Physiology of Blood Purification: Dialysis & Apheresis

Jordan M. Symons, MD
University of Washington School of Medicine
Seattle Children’s Hospital
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
Intermittent 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.

$$K_D = fx \{K_0A, Q_B, Q_D\}$$
Blood Flow and $K_0A$: Effect on Clearance

Dialyzer 2: Higher $K_0A$

Dialyzer 1: Lower $K_0A$
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
• Solutes removed by convection at the same time
• UF capability of a dialyzer described by the UF coefficient ($K_{uf}$) – ml/h/mmHg
Ultrafiltration

- Hydrostatic pressure across membrane
- More water removal with ↑pressure, ↑$K_{uf}$
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
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.
# Apheresis Methods

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

<table>
<thead>
<tr>
<th>Filter CutOff</th>
<th>Filtration Diameter (µm)</th>
<th>Centrifugation Density (specific gravity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td></td>
<td>Plasma (1.025-1.029)</td>
</tr>
<tr>
<td>Platelet</td>
<td>3</td>
<td>Platelet (1.040)</td>
</tr>
<tr>
<td>Red cell</td>
<td>7</td>
<td>Lymphocyte (1.070)</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>10</td>
<td>Granulocyte (1.087-1.092)</td>
</tr>
<tr>
<td>Granulocyte</td>
<td>13</td>
<td>Red cell (1.093-1.096)</td>
</tr>
</tbody>
</table>

## Centrifugation
- Blood component separation by **density**
Effect of Pore Size In Dialysis

- Small molecules pass;
- Plasma proteins are restricted

- Creatinine 113 D
- Urea 60 D
- Glucose 180 D
- Vancomycin ~1,500 D
- Albumin ~66,000 D
- IgG ~150,000 D
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

Blood in from patient

RBCs

Plasma

WBCs, Plts

RBCs

Blood return

Hey!Pheresis®
Fraction Removed from Plasma by Plasma Volume Replaced

- IgG: only 45% intravascular
- 1.5 vol removes ~35% of total body IgG
- Re-equilibration within ~2 days
- Repeated session QOD often needed

\[ y = e^{-x} \]
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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**