The peritoneum
Peritoneal Anatomy

Cross section showing the peritoneal cavity and internal organs
General principles

• A liquid instilled in the peritoneal cavity will equilibrate with the composition of the blood compartment through:

  – **DIFFUSION**: concentration gradient over a semi-permeable membrane

  – **CONVECTION**: “solute drag” by ultrafiltration.
Peritoneal Physiology

Site of Resistance to Solute Movement
A schematic representation of the peritoneal membrane.
Peritoneal Physiology

Diffusion

- concentration gradient
- solute dimensions
- porosity of the membrane
Convection and solute drag:
- independent of solute size to cut off level
- Concentration (and not gradient) dependent
PET test.
A PD dwell

- Dwell time
- IP volume
- Drain
- fill

Time
CAPD - Classic dwell pattern

4 x 2000 or 4 x 2500 ml dialysate

Day

Night

08.00hrs 08.00hrs
APD - alternate CAPD

Day

Night

08.00hrs

08.00hrs
APD - low volume

Day  Night

08.00hrs  08.00hrs
APD - high volume CCPD

Day

Night

08.00hrs

08.00hrs
More is not always better!
ADEMEX: Primary Outcome

ITT Patient Survival Comparing Treatment Groups
Log-rank Test: Chisquare = 0.0004, p-value 0.9842
(Control Group: Events/No. Pts=157/484, Treatment Group: Events/No. Pts=169/481)

p=0.9842
RR(Treated:Control)=1.00
95% CI: (0.80, 1.24)
Efficient use of solution in APD.

BSA 1.71 - 2.0m²
RRF = 0 mL

- 20L APD (8 x 2.5L (Dry Day))
- 20L APD (7 x 2.5L + 2.5L)
- 12.5L APD (4 x 2.5 + 2.5L)
- 15L APD (4 x 2.5L + 2.5L + 2.5L (Mid-day exchange))

CrCl/L/Wk/1.73m²
Efficient use of solution in APD.

BSA 1.71 - 2.0m²
RRF = 0 mL

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- 15L APD (4 x 2.5L + 2.5L + 2.5L (Mid-day exchange))

Blake et al, PDI, 16, 199
Quantified measurement of adequacy

Urea kinetic modelling:

1) $Kt/V$: sum of the peritonal clearance of urea and the residual renal urea clearance, multiplied by 24 hours and divided by the volume of distribution.

\[
Kt/V_{\text{renal}} = \frac{\text{Total urinary volume} \times \text{urinary urea concentration}}{\text{plasma urea concentration} \times V}
\]

\[
Kt/V_{\text{peritoneal}} = \frac{\text{Total dialysate volume} \times \text{dialysate urea concentration}}{\text{plasma urea concentration} \times V}
\]
Delta Kt/V = -.8132 + 1.3696 * D/P
Correlation: r = .58006
## Quantified measurement of adequacy

### Ratio’s of D/P for creatinine and urea

<table>
<thead>
<tr>
<th>Dwell-time (hrs)</th>
<th>1</th>
<th>3</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low transporter</td>
<td>0.48</td>
<td>0.50</td>
<td>0.57</td>
</tr>
<tr>
<td>Low average transporter</td>
<td>0.57</td>
<td>0.62</td>
<td>0.70</td>
</tr>
<tr>
<td>High average transporter</td>
<td>0.68</td>
<td>0.74</td>
<td>0.82</td>
</tr>
<tr>
<td>High transporter</td>
<td>0.79</td>
<td>0.87</td>
<td>0.93</td>
</tr>
</tbody>
</table>
Phosphate clearance in CAPD vs CCPD

Sedlacek et al, AJKD 2000, 36, 1020-1024
The three-pore model and ultrafiltration

Blood in peritoneal capillaries

Endothelium

Urea, Creatinine

Glucose

Macromolecules

Dialysate filled peritoneal cavity

Mesothelium

Dialysate

Cristalloid osmosis

Colloid Osmosis

Ultrafiltration
Modified PET:
Sodium sieving and D/P sodium

D/P sodium

Intact Aquaporin
Deficient aquaporin

min
Changes in the peritoneum during PD

Cumulative exposure to solution Components

“Inflammatory Episodes (cumulative effect of severity / Virulence)

Inflammatory Response

Mesothelial cell repair

FIBROSIS/SCLEROSIS VASCULAR CHANGES

Time on PD (years)

Williams, Data from the “Peritoneal biopsy registry” Cardiff

"Who was first?"
AGE’s and GDP

Pyrraline (pmol/mgprotein) in fluid

- Zeier et al, Kidney Int, 63, 298-305
AGE’s and GDP

Zeier et al, Kidney Int, 63, 298-305
PD patients are (were?) often overhydrated

Plum; NDT 2001
PET test.
INCREASING GLUCOSE CONCENTRATION IS ALWAYS BEST WHEN ULTRAFILTRATION IS INSUFFICIENT
Types of UF failure

- Large vascular surface area
- A decreased osmotic conductance by glucose
- High disappearance rate of macromolecular structures (lymphatic absorption)
- Extremely small peritoneal surface area (e.g. adhesions)

Krediet et al. PDI, 20, S22-S42, 2000
UF Failure

Clinical UF-Failure

Initial evaluation for reversible causes

Dietary incompliance
- salt/fluid
  - Deficient education
  - Complex regimen
  - Burn-out

Appropriate prescription
- Dwell time
- Dialysate tonicity

Mechanical problems
- Leaks
- Entrapment
- Obstruction
- Malposition
Impact of dietary instructions on salt intake

Gunal et al, AJKD, 37, 2001, 588-593
Salt restriction and left ventricular hypertrophy

Figure 1 — Comparison of the echocardiographic (Echo) data of long-term peritoneal dialysis (PD) patients: baseline Echo was performed by mean 36th month of PD; the second Echo was performed 24 months later.
Figure 1. Diagram representing the interrelationship among dietary salt intake, the renin-angiotensin system, and renal TGF-β1 production. While the relationship between salt intake and angiotensin II is well appreciated, perhaps the ability of angiotensin II and increased salt intake to stimulate independently production of TGF-β1 is less well appreciated. In an attempt to control intrarenal production of TGF-β1, both pathways should be considered.

Sanders et al, Hypertension, 2006

TGF-β regulates glucose-induced senescence of mesothelial cells in dialysis patients
See page 345

Ksiazek et al, Lab Invest, 2007
Insulin need in diabetic patients after start of PD: Relation to hypertonic bag use

Fig. 3. The relation between change in insulin requirement and number of 2.5% 2L exchanges per day. All patients received a standard 2L exchange three times daily.
Extensions of PD technique survival in 53 patients with UF failure using Icodextrin (Extraneal).


median survival 22 months
Evolution of TBW after start of Extraneal

Davies et al. JASN. 14. 2338-2344. 2003
S. B. is a 28 year old woman who has had renal failure since adolescence, and high panel reactivity since a failed transplant 15 years ago. After 10 years on haemodialysis she developed major problems with vascular access and switched to PD in March 1992. Latterly she has had increasing problems with fluid balance.

<table>
<thead>
<tr>
<th>PET: Date</th>
<th>4 hour D/P creatinine ratio</th>
<th>UF Capacity ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>0.62</td>
<td>400</td>
</tr>
<tr>
<td>1994</td>
<td>0.5</td>
<td>430</td>
</tr>
<tr>
<td>1995</td>
<td>0.55</td>
<td>250</td>
</tr>
<tr>
<td>1996</td>
<td>0.72</td>
<td>220</td>
</tr>
<tr>
<td>1997</td>
<td>0.85</td>
<td>-100</td>
</tr>
<tr>
<td>1998</td>
<td>0.79</td>
<td>100</td>
</tr>
</tbody>
</table>

Plot the progressive change in peritoneal kinetics, and identify cause of ultrafiltration failure. Design a regime that will improve fluid balance problems.
# Ultrafiltration failure

Mr Jones, weight gain 1.5kg over two days

<table>
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<th>Dialysate</th>
<th>Normal UF</th>
<th>UF obtained yesterday</th>
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<tr>
<td>1.36%</td>
<td>-100</td>
<td>-300</td>
</tr>
<tr>
<td>1.36%</td>
<td>0</td>
<td>-350</td>
</tr>
<tr>
<td>1.36%</td>
<td>-100</td>
<td>-325</td>
</tr>
<tr>
<td>Extraneal</td>
<td>400</td>
<td>-275</td>
</tr>
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</table>
# Ultrafiltration failure

Mr Jones, weight gain 1.5kg over two days

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</tr>
<tr>
<td>1.36%</td>
<td>-100</td>
<td>-325</td>
</tr>
<tr>
<td>Extraneal</td>
<td>400</td>
<td>+750</td>
</tr>
</tbody>
</table>
Lessons to be learned
All patients should be equal
...but some should be more equal than others
THE RIGHT TREATMENT FOR
THE RIGHT PATIENT
Matched – Control Analysis
PD first vs HD

Van Biesen et al, JASN, 11, 116-125, 2000
Patient Survival Probability for Patients Initiating Dialysis with CAPD/CCPD Compared to Hemodialysis (1990-94)

Standardized mortality ratio’s of dialysis vs general population

Villar et al, JASN 2007
Medicare expenditures and type of RRT

Shih et al, KI, 2005, 319
Cost/life year gained of PD vs HD in Finland: a matched pair analysis

PD distribution in Flanders

New reimbursement

NBVN Registry

PD distribution in Flanders

NBVN Registry

New reimbursement

2001 2002 2003 2004

NBVN Registry
The Context - within the Integrated Care Model

Residual Renal Function

Creatinine Clearance (ml/min)

Peritoneal Dialysis

Transplant

Hemodialysis

Initiation of Dialysis

Time on Dialysis
Potential advantages of PD for early start dialysis

- Cost benefit
- Negative effect of HD on residual renal function
- Preservation of vascular access
- Outcome after transplantation
- Lower risk for infection
- Incremental dialysis doses at lower costs
- Lifestyle benefits

Van Biesen et al, PDI
Benefits of Residual Renal Function

Provides endocrine functions
• Erythropoietin production
• Ca\(^{++}\), phosphorus and vitamin D homeostasis

Contributes to total solute clearance (1 ml/min CrCl = 10 liter CrCl/week)

Reduces Mortality

Improves QOL

Improves β\(_2\)-microglobulin and middle molecule clearance

Facilitates volume control

Increases nutritional status

Allows for more liberal diet and fluid intake
“Free choice”
Survival Diabetic patients
Stoke/Gent/ Brescia

N=188
p=0.02

Survival (months)
Cumulative Percent Surviving

PD
HD

0 10 20 30 40 50 60 70 80 90 100 110 120

0 10 20 30 40 50 60 70 80 90 100 110 120

Cumulative Percent Surviving
Survival (months)
Diabetics

One year mortality

<table>
<thead>
<tr>
<th>Year Range</th>
<th>RR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-92 All</td>
<td>1.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>91-93 All</td>
<td>1.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-92 age&lt;50</td>
<td>0.88</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>91-93 age&lt;50</td>
<td>0.89</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Vonesh et al, JASN, 10, 354-365, 1999
Access and septicemia in USRDS wave 2

Ishani et al, KI, 2005
Survival in large patients PD vs HD

Abbot et al, KI, 2004
% mortality in USRDS PD (N= 13000) vs HD(N=93000)

Patient inclusion only if survival > 90 days

Ganesh et al, JASN, 14, 415-424, 2003
Distribution of Deaths According to Day of the Week for PD Patients

Distribution of Deaths According to Day of the Week for M/W/F: HD Patients

RR for de novo cardiac disease in RRT patients in Lombardy

- **Age (per year)**: P<0.0001
- **Male**: P=NS
- **Peritoneal dialysis**: P=NS

Locatelli et al, JASN, 12, 2411-2417, 2001
<table>
<thead>
<tr>
<th></th>
<th>Hemodialysis</th>
<th>Peritoneal dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>• Long term data available</td>
<td>• No need for vascular access</td>
</tr>
<tr>
<td></td>
<td>• Suitable for the majority</td>
<td>• Less risk of hypotension</td>
</tr>
<tr>
<td></td>
<td>• Independent of patient ability</td>
<td>• Patient independence of hospital</td>
</tr>
<tr>
<td></td>
<td>• Manipulation of adequacy</td>
<td>• Ease of travel</td>
</tr>
<tr>
<td></td>
<td>• Less time on treatment</td>
<td>• Maintains residual renal function</td>
</tr>
<tr>
<td></td>
<td>• Provides social support structure</td>
<td>• Can be done by family member</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>• Increased vascular access problems</td>
<td>• Not suitable in all patients</td>
</tr>
<tr>
<td></td>
<td>• Increased use of central catheters</td>
<td>• Increased difficulty in learning</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of sepsis</td>
<td>• Social isolation</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of hypotension</td>
<td>• Peritonitis</td>
</tr>
<tr>
<td></td>
<td>• Reliance of transport</td>
<td></td>
</tr>
</tbody>
</table>
Mortality risk in elderly patients (>70 years)

North Thames dialysis study

P=NS

Harris et al, Perit Dial Int. 2002 Jul-Aug;22(4):463-70
Conclusions

• PD is a simple and efficient treatment
• PD is more than an escape for failed hemodialysis!
Conclusions

• PD is a simple and efficient treatment
• More is not always better
Conclusions

• PD is a simple and efficient treatment
• More is not always better
• Take care of volume: salt and water
Conclusions

• PD is a simple and efficient treatment
• More is not always better
• Take care of volume: salt and water
• Look at the patient, not the numbers