Utilization of Specialty Blood Products

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Objectives

1. Familiarize yourself with the different specialized products
2. Understand when to use

Products:

- Irradiated Units
- Washed RBC
- Volume Reduced Units
- Granulocytes
- HLA-Matched Platelets
- Antigen Negative Units
- HbS Negative Units

Slide 3

AS0 Not needed

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Irradiated Blood Products

Irradiation of Blood Components

GVHD

DEHP Leaching Investigation

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GVHD:

- Cellular blood components are irradiated to destroy viable T lymphocytes, which may lead to graft vs host disease (GVHD)
- GVHD results when immunocompetent viable lymphocytes in donor product engraft in an immunocompromised host. This engrafted lymphocyte recognizes the recipients' cells as foreign attack the tissues.
- This leads to serious consequences involving liver, GI tract and skin
- Chronic or acute

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AS1

Slide 6

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AS1	Not needed Smith, Alex, 2024-11-04T18:40:14.757
AS2	Patient’s Smith, Alex, 2024-11-04T18:42:02

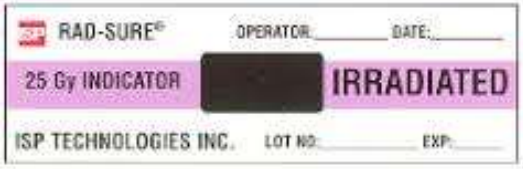
Patients at greatest risk include:

- Severely immunosuppressed
- Immunocompromised
- Receiving blood donation via relatives
- Fetuses receiving intra-uterine transfusions

Irradiation:

- Irradiation inactivates T lymphocytes WITHOUT damaging platelets, RBC and Granulocytes
- Must be labeled "IRRADIATED"
- Expiration date of unit changes to 28 days or keeps the original expiration date, whichever comes first
- May be transfused to normal patient if not used by intended recipient

BEFORE IRRADIATION



AFTER IRRADIATION @ 25 Gy

AS0 Or keeps the original expiration date, whichever is sooner

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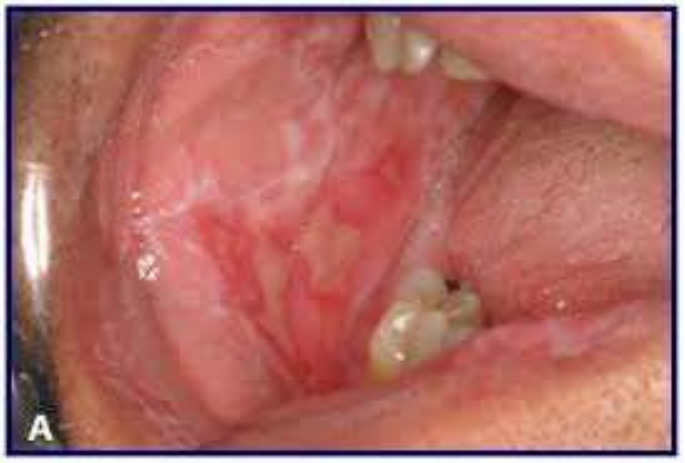
Indications for Irradiation:

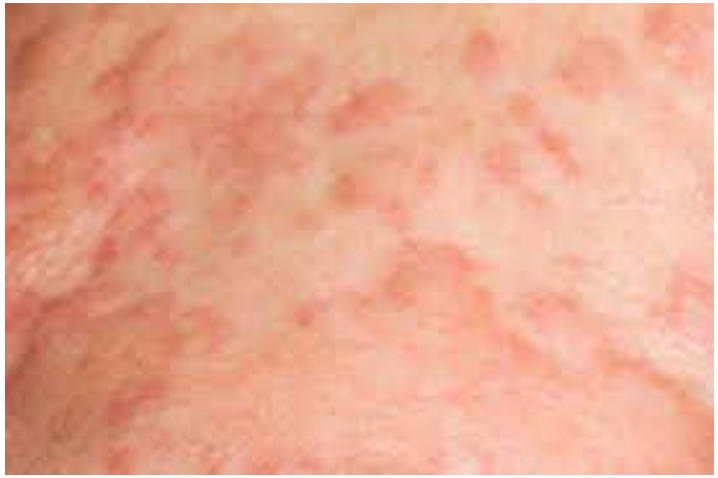
- Intrauterine transfusions
- Donation from blood relatives
- HLA matched platelets
- Granulocyte transfusions
- Hematologic malignancies
- Hodgkin's lymphoma patients
- Known or suspected congenital immunodeficiency due to T-cell defects (SCID, DiGeorge)
- Patients who received purine analog drugs
- Patients who are receiving alemtuzumab (anti-CD52 monoclonal Ab for tx CLL, anaplastic anemia or other hematologic malignancies

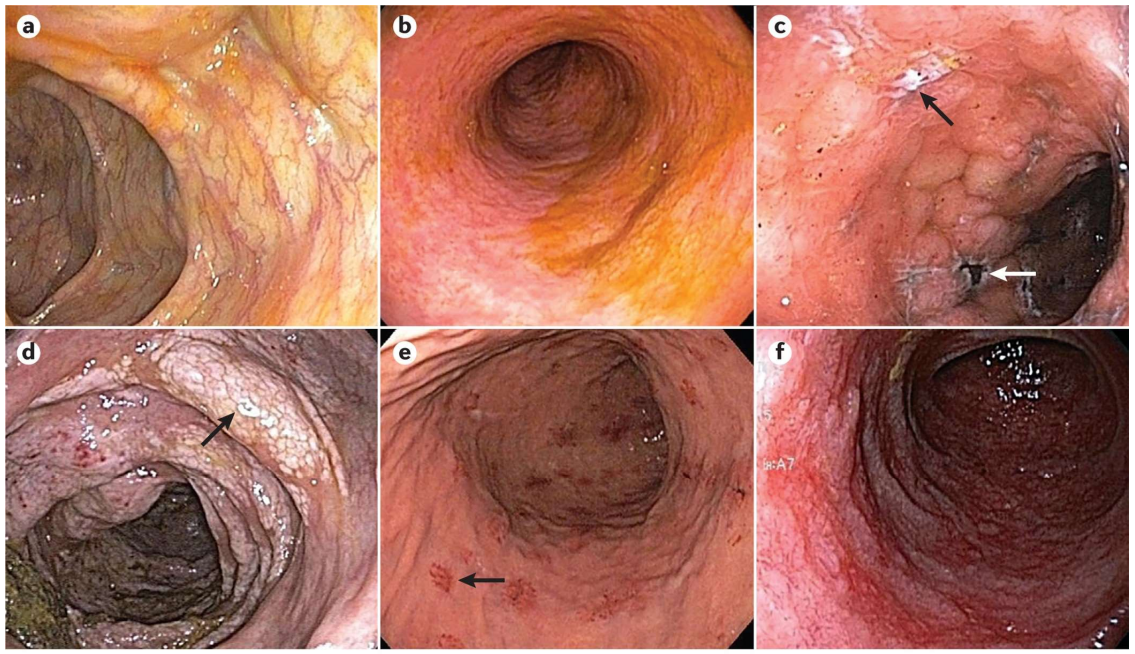
Comments:

- Irradiation of products should be done as close as possible to time of planned transfusion (risk of hyperkalemia; neonatal patients)
- Use of irradiated blood components is **not** routinely required for **solid organ transplant patients**
- There is no indication for irradiation of RBCs or platelets for patients who have HIV
- Pathogen reduction is equally effective as irradiation in preventing proliferation of donor T lymphocytes for prevention of GVHD (UVA light treatment inactivates DNA replication in cells including DNA in any donor T-lymphocyte)

GVHD





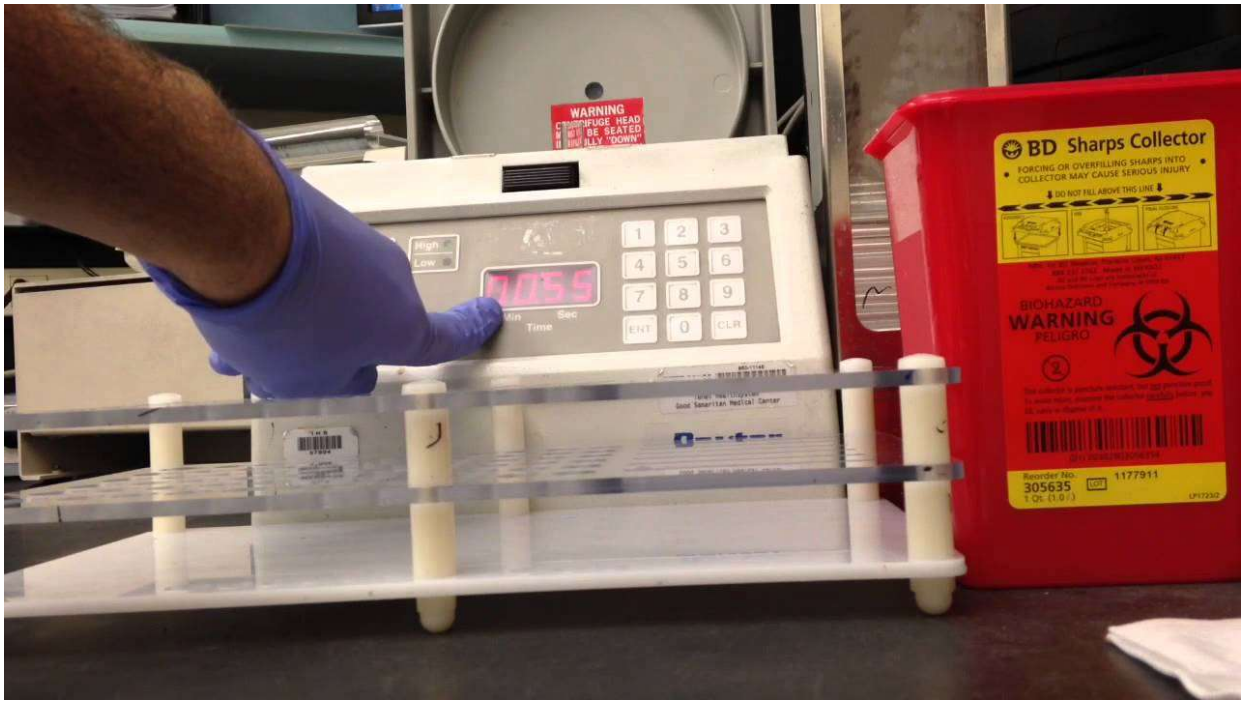


Nature Reviews | Gastroenterology & Hepatology

Washed Blood Products

Cell Washer:


COBE 2991
Cell Processor


WARNING
BD Sharps Collector
FORCING OR OVERFILLING SHARPS INTO COLLECTOR MAY CAUSE SERIOUS INJURY
DO NOT FILL ABOVE THIS LINE
BIOHAZARD
WARNING
PELIGRO
Reorder No.
305635
1177911

Why Wash?

- Necessary for patients with a diagnosis of IgA deficiency **WITH** Anti-IgA Ab's
- Necessary if one has suffered REPEATED severe allergic or anaphylactic reactions with previous blood transfusions
- Recurrent severe allergic reactions not prevented with appropriate premedication
- Necessary if patient is at risk of SEVERE HYPERKALEMIA, (e.g. neonate) – red blood cells only

Low IgA and Selective IgA Deficiency

What is IgA?

IgA is the most common type of antibody
IgA helps **prevent infection** by complexing with bacterial antigens for removal.

IgA Deficiency

IgA deficiency is the most common **immunodeficiency** worldwide
Symptoms of IgA deficiency include:

- Increased **gastrointestinal tract infections**
- Recurrent **respiratory tract infections**
- Increased risk of **allergies**
- More frequent **urinary tract infections** or skin infections
- Increased risk of **autoimmune diseases**

Genetics and IgA deficiency

IFIH1 gene - Variants in IFIH1 that decrease IgA are linked to auto immune diseases
HLA-DQ2.5 - Variants decrease IgA and are linked to celiac disease
HLA-DRB1*1501 - Strongly protective against IgA deficiency, however first strong link to MS

Increasing IgA

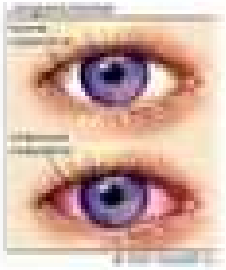
- Probiotics - *Bifidobacterium* and *Lactobacillus* strains of Probiotics may increase IgA
- Vitamin A - Used in IgA transport
- Proper sleep - Lack of REM sleep can cause IgA deficiency

Genetic Lifehacks
Learn. Experiment. Optimize.

Process of Washing:

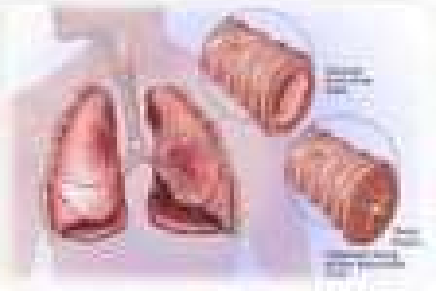
- Process involves 3 wash cycles with 0.9% sodium chloride
- Removes up to 20% of the RBC's and 98% of the plasma
- 20-30% of decreased platelet functions
- RBC units should be used within 24 hr after processing; platelets should be used within 4 hr
- Process takes up to **2 hours** per unit and yields lower quality and quantity of RBC's.
- Key: Washing units removes plasma proteins, antibodies, K+- electrolytes, free hemoglobin, WBC's, platelets and other micro-aggregates which may cause febrile or urticarial reactions

Symptoms (1)

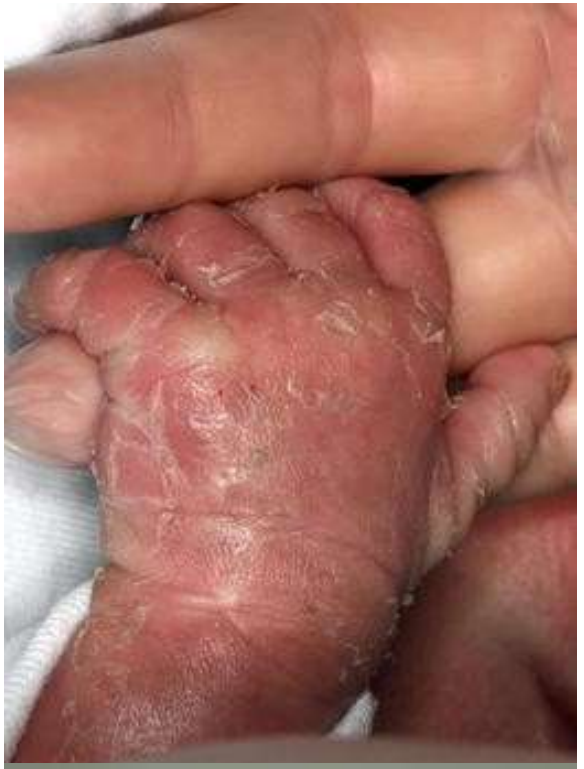


85–90% of IgA-deficient individuals are asymptomatic.

- The most common symptom of Selective IgA Deficiency is susceptibility to infections including:



- Bronchitis.
- Chronic diarrhea.
- Conjunctivitis.
- Gastrointestinal inflammation.
- Mouth infection.



Volume Reduced Blood Products

Volume Reduced Blood Products:

- AKA hyperpacking or hyperconcentrating
- Volume reduction involves the aseptic removal of a portion of the supernatant containing plasma and storage medium additives, following centrifugation.
- Patients in whom fluid status is being aggressively managed (CHF, renal failure) or patients at risk for transfusion associated circulatory overload (TACO)
- Shelf life of volume reduced components is no more than 24 hours if stored at 1-6 C or 4 hours if stored at 20-24C

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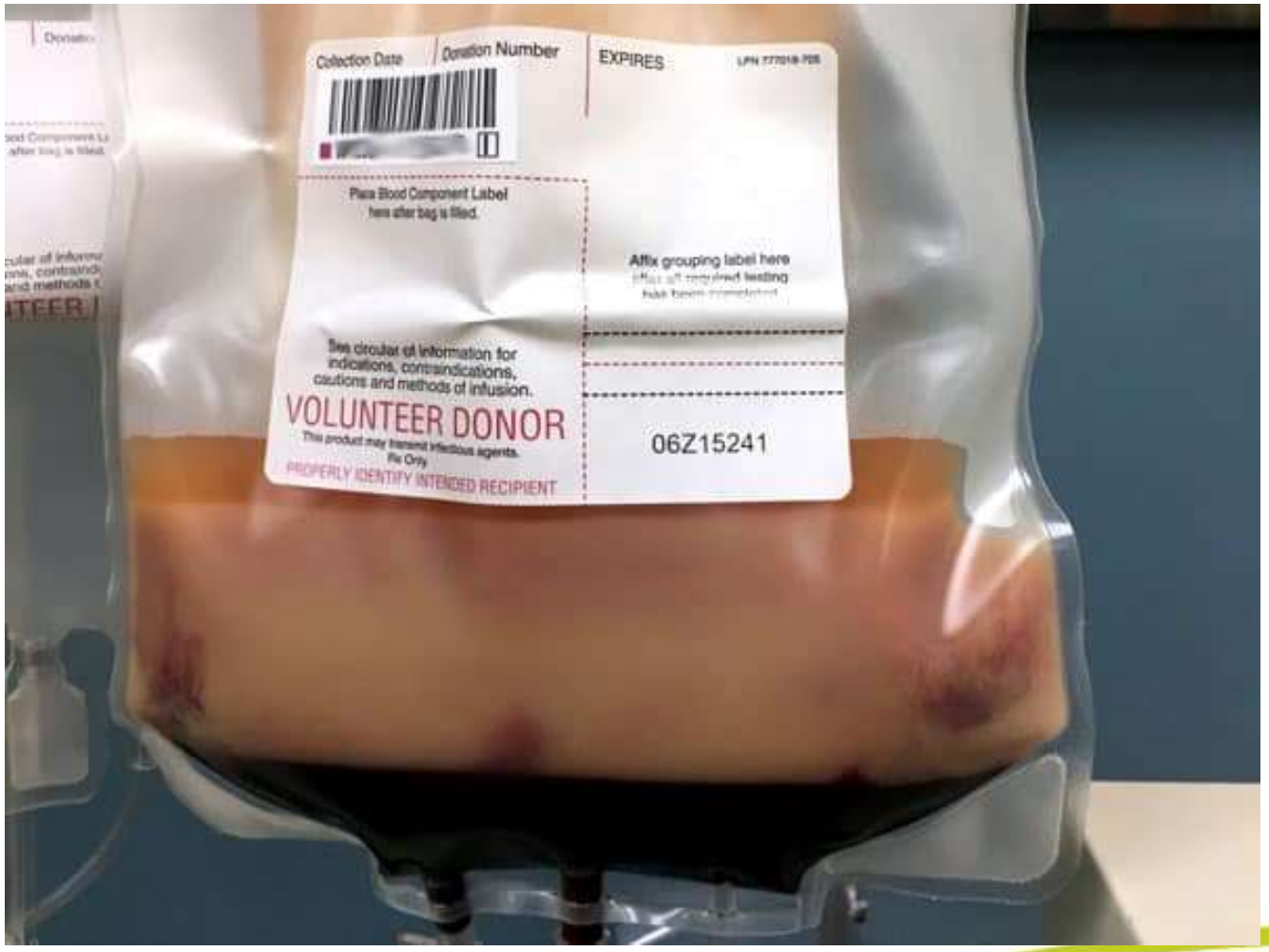
GRANULOCYTES

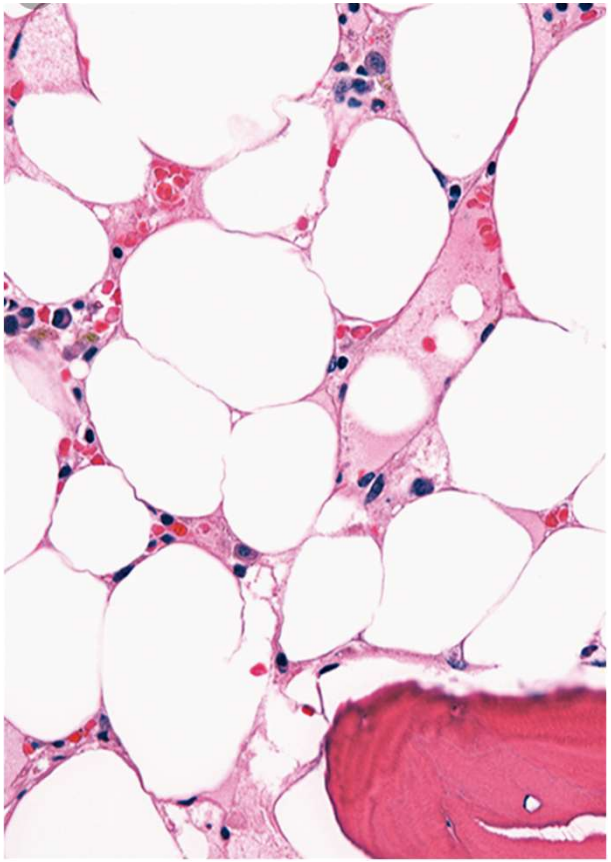


Granulocytes Overview:

- Indications: neutropenic patient with life-threatening bacterial or fungal infections, without response to antibiotics
- Bags must be irradiated to avoid GVHD
- CMV status of donor important as we can not leukoreduce!
- **ABO compatible units ONLY **
- Collected via apheresis after mobilization
- Efficacy remains unproven

Granulocytes Indications

- Patients with prolonged disease-related neutropenia:
  - Aplastic anemia
  - Congenital granulocytic deficiency
  - Neonatal sepsis
- Patients with therapy-related neutropenia:
  - Aggressive chemotherapy recipients
  - Bone marrow or hematopoietic stem cell transplant recipients



Minimal Criteria for Patients:

- Absolute neutrophil count of less than 500 cells/microL
- Evidence of bacterial or fungal infection/clinical symptoms
  - (+) cultures, proven biopsy, (+) x-ray-infiltrates (pneumonia)
- Unresponsive to antimicrobial treatment for at least 48 hours

Granulocyte Collection

- Apheresis: process where only desired cell population is collected
  - Red blood cells, plasma, and other white blood cells are returned
- Should be performed for at least 160 minutes to collect 7-10 L of blood/max granulocyte yield
- Hydroxyethyl starch (HES) is added to donor blood to allow for granulocytes to separate out/ accelerating erythrocyte sedimentation

Stimulating Factors Administered 24 Hours Prior: Corticosteroids and G-CSF

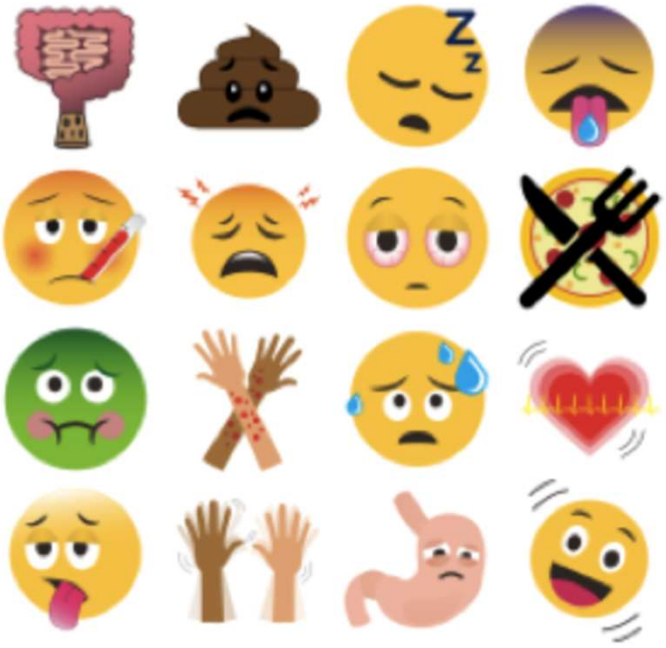
- Corticosteroids can double the number of circulating granulocytes by mobilizing them from the marginal pool
  - 60 mg of oral prednisone / or 8 mg of dexamethasone
  - Keep in mind donor's medical history (HTN, DM, peptic ulcer disease are contraindicated)
- Growth factors: G-CSF (Filgrastim/Neupogen)
  - Cytokine/glycoprotein that stimulates the bone marrow to produce stem cells/granulocytes. They are released into the peripheral blood within 2 hours and peak after 12 hours of administration.
- **NOTE**: In combination, these two drugs increase granulocyte collection to 5 - 10^{10} in one administration, compared to steroid administration alone.

Quality of Granulocytes after G-CSF Stimulation

- Neutrophils collected after the administration of G-CSF have prolonged survival period post-transfusion:
  - Released from bone marrow as an immature population
  - Delayed apoptosis
  - Better respiratory burst
  - Better chemotaxis
  - Better bactericidal activity

Medication Side Effects

- Headache
- Arthralgia
- Bone pain
- Fatigue
- Insomnia
- Hyperglycemia



Donor Qualifications

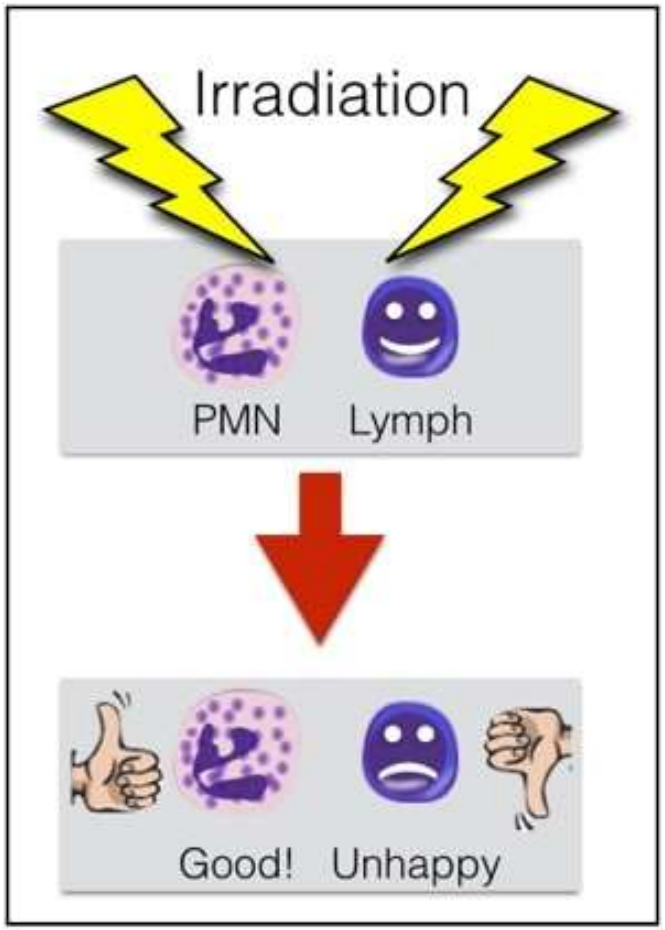
- The willing donors must meet the minimum standards in donor history and physical set by the US FDA:
  - **ABO/RH cross-match compatible to recipient**
    - Difficulty in separating the RBC layer from granulocyte layer of apheresis collection; granulocyte concentrations are usually heavily contaminated with RBCs

Burden on Donors

- Three visits prior to collection for:
  - 1. Initial screen
  - 2. Medication administration
  - 3. Donation
- Two visits for every subsequent donation from there on after
- Procedure time: 4-5 hours

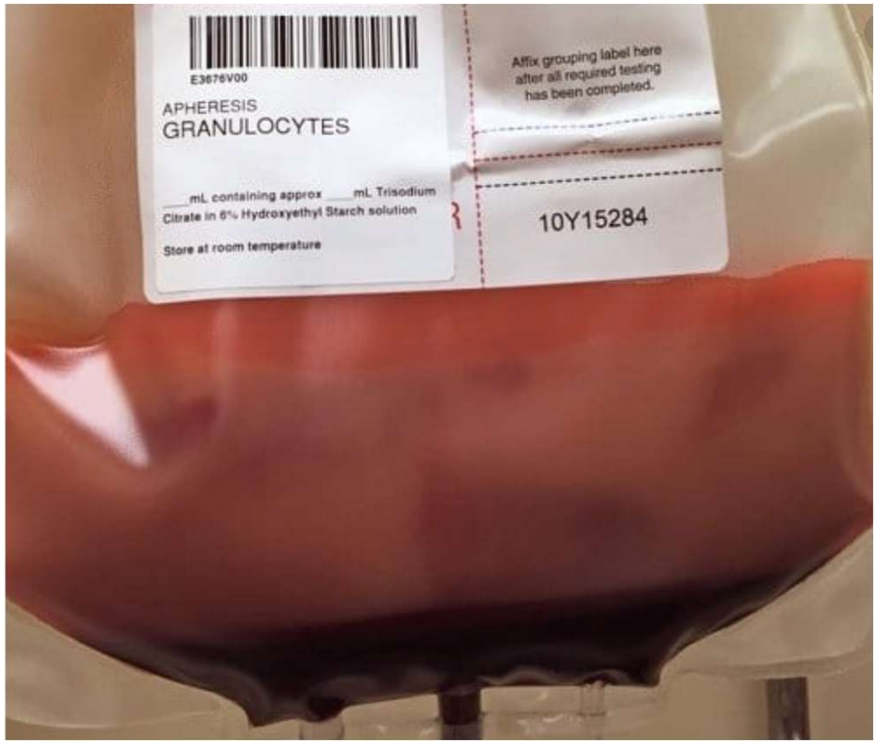
Granulocyte Processing

- All granulocyte concentrates should be irradiated to deactivate lymphocytes in product—> avoid transfusion-associated graft versus host disease (GVHD)
  - ex. Immunodeficient/ immunocompromised patients
- Recruit seronegative CMV donors to provide products specifically for seronegative patients
  - we can not leukoreduce these products!
- STORAGE
  - Granulocyte products can only be stored for 24 hours (***shortest shelf life of any product we obtain from donation---apoptosis***)
  - Stored at room temperature (no agitation required)


Irradiation
PMN
Lymph
Good!
Unhappy

Granulocyte Components

- 1 unstimulated donor unit contains minimally $1x10^{10}$ granulocytes
- 1 stimulated donor unit contains minimally $4\text{-}5 \times 10^{10}$ granulocytes
- You cannot just order casually
- You cannot order STAT



Granulocyte processing cont..

- Must be transfused within 24 hours:
  - Clinicians, therefore, must order on an "as needed" basis, the day before potential transfusion
  - If the clinician does not use the unit, unit must be disposed of

Some Complications

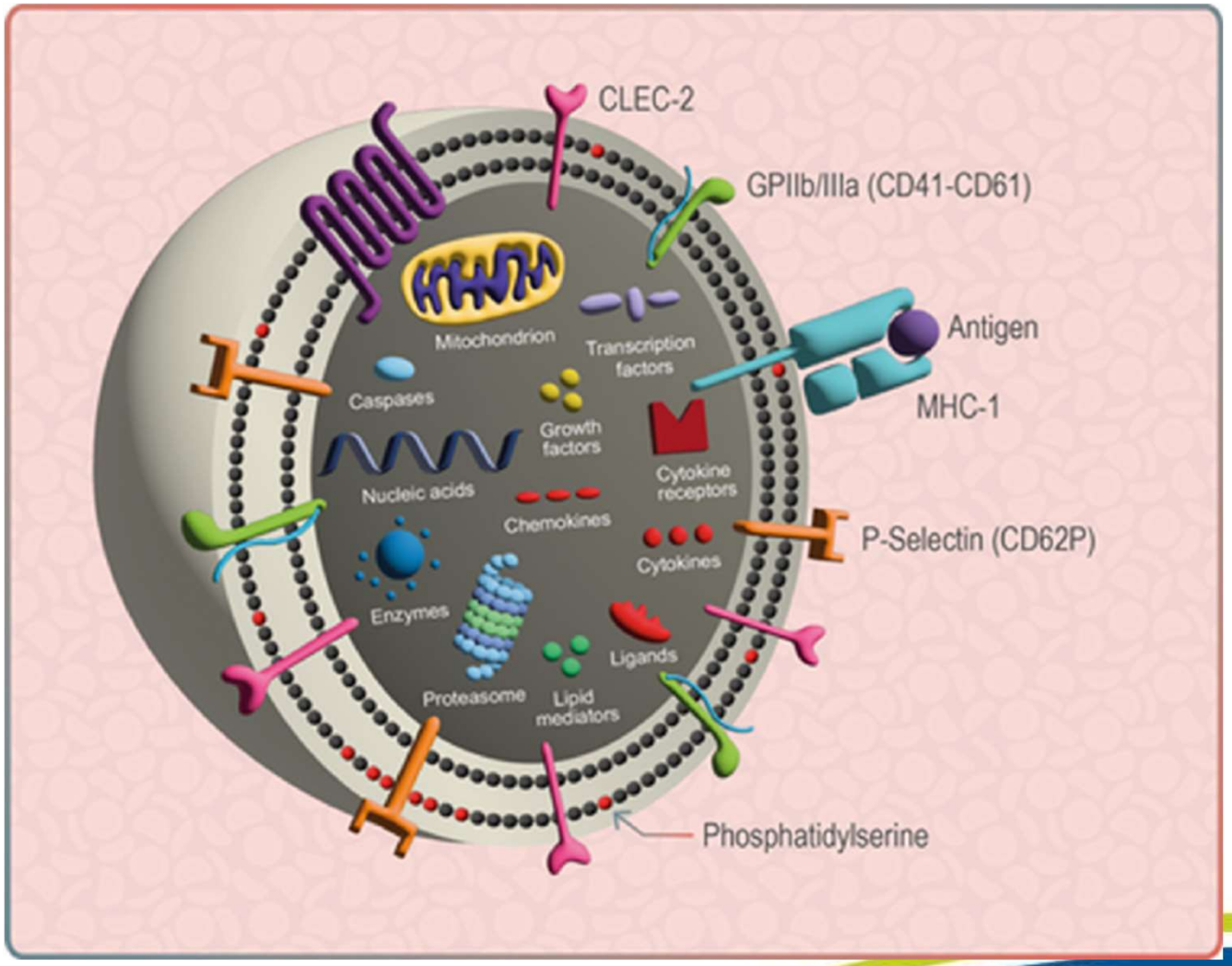
- 1. Pulmonary adverse reactions-TRALI-(granulocytes love the lungs)
  - Degrees of cough, dyspnea, hypoxia, chest x-ray changes
- 2. Transfusion-associated GVHD-donors lymphocytes present in the unit amount an immunologic attack against the recipient (can occur immune competent and compromised patients)- rare (irradiate)
- 3. Alloimmunization- antibodies develop to HLA / granulocyte-specific antigens
  - —> reduction in granulocyte survival and abnormal migration

Variables of Concern:

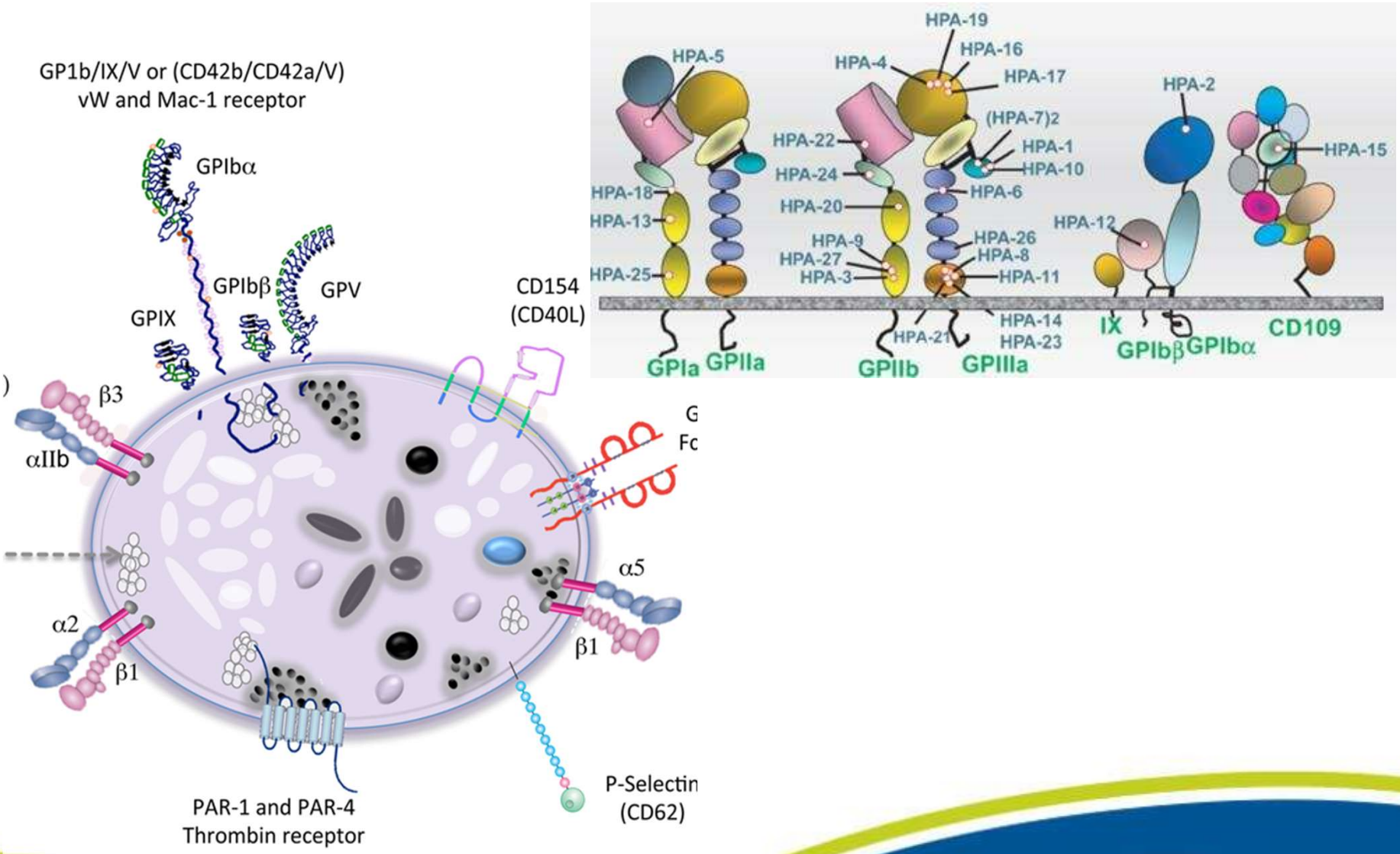
- There have been difficulties in collecting viable, functional granulocytes
- It is still unclear what the adequate number of granulocytes are to administer to reach therapeutic levels
  - The optimal therapeutic dose in adults is still unknown;
  - for children it is 10 to 10ml/kg. This may provide adequate numbers of granulocytes per dose
- Donors must consent to administration of granulocyte stimulating factor; (G-CSF) and Dexamethasone
- Use of hydroxyethyl starch (HES) —> low Hgb, anaphylactoid reactions, interferes with laboratory tests (elevated serum amylase levels), decreases total protein, calcium, fibrinogen levels

HLA-Matched Platelets

HLA Matched Platelets



HLA matched Platelets:



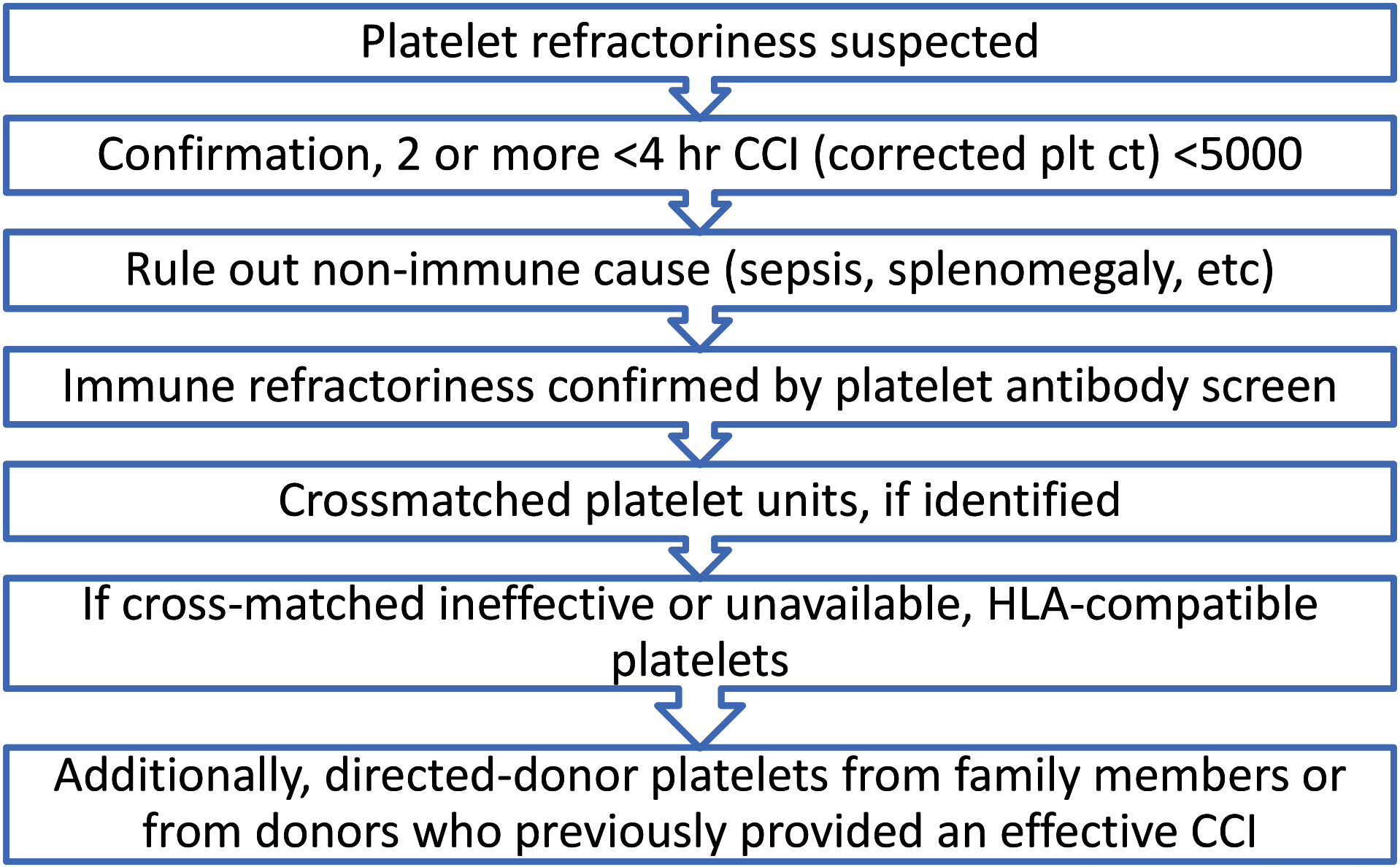
- Patients who fail to respond to platelet transfusions and are at risk of bleeding (Platelet Refractory)
- There are immune and non-immune causes of platelet refractory
- Non-immune causes: DIC, Bleed, Splenomegaly, Fever, Sepsis, Medications
- Immune causes: autoAb and alloAb
  - Auto-Ab: ITP
  - Allo- Ab: HLA (common) and platelet specific (HPA- mostly HPA1)

Corrected Count Increment:

CCI=Apheresis Platelet Concentrations

CCI=(Post-platelet count- Pre-platelet count)(Body Surface Area)/# of platelets transfused (x10^11)

CCI>7500 (1 Hr) or >5000 (20hr)


Platelet refractoriness suspected
Confirmation, 2 or more <4 hr CCI (corrected plt ct) <5000
Rule out non-immune cause (sepsis, splenomegaly, etc)
Immune refractoriness confirmed by platelet antibody screen
Crossmatched platelet units, if identified
If cross-matched ineffective or unavailable, HLA-compatible platelets
Additionally, directed-donor platelets from family members or from donors who previously provided an effective CCI

- HLA sensitization is the most common immune cause of refractoriness and can be diagnosed by demonstration of significant levels of antibodies to class I HLA in the refractory patients' serum
- Poor platelet recovery (1-hour CCI), is usually caused by antibody-mediated destruction

Serologic Testing on Recipient:

- Recipients blood is drawn
- Class I & II screening assay is performed to detect the presence/absence of HLA antibodies on platelet transfused
- If screening assay is positive, a HLA antigen assay is performed to identify the specific HLA antibody present in the serum of the patient
- Ag negative product is requested as a specialized product

Prevention of Alloimmunization

- When HLA-Ab are present, supply apheresis platelets from donors whose HLA-A and HLA-B antigens match those of recipient/patient
- Leukoreduction of products
  - Removes HLA antigen source (WBCs)
- Minimize donor exposure (use apheresis products)
- Minimize transfusions

Antigen Negative/ Antigen Matched Blood Products

Phenotype- matched (red blood cells)

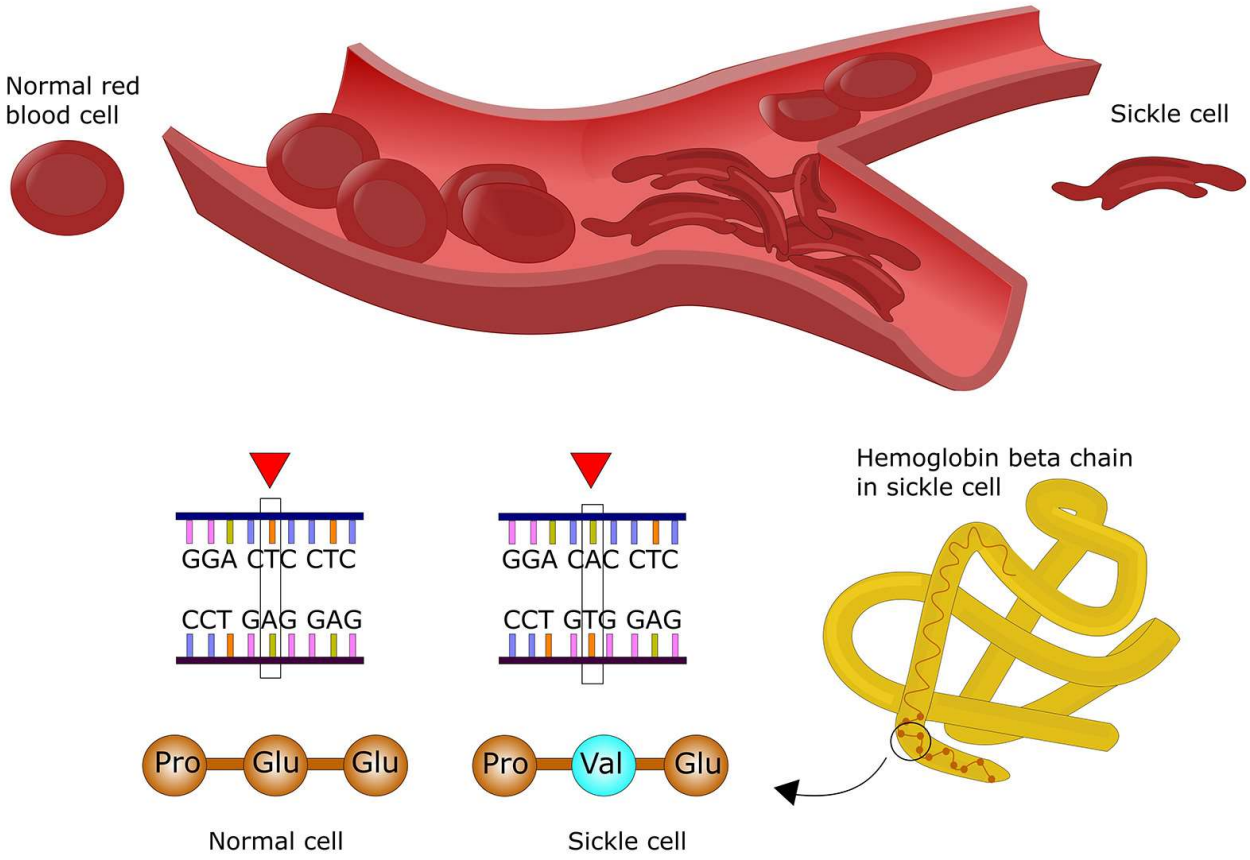
- For patients who require chronic transfusions (HbS, thalassemia)
- Phenotypically red blood cell units are "matched" for patient's Rh and K antigens; (D,C,E,c,e, S, s, Fya, Fyb)
- Matching is done regardless of patient's corresponding red blood cell antibodies
- Phenotype-matched blood decreases rate of red cell alloimmunization from as high as 43% to **2.2%**

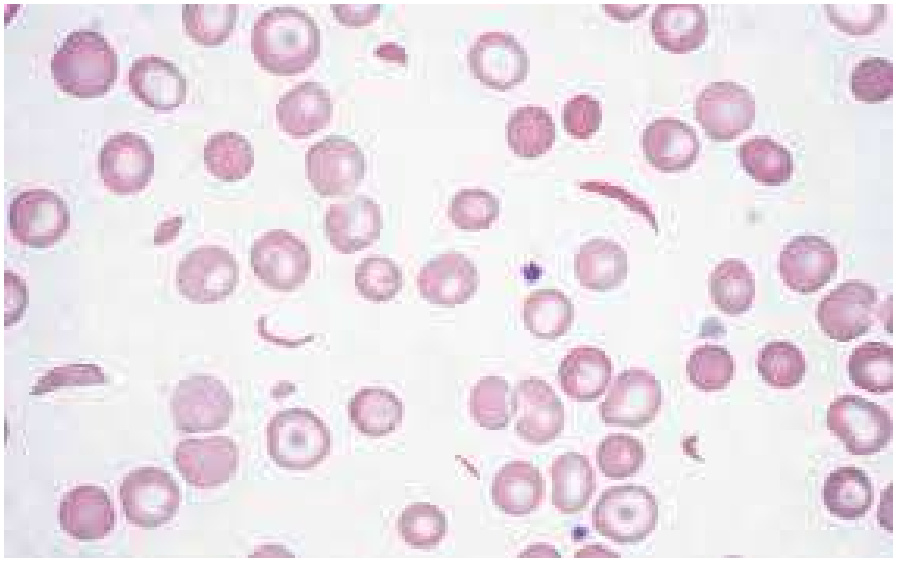
Patients who have developed Antibodies:

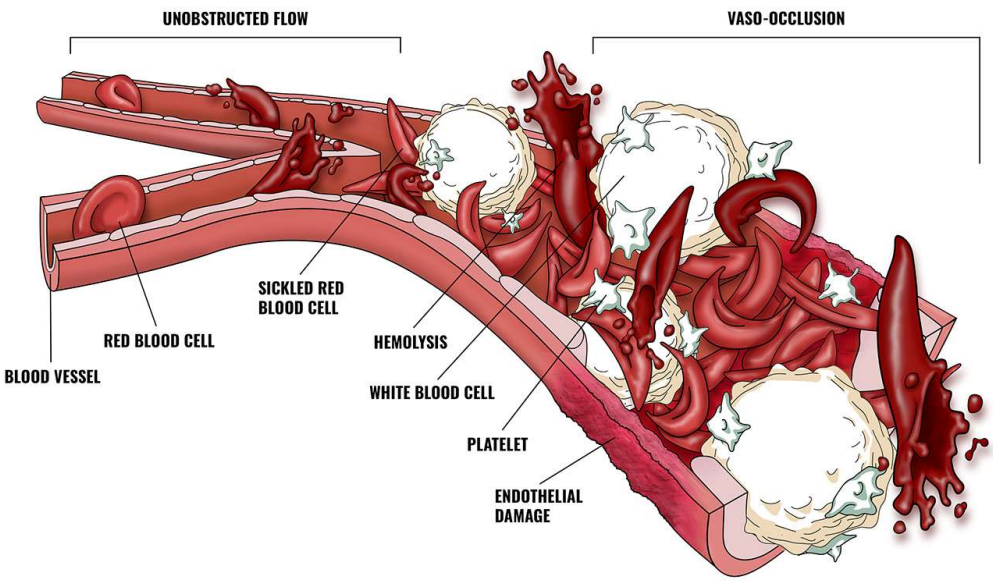
1. Perform the patient's phenotype
2. Strongly consider genotyping the patient if not previously done
3. Transfuse red cells that are matched for all clinically significant antigens against which antibodies are directed. These patients have demonstrated that they are immunologic responders, therefore are more likely to develop antibodies against additional antigens. Prophylactic matching should include Fy^a, Fy^b , Jk^a, Jk^b, S and s, in addition to D, C, c, E, e, and K, if possible.

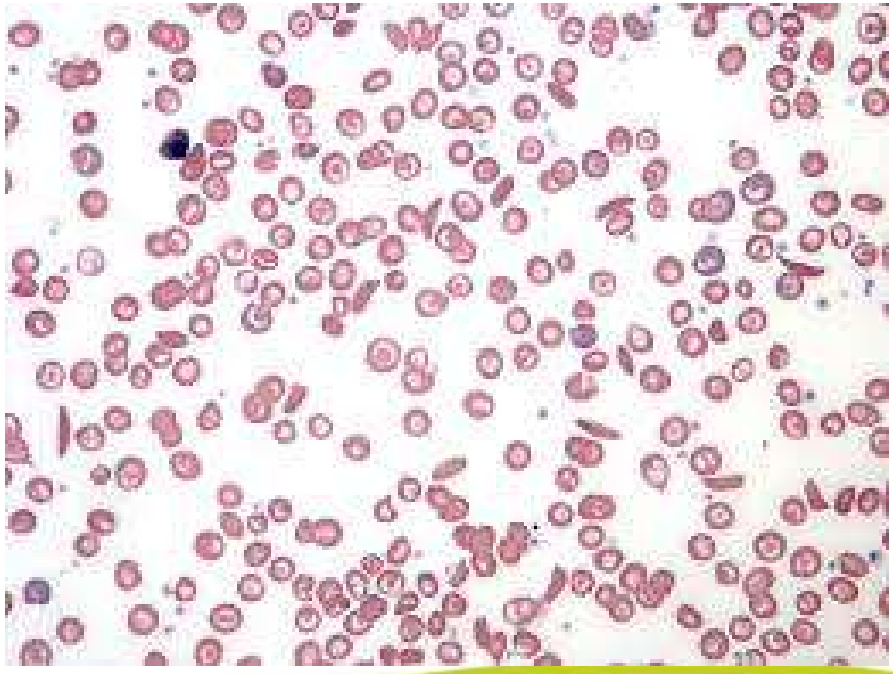
HbS Ag Negative Units

Indications:



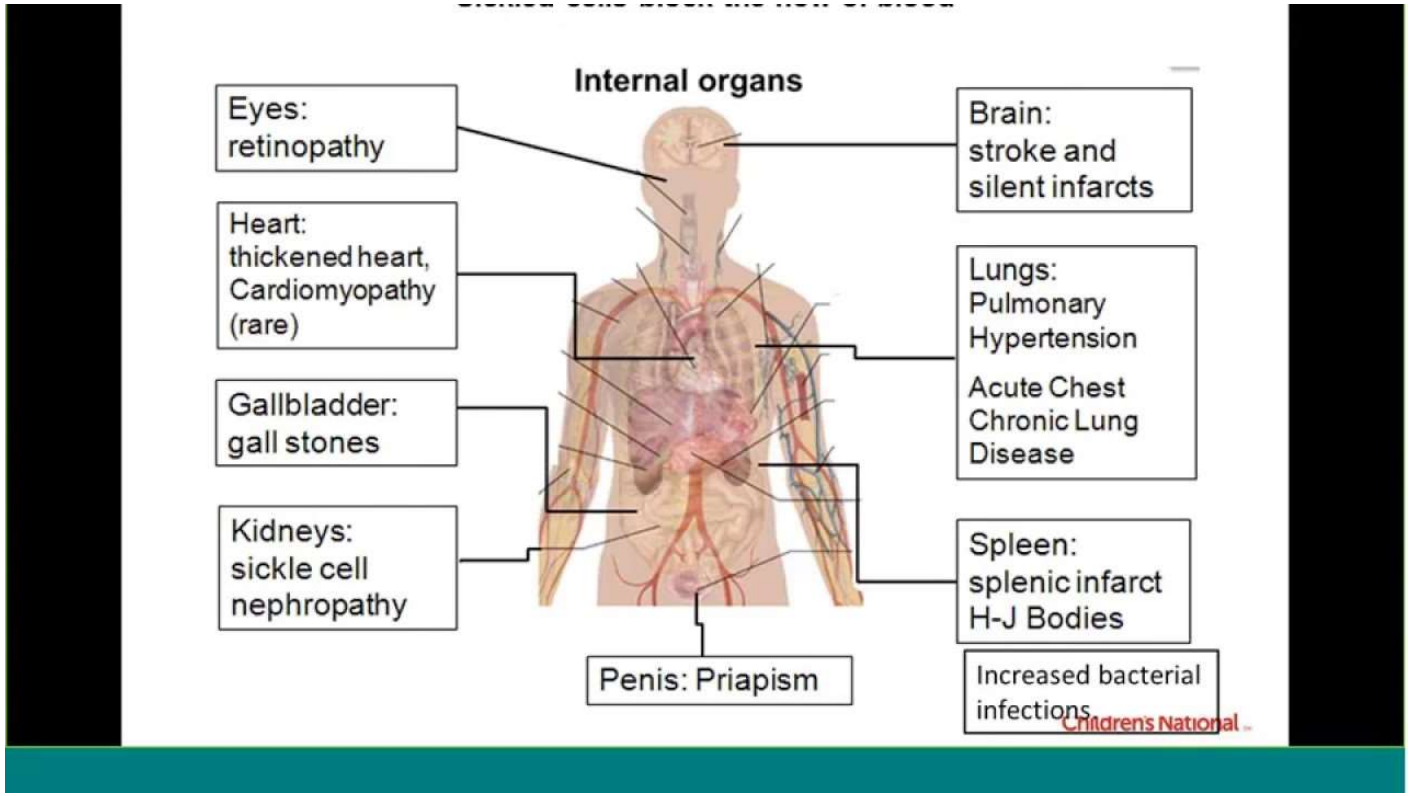






Sickle Cell Anemia

Clinical Symptoms and Risks:



Hemoglobin S- Negative RBC's:

- Indicated for transfusions of patients with HbS/ Sickle cell disease
- Any infant under four months of age needing an RBC transfusion
- Overall: helps prevent worsening of:
  - Sickle cell disease
  - Vascular occlusion
  - Decreased oxygen carrying capacity

Thank You….

Questions??

References

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