TRANSFUSION DELAYED REACTIONS

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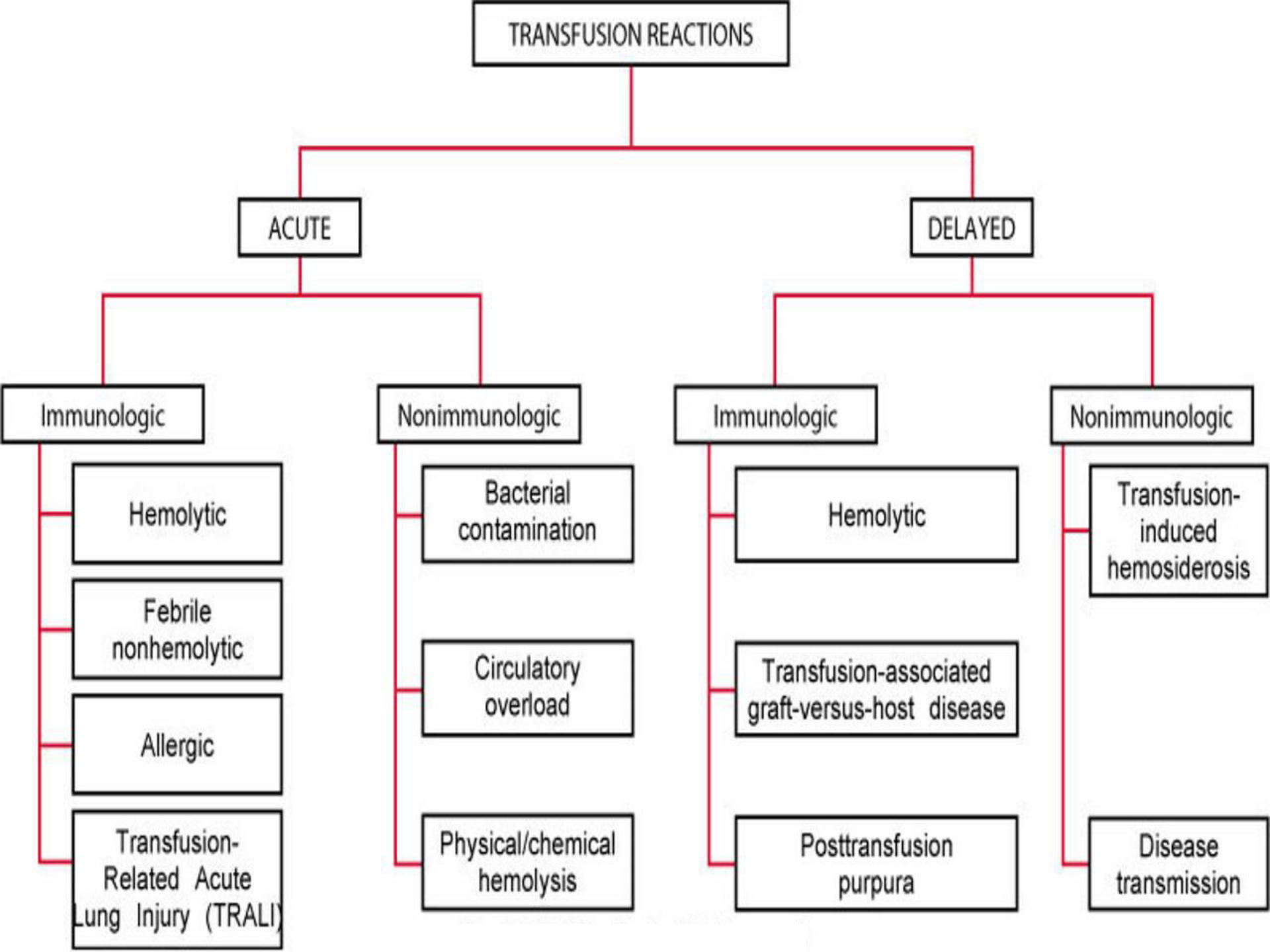
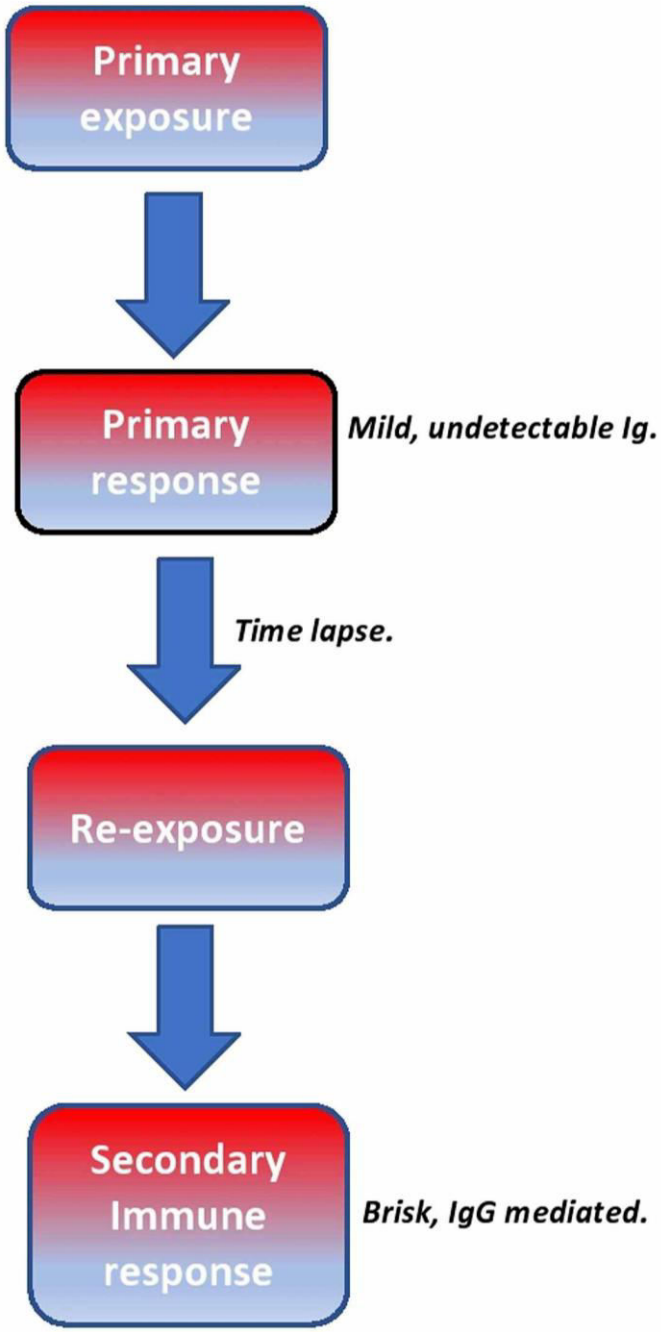
IN THE NAME OF GOD

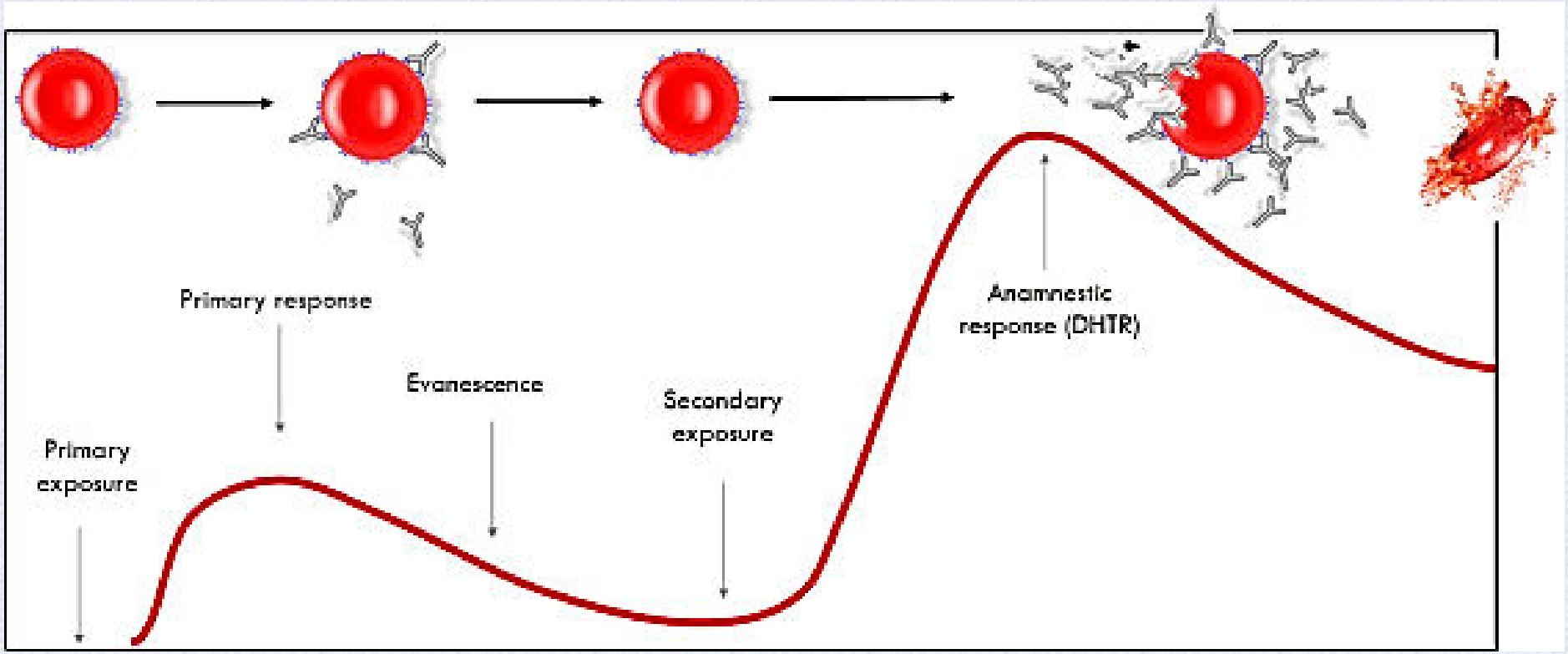

TRANSFUSION REACTIONS
ACUTE
DELAYED
Immunologic
Nonimmunologic
Immunologic
Nonimmunologic
Hemolytic
Febrile nonhemolytic
Allergic
Transfusion-Related Acute Lung Injury (TRALI)
Bacterial contamination
Circulatory overload
Physical/chemical hemolysis
Hemolytic
Transfusion-associated graft-versus-host disease
Posttransfusion purpura
Transfusion-induced hemosiderosis
Disease transmission

DELAYED HEMOLYTIC TRANSFUSION REACTION

- The transfused donor cells may survive well initially, but after a variable delay (2-21 days) they are hemolysed.
- Occurs in recipients sensitized to RBC Ag by previous blood transfusions or pregnancy
- As a result, this type of delayed reaction is more common in females who have a known disposition of alloimmunization
- In which the level of Ab at the time of transfusion is too low & RBC destruction occurs only when the level of Ab is increased after secondary stimulus (***anamnestic response***)
- Often manifested only by a decrease in the post transfusion Hct
- **Jaundice** & **hemoglobinuria** can occur and can cause impairment in renal function, but only rarely lead to death
- Patients experience ***mild fever*** and possible ***rash*** with laboratory and clinical signs of hemolysis such as ***jaundice, hematuria, low haptoglobin, positive direct coombs test, and decreasing Hb levels.***

- Are in the **Rh & kidd systems** rather than the ABO system Not be preventable, because pre transfusion testing is unable to detect very low level of Ab
- The surgical team should include in their D.D. in any patient who has an unexplained decrease in Hct 2 to 21 days after a transfusion, even without obvious manifestation of hemolysis
- **Symptoms** are generally self-limited and **treated** supportively with hydration to protect the renal tubules during hemolysis and further compatible transfusion to support anemia as indicated

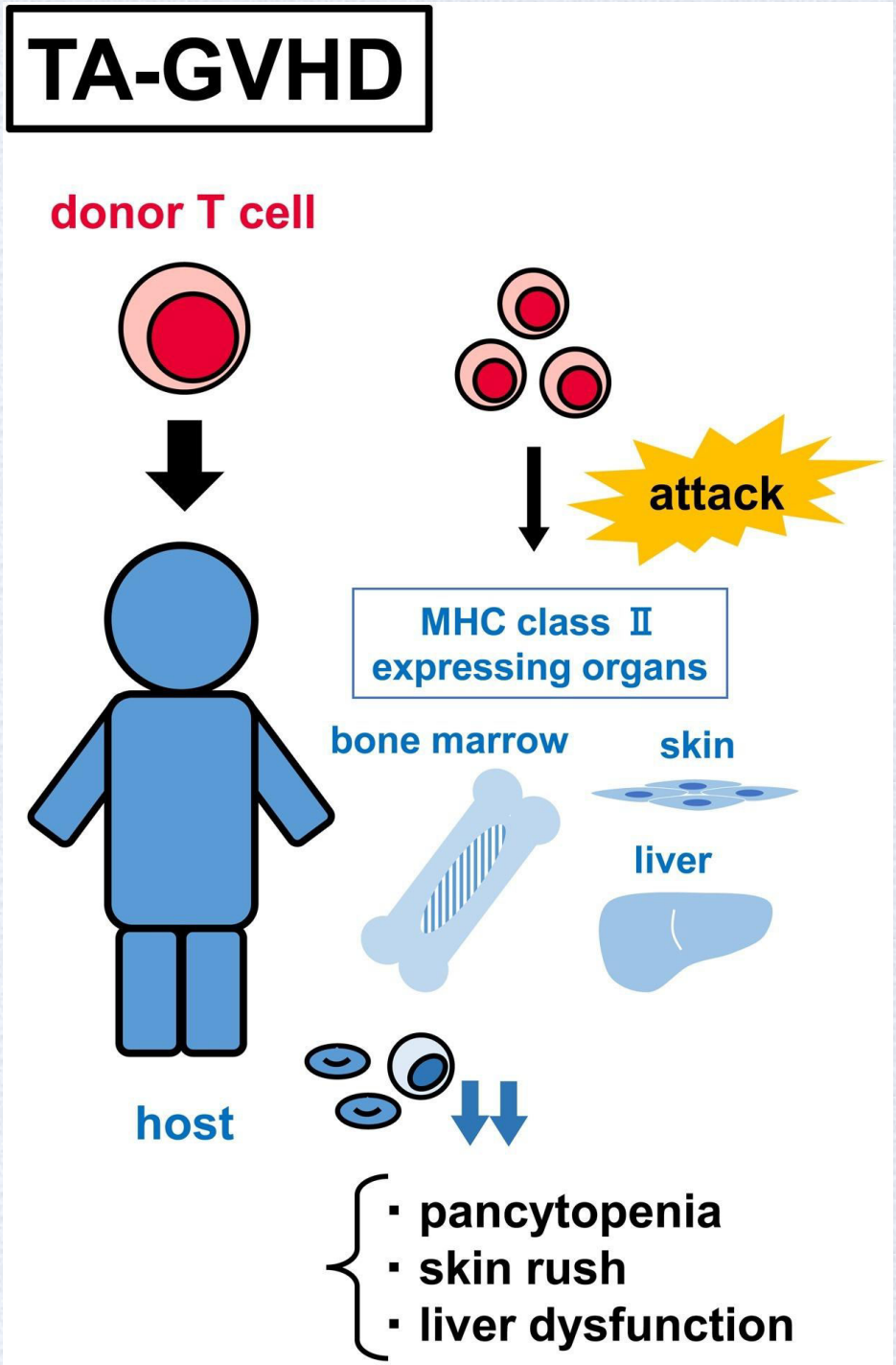

Primary exposure
Primary response
Mild, undetectable Ig.
Time lapse.
Re-exposure
Secondary Immune response
Brisk, IgG mediated.


Primary response
Evanescence
Secondary exposure
Anamnestic response (DHTR)
Primary exposure

TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE (TA-GVHD)

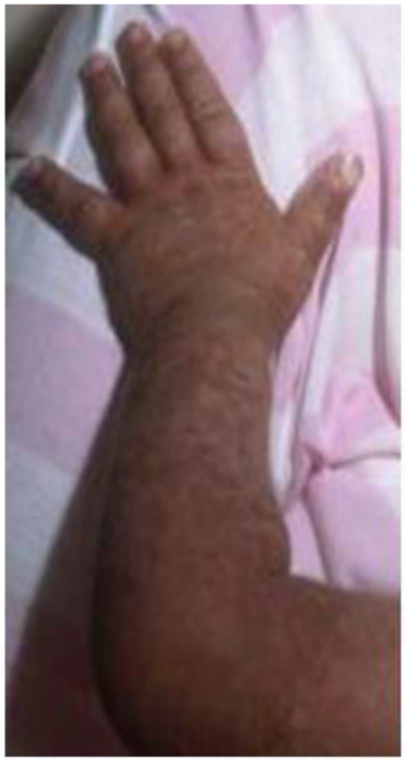
- Is a rare but fulminant and fatal complication of blood products containing cellular components (platelets and RBCs)
- **Mortality** is more than 90%, although incidence is decreasing across the globe secondary to preventative gamma irradiation
- **Patients at risk** include those immunocompromised from stem cell transplants, B-cell malignancies such as multiple myeloma, non-Hodgkin lymphoma, or acute lymphocytic leukemia. Hodgkin's disease and congenital immunodeficiency syndrome
- Classically present 4-21 days after transfusion but clinical suspicion should exist for up to 6 weeks
- **Symptoms** progress rapidly and affect the skin, hepatic, digestive, and hematopoietic organ system causing fever, rash, liver dysfunction, diarrhea, and pancytopenia

TA-GVHD


donor T cell
attack
MHC class Ⅱ
expressing organs
bone marrow
skin
liver
host
・pancytopenia
・skin rush
・liver dysfunction

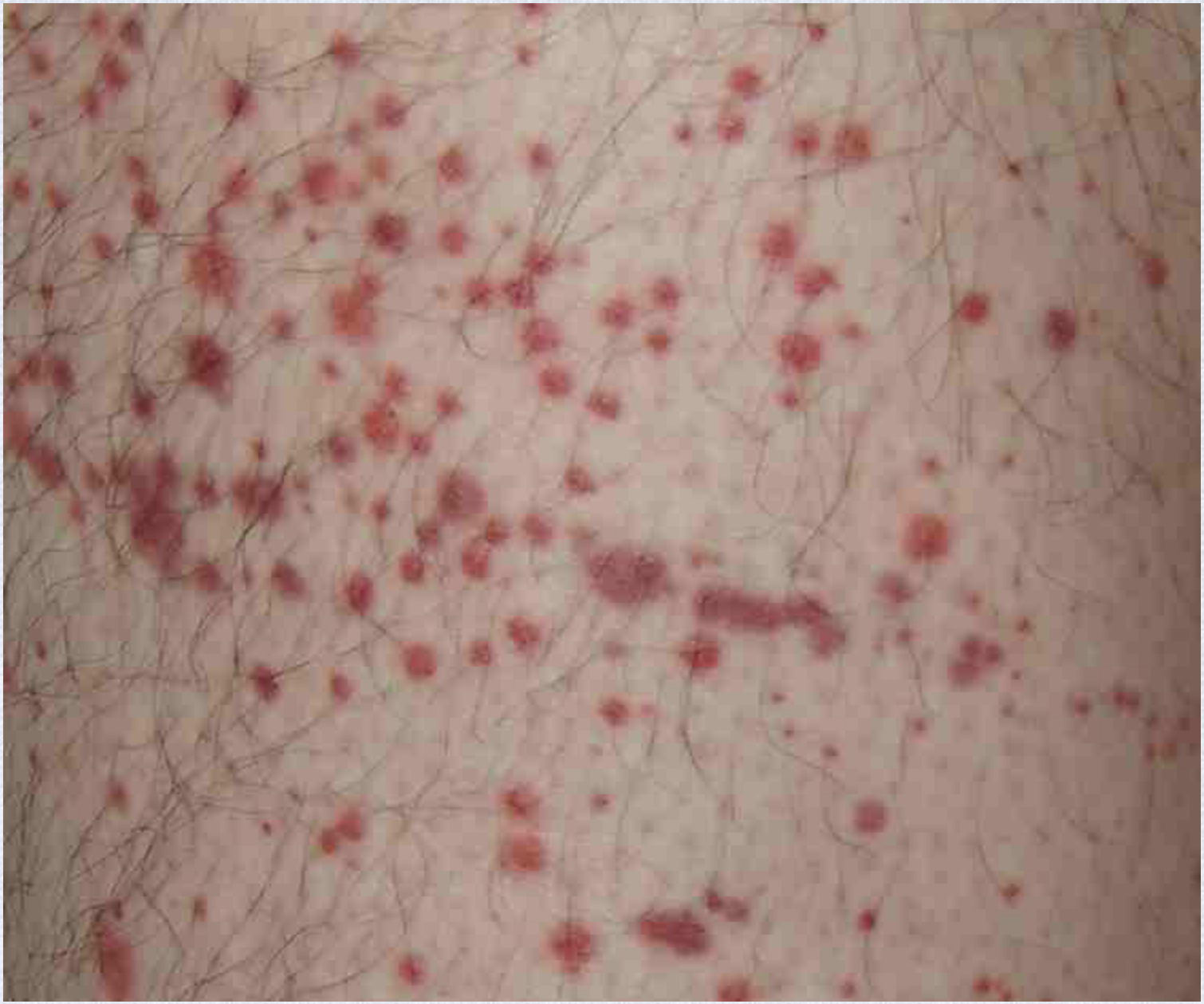
Transfusion Associated Graft-vs-Host Disease (TA-GVHD)

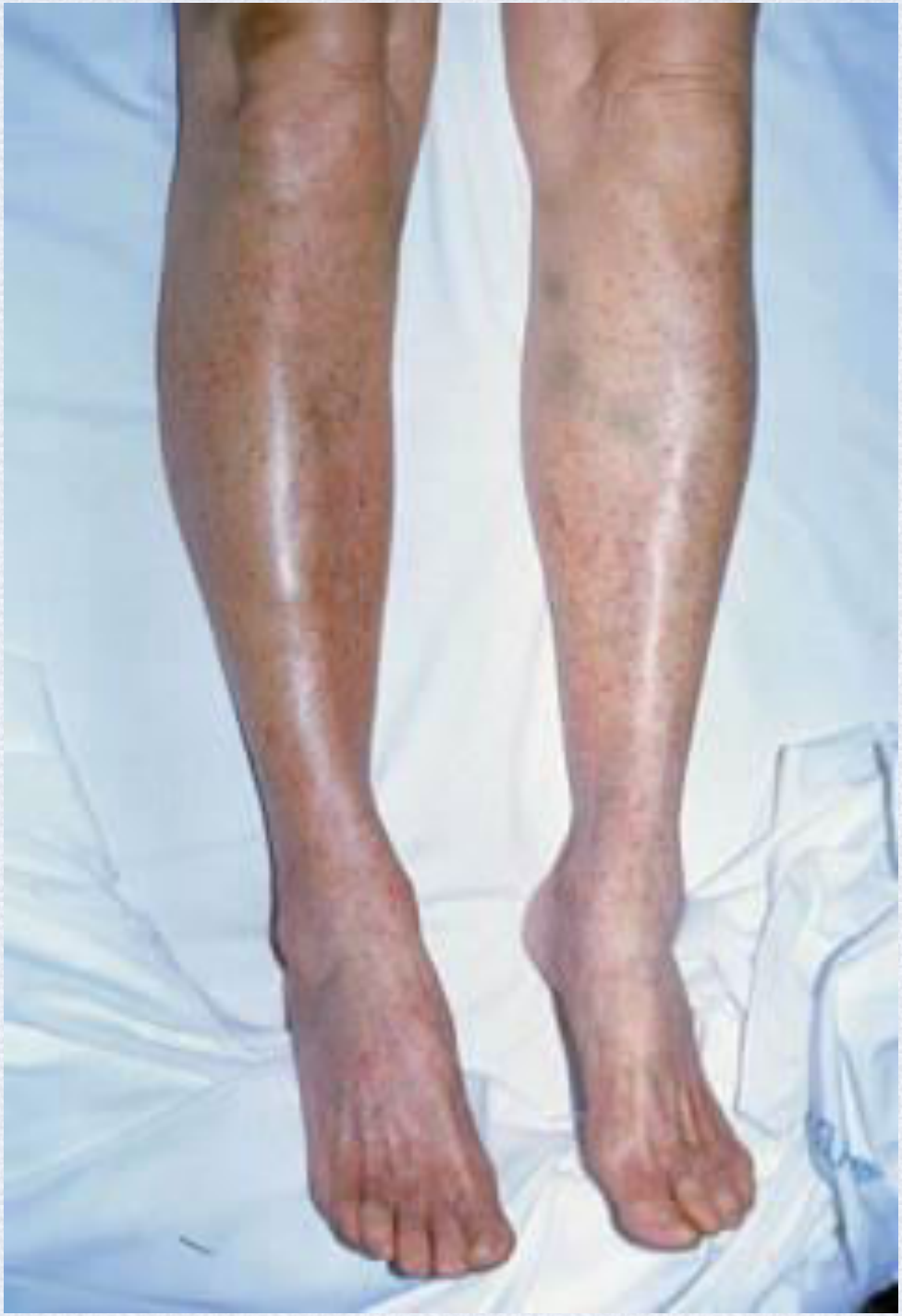
- Incidence: Rare
- Etiology: Donor lymphocytes engraft in recipient and mount an attack on the host tissues
- Presentation: Rash, erythroderma, maculopapular rash, anorexia, nausea, vomiting, diarrhea, hepatitis, pancytopenia, fever, bone marrow fibrosis and failure
- Lab testing:
  - Skin biopsy
  - Bone marrow biopsy and HLA typing



POST TRANSFUSION PURPURA

- is a very rare complication of transfusion (less than 300 reported cases), but associated with high morbidity and mortality
- Was defined as thrombocytopenia arising 5-10 days following transfusion and refers to recipient alloantibodies attacking **donor platelet Ag**
- Most patients have platelet-specific alloantibodies such as anti-HPA-1a, formerly termed anti-PL
- These Abs are almost exclusively found in previously pregnant women and cause platelet destruction of both transfused and autologous platelets
- **IV-IG** is the first line of treatment, but **plasmapheresis** may be necessary to remove Ab and avoid bleeding complications





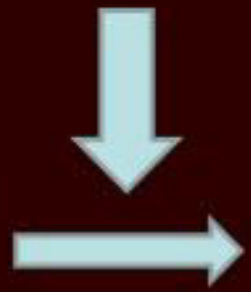
IRON OVERLOAD

- Packed RBCs contain approximately 250 mg of iron/unit which can accumulate in patients who require frequent transfusions for chronic anemia or hemoglobinopathies
- Iron overload occurs when deposit in the **liver, heart**, and **endocrine system** result in organ dysfunction
- ***Chelation therapy*** is the first line of treatment and prevention but difficult to administer secondary to the bioavailability and side effect profile of chelating agents
- ***Exchange transfusion therapy*** decreases the iron load in comparison to traditional transfusion but it is expensive and associated with complication from central venous access and a larger amount of blood products

Iron Overload

- 1 unit of PRCs has ~ 250 mg of Iron

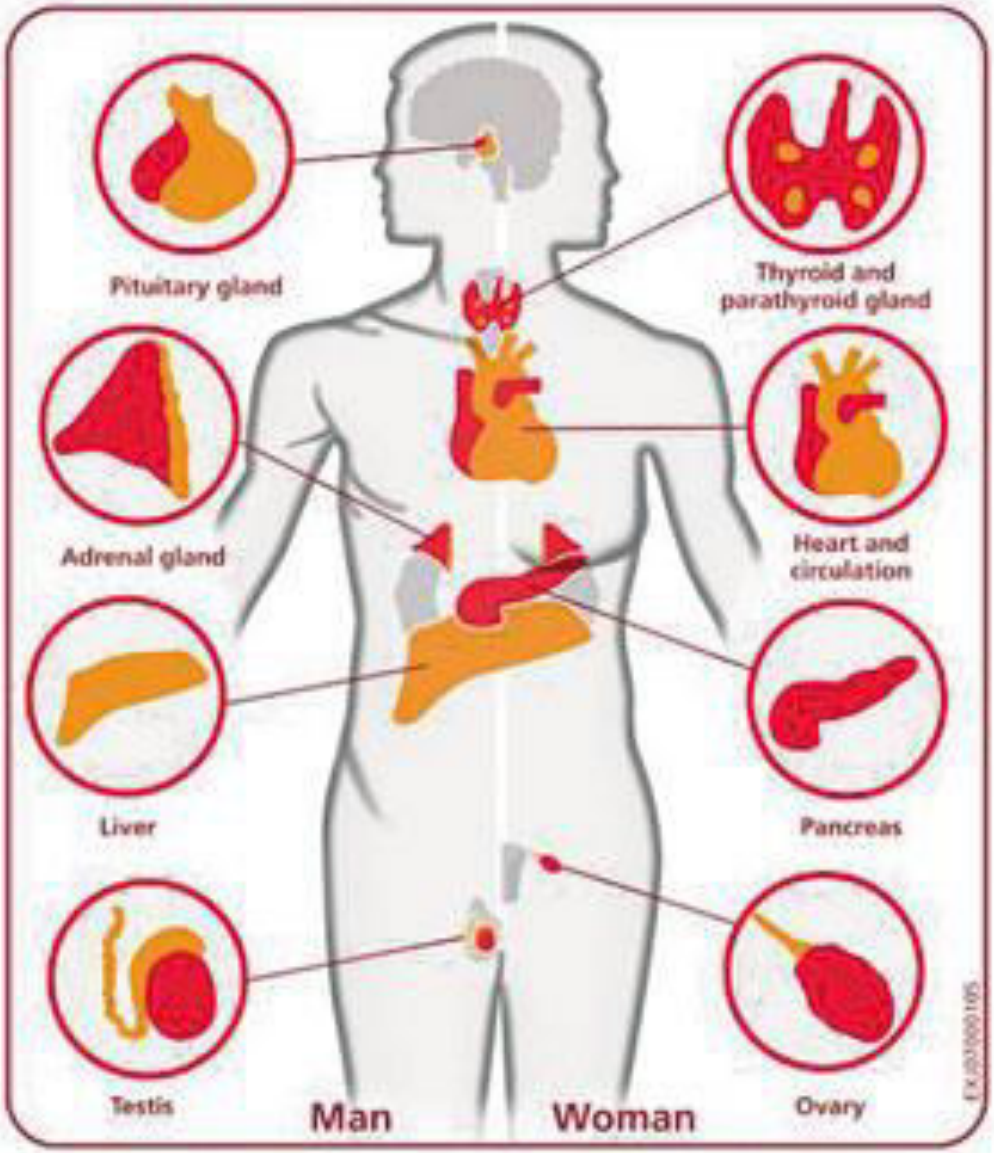
  Removed by body 1 mg / day



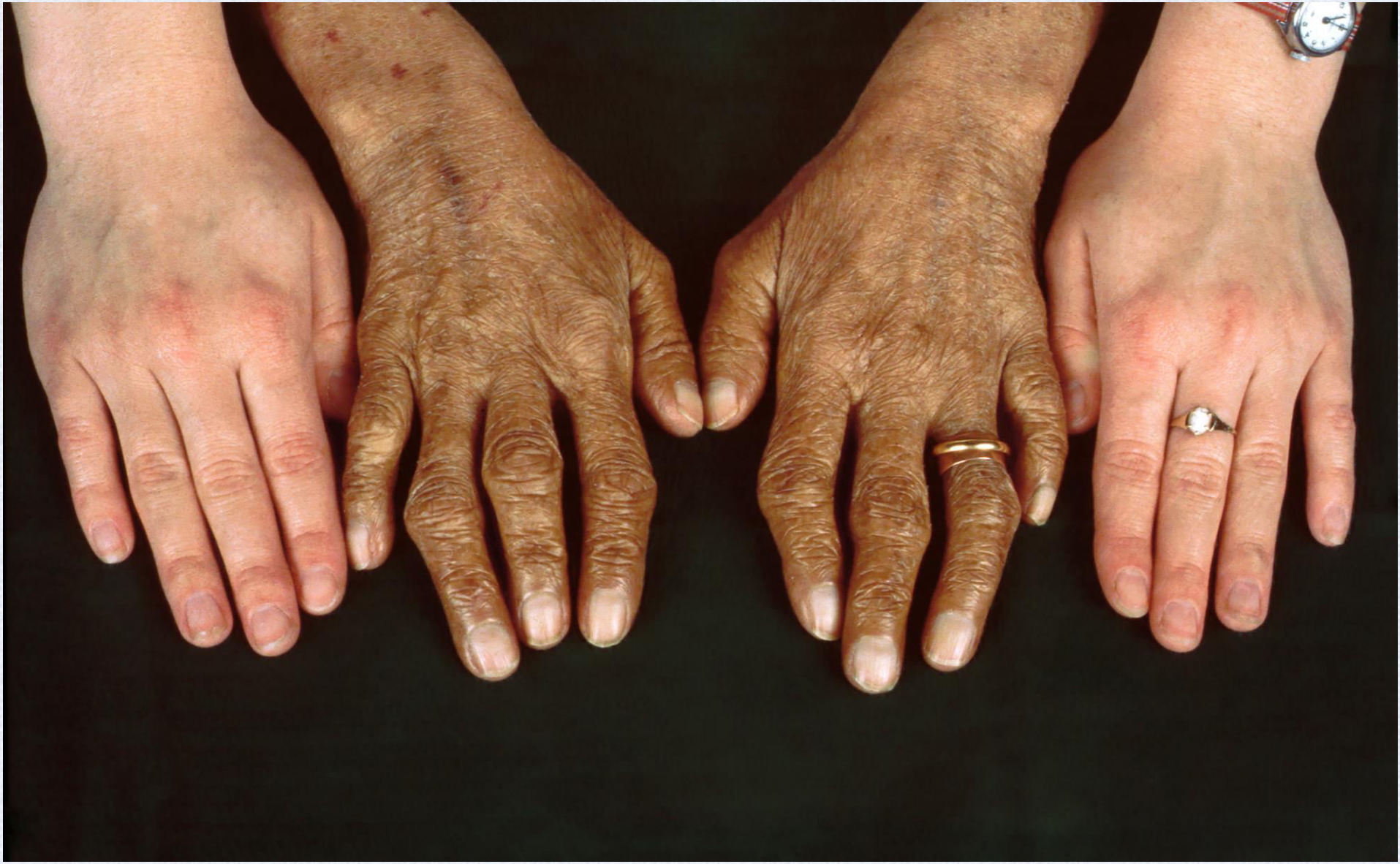
accumulate iron → Hemosiderosis

iron accumulate in tissue → Hemochromatosis

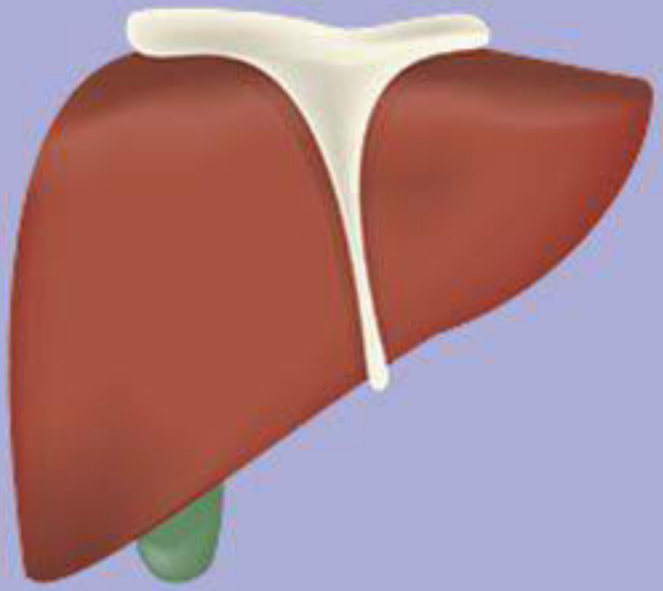
Organs that may be affected by iron overload



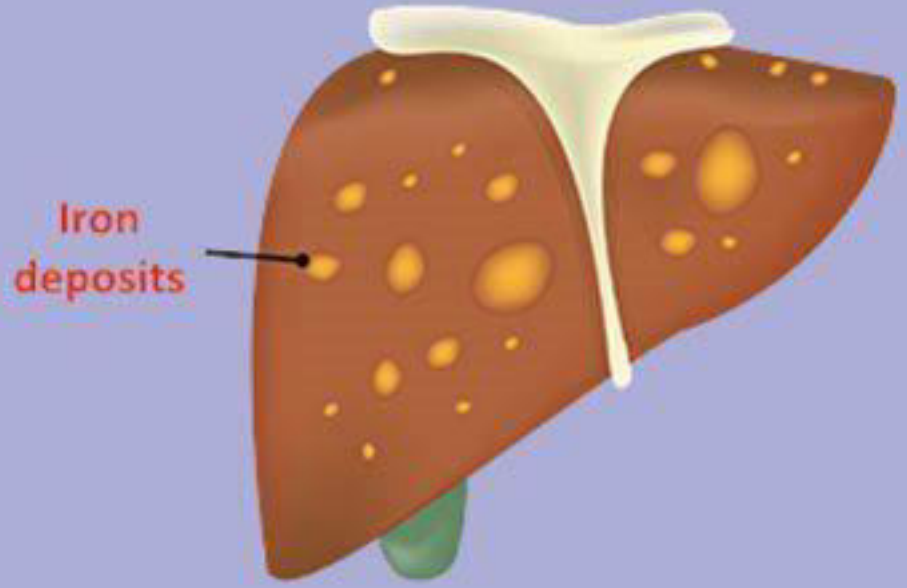
Toxic iron builds up across the body and can cause serious damage to vital organs, including the heart and liver.



Healthy



Iron Overload



TRANSFUSION-TRANSMITTED INFECTION

- The use of more sensitive screening tests and changes in transfusion medicine practices has made these infectious risks quite rare
- The use of **nucleic acid technology** has decreased the window of infectivity (time from being infected to a positive test result), which is a major reason for the decrease in infectivity with hepatitis, HIV, and West Nile virus
- Historically, the FDA has published a table on the risks for infectivity for the year 2011. because the rates of infectivity are so infrequent, the FDA may not published such tables in the future.

PERCENTAGE RISK OF TRANSFUSION-TRANSMITTED INFECTION WITH A UNIT OF SCREENED BLOOD IN THE UNITED STATES*

Infection	Risk	Window Period (Days)
Human immunodeficiency virus-1 and -2	1:1,476,000	5-6
Human T-lymphotropic virus (HTLV-II)	1:2,993,000	51
Cytomegalovirus (CMV)	Infrequent with leukocyte-reduced components	
Hepatitis C virus (HCV)	1:1,149,000	3-4
Hepatitis B virus (HBV)	1: 280,000	24
Hepatitis A virus (HAV00)	1:1,000,000	
Bacteria red blood cells	1:1,000 with septic reaction in 1:500,000	
Pheresis platelets (with early aerobic culture)		
Parasites: Babesia and malaria	<1:4,000,000	7-14
West Nile virus (WNV)	1/1,100,000	?
Acute hemolytic transfusion reactions	1:38,000-1:70,000	

ALLOIMMUNIZATION

- Refers to the induction of an immune response to allogenic antigen exposure
- Occurs occasionally through pregnancy, but the majority of alloimmunization results from transfusion of blood products containing **immunogenic Ags on the surface of RBCs**.
- Unlike classic ABO Ags which consist of carbohydrate chains, most of the non-ABO alloantigens (Kell, Kidd, Duffy, …) results from single amino acid polymorphisms between the recipient and donor
- AHTRs result in an immediate **IgM-mediated** immune response to ABO incompatibility. In contrast, alloimmunization prompts an amnestic **IgG-mediated** humoral immunity to foreign proteins and does not result in RBC destruction until the second Ag exposure
- Only 2-8% of recipients who are chronically transfused develop RBC alloantibodies

TRANSFUSION-RELATED IMMUNOMODULATION (TRIM)

- Blood transfusion **can suppress the immune system** because of circulating lymphocytes
- More than 150 clinical studies have tried to relate allogeneic blood transfusions to recurrence of resected cancers, postoperative infections, and virus activation, with the conclusion that adverse effects may be caused by TRIM.
- Over the past 30 years, several investigators have tried to identify the exact mechanism for TRIM, but results point to a **multifactorial** pathophysiology that implicates the role of transfused WBCs, donor plasma HLA class 1 peptides, cytokines, and immune mediators released during blood product storage as well as the immune function of transfused RBCs within the microvasculature of the recipient.

MICROCHIMERISM

- Refers to more than one cell line in an individual organism
- Specifically donor lymphocytes may persist in a patient
- It is associated with **pregnancy** , **transplant** , and **trauma**
- Out-come is not known

TABLE 61-9 NONINFECTIOUS HAZARDS OF TRANSFUSION

Transfusion Reaction	Incidence (per 10^5 Transfusions)	Etiology	Therapy	Prevention
Febrile	All components: 70-6800	Storage-generated proinflammatory cytokines Patient antileukocyte antibodies bind to donor leukocytes	Stop transfusing Give antipyretics Supportive care	Prestorage leukoreduction
TACO	All components: 16.8-8000 Practice-dependent	Circulatory overload Patients with cardiac or renal disease, infants, and the critically ill are at increased risk	Stop transfusing Give diuretics Oxygen	Identify patients at high risk Transfuse slowly
TRALI	Erythrocytes: 10-20 Platelets/plasma: 50-100	Passive transfusion of donor antibodies Storage-generated toxic lipids	Supportive care	Remove high-risk donors from the donor pool
Allergic	All components: 3000 mild, 2 anaphylactic	Mild reactions: Transfusion of soluble antigens in donor plasma Anaphylaxis: IgA deficiency or other recipient protein deficiency	Stop transfusing ASA monitors Large-bore IV access Epinephrine Antihistamines Supportive care	Pretransfusion antihistamine use remains common practice despite limited evidence
Hemolytic	Erythrocytes: 1.1-9.0	Donor antibodies bind to patient erythrocytes Patient antibodies bind to donor erythrocytes	Stop transfusing Repeat matching Supportive care Treat DIC	Standard operating procedures
TRIM	Unknown	The mechanism is unknown but may depend on the presence of donor leukocytes	Treat complications (e.g., infection, malignancy)	Prestorage leukocyte reduction may be beneficial, but this approach is controversial
Microchimerism	All components: 5000-10,000 massive transfusion	Permanent residence of donor cells in recipient	Unknown	Unknown
Posttransfusion purpura	All components: 2	Recipient alloantibodies attack donor platelet antigens	IVIG	Avoid units positive for implicated HPA antigens in patients with a history of PTP
Hypotensive	Unknown	Production of kinins by the activation of the contact system Patients on ACE inhibitors are at increased risk	Stop transfusing ASA monitors Large-bore IV access Supportive care	Avoid the use of negatively charged leukocyte reduction filters
Graft-versus-host	Varies by patient population	Transfusion into immunocompromised host Transfusion of donor cells closely matching HLA type	No consensus exists Consider bone marrow transplant	Gamma irradiation of cellular products

avoidance of unnecessary transfusions will be the most effective way to reduce complications of blood transfusions !


Thank You