

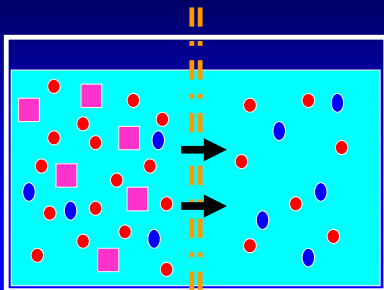
Physiology of Blood Purification: Dialysis & Apheresis

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

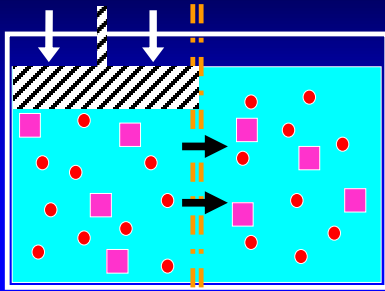
Outline

- 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

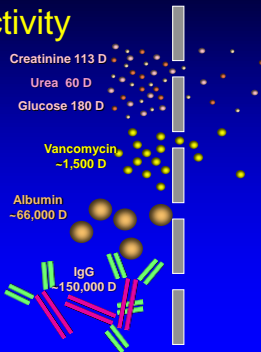
Diffusion



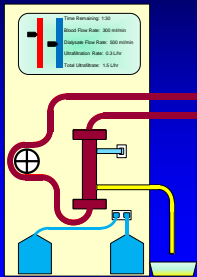
Convection



Effect of Pore Size on Membrane Selectivity



Intermittent Hemodialysis (IHD)

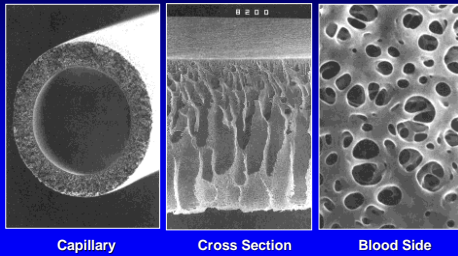


- Blood perfuses extracorporeal circuit
- Dialysate passes on opposite side of membrane
- High efficiency system
- Particle removal mostly by diffusion
- Fluid removal by ultrafiltration (hydrostatic pressure across dialyzer membrane)

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

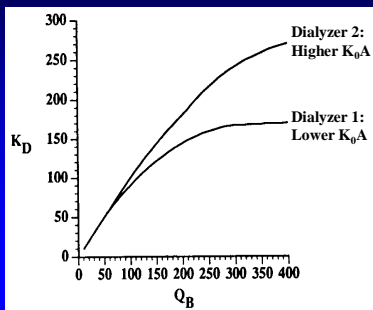
$$K_0A = \text{permeability } (K_0) * \text{surface area } (A)$$

Clearance (K_D)

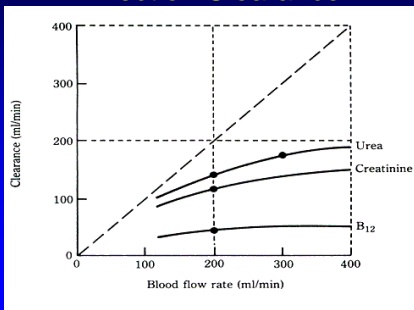
- Clearance (K_D) describes ability of a dialyzer to remove a substance from the blood
- Changes with the dialysis prescription

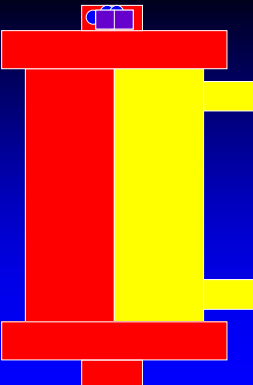
$$K_D = f\{K_0A, Q_B, Q_D\}$$

Blood Flow and K_0A : Effect on Clearance



Blood Flow and Molecular Weight: Effect on Clearance





Small Molecules

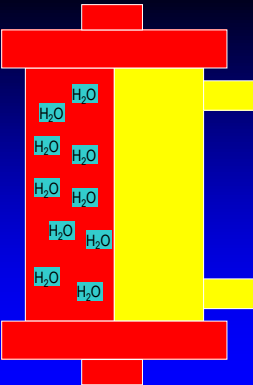
- Diffuse easily
- Higher K_d at given Q_b, Q_d

Larger Molecules

- Diffuse slowly
- Lower K_d at given Q_b, Q_d

Ultrafiltration (UF)

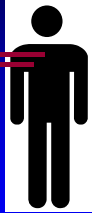
- Removal of water due to effects of pressure
- Solutes removed by convection at the same time
- UF capability of a dialyzer described by the UF coefficient (K_{uf}) – ml/h/mmHg



Ultrafiltration

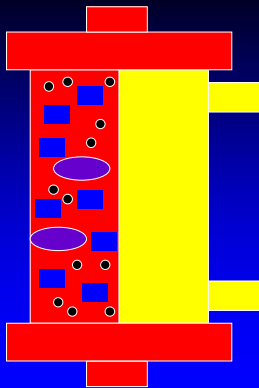
- Hydrostatic pressure across membrane
- More water removal with \uparrow pressure, $\uparrow K_{uf}$

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

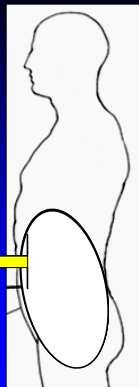
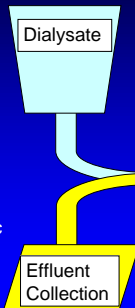
Convection



- 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

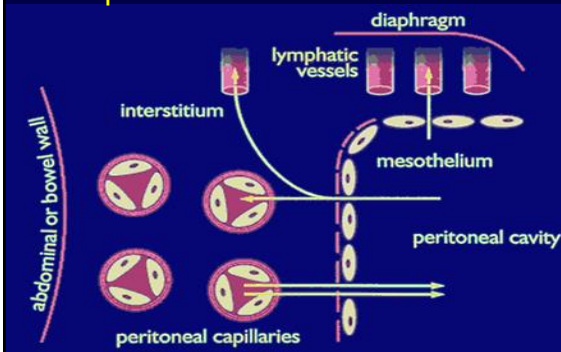
Hemodialysis

- 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)

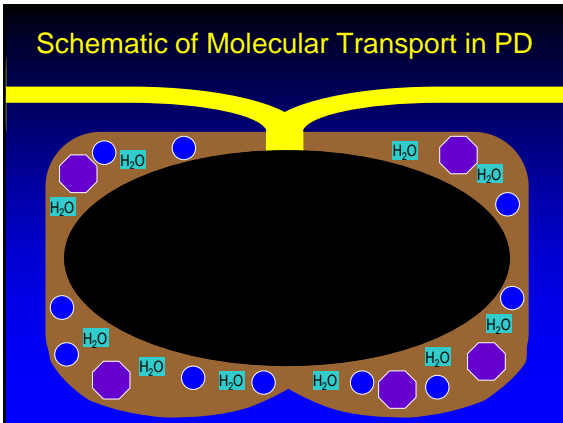
Ultrafiltration in PD: Key Factors

- 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

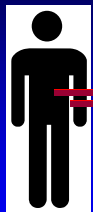
Fluid Absorption in PD

- 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

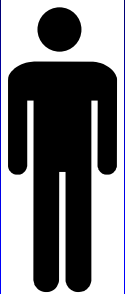


Apheresis

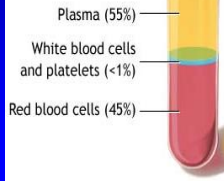


- “Apheresis”: Greek, “To take away or separate”
- Blood perfuses extracorporeal circuit
- Blood components separated; selected component removed
- If large volume removed replacement is required
- Uses include therapeutic indications or for blood component harvest

Components of Whole Blood



Separation and removal of individual components may be required for therapeutic need



Apheresis Methods

Filtration

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

Centrifugation

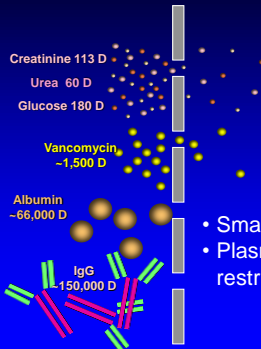
- Blood component separation by **density**

Filtration		Centrifugation	
	Diameter (µm)		Density (specific gravity)
Plasma		Plasma	(1.025-1.029)
○ Platelet	3	○ Platelet	(1.040)
○ Red cell	7	○ Lymphocyte	(1.070)
○ Lymphocyte	10	⊕ Granulocyte	(1.087-1.092)
⊕ Granulocyte	13	○ Red cell	(1.093-1.096)

Filter CutOff

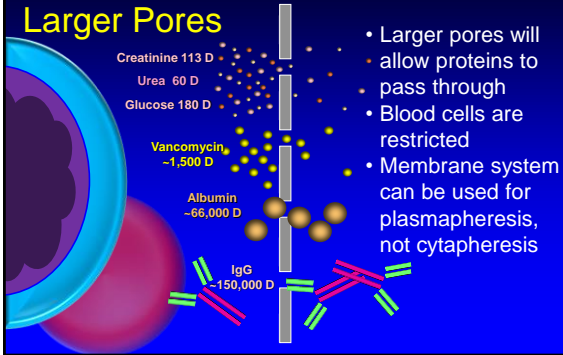
Select

Effect of Pore Size In Dialysis



- Small molecules pass;
- Plasma proteins are restricted

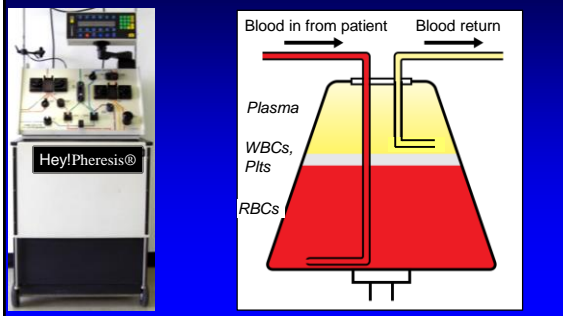
Membrane Apheresis Employs Larger Pores



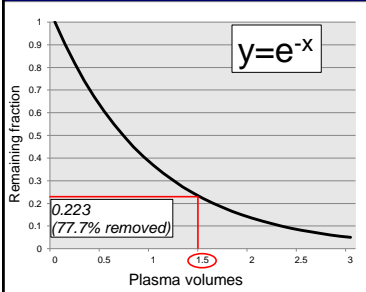
Apheresis by Centrifugation

- 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



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

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**
