Apheresis

Objectives:
- Explain the concept of cell centrifugation
- Explain the concept of extracorporeal volume
- Name 2 methods of venous access for apheresis

General Apheresis

What is Apheresis?
Elements:
- Whole blood removal
- Separation by centrifugation
- Cells removed, replaced or reinfused.

Types of Apheresis

Therapeutic
- Plasma Exchange
- RBC Exchange
- PLT Depletion
- WBC Depletion
- Photopheresis
- LDL Apheresis

Collection
- Red Blood Cells
- Plasma
- Platelets
- White Blood Cells

Key Concept: Separation by Centrifugation
Key Concept: Separation by Centrifugation

Key Concept: Extracorporeal Volume (ECV)

- **ECV** = amount of whole blood in the apheresis circuit
- Average 250mL
- Can be as much as 450mLs with some circuits
- Regulations prohibit removing > 15% of total blood volume
- Sometimes only 10% if safe for the patient
- One size circuit, but may not fit all bodies
- Blood prime option
- ECV impacts patient oxygenation

Key Concept: Anticoagulation

**ACD-A** (anticoagulant citrate dextrose, formula A)
- Binds ionized calcium
- Side-effect: ↓Ca, ↓K, ↓Mg
- Short-acting / regional

**Heparin**
- Potentiates plasma antithrombin
- Long-acting
- Systemic anticoagulation

Key Concept: High-Flow Venous Access

- Two points of access usually required
  - OUT → IN
- Fast, continuous blood flow
  - Up to 150 ml/minute
  - Uninterrupted blood flow for 2-6 hours

Peripheral Venous Access

- 18g or bigger
- AC veins best
- Limited mobility
- AV Fistula Needle
- IV catheter
- Usually for donors

Central Venous Access

**Requirements**
- Dual-lumen
- High-flow
- Short length
- 10 - 14 Fr
- Intra-jugular

**Tunneled:** Hickman-type
- Patients

**Non-tunneled:** Mahurkar-type
- Donors or collecting for storage
General Apheresis Side Effects

- Citrate Toxicity
- Vasovagal reaction
- Bleeding
- Blood Loss
- Transfusion needs
- Allergic Reactions (ETO)
- Fatigue

**Citrate Toxicity**

**Feels like:**
- Lips tingling, body vibration, cramps, chest pain

**Looks like:**
- Low ionized calcium, pallor, tetany

**Resolve:**
- Pause the procedure – resume using slower flow rate
- Oral replacement – TUMS, orange juice, calcium-rich food
- IV replacement – calcium gluconate
- Required: ionized calcium point-of-care testing

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**Pediatric Issues**

Small body, big circuit
- Prime the apheresis circuit with packed RBCs

Side-effects are subtle, fast and strong

IV access:
- usually central
- Peripheral access is possible in larger children (40-50 kg) when patient is highly motivated

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**Type of White Blood Cell Collections (leukapheresis)**

**Hematopoietic Progenitor Cell (HPC)**
- a.k.a Peripheral Blood Stem Cell (PBSC)

**Bone Marrow – Red Blood Cell Reduction**
- Reduce marrow volume and RBC content
- Donor / Recipient incompatible ABO

**Lymphocytes (DLI = donor lymphocyte infusion)**
- From original donor, infused to recipient to induce mild GvHD

**Mononuclear Cells**
- Usually targeting lymphocytes
- T-cells, dendritic cells
- Immunotherapy

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**HPC-A Collection Specifics**

Hematopoietic Progenitor Cells - Apheresis

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**Autologous Preparation**

- Consent
- Venous Assessment
- H&P
- Infectious Disease Testing
- ABO typing
- Storage contract
### Allogeneic Preparation
- Consent
- Venous Assessment
- H&P
- ABO typing / recipient compatibility
- Females - pregnancy testing pre-GCSF
- Donor History Questionnaire
- Infectious Disease Testing
- Donor Eligibility Declaration
  - Eligible / Ineligible, Suitable / Unsuitable
  - Justification for Urgent Medical Need

### Patient / Donor Education
**Pre-procedure instructions**
- Eat pre-procedure: calcium-rich food
- Be warm
- Increase fluid intake
- Hold meds
  - Anticoagulants
  - Antihypertensives
- Bring entertainment!

### HPC-A Mobilization
**Stem cells move from marrow to blood circulation**
- Chemotherapy
- Chemotherapy + G-CSF
- Plerixifor (Mozobil)
  - At SCCA – 4th day of G-CSF injection
  - Repeat up to 4 consecutive days
  - Administered SQ ~ 11 hours prior to apheresis

### HPC-A Collection Timing
**Protocol driven**
**Autologous collection trigger**
- Peripheral CD34 level (PBL) > 10 uL
- Day after WBC > 1,000 uL
- 4th day of G-CSF mobilization

**Allogeneic collection trigger**
- 4th day of G-CSF mobilization

### Procedure Qualification Parameters
**Autologous HPC-A Collections**
- HCT ≥ 30%
- PLT ≥ 20K – 50K
  - Depends on volume processed

**Allogeneic HPC-A Collections**
- HCT ≥ 38%
- PLT ≥ 150,000/uL

* Order to proceed required if lab parameters not met *

### HPC-A Cell Collection Goals
**Protocol and diagnosis driven**
**Allogeneic targets dependent on:**
- non-myeloablative vs. myeloablative transplant
- specific cell quantity
  - typically 5 x 10^6 CD34+/kg recipient weight
  - Some protocols require 2 collections regardless of cell quantity achieved on Day 1

**Autologous targets**
- Myeloma: 10 x 10^6 CD34+/kg
- NHL: 5 x 10^6 CD34+/kg
Allogeneic HPC-A Collection Process

Day -1:
• Donor PBSC collection
• Overnight cell storage for Day 0 infusion

Day 0:
• 2nd collection if Day 1 goal not met or if required by protocol
• Cells from both days of collection infused to recipient

HPC Collection: Procedure Length

Flow rate and blood volume processed impact collection time

- Standard Volume = 12 L
  • 2-3 hours
- Large Volume = 6 x total blood volume
  • 4-5 hours

Regulatory Oversight

In addition to patient care regulation (TJC, DOH), we are manufacturing and transplanting human cells and tissues, and are regulated by:

FDA – Food and Drug Administration.
  • Federal laws that must be followed

FACT – Foundation for the Accreditation of Cellular Therapy
  • Voluntary quality assurance organization granting accreditation

CAP – College of American Pathologists
  • Quality control for laboratory aspects of apheresis

Regulation vs. Accreditation

Regulation
• Law
• 100% Compliance Expectation

Accreditation
• Recognition
• Certification
• Improves performance and safety

Noncompliance can result in non-payment by insurance, program closure, fines, jail

ECP – Indications

• FDA indicated for use in the palliative treatment of skin manifestations of Cutaneous T-Cell Lymphoma (CTCL) that are unresponsive to other forms of treatment.

• Off-label use:
  – GvHD
  – Solid-organ transplant rejection: lung, heart, liver
  – Scleroderma
  – Crohn’s Disease

Extracorporeal Photopheresis (ECP)
**Mechanism of Action – proposed!**

- **EX VIVO:**
  - Uvadex® injected into collected WBC product
  - UVA light activates Uvadex®
  - Uvadex® causes DNA cross-linking in nucleated cells → apoptosis

  ![Apoptosis](image)
  - Programmed cell death
  - Immune pathway regulating cell cycle

**Mechanism of Action - proposed**

- **IN VIVO:**
  - Infused apoptotic cell population induces APC cell response
  - Triggers anti-inflammatory response pathway
    - Increased production of Regulatory T-Cells
    - Decreased production of Effector T-Cells
  - Results in tolerance

  ![Antigen Presenting Cell (APC)](image)

**Treatment Regimens**

- Usually 2 days per week
- Labeling is for consecutive days
- Labeling is for CTCL
  - Monthly x 6 months
- Off-label at SCCA
  - Acute GvHD
    - Weekly x 8 weeks
    - 3 days weekly x 12 weeks (upcoming Acute Peds GvHD Trial)
  - Chronic GvHD
    - Weekly x 4 weeks → bi-weekly x 3-6 mos. → monthly
  - Solid-organ Transplant Rejection
    - Weekly x 1 mo. → bi-weekly x 1 mo. → monthly for 4 mos.

**ECP - Process**

- A leukapheresis procedure:
  - WBCs isolated from whole blood
  - Uvadex® mixed with WBCs
  - UVA light activates Uvadex®
  - WBCs reinfused to the patient

**Photoactivation Module**

- Buffy coat is exposed to UVA lights as it circulates through the module
- Buffy coat recirculates multiple times to receive adequate UVA exposure
  - Average photoactivation time = 20”

**Venous Access**

- Device must allow 50 mL / minute flow rates
- Needs to be reliably patent
Side Effects

- Common
  - Fatigue
  - Photosensitivity

- Less Common
  - Citrate Toxicity
  - Hypotension
  - Fluid overload
  - Bleeding
  - Blood Loss
  - Anemia
  - Infection

Apheresis: Services and Volumes

In 2016, APH performed:

- 583 HPC-A collections
- 251 Research collections
- 7 DLI collections
- 11 HPC-M RBC reductions
- 1283 Extracorporeal Photopheresis (ECP) procedures
- 31 Plasma Exchange procedures

Thank you!