Physiology of Blood Purification: Dialysis & Apheresis

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Outline

• Physical principles of mass transfer
• Hemodialysis and CRRT
  – Properties of dialyzers
  – Concepts that underlie the HD procedure
• Peritoneal Dialysis
  – Peritoneal membrane physiology
  – Concepts that underlie the PD procedure
• Apheresis – basic principles of blood separation

Solute Removal Mechanisms in RRT

• Diffusion
  – transmembrane solute movement in response to a concentration gradient
  – importance inversely proportional to solute size
• Convection
  – transmembrane solute movement in association with ultrafiltered plasma water ("solvent drag")
  – mass transfer determined by UF rate (pressure gradient) and membrane sieving properties
  – importance directly proportional to solute size
Diffusion

Convection

Effect of Pore Size on Membrane Selectivity
- Creatinine: 113 D
- Urea: 60 D
- Glucose: 180 D
- Vancomycin: ~1,500 D
- Albumin: ~66,000 D
- IgG: 150,000 D
Interruption Hemodialysis (IHD)

- Blood perfuses extracorporeal circuit
- Dialysate passes on opposite side of membrane
- High efficiency system
- Particle removal mostly by diffusion
- Fluid removal by ultrafiltration (hydrostatic pressure across dialyzer membrane)

Hollow Fiber Dialyzers

Dialysis/Hemofiltration Membranes

Capillary Cross Section Blood Side
Permeability Surface Area
Product: $K_0A$

- $K_0A$ is a property of the dialyzer
- Describes maximum ability of dialyzer to clear a given substance

$K_0A = \text{permeability} (K_0) \times \text{surface area} (A)$

Clearance ($K_D$)

- Clearance ($K_D$) describes ability of a dialyzer to remove a substance from the blood
- Changes with the dialysis prescription

$K_D = f(x) \{K_0A, Q_B, Q_D\}$

Blood Flow and $K_0A$: Effect on Clearance

![Graph showing the effect of blood flow (Q_B) on Clearance (K_D) for two dialyzers. Dialyzer 2 has a higher $K_0A$ than Dialyzer 1.](graph.png)
Blood Flow and Molecular Weight: Effect on Clearance

Small Molecules
- Diffuse easily
- Higher Kd at given Qb, Qd

Larger Molecules
- Diffuse slowly
- Lower Kd at given Qb, Qd

Ultrafiltration (UF)
- Removal of water due to effects of pressure
- Solute removed by convection at the same time
- UF capability of a dialyzer described by the UF coefficient (Kuf) – ml/h/mmHg
**Ultrafiltration**

- Hydrostatic pressure across membrane
- More water removal with ↑pressure, ↑$K_u$

**Continuous Renal Replacement Therapy (CRRT)**

- Extracorporeal circuit similar to IHD
- Runs continuously
- Particle removal may be by diffusion, convection or a combination
- Fluid removal by ultrafiltration
- Clearance can be approximated by the total effluent rate

**Convection**

- Small and large molecules move equally
- Limit is cut-off size of membrane
- Significant solute loss over time in CRRT
Peritoneal Dialysis (PD)
- Sterile dialysate introduced into peritoneal cavity through a catheter
- Dialysate exchanged at intervals
- Particle removal by diffusion
- Fluid removal by ultrafiltration (osmotic gradient using dextrose)

HD and PD: Physiological Differences

**Hemodialysis**
- Artificial membrane
- Higher blood flow
- Continuous dialysate flow
- Can use hydrostatic pressures for UF

**Peritoneal Dialysis**
- Natural membrane
- Capillary blood flow in peritoneum
- "Stationary" dialysate in most forms of PD
- Different approach to UF is required

PD Transport: A Complex Scheme
The “Three Pore” Model of Peritoneal Transport

- Large pores (>20 nm diameter)
  - Few in number (<10%)
  - Can permit protein transport
- Small pores (4 – 6 nm diameter)
  - Majority (90%)
  - Transport most small molecules
- Ultra-small pores (aquaporins)
  - 1–2%; account for nearly half of water flow

Peritoneal Transport: An Interaction of Three Separate Processes

- Diffusion
- Ultrafiltration
- Fluid absorption

Diffusion in PD: Key Factors

- Concentration gradient of solute (D/P)
- Mass transfer area coefficient (MTAC)
  - Effective peritoneal surface area
    - Surface area + vascularity
  - Diffusive characteristics of membrane for solute in question (permeability)
Ultrafiltration in PD: Key Factors

- Osmotic gradient
- Reflection coefficient
  – i.e., how well the osmotic particle stays in the dialysate ("1" would be perfect)
- UF coefficient
- Hydrostatic and oncotic pressure gradients

Fluid Absorption in PD

- Direct lymphatic absorption of peritoneal fluid
- Tissue absorption of peritoneal fluid
- Limits ultrafiltration and mass transfer
  – Higher levels of peritoneal absorption reduce net ultrafiltration

Schematic of Molecular Transport in PD
Apheresis

- "Apheresis": Greek, "To take away or separate"
- Blood perfuses extracorporeal circuit
- Blood components separated; selected component removed
- If large volume removed replacement is required
- Uses include therapeutic indications or for blood component harvest

Components of Whole Blood

Separation and removal of individual components may be required for therapeutic need
- Plasma (55%)
- White blood cells and platelets (<1%)
- Red blood cells (45%)

Apheresis Methods

**Filtration**
- Blood separation across a membrane by **size**

<table>
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<th>Diameter (µm)</th>
<th>Plasma</th>
<th>Platelet</th>
<th>Red cell</th>
<th>Lymphocyte</th>
<th>Granulocyte</th>
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**Centrifugation**
- Blood component separation by **density**

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<th>Density (specific gravity)</th>
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<th>Platelet</th>
<th>Lymphocyte</th>
<th>Granulocyte</th>
<th>Red cell</th>
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**Effect of Pore Size In Dialysis**

- Small molecules pass;
- Plasma proteins are restricted

**Membrane Apheresis** Employs Larger Pores

- Larger pores will allow proteins to pass through
- Blood cells are restricted
- Membrane system can be used for plasmapheresis, not cytapheresis

**Apheresis by Centrifugation**

- Spinning centrifuge separates blood components by density
- Specific component may be selected for removal by choosing appropriate layer
- Permits plasmapheresis and cytapheresis
Apheresis by Centrifugation

Fraction Removed from Plasma by Plasma Volume Replaced

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• Apheresis – basic principles of blood separation
Physiology of Blood Purification: Summary

• Basic concepts of **diffusion** and **convection** underlie all dialysis methods
  – **HD**: Diffusion + hydrostatic-pressure UF
  – **CRRT**: Diffusion and/or convection + hydrostatic-pressure UF
  – **PD**: Diffusion + osmotic-pressure UF
• Blood components separated by centrifugation or membrane in **apheresis**