Ultrafiltration in PD: Physiologic Principles

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DISCLOSURES

Dr Abu-Alfa has served as a Consultant for Baxter Healthcare, and has received research grants and honoraria for speaking engagements and/or organization of PD educational conferences from Baxter Healthcare.

Dr Abu-Alfa is the immediate past co-President for the North American Chapter of the International Society for Peritoneal Dialysis.
Educational Objectives

- Review physiologic basis of ultrafiltration
- Review the impact of membrane transport characteristics in UF volume.
- Compare osmotic and oncotic forces and effect on UF.
- Discuss Na sieving and Na removal.
- Review membrane changes over time.
Physiology of Ultrafiltration: Mechanisms at Play

- Trans-capillary fluid movement:
  - Osmotic / Oncotic gradient (first and foremost).
  - Hydrostatic pressure (much less so).
  - Membrane function / surface area.

- Lymphatic re-absorption.
Physiology of Ultrafiltration: Structure of Peritoneal Membrane
Physiology of Ultrafiltration: Normal Human Peritoneum

Physiology of Ultrafiltration: Structure of Peritoneal Membrane

- Capillary
  - H₂O
  - Intercellular: 50%
  - Aquaporin mediated: 50%

- Peritoneal Space
  - Glucose
  - Intercellular: >90%
  - Glucose transporter mediated: minimal
Physiology of Ultrafiltration: Sodium Sieving with 4.25% Glucose

Physiology of Ultrafiltration: Role of Aquaporins: Aqp1\(^{-/-}\) mouse

AQP: Aquaporin
V(t): Volume versus time
UF: Ultrafiltration

Physiology of Ultrafiltration: Three-pore model

\[ \pi = \text{Osmotic} \]
\[ P = \text{Hydraulic} \]
\[ r = \text{Radius} \]

Rippe et al: Microcirculation 8, 303–320, 2001
Physiology of Ultrafiltration: Small Pores and Aquaporins

Figure 2 | UF, UFSP and FWT during the test of Double Mini-PET. UF, ultrafiltration; UFSP, ultrafiltration through small pores; FWT, free water transport.

PET: Peritoneal Equilibration test
Physiology of Ultrafiltration: Crystalloid Osmosis

- Normal serum osmolality = 270 mOsm/L
- Uremic serum osmolality = 305 mOsm/L

<table>
<thead>
<tr>
<th>Dialysate Glucose</th>
<th>mOsm/L</th>
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</thead>
<tbody>
<tr>
<td>1.5%</td>
<td>345</td>
</tr>
<tr>
<td>2.5%</td>
<td>395</td>
</tr>
<tr>
<td>4.25%</td>
<td>484</td>
</tr>
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</table>
Physiology of Ultrafiltration: UF with 4.25% Glucose: Small Pores

<table>
<thead>
<tr>
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<th>Capillary Pressure</th>
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<th>Pressure Gradient</th>
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<tbody>
<tr>
<td><strong>Hydrostatic (mmHg)</strong></td>
<td>17</td>
<td>12-18</td>
<td>0 - 6</td>
</tr>
<tr>
<td><strong>Colloid (mmHg)</strong></td>
<td>26</td>
<td>0.1</td>
<td>-26</td>
</tr>
<tr>
<td><strong>Osmolality (mosm/kg H₂O)</strong></td>
<td>305</td>
<td><em>(Glu)</em> 486</td>
<td></td>
</tr>
<tr>
<td><strong>Crystalloid (mmHg)</strong></td>
<td>-</td>
<td>-</td>
<td>105</td>
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Van’t Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

Physiology of Ultrafiltration: UF with 4.25% Glucose: Aquaporins

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<tr>
<td>Crystalloid (mmHg)</td>
<td>Across Small pores</td>
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<td>105</td>
</tr>
<tr>
<td></td>
<td>Across Aquaporins</td>
<td></td>
<td>3559</td>
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Van’t Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

Physiology of Ultrafiltration: Sodium Sieving and Na Removal

![Bar chart showing Na removal meq for CAPD, APD, and Icodextrin]
Phyysiology of Ultrafiltration:
Glucose Absorption and UF Profile

Physiology of Ultrafiltration: Net Ultrafiltration Profile


UF: Ultrafiltration
Physiology of Ultrafiltration: Variables to Consider

- Effect of dwell time
- Effect of fill volume
- Effect of membrane transport profile
- Effect of larger molecules
Physiology of Ultrafiltration: Effect of Fill Volume: Net UF Volume

Dwell Volume, 2.5% Glucose, 4 hours

Abu-Alfa, American Society of Nephrology, Abstract 2001
Physiology of Ultrafiltration: Glucose Kinetics by Transport Status
Physiology of Ultrafiltration: Crystalloid versus colloid osmosis

**Blood in Peritoneal Capillaries**

- Endothelium
  - urea
  - creatinine
  - glucose
  - macromolecules

- Mesothelium
  - crystalloid osmosis
  - colloid osmosis

**Dialysate filled Peritoneal Cavity**

Adapted from Krediet R et al: Peritoneal Dialysis International 17, 35-41; 1997
Colloid Osmosis: Source and Structure of Icodextrin

Corn Starch

Enzymatic hydrolysis

Malto-Dextrin

Membrane fractionation

Icodextrin
### Physiology of Ultrafiltration: UF with 7.5% Icodextrin

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<td>26</td>
<td>66</td>
<td>40</td>
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Van’t Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

Physiology of Ultrafiltration: Transport Status and Icodextrin

TCUFR: Transcapillary UF rate

MTAC: Mean Transport Area Coefficient

Physiology of Ultrafiltration: Transport Status: Icodextrin vs 2.5%

D/P: Dialysate/Plasma
ICO: Icodextrin
GLU: Glucose
Cr: Creatinine

Physiology of Ultrafiltration: Glucose absorption: Caloric Cost

Widening differential

Glucose absorbed (g/8 hrs)

Low | Low Ave. | High Ave. | High

Peritoneal Transport Type

1.50%  2.50%  4.25%

Courtesy of Dr Salim Mujais, Baxter Healthcare 2002
Physiology of Ultrafiltration: Changes in Transport Profile

Glucose exposure (grams/year)

Year 1 | Year 2 | Year 3 | Year 4 | Year 5

Group 1 | Group 2

Time on Treatment

Solute Transport (D/P creatinine at 4 hours)

Start | Year 1 | Year 2 | Year 3 | Year 4 | Year 5

Group 1 | Group 2

Physiologic Principles for UF in PD

Summary

- UF in PD is primarily driven by osmotic (Glucose) or oncotic (icodextrin) forces across the membrane.

- Sodium sieving is maximal at about 60 – 90 minutes of a dwell, and will result in decreased Na concentration in the dialysate if dwell is drained, as with cyclic PD.

- Na sieving negatively impacts total Na removed.

- Many factors modulate UF volume such as glucose concentration, dwell time, dwell volume and intrinsic membrane transport type of each patient.

- Higher transport rates result in less UF with glucose solutions but not with icodextrin solution.
Question 1

The removal of sodium with PD is dependent on convection and diffusion. Calculate the approximate amount of Na removed during a dwell for each of the following conditions:

1) No net ultrafiltration after a 4 hours dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and plasma [Na]=140 meq/L.

2) 500 cc of net ultrafiltration after a 10 hours dwell using 2 liters of 7.5% icodextrin solution with [Na]=132 meq/L and plasma [Na]=140 meq/L.

3) 250 cc of net UF after a 1 hour dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and 60 mins dialysate [Na]=128 meq/L, with a short APD cycle.
The removal of sodium with PD is dependent on convection and diffusion. Calculate the approximate amount of Na removed during a dwell for each of the following conditions:

1) No net ultrafiltration after a 4 hours dwell using 2 liters of 2.5% dextrose solution with \([Na]=132\) meq/L and plasma \([Na]=140\) meq/L. Answer: 16 meq

2) 500 cc of net ultrafiltration after a 10 hours dwell using 2 liters of 7.5% icodextrin solution with \([Na]=132\) meq/L and plasma \([Na]=140\) meq/L. Answer: 16+70=86 meq

3) 250 cc of net UF after a 1 hour dwell using 2 liters of 2.5% dextrose solution with \([Na]=132\) meq/L and 60 mins dialysate \([Na]=128\) meq/L, with a short APD cycle. Answer: 24 meq