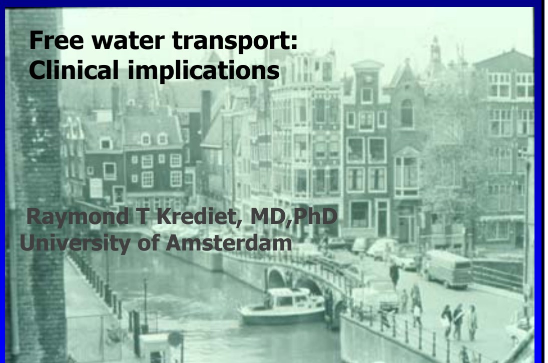
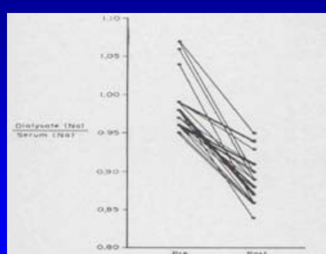


Free water transport: Clinical implications

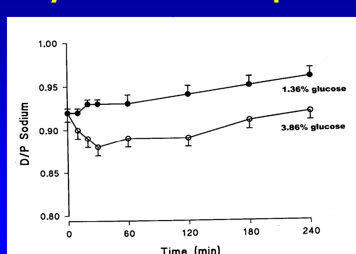
Raymond T Krediet, MD,PhD
University of Amsterdam

Sodium sieving during short very hypertonic dialysis exchanges



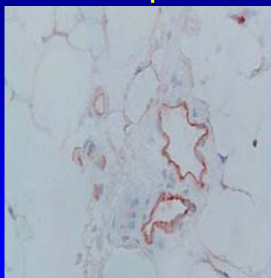
Nolph KD et al. Ann Int Med 1969;70:931-947

Sodium sieving during the initial phase of a 4 hrs dwell is due to dilution, caused by free water transport



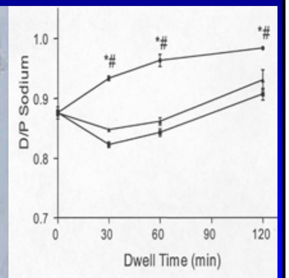
Monquil et al. Perit Dial Int, 1995

Peritoneal AQP-1 is present in human venules and capillaries



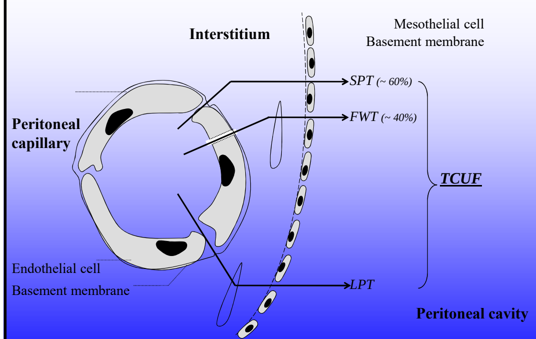
Pannekeet et al. Perit Dial Int, suppl 1,1996

No Na^+ sieving in AQP-1 knock-out mice



Ni et al. Kidney Int,2006

Fluid transport according to the 3-pore model



Clinical assessment and potential importance of free water transport

- Both small pore fluid transport and free water transport are influenced by the cristalloid osmotic pressure gradient
- It is therefore most informative when the assessments are done during the first hour of a dwell, when the cristalloid gradient is high
- A 3.86%/4.25% glucose solution provides the best signal/arousal ratio for volume measurements
- Calculations based on Na^+ removal are appropriate for use in routine clinical practice

Principle of calculating free water transport

Ultrafiltered volume by crystalloid osmosis (1)

- Na^+ associated through interendothelial channels (small pores) → Peritoneal Na^+ clearance (2)
- Not Na^+ associecated through AQP-1 → Free water transport: differencee (1) en (2)

Quantification of free water transport

(Smit et al. Kidney Int,2004; La Milia et al. Kidney Int, 2005)

- 1 hour PET, 3.86%/4.25% glucose
- Na^+ removal = (drained volume x $D_{Na}{}^+$) – (instilled volume x $D_{Na}{}^+$)
- UF small pores: Na^+ removal / $P_{Na}{}^+$~ Na^+ clearance, which occurs through the small pores
- Free water transport: total UF – UF small pores

Combination of a modified PET with drainage after 1 hour followed by reinfusion

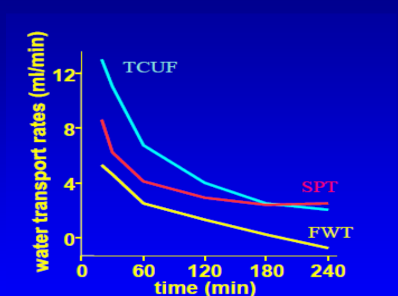
- **Rationale:** volume measurement ,plasma and dialysate Na^+ after one hour, are required to use the La Milia method
- **Procedure:**
- Temporary drainage after one hour for volume assessment by weight and sampling, followed by reinfusion
- Final drainage after 4 hours for assessment of solute transport and effluent biomarkers when necessary
- **Names:**
- The two- in- one procedure of the modified PET; MoPET 1/4

From: Cnossen et al. Perit Dial Int, 2009

Transcapillary ultrafiltration

- **Pressure:**
  - -hydrostatic pressure: only relevant for small pore fluid transport
  - -osmotic pressure: crystalloid (glucose)
    colloid (icodextrin)
- **Crystalloid osmotic pressure:**
  - -influences both small pore fluid transport and free water transport
- **Pathways:**
  - - interendothelial pores ~ small pore fluid transport
  - - endothelial AQP-1 ~free water transport
  - - hydraulic permeability (interstitial tissue)

Water transport pathways

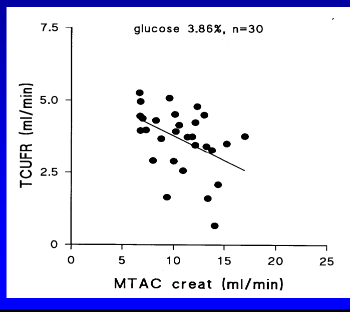


From: Parikova et al. Kidney Int, 2005

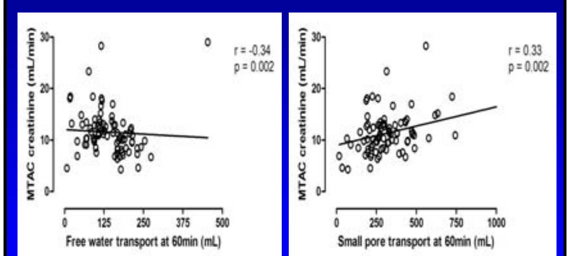
Consequences of the effective vascular surface area for net ultrafiltration

- A large number of perfused peritoneal capillaries allows high ultrafiltration rates.
- This is counteracted by a high glucose absorption rate leading to a rapid disappearance of the osmotic gradient.
- How does this work out for net UF, SPFT and FWT?

Relationship between transcapillary UF rate and effective surface area, reflected by MTAC creatinine

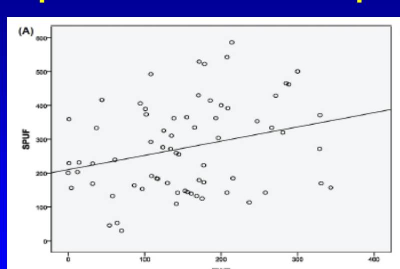


Relationship between effective surface area and pathways for fluid transport



From: Lopes Barreto et al. Perit Dial Int, 2013

Relationship between small pore fluid transport and free water transport



From: Bernardo et al. Perit Dial Int, 2012

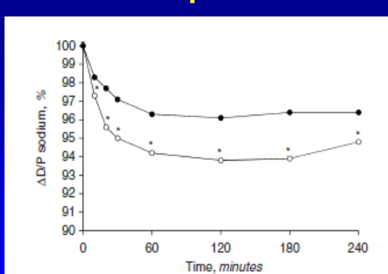
Free water transport in various conditions

- FWT and age
- FWT and peritonitis
- FWT and time on PD
- FWT with biocompatible solutions
- FWT in early and late UF failure
- FWT preceding EPS

Cross-sectional studies on free water transport

Group	Number patients	Median / mean	Range/ CI	Ref.
Children < 5	29	170 mL	10-71%	Raaijmakers, NDT,2011
Children >5	36	221 mL	17-75%	Raaijmakers, NDT,2011
Adults, AMC, 2004	40	164 mL	15-62%	Smit, Kidney Int, 2004
Adults, AMC, 2005	80	180 mL	13-87%	Parikova, KI, 2005
Adults, Porto	70	152 mL	32-40%	Bernardo, PDI, 2012

Effect of acute peritonitis on Na^+ sieving

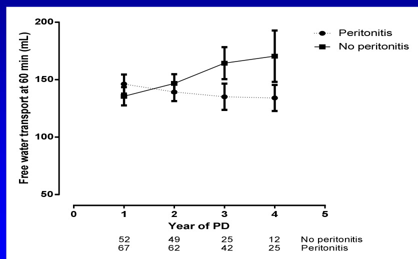


open circles: peritonitis
closed circles: long-term PD

Patients matched for MTAC creatinine

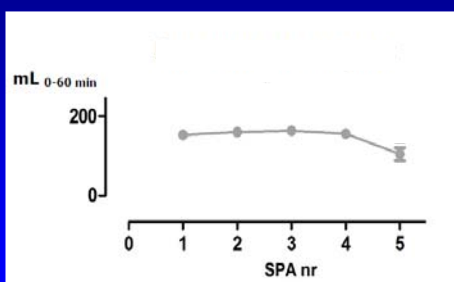
from: Smit et al. Kidney Int, 2004

Time-course of FWT according to no, or at least one peritonitis episode



Van Esch et al, Perit Dial Int 2016

Time course of free water transport on a conventional dialysis solution

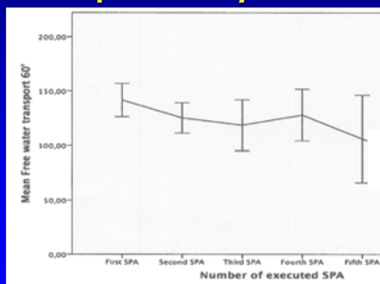


from: Coester et al. Perit Dial Int, 2014

Free water transport in various conditions

- FWT and age
- FWT and peritonitis
- FWT and time on PD
- FWT with biocompatible solutions
- FWT in early and late UF failure
- FWT preceding EPS

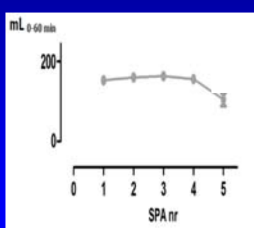
Time course of FWT on a biocompatible dialysis solution



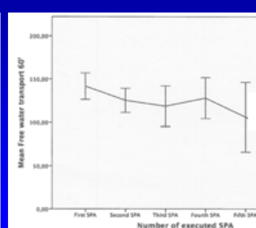
van Diepen et al, 2017

Time course of FWT

Conventional solution



Biocompatible solution



Free water transport in various conditions

- FWT and age
- FWT and peritonitis
- FWT and time on PD
- FWT with biocompatible solutions
- FWT in early and late UF failure
- FWT preceding EPS

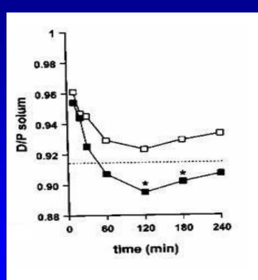
Impaired Na^+ sieving (FWT) in late UFF failure

	Early UF failure ≤ 2 years	Late UF failure ≥ 4 years
Number of patients	25	23
D/P creatinine	0.83	0.82
Max dip D/P Na^+	0.08	0.05*

*$p < 0.01$

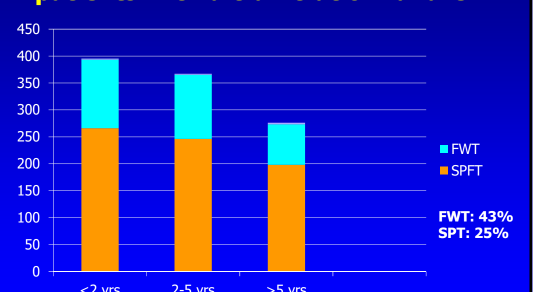
Smit et al. Perit Dial Int; Suppl 3,2005

Na^+ sieving in early (.) and late (□) UFF



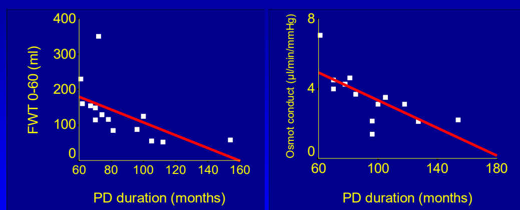
Smit et al. Perit Dial Int;Suppl 3, 2005

Small-pore fluid- and free watertransport during the first hour of an exchange in patients with ultrafiltration failure



From: Parikova et al. Kidney Int, 2006

The time course of free water transport and osmotic conductance in patients with late UF failure

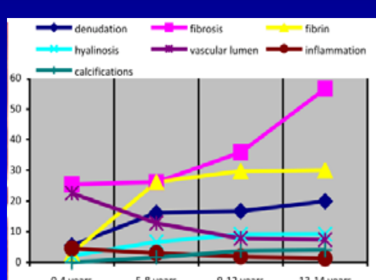


From: Parikova et al. Kidney Int, 2006

Why is FWT severely impaired in long-term UF failure?

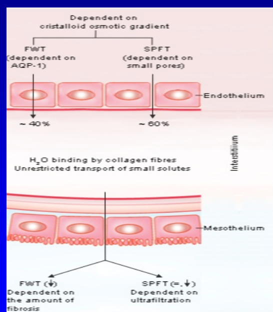
- The effective peritoneal vascular surface area is not different from that in early UF failure
- AQP-1 expression is normal
- AQP-1 function may be altered, but no data
- Peritoneal interstitial collagen increases with the time on PD
- Collagen 1 can bind water, without binding small solutes and electrolytes

Time course of the development of morphological abnormalities



From: Taranu et al. Rom J Morphol Embryol, 2014

Relationship FWT and fibrosis

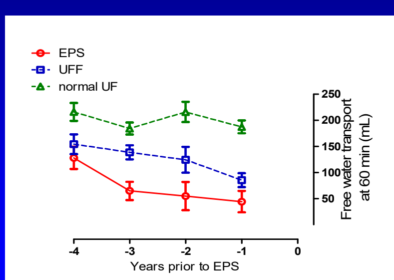


Krediet RT, Lopes Barreto D et al. Peit dial Int, in press

Free water transport preceding EPS

- **Sampimon et al. Nephrol Dial Transplant,2011**
  – 12 EPS patients with preEPS data on FWT, compared to 21 "matched" controls without UFF and 26 with normal UF.
  @ No histology
- **Morelle et al. Clin J Am Soc Nephrol, 2015**
  - 7 EPS patients with preEPS data on Na^+ sieving, compared to 28 time matched controls, irrespective of their fluid kinetics.
  @ Histology on peritoneal collagen and AQP-1 expression

Time-course of FWT in patients preceding EPS, controls with UFF and with normal UF



Sampimon et al. Nephrol Dial Transplant, 2011

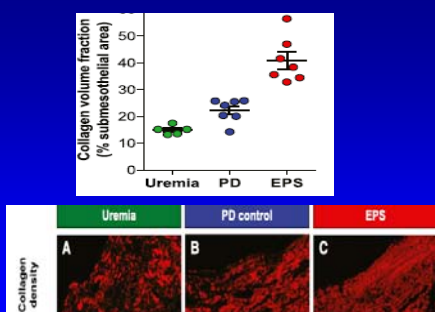
Area under the reciever operating curve for the prediction of EPS within one year

	AUC
Net UF	0.54
Osmotic conductance	0.60
Ultrafiltration coefficient	0.60
Reflection coefficient	0.49
Free water transport $_{0\text{-}60}$	0.82

0.5: no prediction; 1.00: perfect prediction

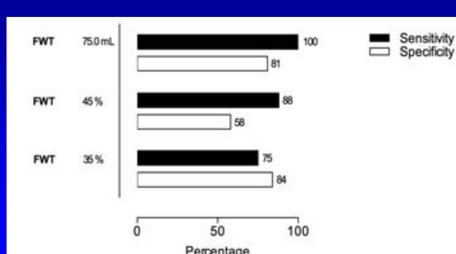
Sampimon, Lopes Barreto et al. Adv Perit Dial, 2014

Peritoneal collagen



Morelle J et al. J Am Soc Nephrol, 2015

Sensitivity and specificity of FWR one year prior to the diagnosis of EPS



From: Lopes- Barreto et al, 2014

What to remember on free water transport?

- $FWT_{0\text{-}60\ min}$ can be assessed easily in routine clinical practice using a MoPET 1/4
- Both SPFT and FWT are dependent on the osmotic gradient and therefore often related
- FWT is high in children. A difference is present between acute peritonitis and its long-term effects
- FWT decreases with the duration of PD without marked effects of biocompatibility. It is especially decreased in late UFF
- FWT< 75 mL is the best predictor of EPS