

Overview of Therapeutic Apheresis (TA)

History



***Apheresis
(Greek Term) =
Removal or Withdrawal***

Definition of a TA Procedure

The removal of a blood component from a patient using apheresis technology for the purpose of removing defective cells or depleting a disease mediator

Rationale For Performing TA Procedures

- An apheresis procedure can more effectively remove a pathogenic substance in the circulating blood that contributes to a disease state than the body's own homeostatic mechanisms
- The patient may benefit from both the removal of the blood component and the fluid given as replacement

Types of TA Procedures

- Therapeutic Plasma Exchange (TPE)
- Red Blood Cell Exchange (RBCX)
- Cellular Depletions

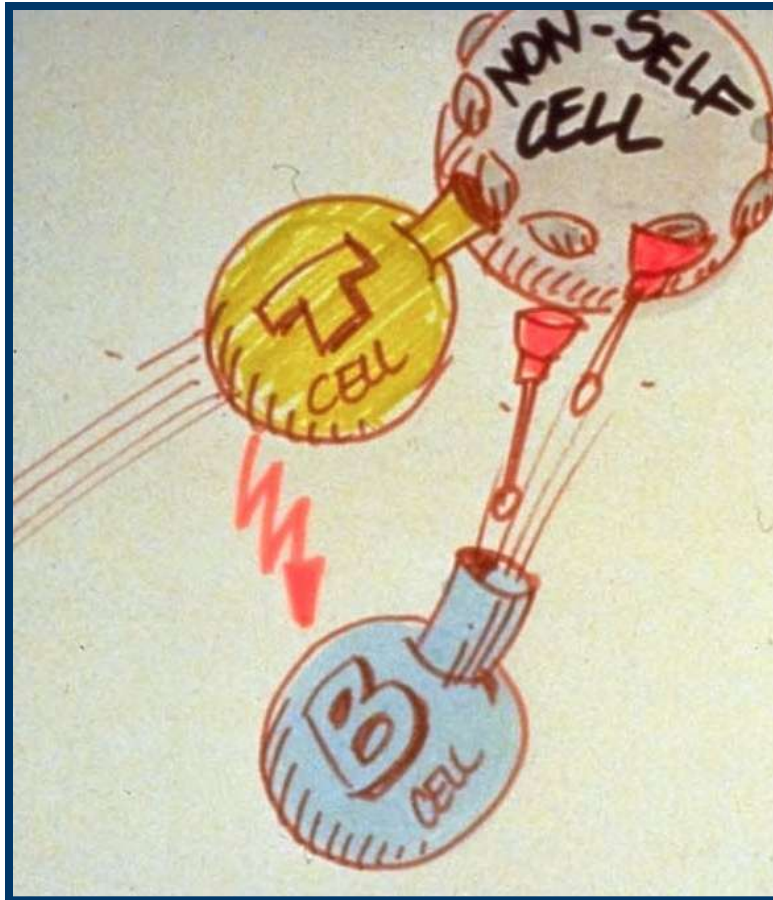
Therapeutic Plasma Exchange (TPE)

- The removal of large volumes of patient plasma and replacement of the plasma with appropriate fluids
- Specialty areas include:
 - Renal and metabolic diseases
 - Hematologic diseases
 - Neurologic disorders

Therapeutic Plasma Exchange

- The most common use of TPE is for the treatment of autoimmune or immune mediated diseases or disorders
- TPE removes:
 - Monoclonal antibodies
 - Paraproteins
 - Autoimmune antibodies
 - Antigen-antibody complexes

Normal Immune Response

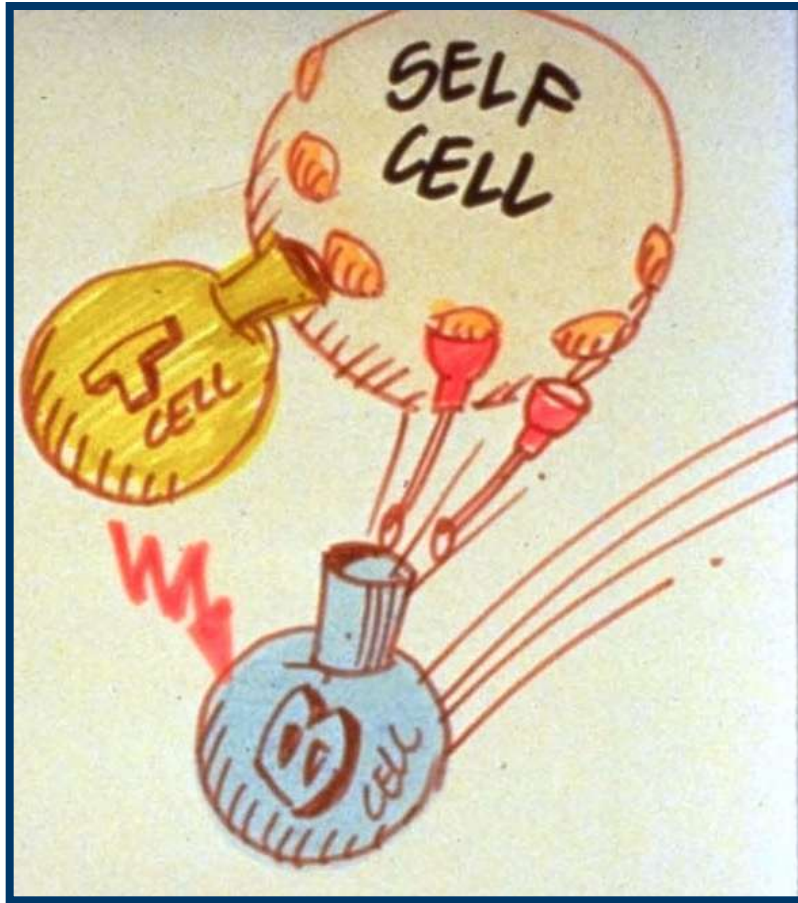


1. Antigen presenting cells(APC's) engulf foreign antigens
2. APCs "present" antigen to T cells
3. T cells initiate cellular immune response and signal B cells to proliferate and produce antibodies
4. Cell and antibody mediated immune responses destroy non-self cell and cause inflammatory effects:
 - Fever
 - Pain
 - Swelling

Autoimmune Disease

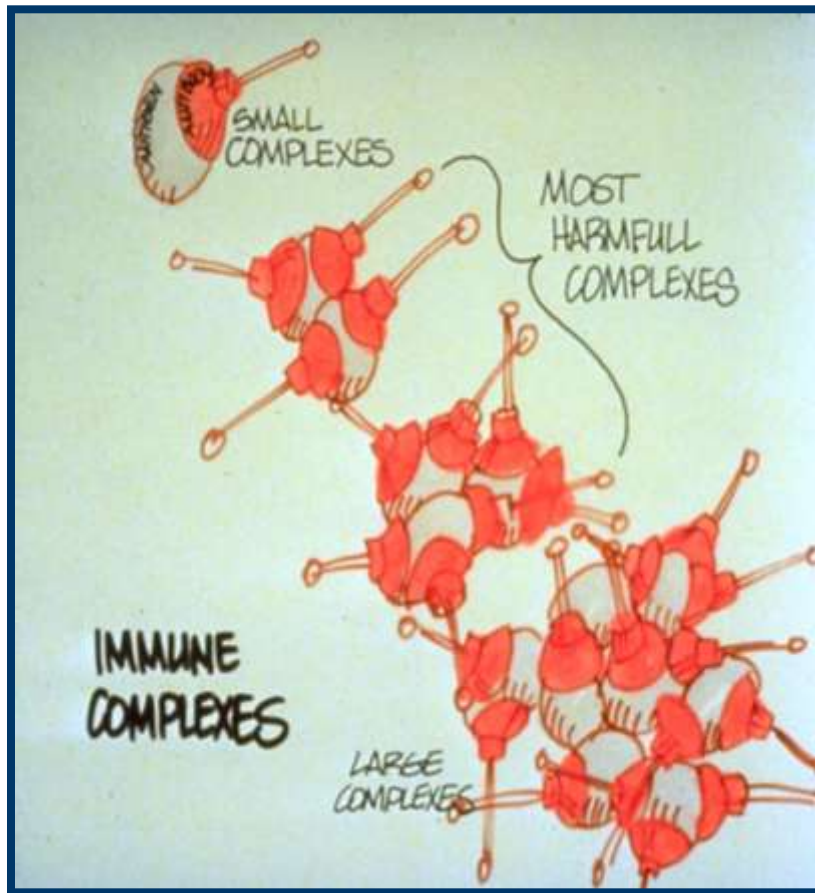
- Autoimmune disease occurs when an immune response is triggered inappropriately against self antigens
- Clearance of antigen by normal immune processes does not occur and the result is a sustained immune response and chronic injury to tissues

Autoimmune Disease



1. Self cells are inappropriately identified as non-self cells
2. T cells activate B cells to produce antibodies against the self cells
3. An immune response is initiated with resulting inflammatory effects:
 - Fever
 - Pain
 - Swelling
4. Self cell is destroyed

Immune Complex Disease



1. An antibody and an antigen combine to form a complex
2. Middle-size complexes become entrapped in blood vessels, kidneys, or joints

Effects:

- Vasculitis
- Nephritis
- Arthritis

Autoimmune Therapy

Purpose:

- Suppress the abnormal immune response
- Remove the causative factor
- Relieve/eliminate symptoms

Therapy:

- Drugs
- Surgery
- Drugs and TPE



Therapeutic Plasma Exchange

- Removing the plasma removes disease mediators circulating in the patient's plasma, including:
 - Alloantibodies, autoimmune antibodies and antigen-antibody complexes
 - Abnormal or increased amount of plasma protein
 - Very high cholesterol levels
 - High levels of plasma metabolic waste products or plasma-bound poisons or drugs
- Decreasing levels of disease mediator can relieve symptoms, but is not curative

Therapeutic Plasma Exchange

- Also removes normal plasma components important in the maintenance of homeostasis:
 - Immunoglobulins (IgG, IgM, IgA)
 - Cholesterol
 - Albumin
 - Fibrinogen
 - Creatinine, uria
 - Electrolytes
 - Plasma-bound drugs

Red Blood Cell Exchange

- Removal of large volumes of abnormal patient red blood cells and replacement with normal donor red blood cells
- RBCX removes RBCs containing abnormal hemoglobin, infected RBCs, abnormal short lived RBCs that contribute to iron overload

Cellular Depletion

- Rapid reduction of a greatly elevated number of cells from the intravascular space to decrease the risks associated with vascular stasis
- According to the ASFA evidenced based guidelines, cellular depletions are generally considered when:
 - Leukocytosis: $> 100,000/\mu\text{L}$ white blood cells (WBC)*
 - Thrombocytosis: $> 500,000 - 1,000,000$ platelets*
 - Erythrocytosis: $> 60\%$ hematocrit*
- Supportive therapy used in combination with drugs or chemotherapy

*or when the patient is symptomatic

WBC Depletion

- Considered when symptoms occur due to the large number of circulating WBCs
- Symptoms generally occur at WBC concentrations greater than $100 \times 10^3/\mu\text{L}$ but will vary depending on individual patient variables and disease
 - Symptomatic leukocytosis reported range is $50 \times 10^3/\mu\text{L}$ (AML) to $300 \times 10^3/\mu\text{L}$ (CLL)

Platelet Depletion

- Platelet depletions are performed in order to prevent recurrent or progressive thrombotic or hemorrhagic events or to quickly reduce elevated counts in high risk or symptomatic patients

Red Blood Cell Depletion

- Erythrocytapheresis or RBC depletion is defined as the rapid reduction of a greatly elevated number of RBCs to:
 - Reduce blood viscosity
 - Reduce red cell volume
 - Reduce iron overload and maintain normal iron levels

CaridianBCT Apheresis Devices



Spectra Optia®
Apheresis Sytem

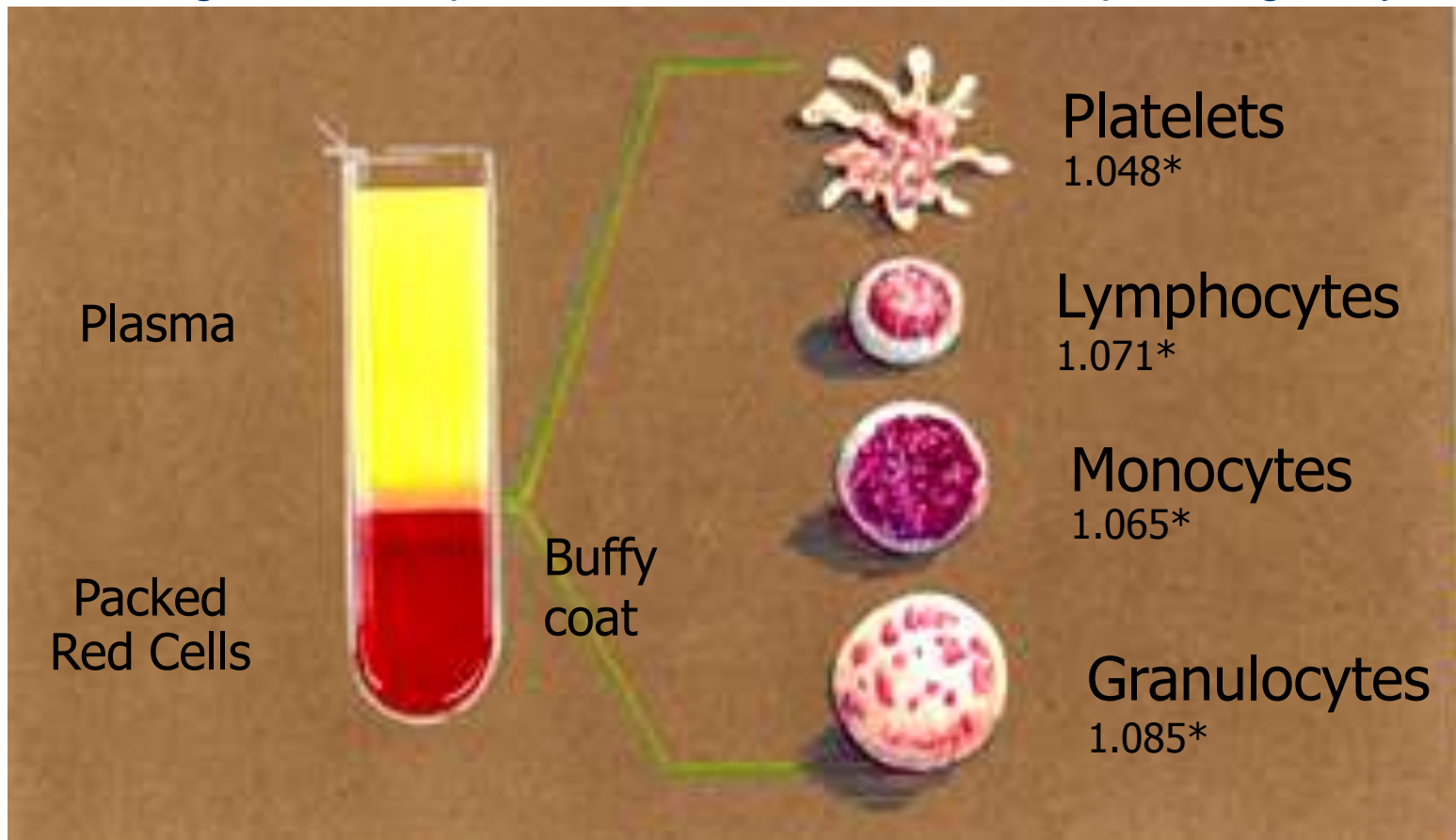
COBE® Spectra
Apheresis System



Therapeutic Plasma Exchange and Mononuclear Cell Collection protocols on the Spectra Optia apheresis system are available in selected markets. Contact your CaridianBCT representative for local availability.

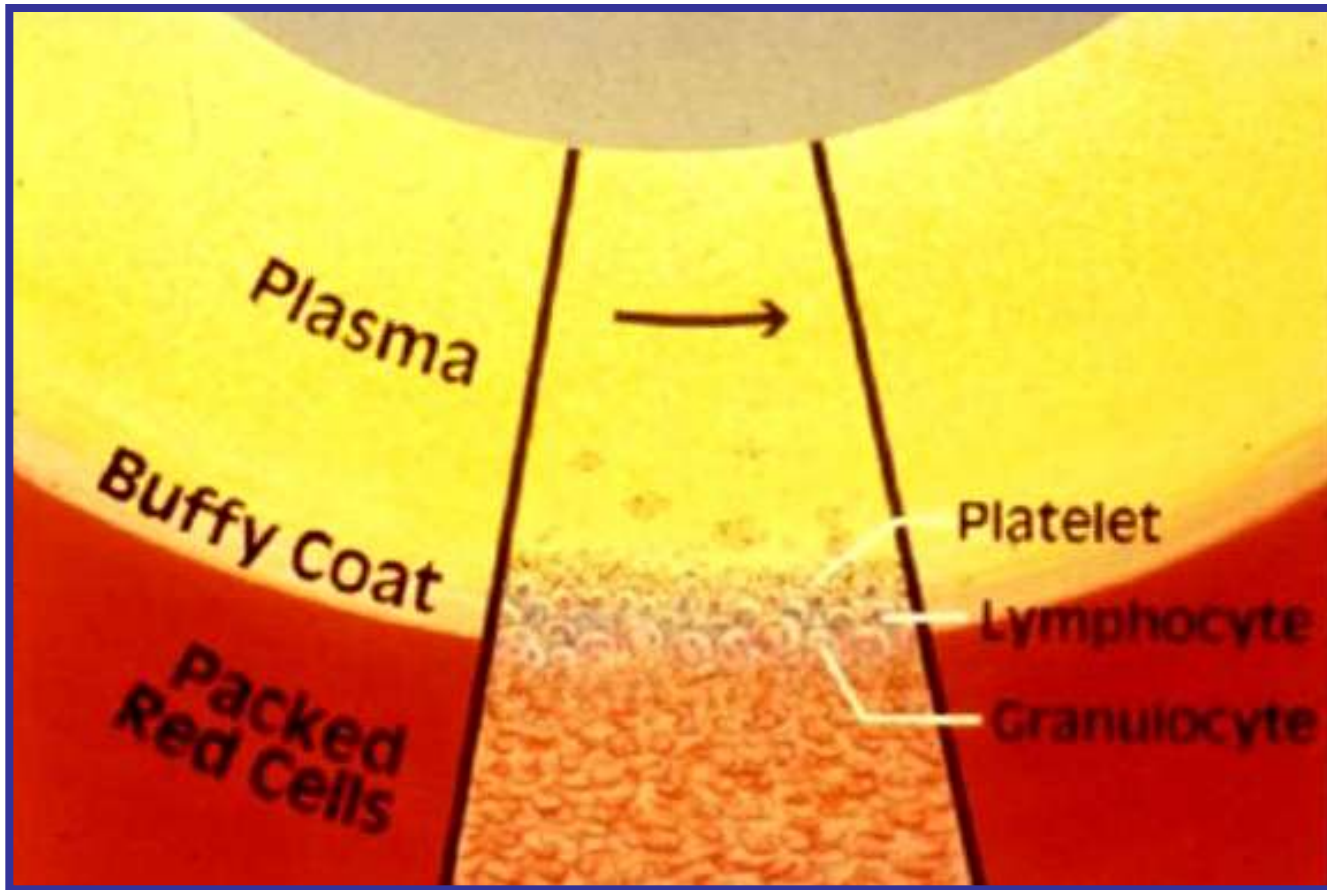
Separation of Blood Components

Centrifugal force separates cells based on their specific gravity

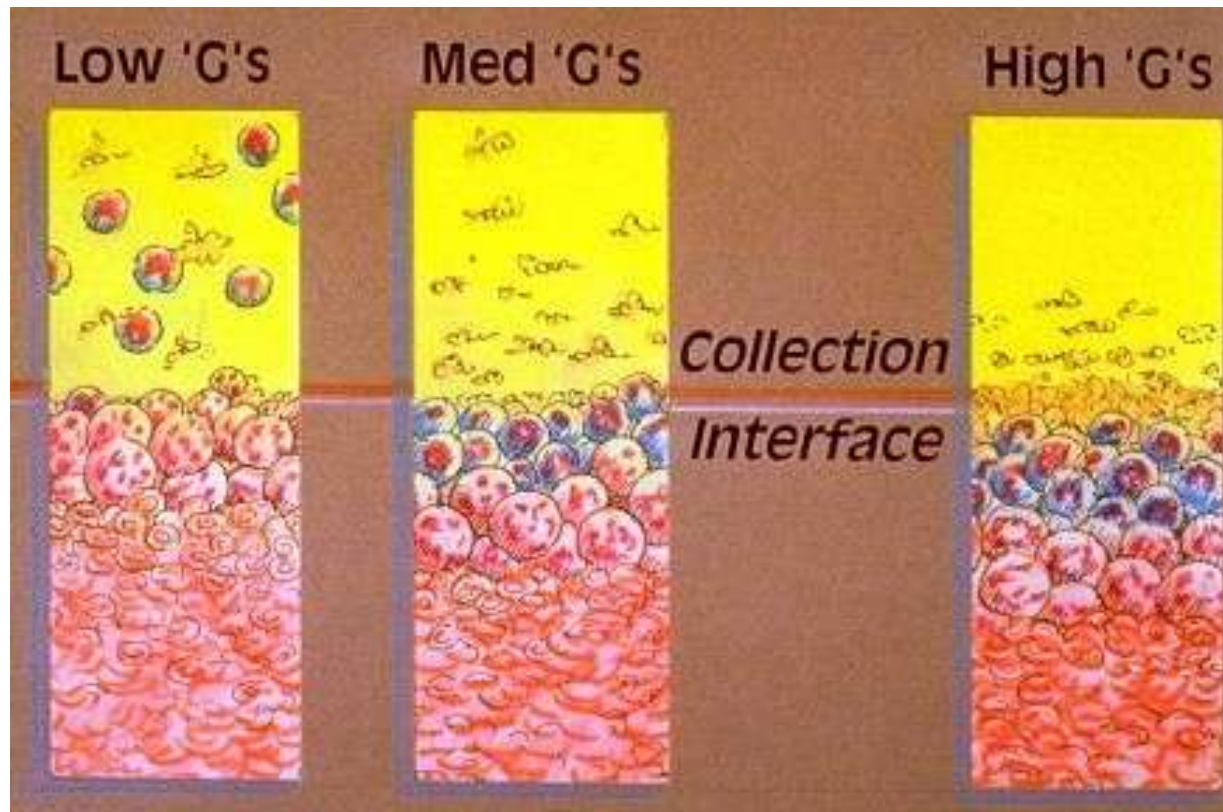


*Average specific gravity of cell type shown

Separation of Blood Components



Effects of G-Force on Separation



Procedural Elements of TA

- Vascular access
- Anticoagulation
- Replacement fluids
- Treatment frequency
- Potential side effects

Vascular Access

- Antecubital/peripheral venipuncture
- Femoral catheter
- Subclavian catheter
- Jugular access
- Ports
- Arteriovenous fistula or graft

Anticoagulation



- ACD-A
- Heparin

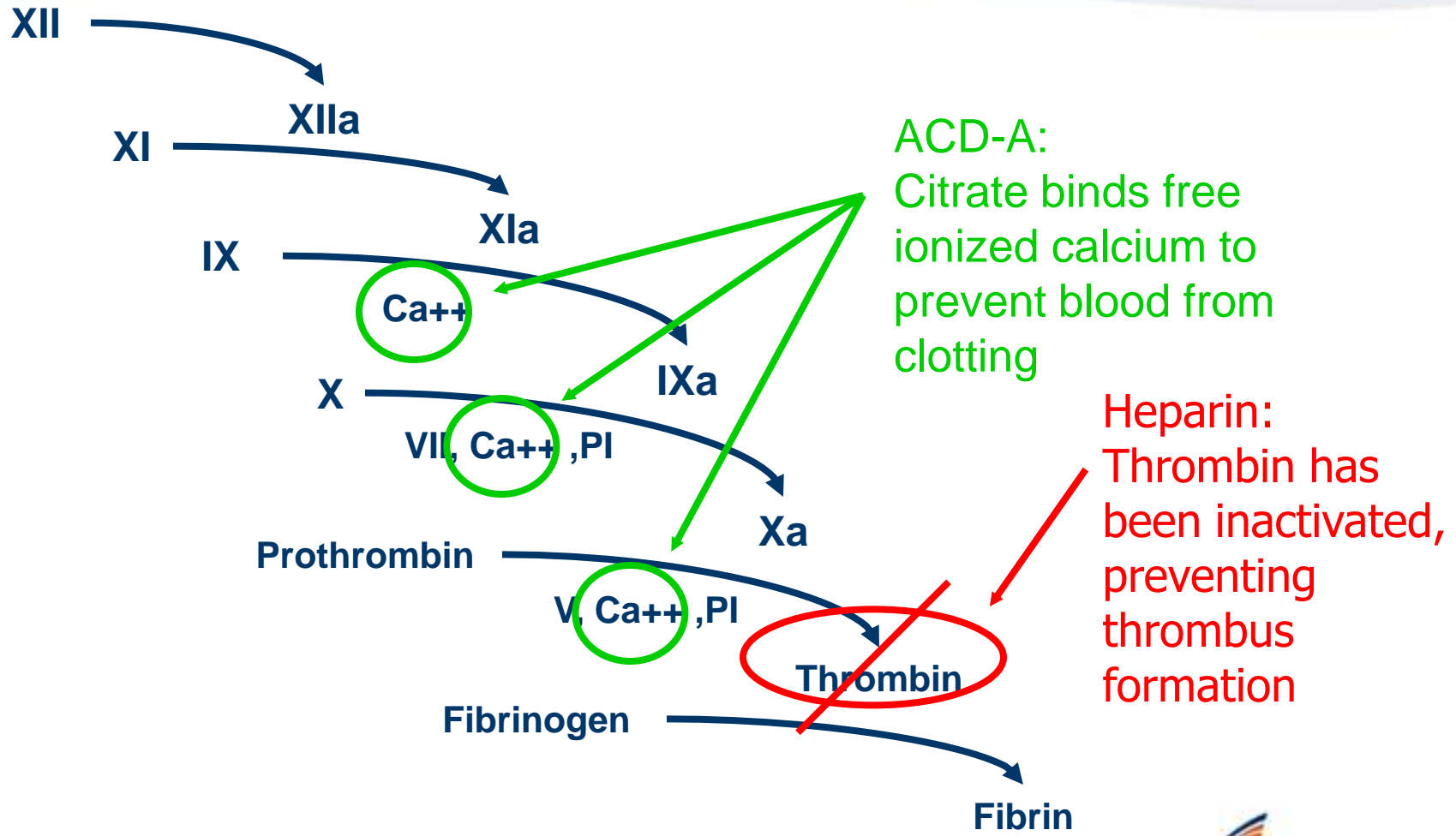
ACD-A (Acid Citrate Dextrose-Formula A)

- Binds to ionized calcium
- Lowers the pH of the blood
 - Inhibits platelet clumping
- Anticoagulates extracorporeal blood circuit
 - Is rapidly metabolized
- May cause hypocalcemia

Heparin

- Complexes with antithrombin and increases its activity, which inactivates thrombin and other factors and prevents thrombus formation¹
- Anticoagulates systemically
 - Metabolized slowly (1 to 2 hours)
- Can cause heparin-induced thrombocytopenia

Clotting Cascade



Replacement Solutions

TPE procedures:

Crystalloids (contain no protein)

- 0.9% sodium chloride
 - In combination with 5% albumin replacement

Colloids (contain macromolecules)

- 5% albumin
- Fresh frozen plasma/cryo-poor plasma
- Hydroxyethyl starch (HES)

Replacement Solutions

RBC exchange procedures:

- Packed red blood cell units

Cellular depletion procedures:

- Saline and/or 5% albumin, according to physician's order

Treatment Frequency

Acute disease

- Rapidly progressive
- Requires frequent treatments (every 24 to 48 hours, sometimes every 12 hours)

Chronic disease

- Slowly progressive
- Requires less frequent treatments (weekly or monthly)

Potential Side Effects

- Hypocalcemia
- Other electrolyte imbalances
- Hypotension
- Vasovagal syncope
- Allergic reactions
- Transfusion related acute lung injury (TRALI)

How Does TA Impact the Lab/Blood Bank?

- Possible increased inventory of plasma or cryo-poor plasma for ongoing TPE procedures
- Capacity for thawing large amounts of plasma
- Possible increase in transfusion reaction work ups due to transfusion of multiple units of blood products
- Type and crossmatch needed for replacement RBC units for RBCX procedures

How Does TA Impact the Lab/Blood Bank?

- Screening RBC units for sickle cell trait, if patient has sickle cell disease
- Apheresis staff may request a hematocrit on each of the replacement RBC units for RBCX procedures

How Does TA Impact the Lab/Blood Bank?

- For depletion procedures, the apheresis staff may request a cell count from the product to help determine the efficiency of the procedure
 - Sample may need to be further diluted by the laboratory

Overview of Therapeutic Apheresis

Questions?