Osmotic Conductance to Glucose: What does it mean?

B. Bammens, MD, PhD
Brussels, May 22 2014

2nd self-care dialysis symposium
Essentials of Peritoneal Dialysis

Osmotic Conductance to Glucose

Aristoteles

384-322 B.C.
Aristotelian Dramatic Arc

START

action
tension grows

climatic event
maximum confusion

resolution
of confusion

unravelling of plot

END
Osmotic Conductance to Glucose

- Essential peritoneal membrane physiology
- Please welcome: OCG!
- OCG: what does it mean?

Aristotelian Dramatic Arc

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‘6 barriers for transport’

Stagnant layers at mesothelial and capillary side: not relevant
Mesothelial cell layer: not relevant
Interstitial tissue: (minor) diffusive resistance
Capillary wall: most important restriction barrier

Capillary wall is the most important restriction barrier and determines the peritoneal membrane’s size-selectivity through a system of pores

→ the “PORE THEORIES”
‘Old’ theory: TWO pores

Small pores with constant radius 40-50Å (majority) for transport of low molecular weight solutes

Large pores with various radii, average > 150Å (minority, less than 0.1% of total pore count) for transport of macromolecules
‘Old’ theory: TWO pores

The two-pore theory perfectly explains the diffusive transport of molecules.

DIFFUSION

movement of solutes along their concentration gradient
Diffusive transport

\[ J_s = \frac{D_f}{\Delta x} \cdot A \cdot \Delta C \]  

(diffusive permeability (membrane- and solute-specific))
Diffusive transport

\[ J_s = \frac{D_f}{\Delta x} A \Delta C \]  

(Fick’s first law of diffusion)

diffusive permeability (membrane- and solute-specific)

surface area (membrane-specific)
Diffusive transport

\[ J_s = \frac{D_f}{\Delta x} . A . \Delta C \]  

(Fick's first law of diffusion)

- Diffusive permeability (membrane- and solute-specific)
- Surface area (membrane-specific)
- Concentration difference between plasma and dialysate
Diffusive transport

$$J_s = \frac{D_f \cdot A \cdot \Delta C}{\Delta x}$$

(Fick’s first law of diffusion)

diffusive permeability (membrane- and solute-specific)
surface area (membrane-specific)
concentration difference between plasma and dialysate
mass transfer area coefficient (MTAC)
Diffusive transport

\[ J_s = \frac{D_f \cdot A \cdot \Delta C}{\Delta x} \]  
(Fick’s first law of diffusion)

\[ J_s = MTAC \cdot \Delta C \]

Transport of small molecules up to MW of \( \beta_2M \) (11,8 kDa) NOT limited by size of (large) pores

MTAC for a given solute ONLY determined by effective vascular peritoneal surface area (number of pores)
The two-pore theory perfectly explains the diffusive transport of molecules.

However, it does not explain all aspects of the convective transport of molecules and ultrafiltration.
‘Old’ theory: TWO pores

However, it does not explain all aspects of the convective transport of molecules and ultrafiltration.

**CONVECTION**

movement of solutes along with fluid as it moves across the membrane (solvent drag)

Bammens Semin Nephrol 31: 127-137, 2011
Convective transport
Convective transport

\[ J_s = J_v \cdot \bar{C} \cdot (1 - \sigma) \]
Convective transport

\[ J_s = J_v \cdot \bar{C} \cdot (1 - \sigma) \]

water flux (membrane-specific)
Convective transport

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- water flux (membrane-specific)
- mean solute concentration in the membrane \((P+D)/2\)
Convective transport

\[ J_s = J_v \cdot \bar{C} \cdot (1 - \sigma) \]

water flux (membrane-specific)

mean solute concentration in the membrane \((P+D)/2\)

Staverman’s reflection coefficient

= how difficult it is for a solute to be transported by solvent drag across a semi-permeable membrane

(membrane- and solute-specific)
Convective transport

$\sigma$ Staverman’s reflection coefficient

$= \textit{how difficult it is for a solute to be transported by solvent drag across a semi-permeable membrane}$

$S$ sieving coefficient

$= \textit{how easy it is for a solute to be transported by solvent drag across a semi-permeable membrane}$
For a semi-permeable membrane, $S$ and $\sigma$ are expected to be perfectly interchangeable concepts!

\[
S = 1 - \sigma
\]

the "ideal" two-pore membrane
Convective transport

\[ \sigma \quad \text{Staverman's reflection coefficient} \]

= how difficult it is for a solute to be transported by solvent drag across a semi-permeable membrane

= fraction of maximal osmotic pressure a solute can exert across a semi-permeable membrane

\[ S \quad \text{sieving coefficient} \]

= how easy it is for a solute to be transported by solvent drag across a semi-permeable membrane

= fraction of maximal solute transport by solvent drag across a semi-permeable membrane
Convective transport

For a semi-permeable membrane, $S$ and $\sigma$ are expected to be perfectly interchangeable concepts!

![Diagram showing the relationship between $S$ and $\sigma$ with the equation $S = 1 - \sigma$.](image)

$\sigma_{\text{glucose}}$ very low!
For a semi-permeable membrane, \( S \) and \( \sigma \) are expected to be perfectly interchangeable concepts!

However, the peritoneal membrane seems not to fulfill this “ideal semi-permeable membrane” criteria.

\[ \sigma_{\text{glucose}} = 0.03 \]

\[ S = 1 - \sigma \]
‘New’ theory: THREE pores

Small pores with constant radius 40-50Å
Large pores with various radii, average > 150Å

Ultra-small pores with radius 3-5Å

for transport of water only
accounts for 1/2 of transcapillary water transport

(explains good osmotic properties of glucose)
‘New’ theory: THREE pores

Ultra-small pores with radius 3-5Å

Fig. 1. Schematic model representing CHIP integral membrane protein within the membrane lipid bilayer. Notable features include 1) homotetrameric complex with 1 subunit bearing a polylactosaminoglycan, 2) minimal polypeptide mass extending above or below the lipid bilayer, and 3) possible individual water pore within each subunit.

‘New’ theory: THREE pores

ULTRAFILTRATION

Davies Kidney Int 70 (Suppl 103): 76-83, 2006
‘New’ theory: THREE pores

ULTRAFILTRATION

[Graph showing ultrafiltration volume over time for different categories: Net UF, Small pores, Aquaporins, Large pores, Lymphatics.]

Davies Kidney Int 70 (Suppl 103): 76-83, 2006
Aristotelian Dramatic Arc

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The original 2.27% PET test

SOLUTE TRANSPORT

(D/Pcreatinine reflects effective vascular surface area, rather than the intrinsic permeability of the membrane!)

The original 2.27% PET test

The original 2.27% PET test

ULTRAFILTRATION

SOLUTE TRANSPORT

The original 2.27% PET test

ULTRAFILTRATION

Davies Kidney Int 70 (Suppl 103): 76-83, 2006
The aquaporins?

ULTRAFILTRATION

Davies Kidney Int 70 (Suppl 103): 76-83, 2006
With a hypertonic dialysate solution, dialysate $\text{Na}^+$ concentration will decrease initially due to water-only transport across aquaporins.

= SODIUM SIEVING

Time profile $D/P_{\text{sodium}}, D_{\text{sodium}}$ (or $D/D_0$ or $\Delta D_{\text{sodium}}$ at 1 hour) CAN BE USED TO ASSESS THE CONTRIBUTION OF AQUAPORIN TRANSPORT TO ULTRAFILTRATION

ISPD definition of UF failure = $< 400\text{ml UF after 4 hours of 3.86% glucose}$
Aristotelian Dramatic Arc

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- unravelling of plot
- resolution of confusion
BUT:
A flat SODIUM SIEVING profile may have different meanings! (at least theoretically)

aquaporin deficiency
“very very fast” small solute transport (small pores)
BUT:
A flat SODIUM SIEVING profile may have different meanings!
(at least theoretically)

aquaporin deficiency
“very very fast” small solute transport (small pores)
fibrotic peritoneal interstitium (“closed membrane”, uncoupling)
Pore models: interstitium?

Morphological changes in peritoneal membrane
THICKNESS OF SUBMESOTHERelial COMPACT ZONE

Pore models: interstitium?

the serial three-pore membrane/fiber matrix model

A  Three pore membrane with a normal ("loose") serial fiber matrix

\[ \varepsilon = 0.995 \]
\[ r_f = 6 \text{ (Å)} \]

\[
\begin{aligned}
L_p S & = 3.66 \text{ μL/min/mmHg} \\
PS_g & = 9.30 \text{ mL/min} \\
\sigma_g & = 0.047 \\
L_p S & = 0.078 \text{ mL/min/mmHg}
\end{aligned}
\]

B  Three pore membrane with a fibrotic ("dense") serial fiber matrix

\[ \varepsilon = 0.96 \]
\[ r_f = 7.5 \text{ (Å)} \]

\[
\begin{aligned}
L_p S & = 3.02 \text{ μL/min/mmHg} \\
PS_g & = 13.46 \text{ mL/min} \\
\sigma_g & = 0.039 \\
L_p S & = 0.078 \text{ mL/min/mmHg}
\end{aligned}
\]

Pore models: interstitium?

the serial three-pore membrane/fiber matrix model

A. Three pore membrane with a normal ("loose") serial fiber matrix

- $E = 0.995$
- $r_f = 6 \, \text{Å}$

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  - Action
  - Tension grows

- **climatic event maximum confusion**

- **unravelling of plot**

- **END**
  - Resolution of confusion
The Osmotic Conductance to Glucose

= the ability of glucose to exert an osmotic pressure sufficient to cause transperitoneal ultrafiltration

= \( L_p S \sigma \) (\( \mu l/min/mmHg \))

OCG: the Dummy’s view

$L_p.S.\sigma$ ($\mu$l/min/mmHg)

- Reflection coefficient of glucose
  - lower in case of aquaporin dysfunction
  - lower in case of increased small solute transport

- Surface area
  - higher in case of increased small solute transport

- Hydraulic conductivity
  - lower in case of fibrosis
OCG: the Dummy’s view

A flat SODIUM SIEVING profile may have different meanings! (at least theoretically)

- aquaporin deficiency
- “very very fast” small solute transport (small pores)
- fibrotic peritoneal interstitium (“closed membrane”, uncoupling)

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\[ L_{p.S.\sigma} (\mu l/min/mmHg) \]
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\[
L_p S \sigma \text{ (}\mu\text{l/min/mmHg)}
\]

‘isolated aquaporin dysfunction probably non-existent’ (Rippe a.o.)
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resolution of confusion

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OCG: what does it mean?

- **Normal OCG**: Curve A
- **Low OCG**: Curve C

OCG: what does it mean?

Double mini-PET test

OCG: what does it mean?

Double mini-PET test

OCG: what does it mean?

The peritoneal osmotic conductance is low well before the diagnosis of encapsulating peritoneal sclerosis is made.

Mark L. Lambie¹,², Biju John¹,², Lily Mushahar¹,², Christopher Huckvale¹,² and Simon J. Davies¹,²

Lambie et al. Kidney Int 78: 611-618, 2010
Aristotelian Dramatic Arc

- Action: tension grows
- Climatic event: maximum confusion
- Resolution: unravelling of plot
- Start
- End
Aristotelian Dramatic Arc

climatic event
maximum confusion
unravelling of plot
resolution of confusion
This is me!

action
tension grows

This is me!

This is Johann Morelle.
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