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
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
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.

\[ K_D = f(x) \{ K_0 A, Q_B, Q_D \} \]
Blood Flow and $K_0A$: Effect on Clearance

The graph illustrates the relationship between $K_D$ (dialysis clearance) and $Q_B$ (blood flow) for two dialyzers:

- **Dialyzer 1:** Lower $K_0A$.
- **Dialyzer 2:** Higher $K_0A$.

As $Q_B$ increases, $K_D$ also increases for both dialyzers, but the curve for Dialyzer 2 is higher, indicating a greater clearance for the same flow rate compared to Dialyzer 1.
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 $\uparrow$ pressure, $\uparrow K_{uf}$
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
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*

**Centrifugation**
- Blood component separation by *density*

<table>
<thead>
<tr>
<th>Diameter (µm)</th>
<th>Plasma</th>
<th>Platelet</th>
<th>Red cell</th>
<th>Lymphocyte</th>
<th>Granulocyte</th>
</tr>
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<tbody>
<tr>
<td>Filter CutOff</td>
<td>○</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td>13</td>
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</table>

<table>
<thead>
<tr>
<th>Density (specific gravity)</th>
<th>Plasma</th>
<th>Platelet</th>
<th>Lymphocyte</th>
<th>Granulocyte</th>
<th>Red cell</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(1.025-1.029)</td>
<td>(1.040)</td>
<td>(1.070)</td>
<td>(1.087-1.092)</td>
<td>(1.093-1.096)</td>
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</tbody>
</table>
Effect of Pore Size In Dialysis

- Small molecules pass;
- Plasma proteins are restricted
**Membrane Apheresis**

Larger Pores

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

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

Plasma

WBCs, Plts

RBCs

Blood return

Hey!Pheresis

OPTIMUM®
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

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

Remaining fraction

<table>
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<tr>
<th>Plasma volumes</th>
<th>0.223 (77.7% removed)</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>2.5</th>
<th>3</th>
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<td>0</td>
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<td>0.8</td>
<td>0.7</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
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</table>
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**
Physiology of Blood Purification

Thanks!