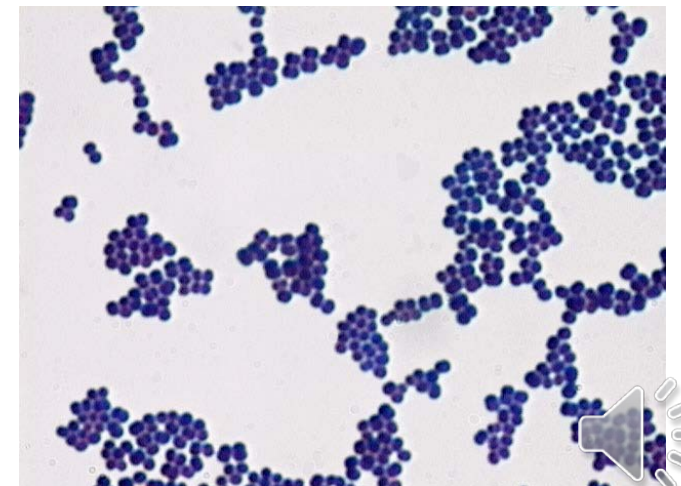
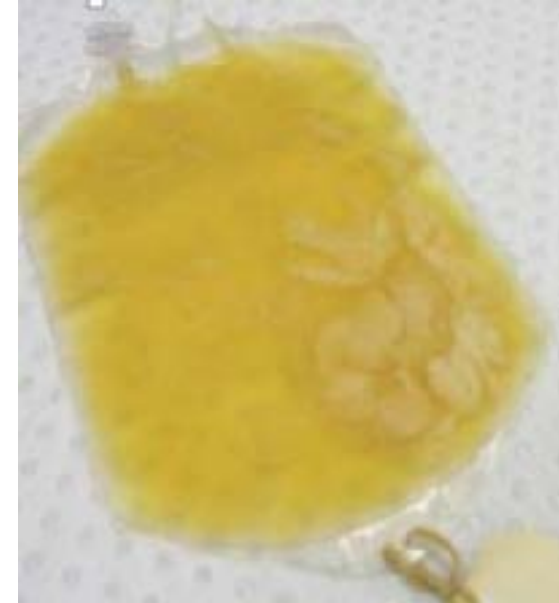
# **Non-immune Acute Hemolytic Transfusion Reactions**

- **Occurs independently from presence of antibodies**
- **Symptoms:**
  - **Asymptomatic hemoglobinuria**
- **Diagnostics:**
  - **DAT negative**



# Transfusion Associated Sepsis (TAS)

- Non-immune transfusion reaction
- Occurs when bacteria contaminated blood product is transfused
  - Platelets: skin contaminants from collection
  - RBCs: organism growing asymptotically in donor blood
- Platelets usually cause TAS (room temp storage)



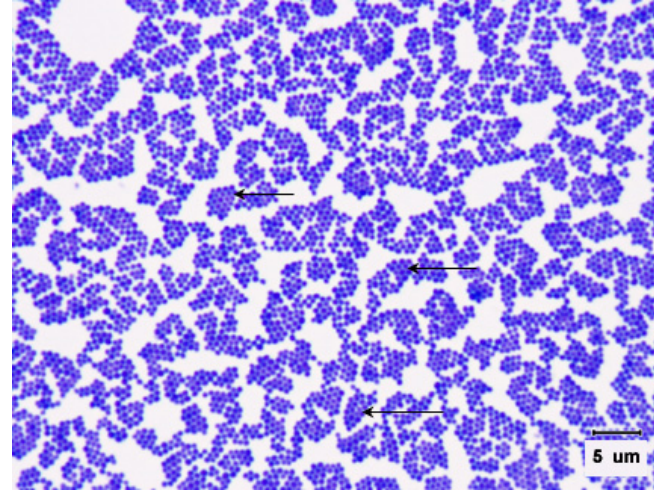
# TAS Signs and Symptoms

- Rapid onset high fever
- Rigors/chills
- Abdominal cramping, nausea, vomiting
- Hypotension/shock



# TAS Lab Findings

- Discolored blood product
- Non-immune hemoglobinuria/emia
- DAT negative
- 2/3 of proven positives: positive gram stain
- Positive culture of both unit and recipient





# TAS Prevention

- Careful donor history
- Proper phlebotomy technique
- AABB requires all platelets to be cultured
- Quarantine other products from a positive donation

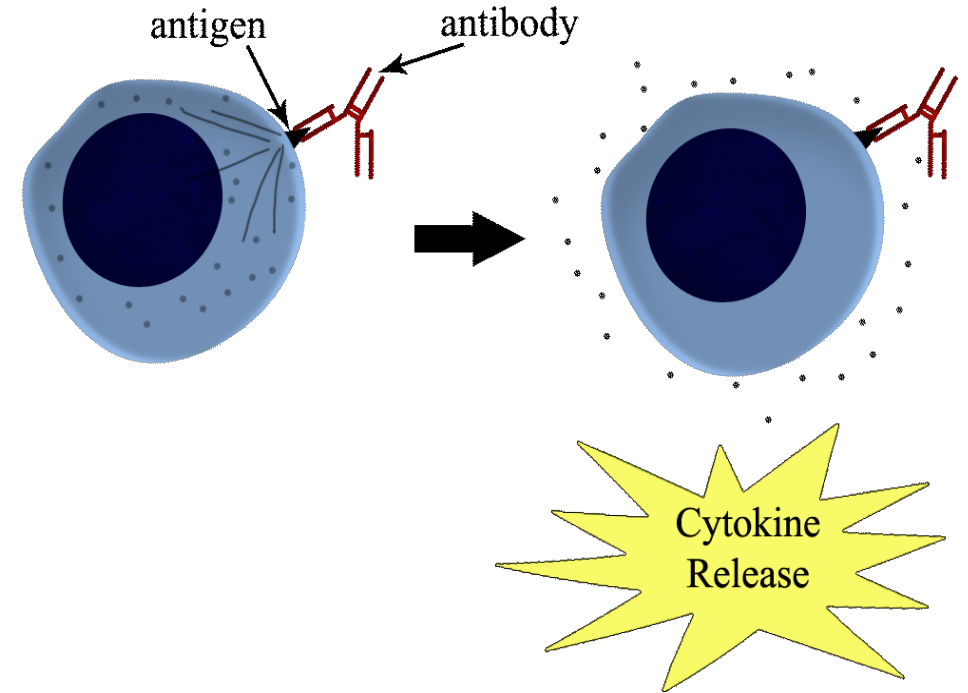


<b>QUARANTINE</b>	
REASON _____	
_____	
_____	
SIGNED _____	DATE _____
QA Supplies 08 8396 5838 Re-order L306	



# Febrile Non-hemolytic Transfusion Reactions (FNHTR)

- Unexplained increase in temperature 1°C or 2°F due to increased pyrogenic substances from WBCs
- Two white cell related mechanisms:
  - Donor WBCs secrete cytokines in bag before transfusion
  - Recipient antibodies against HLA antigens on WBCs leading to fever-inducing substance released
  - Both release pyrogens causing fever



# FNHTR Signs/Symptoms

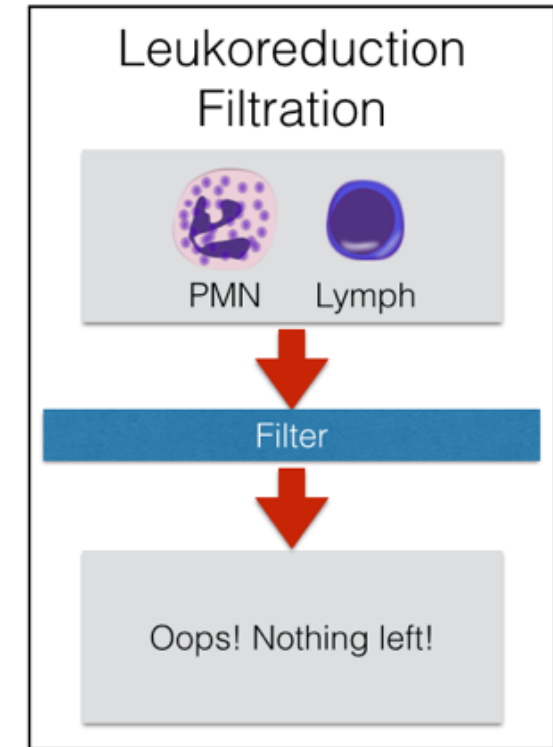
- Fever and chills during or up to 2 hours after transfusion
- Reaction usually resolves on its own
- Nausea/vomiting
- Increased blood pressure
- Increased heart rate and breathing
  - Tachycardia/Tachypnea





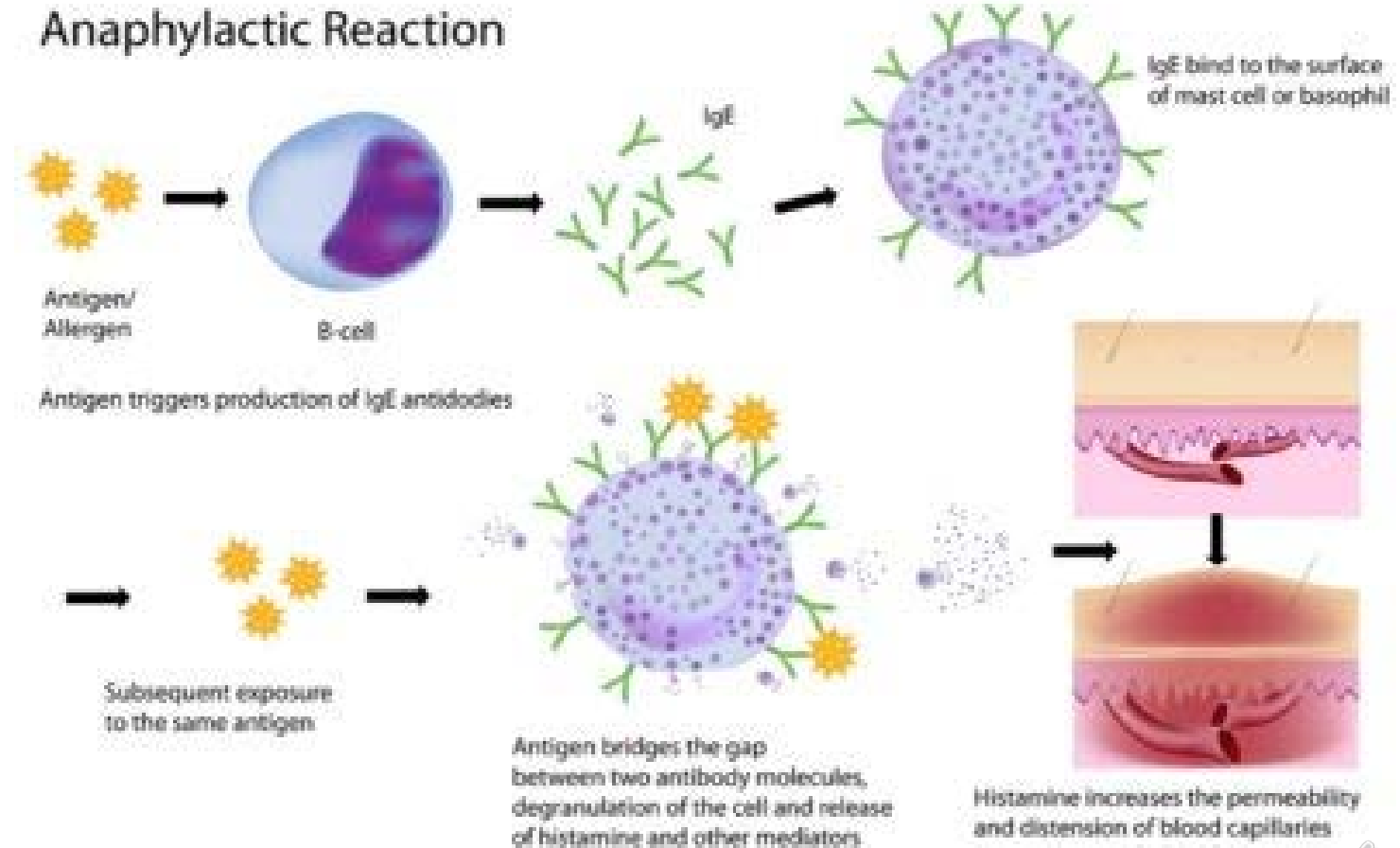
# FNHTR

- Lab Findings:
  - None: Negative hemolysis workup
  - Diagnosis is made by exclusion
- Prevention:
  - Leukocyte reduction of red cells (remove WBCs)
  - Pre-medicate with acetaminophen to reduce fever
- Treatment:
  - Stop transfusion
  - Acetaminophen to reduce fever



# Allergic Transfusion Reactions

- IgE antibodies bind to allergen bound to mast cells resulting in release of histamine
- Severe reactions in IgA deficiency
  - Form an anti-IgA IgE antibody
  - Causes anaphylactic shock
- Allergens: IgA, latex, drugs, food, proteins



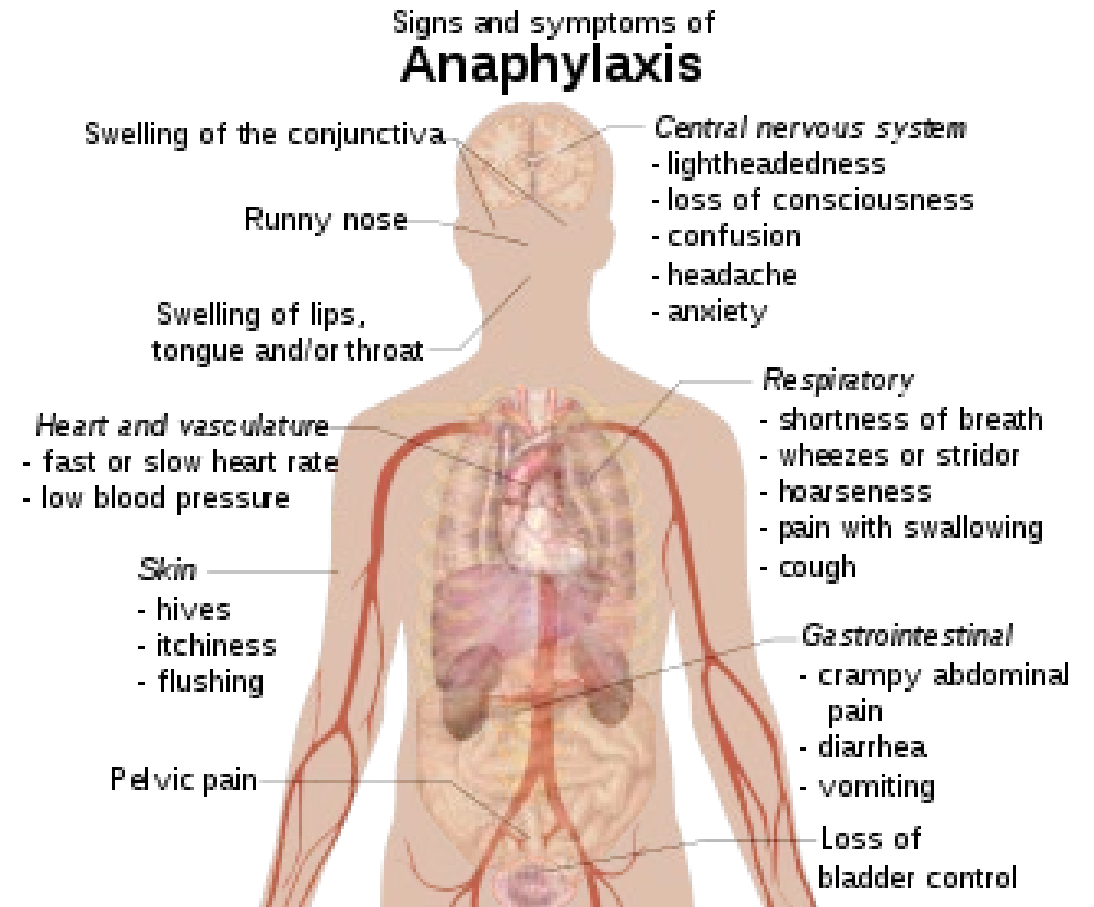
# Mild Allergic Reaction Symptoms

- Anytime during transfusion
- Hives
- Mild respiratory symptoms
- Urticaria
- Redness
- Swelling
- May continue transfusion once symptoms disappear



# Severe Allergic Reaction Symptoms

- Shortly after starting transfusion
- Angiodema (swelling under skin)
- Wheezing
- Hypotension
- Anaphylaxis



# Allergic Transfusion Reaction

- Lab Findings:
  - None
  - DAT Negative
  - Based on symptoms and response to treatment
- Treatment/Prevention:
  - Benadryl for mild symptoms
  - Epinephrine for anaphylactic
  - Washed red cells in future for IgA deficient patients



# Transfusion-Related Acute Lung Injury (TRALI)

- Leading cause of transfusion related fatalities
- Two hypothetical pathways of pathogenesis:
  - Immune TRALI
  - Nonimmune TRALI



# Immune TRALI

## Principle

- Involve antibody-mediated event.
- Alloantibodies are responsible for TRALI.

## Types of Alloantibodies involve

- Anti-human leukocyte antigen(anti-HLA) class I or class II antibody
- Also associated with antilymphocyte, antimonocyte
- Specific neutrophil alloantigen: HNA-1a, HNA-1b, HNA-3a and HNA-2a

Donor antibodies react with recipient leukocytes/neutrophils

Aggregates obstruct pulmonary circulation

Activate complement/release cytokines

Damage endothelium/destroy capillaries in lung

\*Can occur in healthy individuals with no underlying lung injury



# Nonimmune TRALI

## First Hit

Predisposing condition

Primes patient's neutrophils

Sequester neutrophils in pulmonary endothelium

## Second Hit

Transfusion of blood product

Antibodies or biologically active lipids activate primed neutrophils

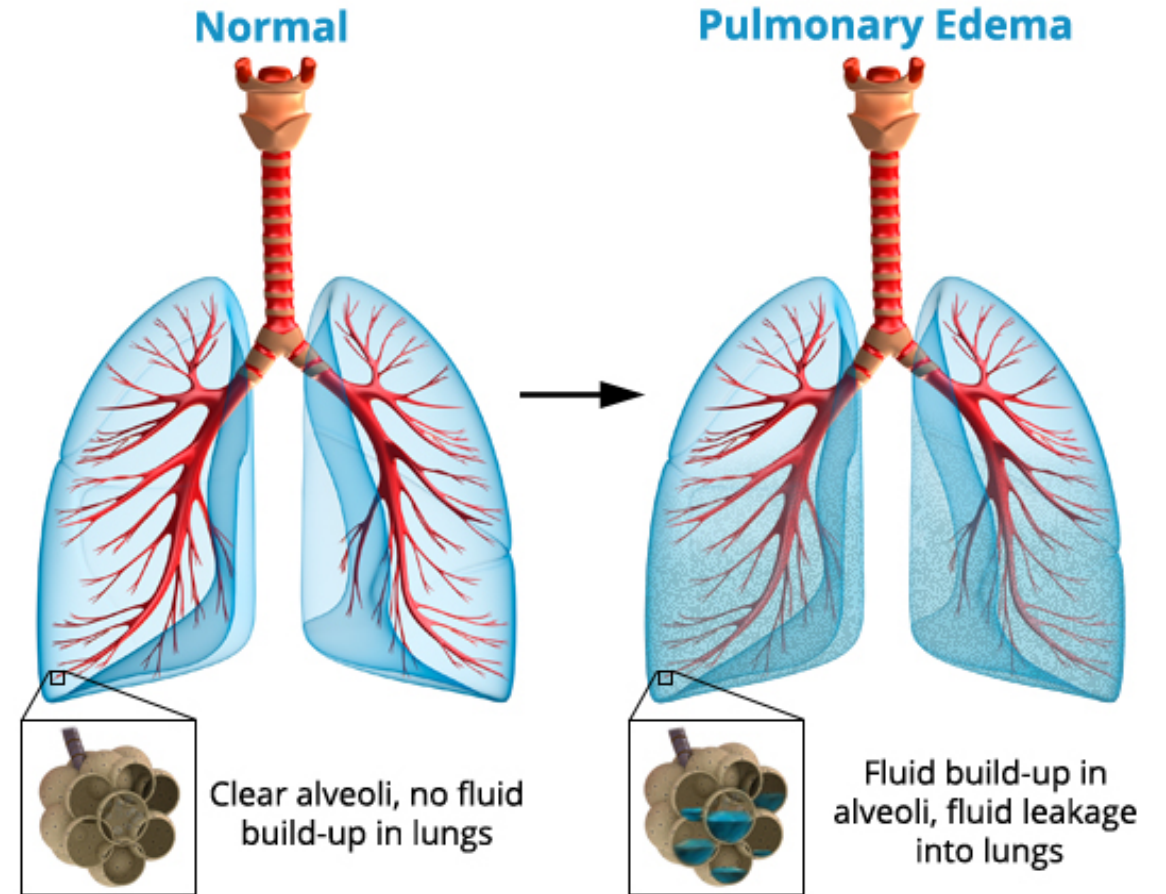
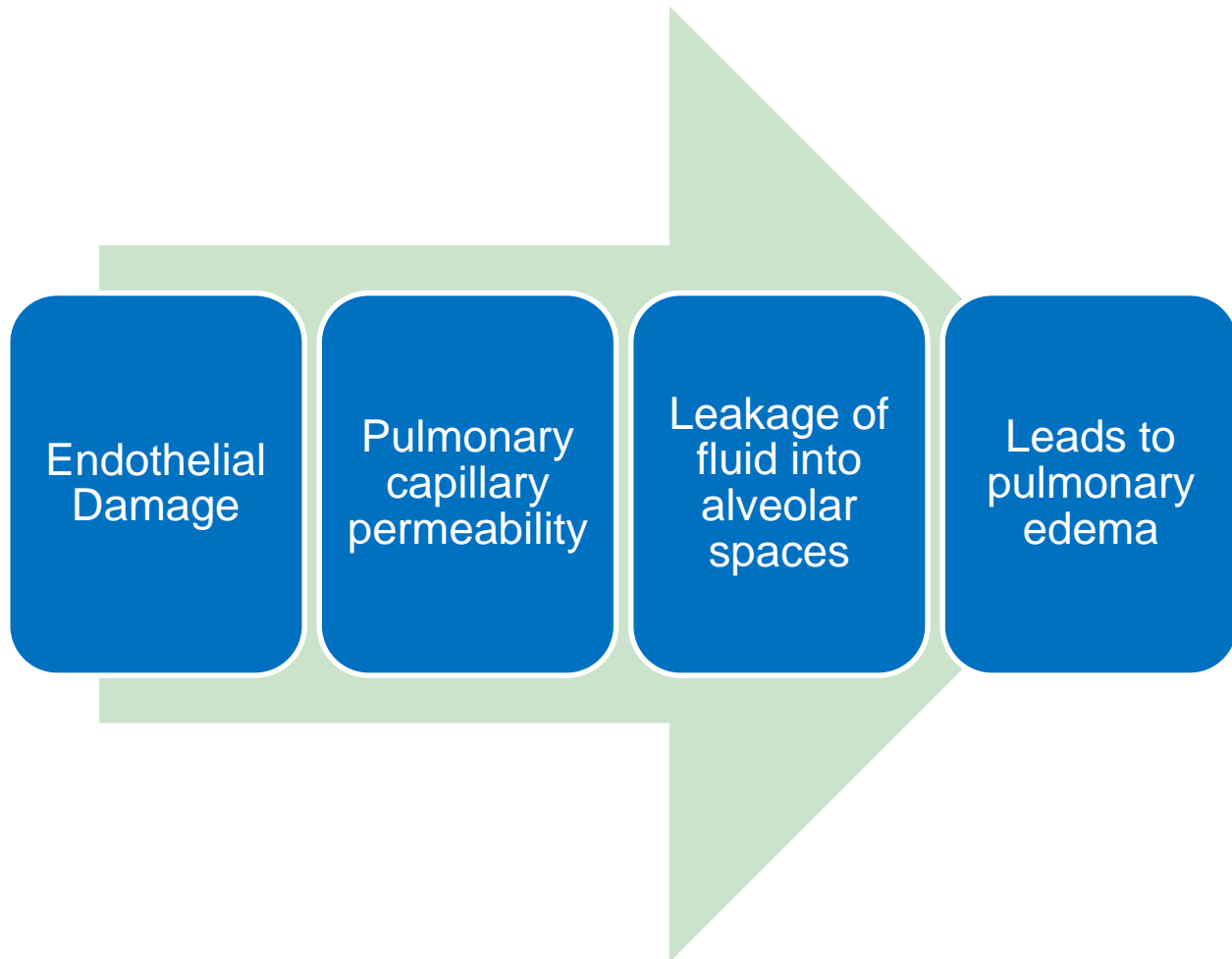
Damage endothelium





# Final Common Pathway

- Immune and nonimmune have final common pathway



Pulmonary Edema= fluid buildup in lungs



# TRALI Signs and Symptoms

- New acute lung injury within 6 hours of transfusion
- Lack other risk factors for pulmonary edema
- Respiratory distress
- Fever/chills
- Hypotension
- Severe hypoxemia
  - Decreased O<sub>2</sub> in blood

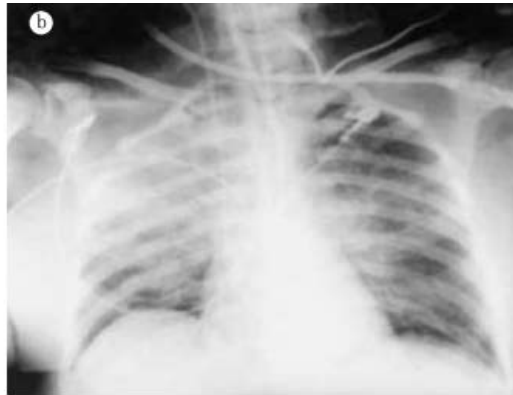


# TRALI Diagnostics

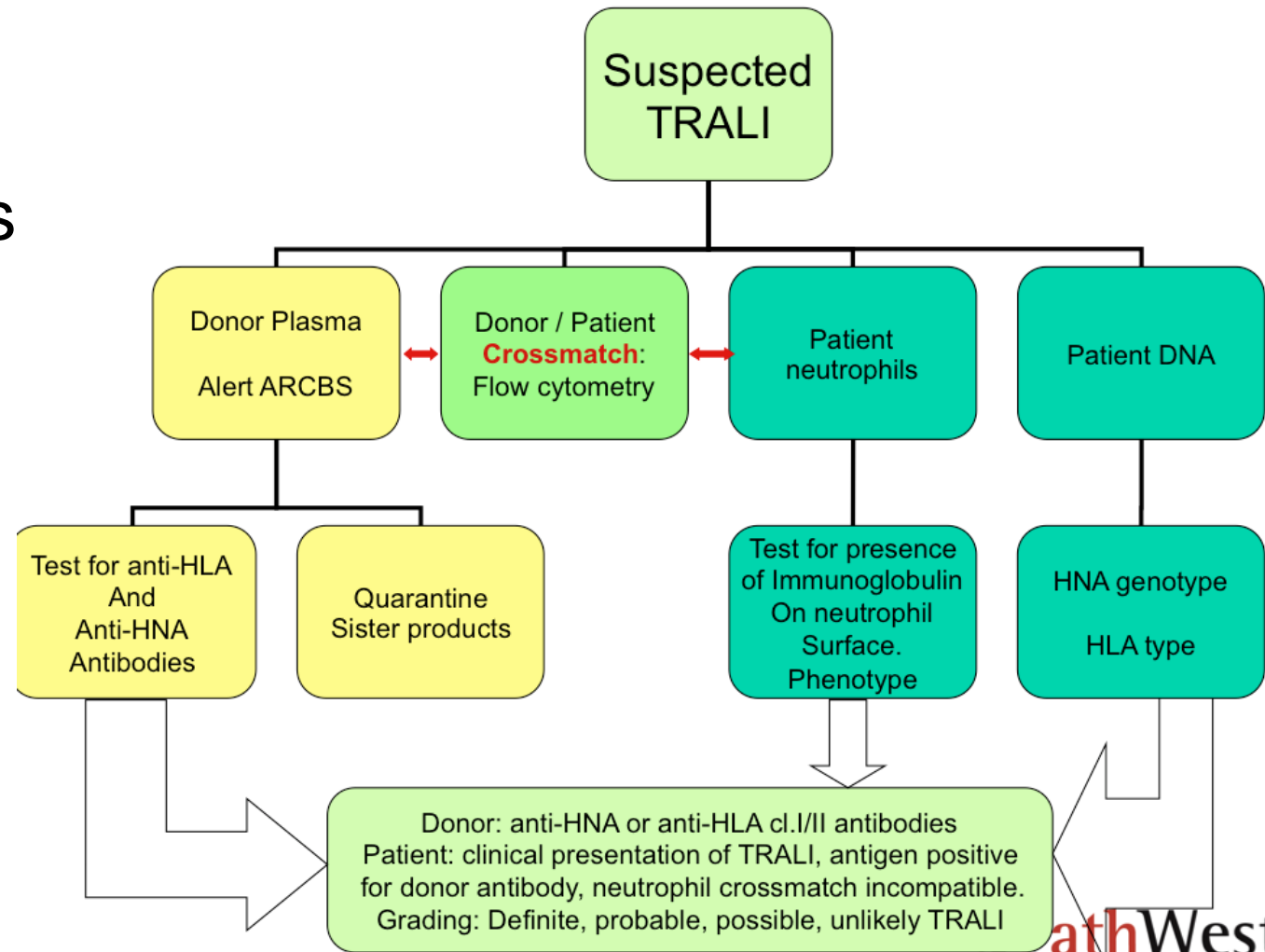
- Difficult to diagnose
- Chest X-ray- bilateral infiltrates
- Donor/Recipient tests for HLA/HNA antibodies
- O2 saturation <90%



Before TRALI



After TRALI



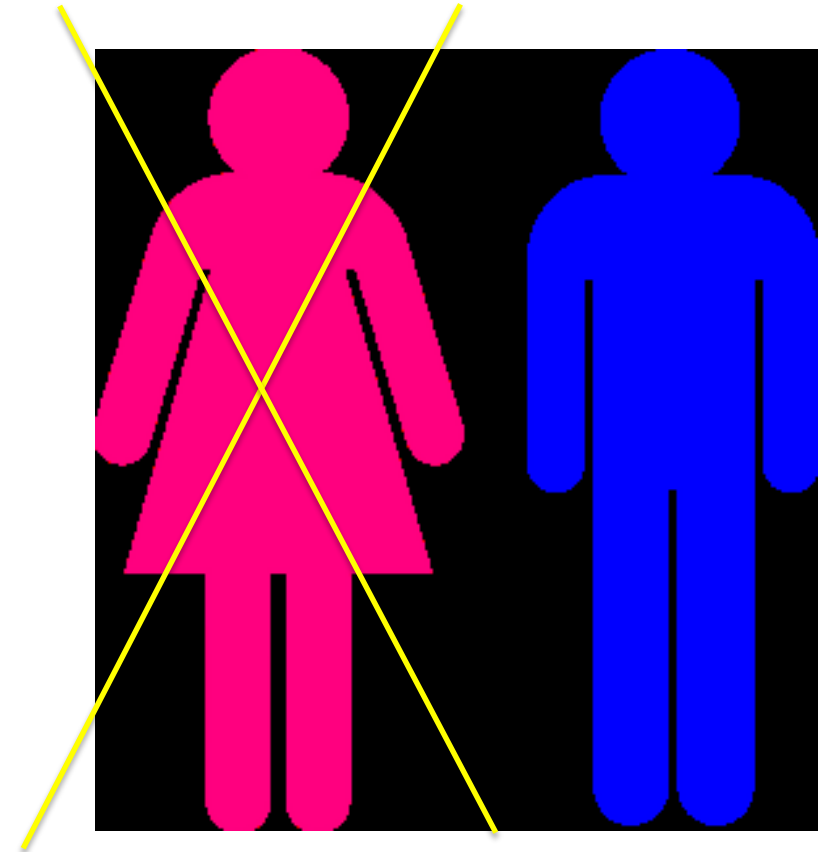
# TRALI Treatment

- Treatment:
  - Largely supportive
  - Mild TRALI- supplemental oxygen therapy
  - Severe TRALI- mechanical ventilation and ICU support
  - Cases usually improve within 48-96 hours
  - 15-20% fatal



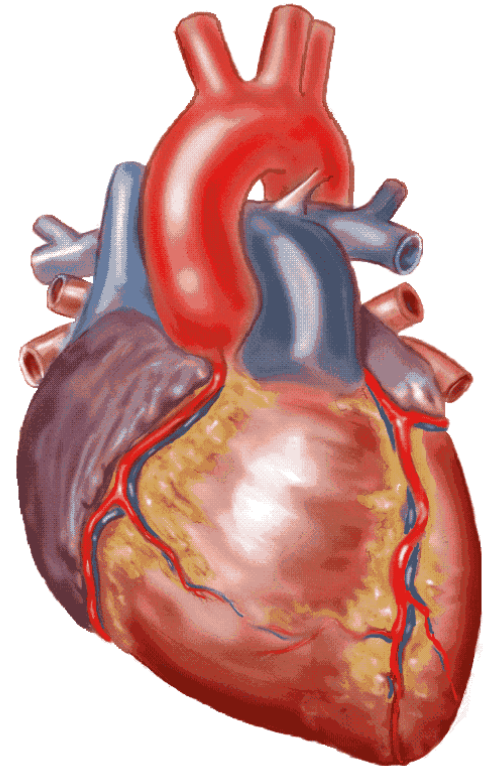
# TRALI Prevention

- Plasma and platelets contain largest plasma volumes
  - Highest risk of immune-mediated TRALI
- Donors found to have antibodies deferred from donation
- Some donor centers only accept male plasma donors
  - Or reject multiparous females



# Transfusion-Associated Circulatory Overload (TACO)

- Patient's cardiovascular system is unable to handle additional workload
- Manifests as congestive heart failure
- Patients at risk:
  - Preexisting CHF
  - Very old/very young
  - Renal failure
  - Chronic anemia
  - Rapid or massive transfusion





# TACO Signs/Symptoms

- Respiratory distress
- Hypoxemia
- Cough
- Headache
- Jugular vein distention
- Elevated blood pressure
- **Afebrile**



# TACO Diagnostics

- Chest X-ray:
  - Bilateral infiltrates
  - Pulmonary edema
  - Cardiomegaly
  - Distended pulmonary artery
- Elevated BNP





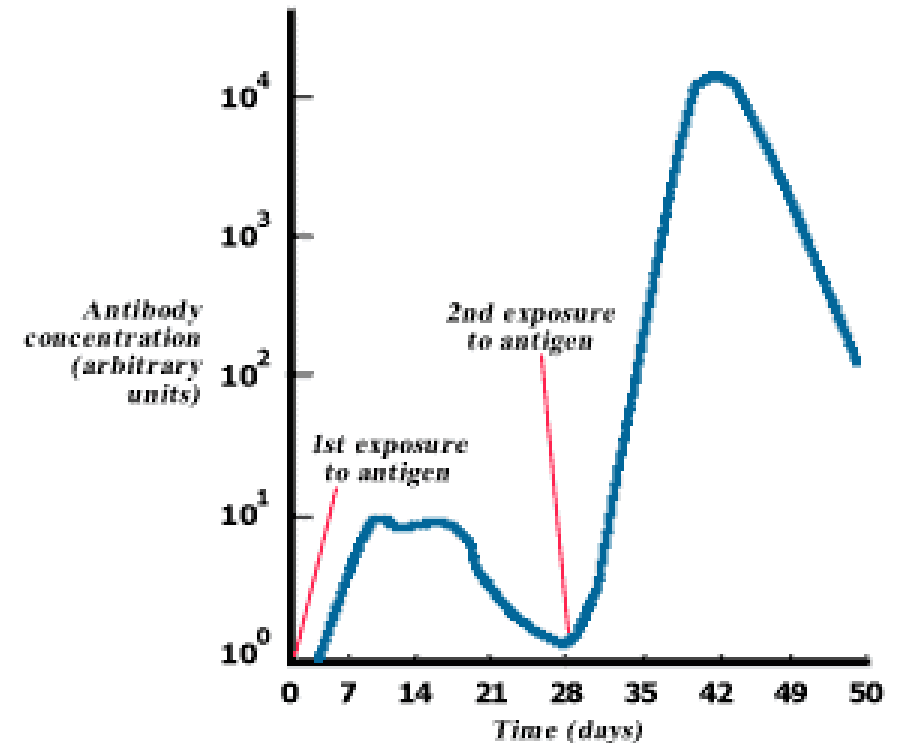
# TACO Treatment and Prevention

- Treatment:
  - Upright sitting position
  - Supplemental oxygen
  - Diuresis- increase urine output, reduce blood volume
- Prevention:
  - Control infusion rates
  - Split units into aliquots
  - Consider low volume units for at risk patients



# Delayed Hemolytic/Serologic Transfusion Reaction (DHTR)

- Hemolysis 24 hours to 28 days after transfusion
- Anamnestic response:
  - Patient exposed to foreign non-ABO antigen
  - Antibody forms, but fades over time and is never tested or found
  - Patient has negative screen and is re-exposed to antigen with transfusion
  - Rapid production of IgG antibody vs. target antigen



# DHTR

- Usually extravascular hemolysis- RBCs removed by liver/spleen
- Common for Kidd, Duffy, and Kell
- Sometimes may be asymptomatic- many times only discovered with new sample
- Degree of RBC destruction depends on:
  - Antibody specificity
  - Thermal activity range
  - Ability to fix complement



# DHTR Symptoms

- Often asymptomatic
- Fever
- Anemia
- Mild jaundice
- Pallor



Normal

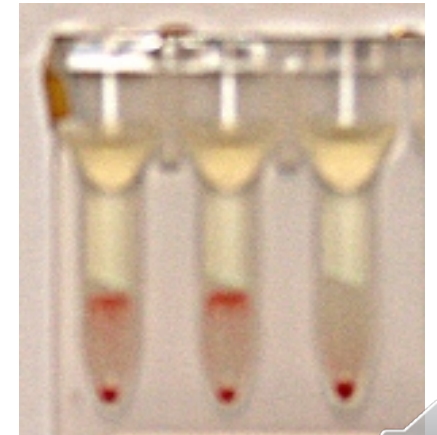
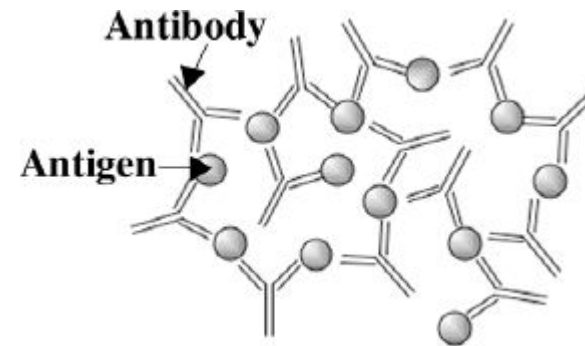
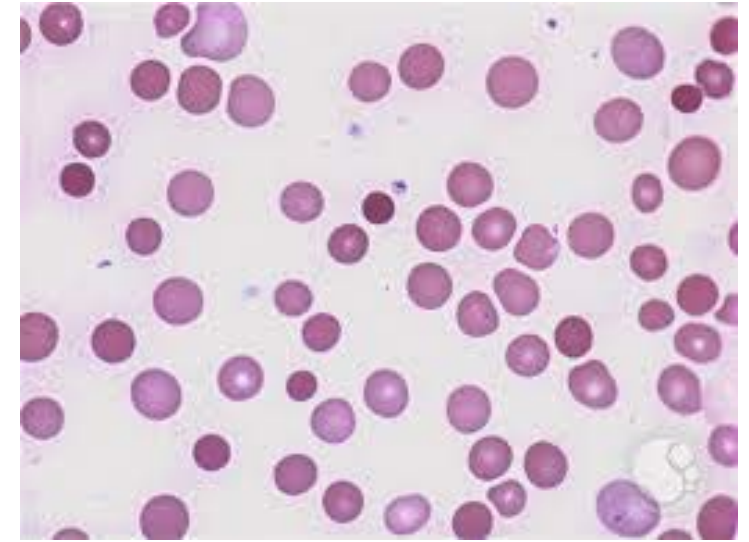


Anemia



# DHTR Lab Findings

- Decreased hemoglobin and haptoglobin
- Newly positive antibody screen
- Positive DAT
- Anemia
- Spherocytes
- Elevated LDH and bilirubin



# DHTR Prevention and Treatment

- Obtain antibody history from other hospitals
- For the most part difficult to prevent if the antibody titer falls below detectable levels





# Transfusion-Associated Graft-Versus-Host Disease (TA-GVHD)

- Donor lymphocytes in component launch immune response against recipient cells (foreign HLA tissues)
- Usually fatal
- Three requirements:
  - Viable T-lymphocytes transfused
  - Donor and recipient not HLA-identical
  - Recipient can not launch counterattack

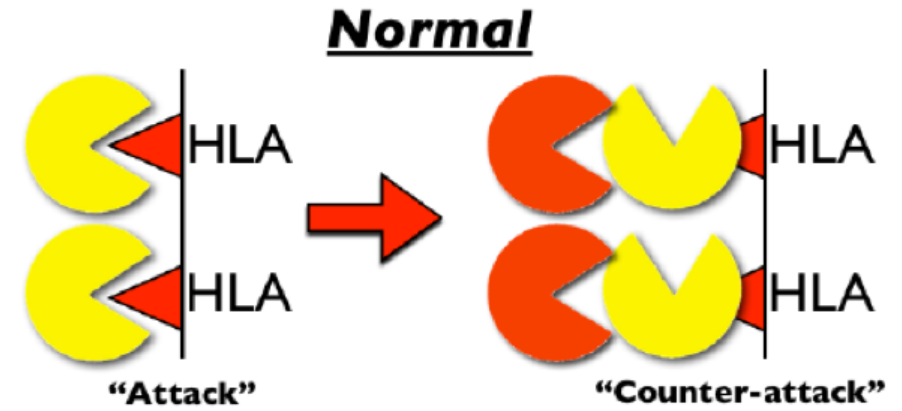
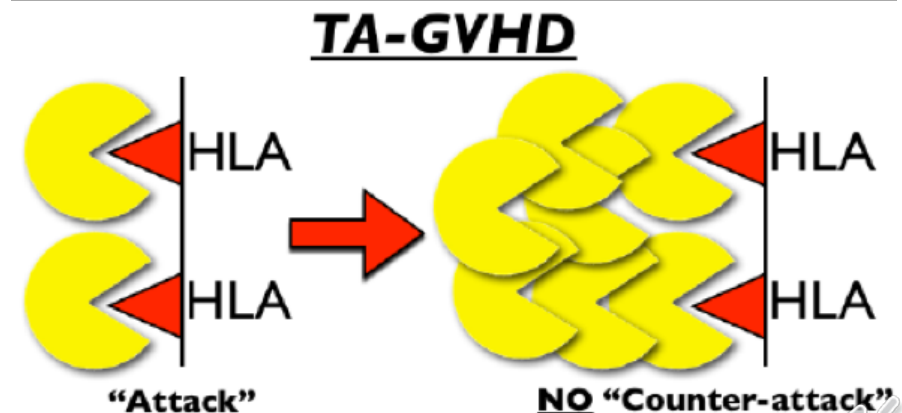





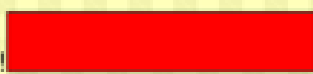
Figure 11: Normal Sequence



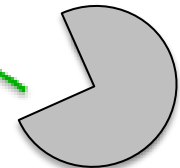
# Patients at Risk for TA-GVHD

- Immunosuppressed (T-cell deficiency, bone marrow transplants, chemotherapy, aplastic anemia)
- Intrauterine and neonatal transfusions
- Hematologic malignancies (Hodgkins)
- Granulocyte transfusions
- Receiving blood from relative

Blood from a relative:

Recipient HLA	Donor HLA
	
	

Mismatch!

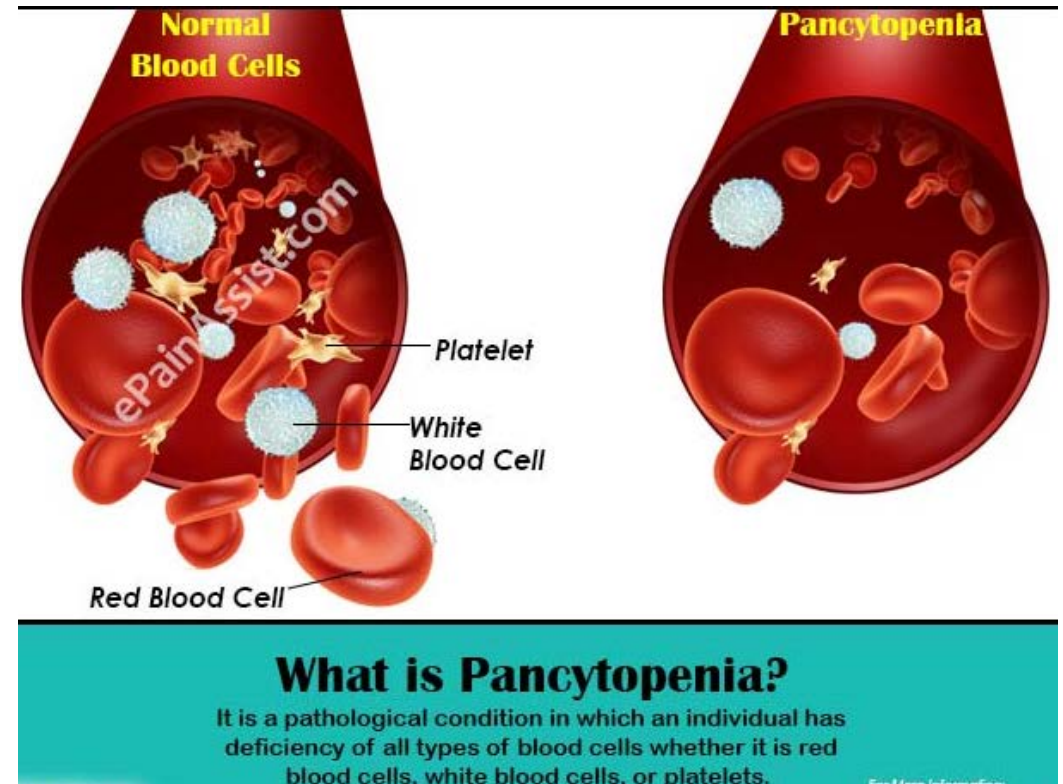


Doesn't counterattack  
because donor  
lymphocyte doesn't  
look foreign



# TA-GVHD Signs and Symptoms

- Fever 7-10 days post-transfusion
- Face/trunk rash
- Nausea/vomiting
- Watery diarrhea
- Hepatitis
- Pancytopenia- leads to infections and fatal consequences



# TA-GVHD Lab Findings

- Pancytopenia
- Skin biopsy- perivascular lymphocyte infiltrate
- Bone marrow aspirate- hypocellular or aplastic marrow
- Liver biopsy- necrosis of small bile duct
- Molecular studies- determine donor vs. recipient HLA types



# TA-GVHD Prevention

- Irradiation- deactivates lymphocytes without damaging other cells
- Leuko-reduction may not be enough- some cases reported from leukoreduced units
- No standard therapy
- 90% mortality rate



RAD-SURE®	OPERATOR: _____	DATE: _____
25 Gy INDICATOR	<b>NOT</b>	IRRADIATED
ISP TECHNOLOGIES INC.	LOT NO: _____	EXP: _____

BEFORE IRRADIATION

RAD-SURE®	OPERATOR: _____	DATE: _____
25 Gy INDICATOR	<b>IRRADIATED</b>	
ISP TECHNOLOGIES INC.	LOT NO: _____	EXP: _____

AFTER IRRADIATION @ 25 Gy



# Post-Transfusion Purpura

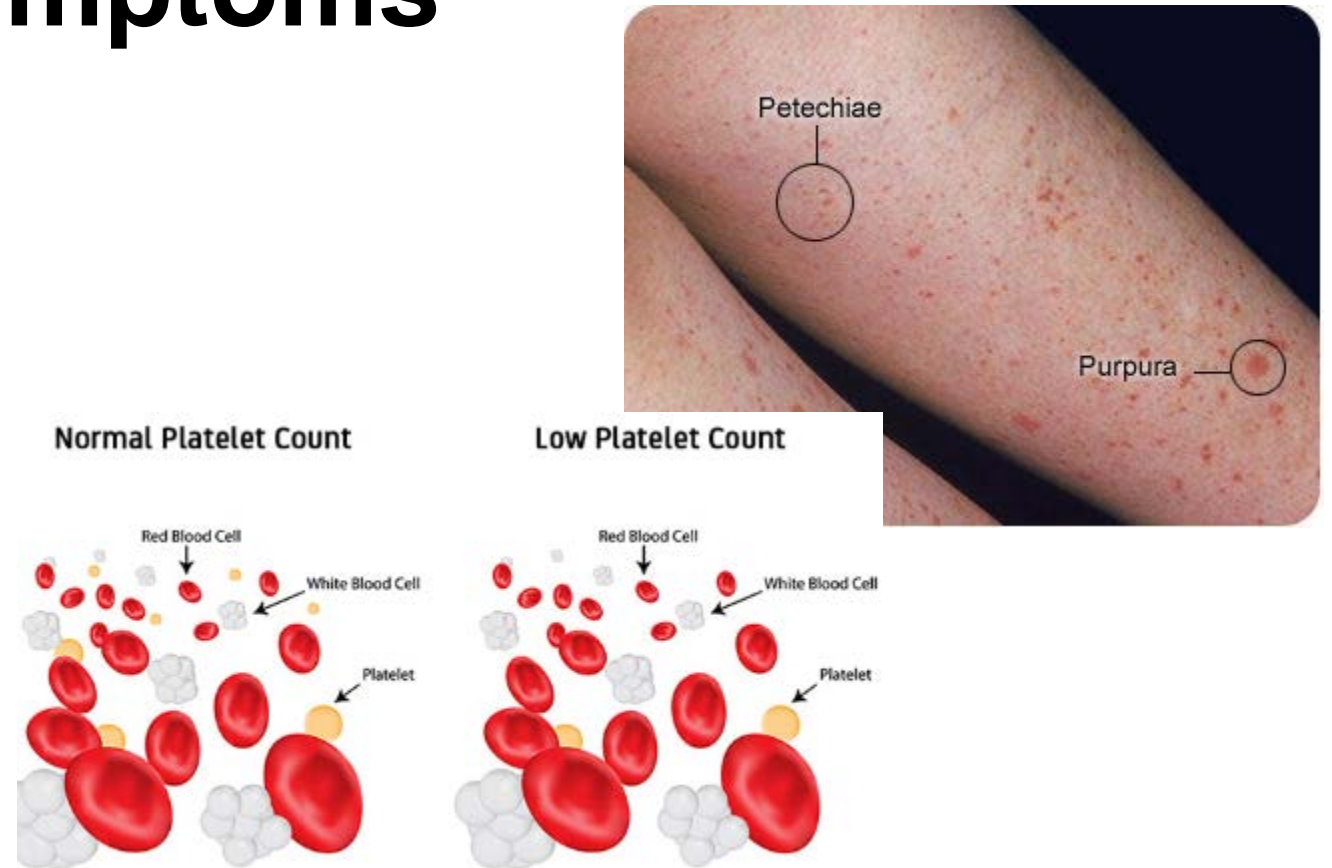
- 2-14 days after transfusion
- Patient makes antibody to a human platelet antigen from pregnancy or transfusion
  - HPA-1a antibodies
- Leads to destruction of platelets
  - Destroys both donor and patient's platelets





# Post-Transfusion Purpura Signs and Symptoms

- Thrombocytopenia
- Purpura, rash, bruising, mucosal bleeding
- Sometimes febrile
- Difficult to diagnose
- Self-limiting: platelet count usually returns to normal in 2 weeks



**Thrombocytopenia**  
**(Low Platelet Count)**



# PTP Treatment Prevention

- Treatment: IVIG
  - Binds to platelet antibodies
  - Blocks antibody Fc receptors
  - Breaks down IgG molecules
- Once antibody has been identified as the cause:
  - Avoid platelet transfusions if possible
  - Future platelet transfusions should be negative for antigen

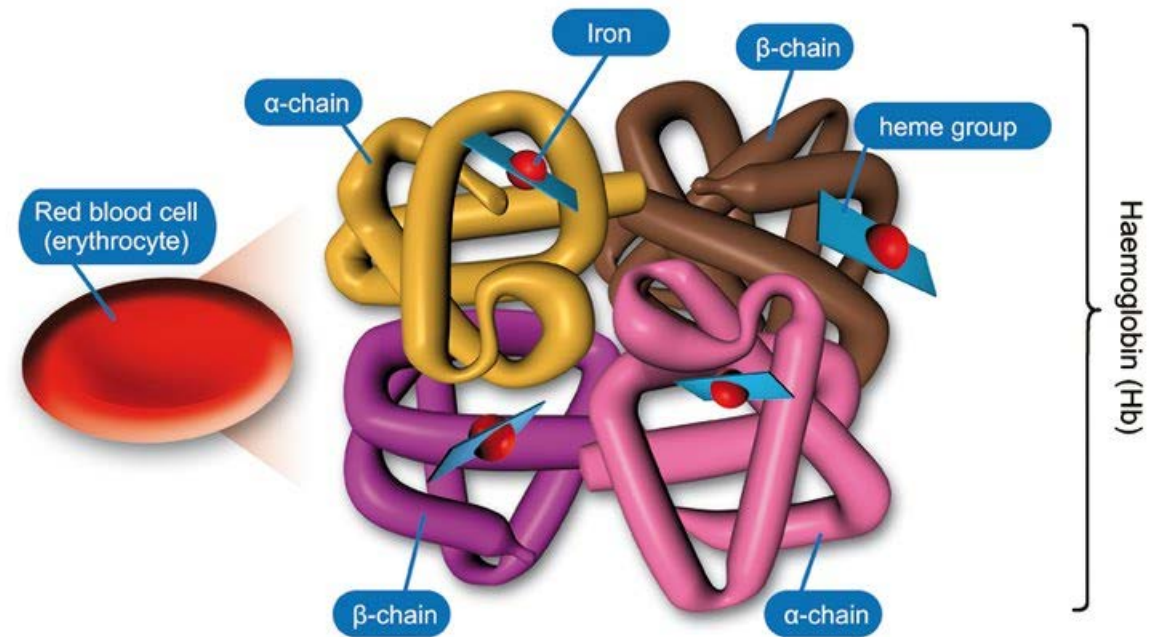


# Iron Overload

- Iron accumulation due to many transfusions
- RBC units contain: 200-250 mg iron
- Average male: 3-3.5g iron
- 1-2 mg of iron in daily diet
- Lifetime load of 50-100 transfusions = risk for iron overload
- Greatest risk: chronic red cell transfusion recipients



Structure of haemoglobin

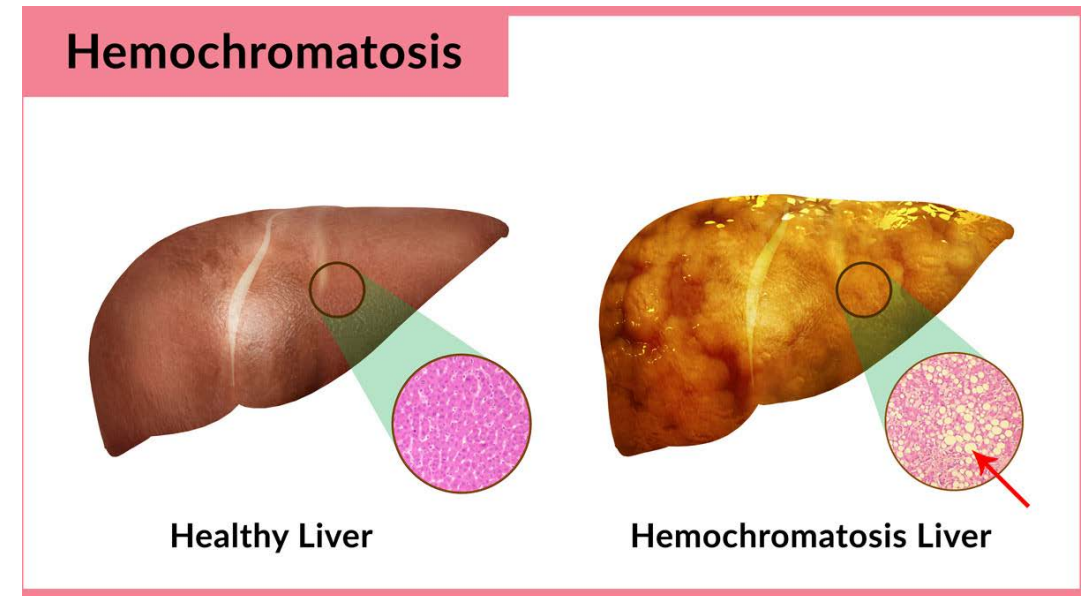


Each erythrocyte (RBC) contains ~270 million haemoglobin molecules



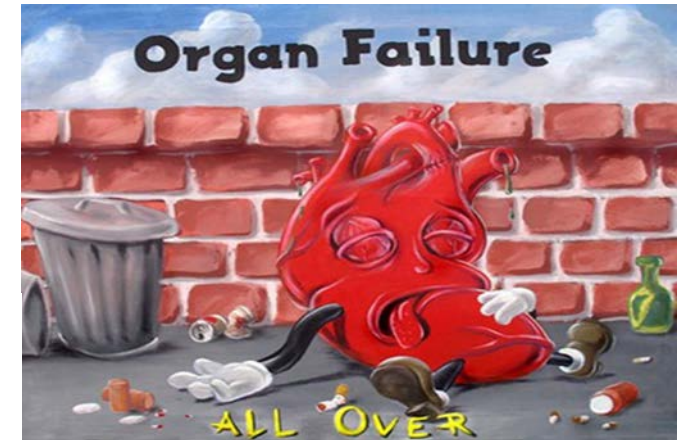
# Iron Overload Diagnosis

- Excess iron accumulates and deposits in tissues
- Leads to multi-organ damage/failure
  - Liver, heart, pancreas, endocrine organs
- Elevated ferritin levels
- Liver biopsy



# Iron Overload Symptoms

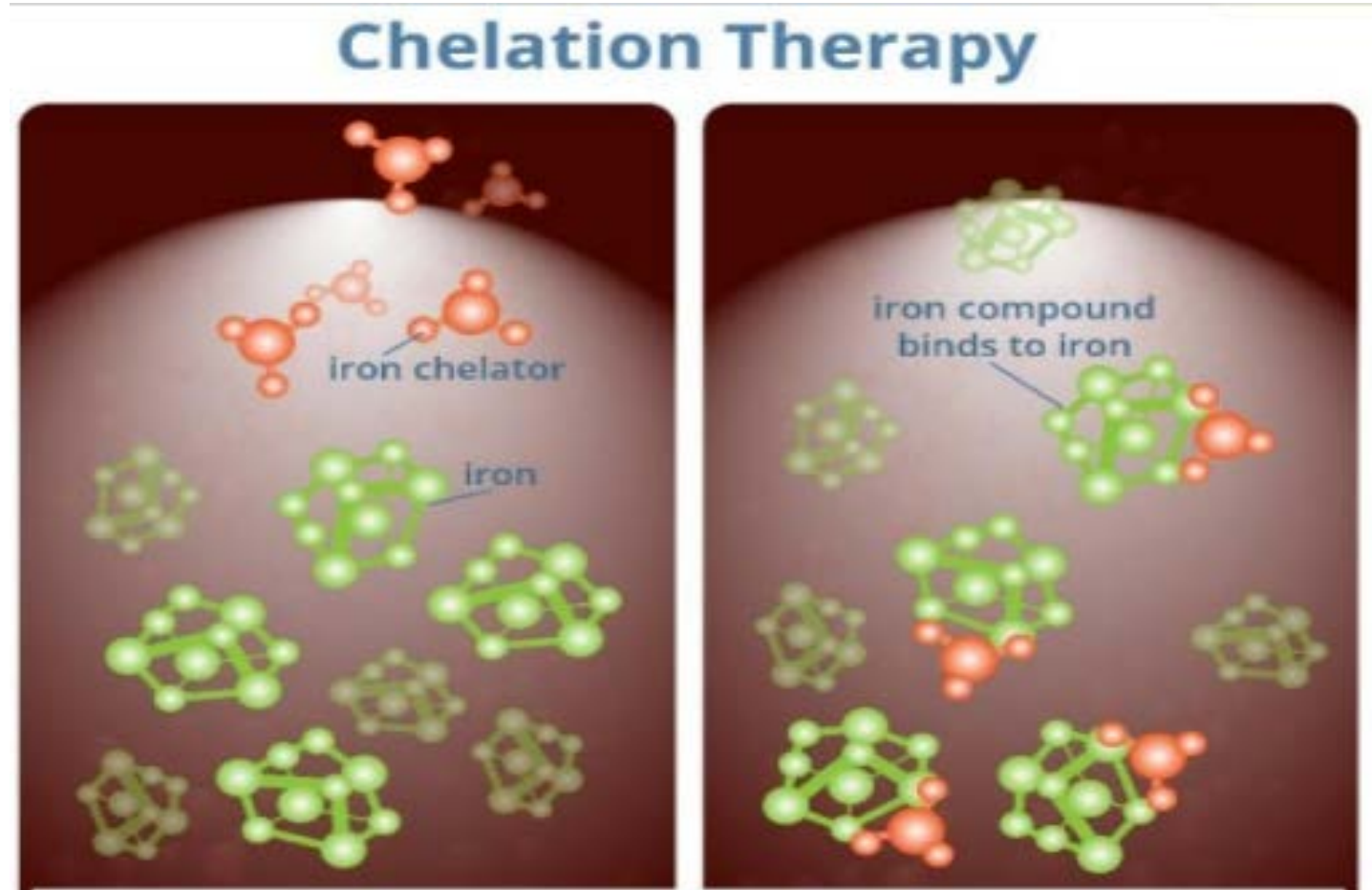
- Weakness
- Fatigue
- Jaundice/hepatic dysfunction
- Anemia
- Cardiac arrhythmia
- Diabetes
- Organ failure





# Treatment and Prevention

- Treatment
  - Iron chelation therapy
  - Chelating agent forms complex with iron
  - Facilitate excretion through urine/feces
- Prevention
  - Limit transfusion of red blood cells







**Every life deserves world class care.**

