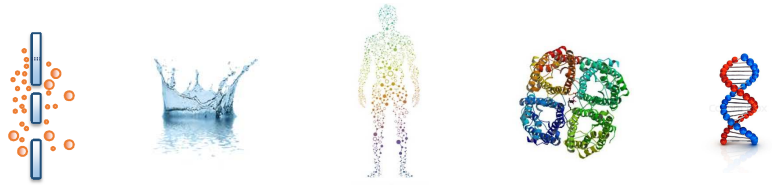

# Peritoneal Function Testing
## *should be performed in PD patients*

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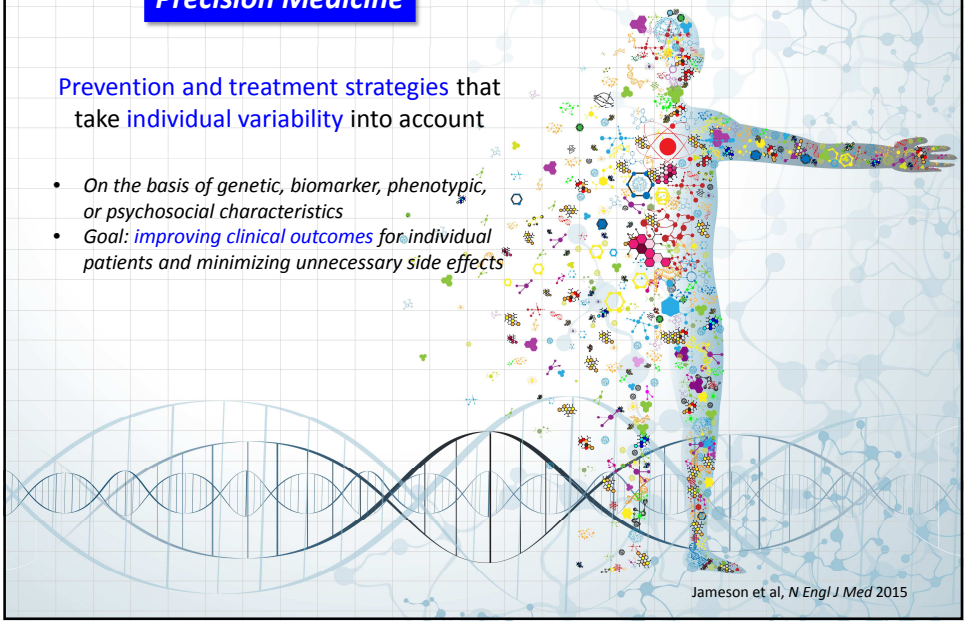
## ***Precision Medicine***

Prevention and treatment strategies that take individual variability into account

- *On the basis of genetic, biomarker, phenotypic, or psychosocial characteristics*
- *Goal: improving clinical outcomes for individual patients and minimizing unnecessary side effects*



Jameson et al, *N Engl J Med* 2015

## Precision Medicine Initiative®

- *Barack Obama - Jan 20, 2015*
- *Coll. NIH*
- *$215 Mo in 2016*
- *Research, technology and policies that empowers patients*
  *→ Individualized care*


## Peritoneal transport testing
## Experience at the Cliniques universitaires Saint-Luc

| Test | Period | n |
|---|---|---|
| 3,86% 4h PET | 1994-2016 | 387 |
| 3,86% 1h PET | 2005-2012 | 104 |
| Uni-PET | 2013-2016 | 40 |

531 peritoneal tests

16705 dosages on dialysate effluents

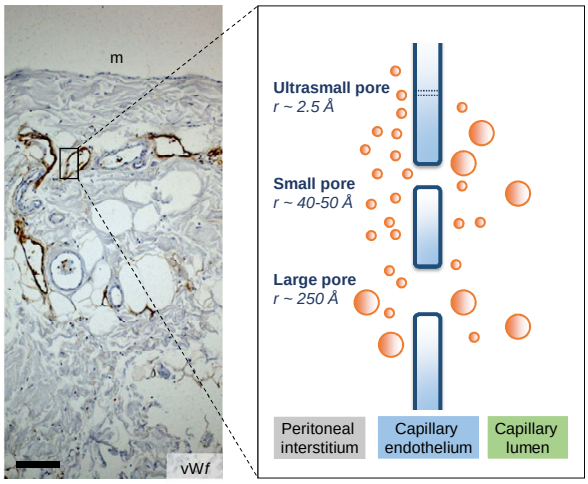
~ 2000 hours of work

~ 250 working days

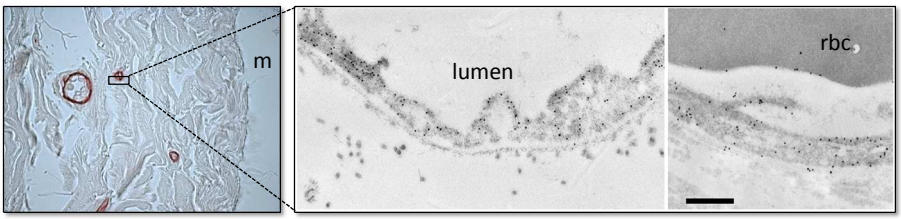
~ 100 PET in mice/year

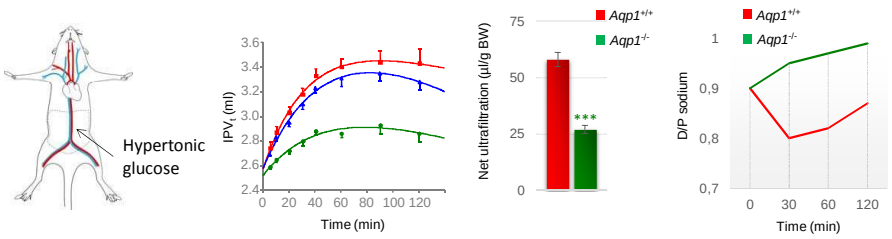
***Peritoneal transport, an open window on the peritoneal membrane!***

## The basics of peritoneal transport




## Role of Aquaporin-1 in Water Transport during Peritoneal Dialysis



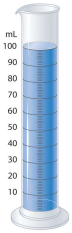



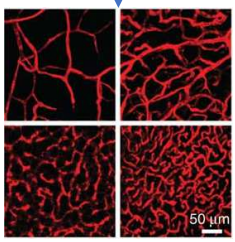

*Endothelial AQP1 ⟶ critical role in water removal during peritoneal dialysis*

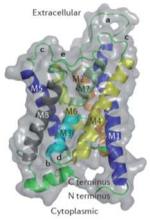
Devuyst et al, *Am J Physiol* 1998 ; Ni et al, *Kidney Int* 2005

## Peritoneal transport testing – expectations from clinical practice

3.86% glucose-based 4h PET
(or Uni-PET)



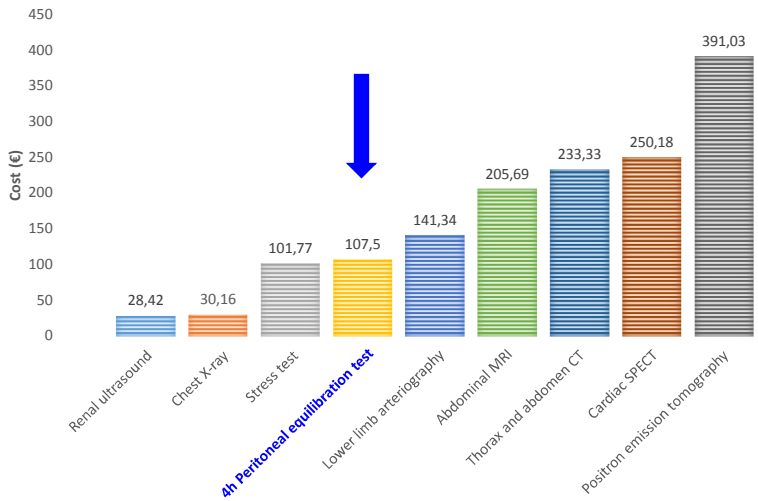

*Accurate assessment of net ultrafiltration (diagnosis of UF failure)*

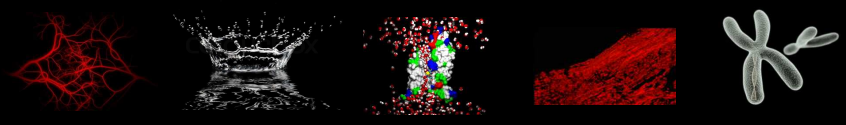
*Peritoneal solute transport and effective vascular surface area*

*Estimation/quantification of AQP1-mediated water transport*

## Peritoneal transport testing is easy, safe, reproducible…

## …and affordable

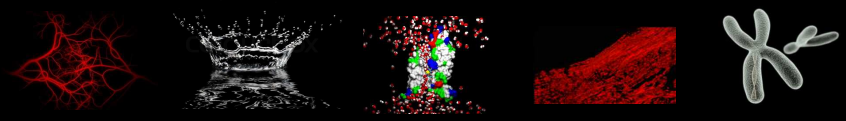




*Why should we perform peritoneal transport testing in our PD patients?*

*Peritoneal solute transport and the risk of death and fluid overload*

*Changes in peritoneal water transport in long-term PD and the risk of EPS*



*Why should we perform peritoneal transport testing in our PD patients?*

*Peritoneal solute transport and the risk of death and fluid overload*

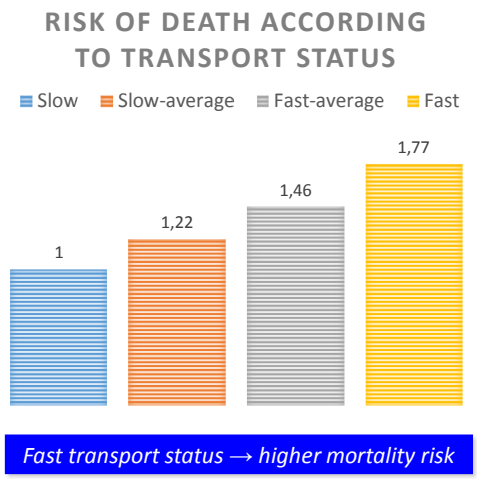
*Changes in peritoneal water transport in long-term PD and the risk of EPS*


***« Prediction is very difficult, especially if about the future »***

- Niels Borh

## Impact of baseline peritoneal solute transport on the risk of death

**2006 – meta-analysis -** 20 observational studies
*Mainly CAPD, glucose only*

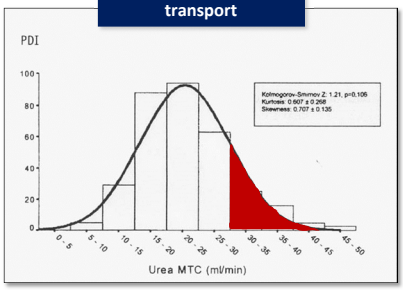



*Fast transport status → higher mortality risk*

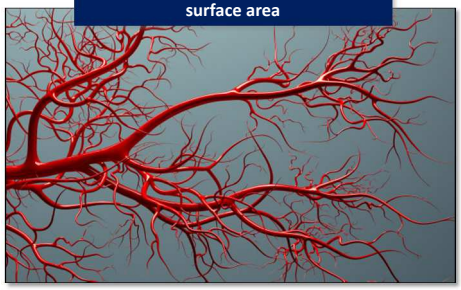
Brimble, *J Am Soc Nephrol* 2006

## Fast transport status and UF capacity

**Fast peritoneal transport**



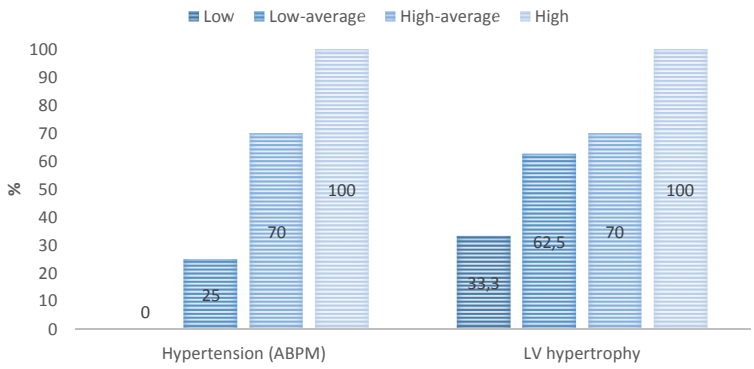

**Large effective peritoneal vascular surface area**



*Fast transport status → Large effective vascular surface area*
*→ Rapid glucose absorption and dissipation of the osmotic gradient → Poor UF*

## Fast transport status, fluid overload and the risk of death

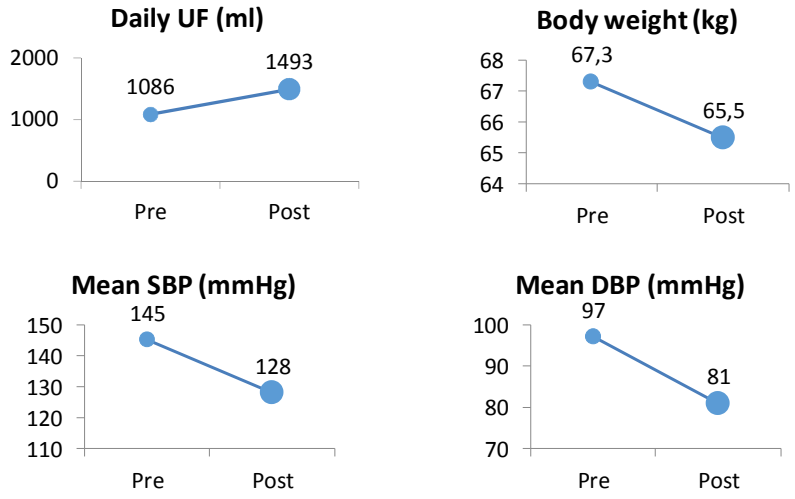
*Prevalence of hypertension (24-h ABPM) and LV hypertrophy in prevalent PD patients according to transport status*




*Patients with fast transport status on CAPD*
*Fluid overload → Increased risk of death from cardiovascular events*

Tongul, *Perit Dial Int* 2003

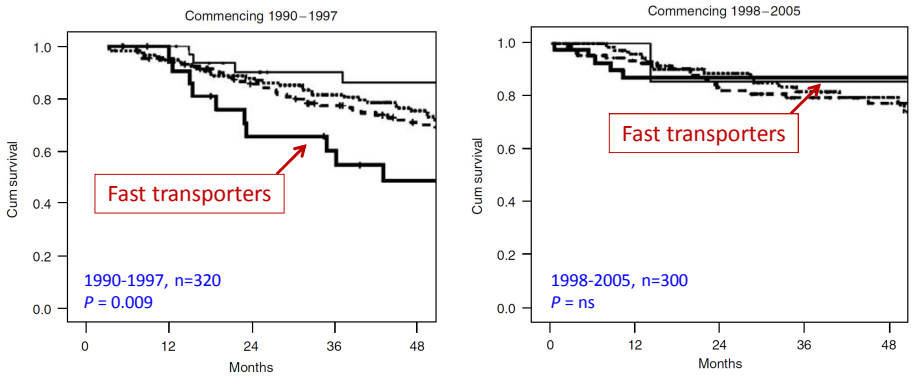
## Individualizing PD prescription can mitigate peritoneal membrane characteristics and improve survival




Tongul, *Perit Dial Int* 2003

## New era: individualizing PD prescription

*Survival on PD according to transport category at the start of treatment (Stoke experience)*




*Important changes in management of PD patients:*

- Routine use of **APD with short dwells** in patients with fast transport status
- Use of **icodextrin** → avoid dialysis exchanges with net fluid reabsorption

Davies, *Kidney Int* 2006

## Baseline peritoneal solute transport rate should be evaluated in PD patients

National Kidney Foundation®

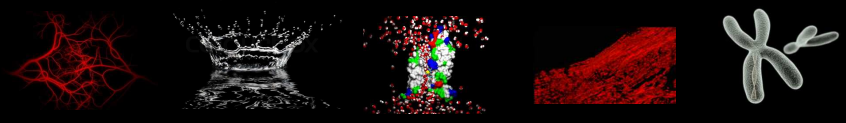
**NF/KDOQI**
Baseline peritoneal membrane transport characteristics should be established after initiating a daily PD therapy.

ERBP

**European Renal Best Practice – ERA-EDTA**
An evaluation of peritoneal membrane characteristics should be used to guide prescription of PD therapy

Kidney Health Australia

**CARI (Caring for Australians with Renal Impairment)**
Patient's membrane transport status should be evaluated by the standard peritoneal equilibration test (PET).

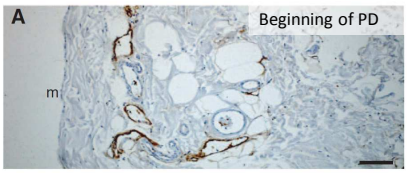


*Why should we perform peritoneal transport testing in our PD patients?*

*Peritoneal solute transport and the risk of death and fluid overload*

*Changes in peritoneal water transport in long-term PD and the risk of EPS*

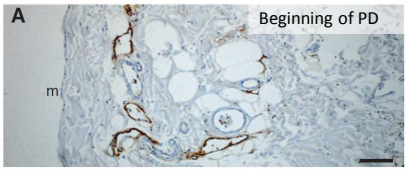
## Changes in pertioneal membrane during long-term PD

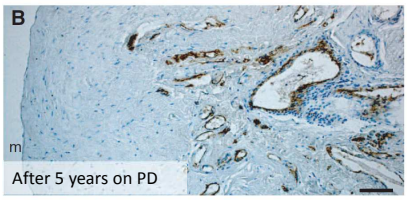



*The peritoneum is a living tissue*

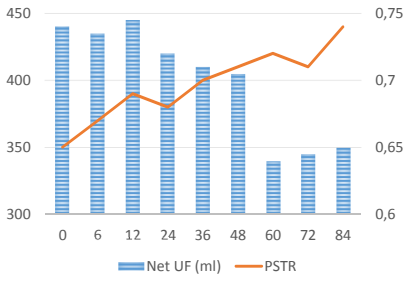
Devuyst, *J Am Soc Nephrol* 2010; Davies, *J Am Soc Nephrol* 2004

## Changes in pertioneal membrane during long-term PD




*n = 574 incident PD patients*
*Stoke-on-Tent (UK) cohort*




*Progressive increase in PSTR*
*Loss of UF capacity*

Devuyst, *J Am Soc Nephrol* 2010; Davies, *J Am Soc Nephrol* 2004

## Peritoneal function should be monitored during PD

National Kidney Foundation®

**NF/KDOQI**
Peritoneal membrane transport testing should be repeated when clinically indicated

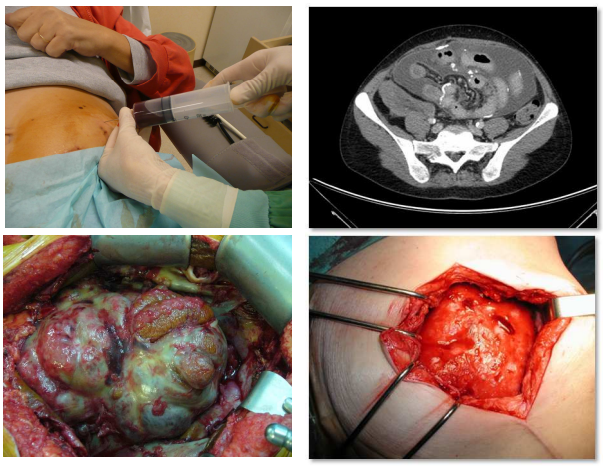
ERBP

**European Renal Best Practice – ERA-EDTA**
An evaluation of peritoneal membrane characteristics should routinely be repeated at least once per year or when new clinical problems (overhydration, malnutrition, metabolic disturbances) are noticed.

Kidney Health Australia

**CARI (Caring for Australians with Renal Impairment)**
PETs should be repeated at 2 years and then annually. PETs should be repeated earlier if there is clinical evidence of fluid overload with a significant decrease in ultrafiltration, hypertension or elevated serum urea levels (…).

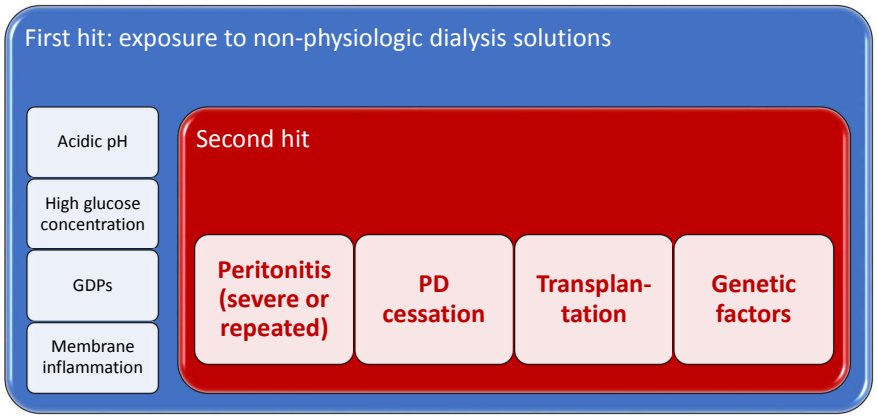
## Encapsulating peritoneal sclerosis (EPS)



*Devastating syndrome of excessive fibrotic peritoneal thickening that can eventually encapsulate the bowel, leading to partial or total bowel obstruction*

Courtesy Prof. C. Verger, T. Augustine and E. Goffin

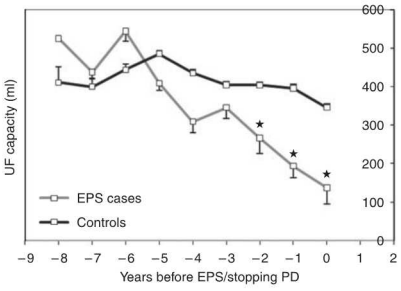
## Physiopathology of EPS: the 'two hit theory'



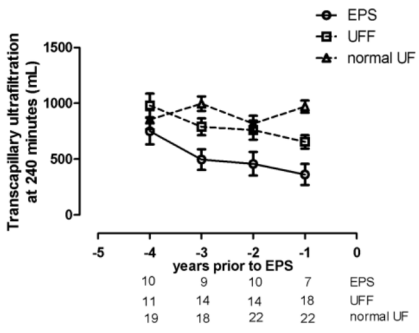

*>2/3 of the patients develop EPS after PD has been stopped*
*No predictive tool to identify patients at risk for EPS*

## Changes in peritoneal transport before EPS onset

UK cohort (2.27% PETs)




Dutch cohort (3.86% PETs)

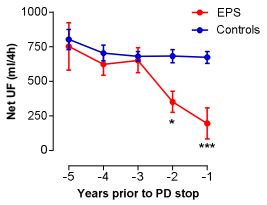


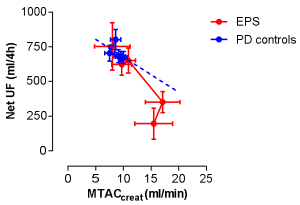

*Loss of UF capacity and UF failure frequently occur before the onset of overt EPS*

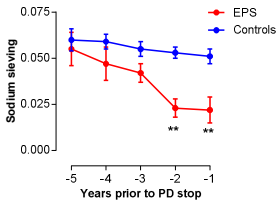
Lambie et al, *Kidney Int* 2010; Sampinon, *Nephrol Dial Transplant* 2011

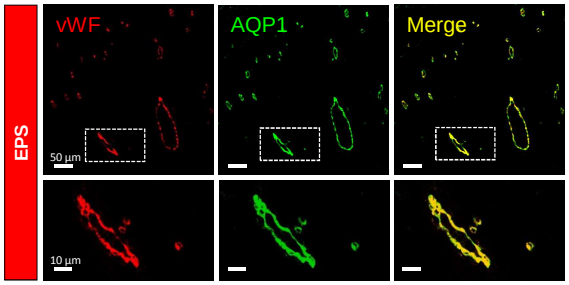
## Mechanisms of loss of ultrafiltration in patients with EPS

UCL Brussels, 1994-2013, yearly 3.86% PET
7 EPS cases *versus* 28 PD-duration and gender-matched controls



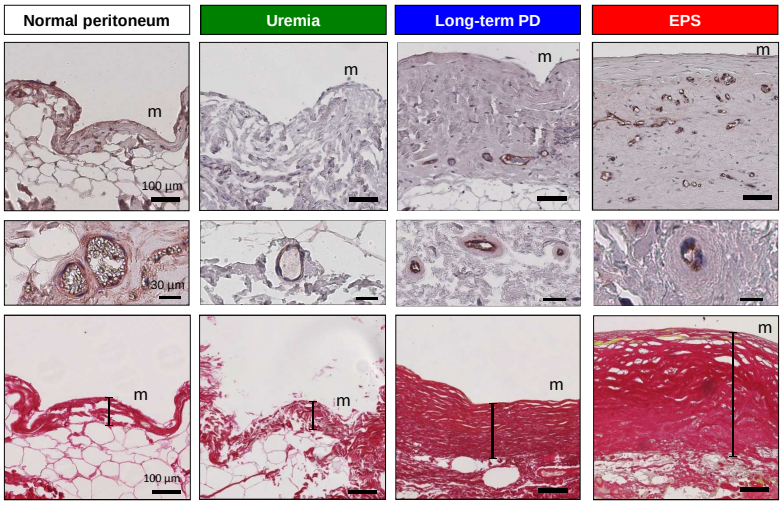

**Patients who will develop EPS**
→ *Loss of UF (uncoupling)*
→ *Loss of sodium sieving*
→ *Preserved AQP1 expression*

Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

*Patients who will develop EPS*
*have a premature loss of water transport*

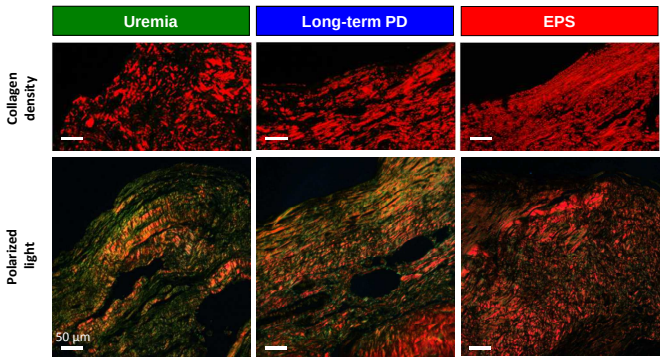
→ *Effect of peritoneal remodelling/fibrosis?*

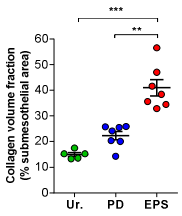
## Vascular and fibrotic changes in the EPS peritoneum

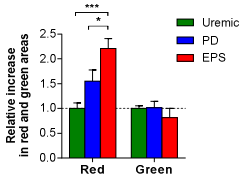



Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

## Collagen density and optical properties under polarized light microscopy



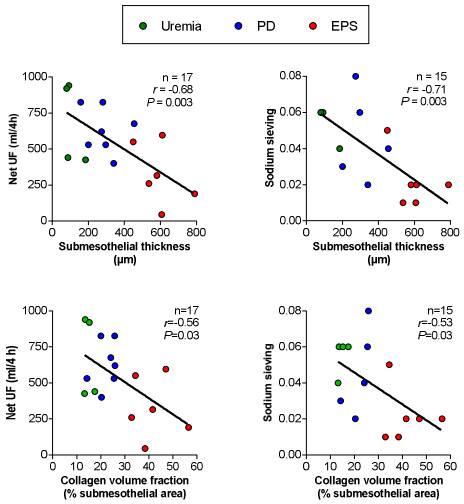




| Polarized light | Orange-red | Green |
|---|---|---|
| Fiber Ø | > 60 nm | 20-40 nm |
| Collagen | Type I | Type III |
| Wound-healing | Late stages | Early stages |

Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

## Effect of fibrosis on water transport across the peritoneum



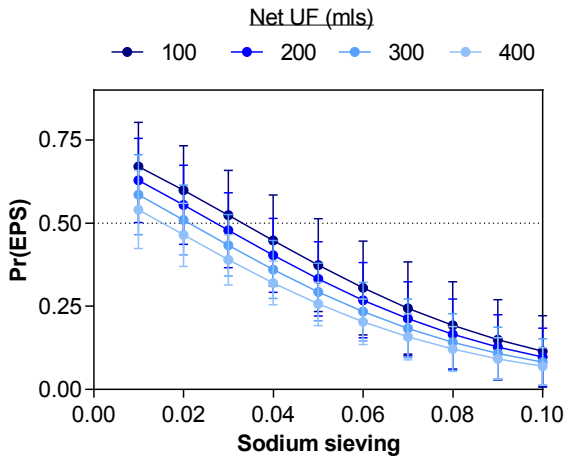

***The thicker and more dense in collagen fibers the peritoneum is,***

***less it is capable of transporting water***

Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

*Clinical relevance of impaired osmotic water transport before onset of overt EPS?*

Loss of free-water transport in long-term PD patients
= *powerful and independent indicator for the development of EPS*
*(Multivariate analysis & random-effect model)*




Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

The Value of Osmotic Conductance and Free Water Transport in the Prediction of Encapsulating Peritoneal Sclerosis

Denise E. Sampimon,* Deirisa Lopes Barreto,* Annemieke M. Coester, Dirk G. Struijk, Raymond T. Krediet

52nd ERA-EDTA CONGRESS London2015 United Kingdom MAY 28 '15
www.era-edta2015.org

**A simple model to predict encapsulating peritoneal sclerosis in patients undergoing peritoneal dialysis: a 20 years prospective controlled longitudinal cohort study of peritoneal membrane function**

*Vincenzo La Milia, Elisabetta Sironi, Selena Longhi and Giuseppe Pontoriero*
Nephrology and Dialysis, A. Manzoni Hospital, Lecco, Italy

## *How should long-term PD patients with loss of sodium sieving be managed?*

*What we have (recently) learned*

| | |
|---|---|
| Development of UF failure | May precede EPS (50% of patients at 3 years) |
| Loss of sodium sieving during the course of PD | Reflects interstitial fibrosis and higher risk of EPS |
| CT scan or surgical exploration | Diagnosis of encapsulating peritoneal sclerosis |
| Stopping peritoneal dialysis | May trigger the onset of EPS |