Nutritional Challenges and Interventions in Peritoneal Dialysis (PD)

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DISCLOSURE

I am a full time employee of Pentec Health Inc.
1. Causes of Protein Energy Wasting (PEW)

2. Factors Unique to PEW in PD

3. Malnutrition and Outcomes
   - Albumin
   - Creatinine

4. Interventions:
   - Nutrition Interventions: What do the experts say?
     ONS
     Tube Feeding
     IPAA, IPN
   - Alternative PD solutions: Clinical Benefits

5. Summary
The Current Challenges in PD Include:

Li PK, Kwong VW. *Semin Nephrol* 2017

-How to tackle technique failure and sustain long-term PD

-Manage and/or prevent:
  - Peritoneal infections
  - *Malnutrition*
  - *Inflammation*
  - Cardiovascular mortality
  - Volume overload
  - *Glucose exposure*
  - Adequacy of solute removal
  - Peritoneal access
  - *Peritoneal physiology and changes with long-term PD*
  - Patient fatigue
  - Psychosocial issues, and care of elderly patients on PD
Representation of Causes and Manifestations of PEW in CKD


**Nutrient Loss During Dialysis**

- Anorexia
- Production of Inflammatory Cytokines
- Oxidative and Carbonyl Stress
- Volume Overload

**Dialysis Treatment Related Factors**

- AV Graft, Dialysis Membrane

**Endocrine Disorders**

- Vit D deficiency, ↑PTH, DM
- Decreased Insulin/IGF signaling

**Co-morbid conditions**

- DM, CVD, Infection, Aging

**Uremic Toxins**

- Protein Energy Wasting (PEW)
- Cachexia

**Inflammation**

- Hypercatabolism

**Survival Paradoxes**

- ↓Mortality  ↑Hospitalization
- ↓Quality of Life

**ASCVD, Vascular Calcification**

**↓ Nutrient intake Prescribed Dietary Restriction**

**Malnutrition (Under Nutrition) Low Nutrient Intake**

**↓ Albumin Transthyretin Lipids**

**↑ CRP**

**↓ Weight  ↓ BMI**

**↓ Body Fat Sarcopenia**

**↓ Quality of Life**
Factors Unique to PD Contributing to PEW

- Albumin losses and turnover
- Higher prevalence of gastrointestinal symptoms than HD
- Residual Renal Function (RRF)
- Glucose Absorption: Insulin Resistance, Inflammation
- Incompatibility of IPN Solutions to the Peritoneal Membrane
- Transporter Type
- Peritonitis
Turnover of albumin is increased in PD & HD due to increased external losses, normally leading to compensatory increases in hepatic albumin synthesis.

Normal rate of albumin synthesis is ~12 g/day and the fractional catabolic rate of albumin is ~4% daily.

*In PD daily loss of proteins is ~5g, of which ~4g is albumin.

In automated PD (APD) loss is ~10g of protein per 24 hours and is increased by dwell time & number of night-time exchanges.

External loss of albumin particularly when high-performance membranes are used in HD with losses per session ranging between 1 and 8 g (or more).

6-8g protein losses/day; exaggerated during peritonitis.
**Gastrointestinal Issues in PD**


61 PD patients. **Gastric emptying** in PD patients with glucose dialysate, AA dialysate, icodextrin and no dialysate impaired in all.


Compared to healthy controls, **PD patients had lower peak hunger, less change in fullness rating around mealtimes & lower nutrient intake**


55% of PD patients in this study (112 PD & 157 HD) had dyspepsia/GE reflux


112 PD patients. **Prevalence of eating dysfunction, reflux & indigestion was:** 44.2%, 32.7% and 32.7% respectively


Study of (122 PD & 172 HD). In PD patients: 85% reported at least 1 GI symptom; 55% reported symptoms were related to onset of dialysis; 53% reported a ↓ in food intake.
Preservation of RRF is an important goal and is associated with:

- better long-term survival (strong independent marker)
- ↓ blood pressure
- improved fluid status
- higher hemoglobin levels
- ↓ inflammatory markers
- ↑ serum β2-macroglobulin clearance
- contributes to adeq achievement targets
- ↑Na+ removal

Loss of RRF is associated with

- volume overload
- anemia
- cardiovascular disease
- LVH
- inflammation
- hypertension
- malnutrition
- increased mortality
PD Glucose Absorption: Pros and Cons

**Pro:**
Burkhart J. *Semin Dial* 2004;17:498-504
Szeto CC, Johnson D 2017 *Seminars in Nephrology* 37:30-42

- Inexpensive, safe & effective osmotic agent
- Absorption of CHO provides ~ 500-800 kcal/day depending on type of PD glucose conc., dwell time & membrane transport status. “Protein sparing” effect.

**Cons:**
Saxena R, West C *JABFM* 2006;19:380-389

- Rapidly absorbed (small size) with progressive loss of the osmotic gradient and long-term metabolic consequences.
- ~60% absorbed into blood during a 4-hr dwell

Holmes C., Mujais S. *Kidney Int.* 2006;70: S104-9

- Hyperinsulinemia, insulin resistance, dyslipidemia, oxidative stress, inflammation


- Body composition analysis showed visceral to subcutaneous fat ratio was increased in incident patients on PD compared to those on HD.


- Increased BG and insulin requirement in patients with DM
Characteristics of glucose based dialysate:

- Hyperosmolar: PD solutions are limited to osmolarities of 500-600 mOsm to avoid inflammatory complications.
- Acidic
- Contains toxic glucose degradation products

Glucose degradation products (GDPs) are a result of heat sterilization and storage of glucose containing PD fluids. GDP’s induce formation of AGE’s which bind to the peritoneal membrane cause fibrosis and microvascular sclerosis.
Transporter Type: High Transporters

**High transporters:**

↑ Transport rate for small solutes & lesser fluid removal after 4-6 hrs. as compared to other transporters which results in:

↑ Glucose absorption from dialysate
↑ Protein losses into dialysate
Loss of ultrafiltration capacity.

High transporters require more frequent exchanges & often do better on a cycler. High transporter ‘type’ is linked to ↑ M& M and associated with ↑ time on PD, DM, peritonitis, exposure to GDP’s.

Several studies associate high transporters with markers of malnutrition: low albumin, low nPCR and lower LBM. (1-6)

Peritonitis is the main complication of PD & major cause of:
- Death
- Hospitalization
- Catheter loss
- Technique failure (functional & structural alterations of peritoneal membrane)
- Conversion to long term HD

Protein losses (most of which are albumin) may \( \uparrow \) to 20g during an episode of peritonitis.

A recent study by van Diepen et al followed 541 patients after the 1\textsuperscript{st} episode of peritonitis observing peritoneal transport characteristics.(1)

Data collected from 1990-2010

Results demonstrated that when compared to controls (patients w/o peritonitis), a 1\textsuperscript{st} peritonitis episode later remained with a faster small solute transport. This may indicate that cured peritoneal infection may lead to a latent state that later causes long lasting alterations.

Introduction: Peritonitis is a major complication of PD

Purpose: Perform a comprehensive collection of studies on modifiable and non-modifiable risk factors for PD associated peritonitis

METHOD: Studies identified (PubMed) 1990-2012; assessed for methodological quality. 415 down to 35 studies for final analysis

RESULTS:

<table>
<thead>
<tr>
<th>NON-MODIFIABLE</th>
<th>MODIFIABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity, Female Gender, CHF, CAD, HTN, DM, Chronic Lung Disease, Anti-hep C virus antibody positivity, Lupus nephritis, No RRF, Glomerulonephritis as renal disease</td>
<td>Malnutrition, Overweight, Smoking, Imunosuppression, No use oral active Vit. D, Psychosocial factors, Low socioeconomic status, PD against patient choice, HD as former modality</td>
</tr>
</tbody>
</table>
Malnutrition Risk:

- In 3 studies, albumin <3.0 g/dL and <2.9 g/dL respectively were associated with ~ two fold risk for peritonitis.

- In 3 studies, association between low albumin levels and a higher peritonitis risk was seen.

- In 1 study, significant increased risk for subsequent peritonitis when albumin levels were declining.

- In 3 studies association between low levels of albumin and risk for peritonitis could not be confirmed.

- 1 study significant ↓ for peritonitis in patients w/o malnutrition (SGA)

Authors state: “It might be hypothesized that hypoalbuminemia as a result of malnutrition, inflammatory response or of uremia itself may lead to higher susceptibility to infection.
## Peritonitis


<table>
<thead>
<tr>
<th>Organism</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GRAM -POSITIVE COCCI</strong></td>
<td>Commonest cause of PDAI</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>and B-haemolytic Streptococcus</td>
<td>Micrococci</td>
</tr>
<tr>
<td><strong>GRAM NEGATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>VRE</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>Acinetobacter sp</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>Enterococci</td>
</tr>
<tr>
<td><strong>FUNGI</strong></td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td>Candida parapsilosis</td>
</tr>
<tr>
<td>Candida glabrata</td>
<td>Neosartorya hiratsukae</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td></td>
</tr>
<tr>
<td><strong>ANAEROBES</strong></td>
<td></td>
</tr>
<tr>
<td>Mycobacteria sp</td>
<td>Rapidly growing nontuberculous</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>Listeria monocytogenes</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>Bordetella bronchiseptica</td>
</tr>
<tr>
<td>Corynebacterium ulcerans</td>
<td>Acanthamoeba</td>
</tr>
<tr>
<td></td>
<td>Unusual. India and mainly developing economies</td>
</tr>
</tbody>
</table>
Variability of Peritonitis Rates Around the World


<table>
<thead>
<tr>
<th>Country</th>
<th>Reference</th>
<th>Year</th>
<th>Adults</th>
<th>Children</th>
<th>Centers</th>
<th>Episodes per year at risk (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>Kavanaugh (1)</td>
<td>2004</td>
<td>1205(^a)</td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Japan</td>
<td>Hoshi (2)</td>
<td>2006</td>
<td></td>
<td>130</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Canada</td>
<td>Mujais (3)</td>
<td>2006</td>
<td></td>
<td>26</td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>United States</td>
<td>Mujais (3)</td>
<td>2006</td>
<td></td>
<td>35(^a)</td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Japan</td>
<td>Nakamoto (4)</td>
<td>2006</td>
<td>139</td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>Portugal</td>
<td>Rodrigues (5)</td>
<td>2006</td>
<td>312</td>
<td></td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>Canada</td>
<td>Fang (6)</td>
<td>2008</td>
<td>312</td>
<td></td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>China</td>
<td>Fang (6)</td>
<td>2008</td>
<td>496</td>
<td></td>
<td></td>
<td>0.20</td>
</tr>
<tr>
<td>Taiwan</td>
<td>Tzen–Wen (7)</td>
<td>2008</td>
<td>100</td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Turkey</td>
<td>Akman (8)</td>
<td>2009</td>
<td></td>
<td>132</td>
<td></td>
<td>0.77</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Davenport (9)</td>
<td>2009</td>
<td></td>
<td>1904 pt–yrs(^a)</td>
<td></td>
<td>0.82 CAPD 0.66 APD</td>
</tr>
<tr>
<td>Austria</td>
<td>Kipriva–Alftart (10)</td>
<td>2009</td>
<td>332</td>
<td></td>
<td></td>
<td>0.24</td>
</tr>
<tr>
<td>Brazil</td>
<td>Mores (11)</td>
<td>2009</td>
<td>680(^a)</td>
<td></td>
<td></td>
<td>0.74</td>
</tr>
<tr>
<td>Canada</td>
<td>Nessim (12)</td>
<td>2009</td>
<td>4247(^a)</td>
<td></td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Spain</td>
<td>Perez Fontan (13)</td>
<td>2009</td>
<td>641</td>
<td></td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>United States</td>
<td>Qamar (14)</td>
<td>2009</td>
<td>137(^a)</td>
<td></td>
<td></td>
<td>0.24</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Ruger (15)</td>
<td>2009</td>
<td>205(^a)</td>
<td></td>
<td></td>
<td>0.60</td>
</tr>
<tr>
<td>France</td>
<td>Castrale (16)</td>
<td>2010</td>
<td>1631(^b)</td>
<td></td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Israel</td>
<td>Cleper (17)</td>
<td>2010</td>
<td>29</td>
<td></td>
<td></td>
<td>1.66</td>
</tr>
<tr>
<td>Australia/New Zealand</td>
<td>Fahim (18)</td>
<td>2010</td>
<td>4675(^a)</td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Australia</td>
<td>Jarvis (19)</td>
<td>2010</td>
<td>4675(^a)</td>
<td></td>
<td></td>
<td>0.60</td>
</tr>
<tr>
<td>Qatar</td>
<td>Shigidi (20)</td>
<td>2010</td>
<td>241</td>
<td></td>
<td></td>
<td>0.24</td>
</tr>
</tbody>
</table>

CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis.

\(^a\) Registry data.

\(^b\) Elderly patients.

The Position Statement provides a chart for ‘modifiable risk factors’ and includes hypoalbuminemia as a ‘well-known risk factor for peritonitis’.


*These evidence based guidelines were again updated in 2016 and include the following 5 sections:*

1. Peritonitis rate
2. Prevention of peritonitis
3. Initial presentation and management of peritonitis
4. Subsequent management of peritonitis
5. Future research
NUTRITION STATUS & OUTCOMES IN PD

Numerous studies associate indices of nutritional status to outcome and several studies associate factors which influence nutritional intake to outcome.
<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Study Components</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yun T et al <em>Medicine</em> 2017; 96:44(e8421)</td>
<td>365 PD</td>
<td>2009-2015 SGA and modified SGA in incident PD patients in predicting mortality</td>
<td>Survival rate in pts with ‘good nutrition’ (SGA) significantly ↑ than those w/‘mild to severe’ malnutrition. Evaluation of nutr’l status based on SGA predicts mortality; weighted SGA w/alb. &amp; TIBC can provide add’l predictive power for mortality.</td>
</tr>
<tr>
<td>Querido S, et al. <em>Rev Port Cardiol.</em> 2017; 36:599-604</td>
<td>112 PD</td>
<td>Demographic, clinical and lab parameters, valvular calcifications, types of PD solutions, hospitalization, CV events and death analyzed</td>
<td>Hypervolemia, mitral calcifications and hypoalbuminemia were independent predictors of CV events or mortality.</td>
</tr>
<tr>
<td>Chiu P-F <em>Medicine</em> 2016;95: 1-7</td>
<td>516 PD (1999-2014)</td>
<td>Categorized pts into 2 groups by difference in Δ initial and peak alb. level. (&lt;0.2g/dl and &gt; 0.2g/dL). Further stratified into quartiles of change of alb. Mortality risk assessed</td>
<td>Initial alb level of all pts: 3.35+ 0.64g/dL Peak 3.7 + 0.34g/dL. End PD alb 2.92 + 0.74g/dL. &lt;0.2g/dL Δ had poorer survival &amp; more frequent &amp; longer hospitalizations. Patients in quartile w/least alb. increment had worst survival. Analysis showed better outcome if initial alb. is at least &gt;3.15g/dL</td>
</tr>
<tr>
<td>Huang R, et al <em>British Journal of Nutrition</em> 2015;133:627-633</td>
<td>885 PD</td>
<td>Retrospective Cohort Nutrition status assessed at initiation of CAPD. 3 components were extracted: visceral proteins, muscle-mass surrogate and BMI Primary Outcome: All Cause Mortality</td>
<td>~ 50% albumin &lt;3.8 ~34% pre-albumin &lt;30 ~ 46% transferrin &lt;200mg/dL After adjustment, the factor score including albumin, pre-alb. &amp; transf. independently associated with mortality. Lower visceral protein conc. independently associated with ↑ mortality</td>
</tr>
<tr>
<td>Study</td>
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<td>Study Components</td>
<td>Results</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Vehakama P. et al. <em>BMC Nephrology</em> 2013;1-9</td>
<td>1,177 PD</td>
<td>Cohort study with 3 yrs flu observing Kt/V and Crcl to outcomes from first initiation PD to death. Other variables included in the prognostic model: BMI, alb., Hgb., BP’s, UF volume</td>
<td>Min tKt/V of 1.75. should be targeted. Age, albumin, Hgb SBP and UF volume significantly affected mortality outcomes</td>
</tr>
<tr>
<td>Chen JB et al. <em>BMC Nephrol</em> 2012;13:39:1-7</td>
<td>77 PD</td>
<td>Prospective study investigates assoc between PD adequacy, and measures of QOL in cohort of incident PD patients</td>
<td>Baseline level of Kt/V affects components of QOL after PD initiation. Lower baseline nPCR assoc. w/deterioration in QOL after PD therapy</td>
</tr>
<tr>
<td>Li, ZJ <em>Int Urol Nephrol</em>. 2011;43:875-82</td>
<td>142 PD</td>
<td>2 groups: those with depression and those without. Clinical, MIS, socio-economic factors compared</td>
<td>~26% had depression; ~49% had potential depression. Compared to non-depressed pts, depressed pts showed lower albumin &amp; higher CRP levels.</td>
</tr>
<tr>
<td>Study</td>
<td>Number</td>
<td>Study Components</td>
<td>Results</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>--------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Leinig CE et al <em>J Ren Nutr.</em> 2011;21:176-183</td>
<td>199 PD</td>
<td>Evaluate predictive value of malnutrition markers for mortality rates on the basis of the PEW definition of PD patients. Observed BMI, AC, MAMC, pro/kcal intake albumin, SGA &amp; presence of PEW.</td>
<td>Mean BMI: 26.6±5.0kg/m². PEW in 17.5% of patients. SGA, alb &amp; PEW were only nutrition markers assoc. w/mortality. After adjusting for classic mortality risk factors, only patients w/hypalbuminemia were at high risk for mortality at follow up.</td>
</tr>
<tr>
<td>Chen KH et al. <em>Kidney Blood Press Res.</em> 2010;33:174-80</td>
<td>552 PD</td>
<td>PNI (alb., LBM, nPNA) used to investigate mortality risk. Demographic, biochem, nutr’l markers, comorbidity &amp; dialysis related data obtained</td>
<td>Age, Comorbidity index &amp; PNI independent predictors of mortality. PNI at start of PD assoc. with all cause mortality and each ↑ by a score of 1 in PNI leads to a 16% ↓ risk of mortality</td>
</tr>
<tr>
<td>Avram MM <em>Kidney Int</em> Suppl. 2010;Aug 117: S37-40</td>
<td>62 PD</td>
<td>Explore extracellular mass (ECM) and body cell mass (BCM) on survival. ECM/BCM ratio highly sensitive index of malnutrition.</td>
<td>ECM/BCM ratio a significant independent predictor of mortality. For every 10% ↑ in ECM/BCM ratio, the RR of death ↑ ~35%. ECM/BCM correlated inversely w/alb, creatinine, BUN &amp; TP. This ratio, was an independent predictor LT survival in PD pts</td>
</tr>
</tbody>
</table>
INTRODUCTION: Conflicting regarding relationships between estimates of adequacy of dialysis and clinical outcomes.

STUDY PURPOSE: Evaluate the association of adequacy of PD patients with mortality, technique failure and hospitalization and to evaluate association of nutritional status with those same variables.

METHOD: Prospective Cohort Study of patients commencing PD in 14 centers in Canada and the U.S. from 9/1/1990-12/31/1992

RESULTS: n= 680 PD
137 transplants
90 deaths
118 technique failures
↑ RR death associated with: Age, DM, CVD, SGA, decrease in adequacy
Creatinine kinetics were used to determine LBM association with survival.

### RESULTS (cont’d)

<table>
<thead>
<tr>
<th>Albumin Level</th>
<th>Days/year Hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 4.0</td>
<td>7.3</td>
</tr>
<tr>
<td>3.5 – 4.0</td>
<td>12.7</td>
</tr>
<tr>
<td>3.0 – 3.4</td>
<td>23.6</td>
</tr>
<tr>
<td>&lt; 3.0</td>
<td>35.6</td>
</tr>
</tbody>
</table>

A 0.1 g/dl ↓ in serum albumin concentration was associated with:
- 6% ↑ in Relative Risk of Death
- 5% ↑ in Relative Risk of technique failure
- 5% change in days hospitalized

<table>
<thead>
<tr>
<th>%LBM</th>
<th>2 yr Survival Probability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;73</td>
<td>88.3</td>
</tr>
<tr>
<td>63-73</td>
<td>81.2</td>
</tr>
<tr>
<td>&lt;63</td>
<td>65.2</td>
</tr>
</tbody>
</table>

Creatinine kinetics were used to determine LBM association with survival.
INTRODUCTION:
Hypoalbuminemia is used to assess mortality risk and is a powerful predictor of outcomes in HD. In PD patients, there is an association (inconsistent) between low albumin and all-cause mortality and peritonitis risk.

There is little information on cause-specific mortality in PD.

5yr survival in PD is (40%) vs. HD (34%) yet PD patients have lower albumin levels. Authors felt it is reasonable to assume that perhaps a given level of albumin may be associated with ↓ risk of death in PD pts.

The threshold for clinical intervention or use to judge quality of care may differ by dialysis modality

STUDY PURPOSE: To define the relationship between albumin level and mortality risk in a large cohort of PD patients and compare the relationship with HD patients.
CRITERIA FOR STUDY: All Davita patients receiving dialysis treatments between 7/1/2001 and 6/30/2006

METHODS  

N= 130,052  
Observational Cohort

Data was extracted from patient records and then merged with USRDS data
10 co-morbid conditions were considered
Albumin levels were averaged quarterly
Weight was averaged over 13 weeks & used with baseline height to determine BMI
Cause of death available from USRDS data

RESULTS

PD patients were younger and less likely to have DM. Less prevalence of ASCHD
Higher values for Creatinine, iPTH, TIBC
Lower values for Ferritin, Phosphorus, Alkaline Phos
<table>
<thead>
<tr>
<th>Variable</th>
<th>PD</th>
<th>HD</th>
<th>&lt; 2 yr PD</th>
<th>&lt; 2 yr HD</th>
<th>&gt; 2 yr PD</th>
<th>&gt; 2 yr HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dL)</td>
<td>3.6±0.5</td>
<td>3.7±0.5</td>
<td>3.6±0.5</td>
<td>3.6±0.5</td>
<td>3.6±0.5</td>
<td>3.8±0.4</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>8.4±3.8</td>
<td>8.0±3.3</td>
<td>7.8±3.6</td>
<td>7.2±3.1</td>
<td>11.2±4.0</td>
<td>10.0±3.2</td>
</tr>
<tr>
<td>Ferritin (ng/dL)</td>
<td>245</td>
<td>388</td>
<td>223</td>
<td>314</td>
<td>394</td>
<td>656</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>54±16</td>
<td>62±16</td>
<td>55±17</td>
<td>63±16</td>
<td>52±15</td>
<td>59±15</td>
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<tr>
<td>Women (%)</td>
<td>47</td>
<td>45</td>
<td>46</td>
<td>45</td>
<td>51</td>
<td>46</td>
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<tr>
<td>Diabetes (%)</td>
<td>38</td>
<td>45</td>
<td>41</td>
<td>47</td>
<td>26</td>
<td>38</td>
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<tr>
<td>Vintage (mo)</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>46</td>
<td>50</td>
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<tr>
<td>Weight (kg)</td>
<td>76±20</td>
<td>75±21</td>
<td>76±20</td>
<td>75±21</td>
<td>78±22</td>
<td>74±21</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27±8</td>
<td>27±7</td>
<td>27±8</td>
<td>27±7</td>
<td>27±6</td>
<td>26±7</td>
</tr>
</tbody>
</table>
RESULTS

ALBUMIN: PD Patients

BASELINE: ≤3.0 11%
3.0-3.79 52%
3.8-3.99 16%
>4.0 21%

In 6 mo. albumin: 31% unchanged 37% ↑ > 0.1 g/dL 32% ↓ > 0.1 g/dL

PD patients with ↓ in albumin > 0.3 over 6 months
- Higher prevalence of CHF, Acute MI, Ischemic Heart Ds, PVD
- Lower body weight
- Higher TIBC and PTH compared to other groups
| PD Albumin < 3.0 | 3.0 fold ↑ risk of all cause mortality  
| | 3.4 fold ↑ risk infection related mortality  
| (reference +0.1 to -0.1) |  
| PD patients with > 0.3 increase in albumin over 6 months | All cause mortality significantly lower  
| PD patients with > 0.2 decrease in albumin over 6 months | All cause mortality significantly higher  
| PD < 3.8 | HD < 4.0  
| 37% PD had > 3.8  
| 46% HD had > 3.8 | Significant increase in death risk.  
| Risk of all cause mortality lower for PD than HD for each 0.2 albumin category  
| Risk of infection related mortality higher in PD vs. HD patients for every albumin category (septicemia, pulmonary) |
DISCUSSION:

2 contributors to low albumin in dialysis patients: systemic inflammation & low nutrient intake.

“There is no evidence that a higher prevalence of either of these 2 abnormalities accounts for the ↑ prevalence of hypoalbuminemia”
Likely that obligatory protein losses with PD account for the lower serum albumin level in PD patients.

CONCLUSIONS:
Prognostic value of serum albumin was validated
Hypoalbuminemia predicts ↑ CV and infection-related mortality in PD
Serum albumin mandating clinical evaluation and intervention to judge quality of care should be modality specific.
PD patient threshold should be 0.2-0.4 g/dL lower than HD
Periodic measurement of serum albumin provides more valuable information than a single baseline measurement
Higher serum creatinine represents larger muscle mass & predicts greater survival in HD patients and low creatinine is associated with ↑ mortality. This association remains uncertain in PD patients.

PD patients have greater preservation of residual GFR which is independently associated with mortality as well as serum Cr level.

In studies of PD patients, there have been variable associations between serum Cr level and mortality (in part related to greater preservation of residual GFR).

STUDY PURPOSE: Examine association of baseline serum Cr levels and Δ in serum Cr level during first 3 months with all-cause mortality and examine effect of PD treatment duration on serum Cr-mortality association.
CRITERIA: All Davita patients receiving PD treatments between 7/1/2001 – 6/30/2006

METHODS: 10,896 PD patients

Data was extracted from patient records and merged with USRDS data
10 co-morbid conditions were considered
Weight was averaged over 13 weeks & used with baseline ht. to determine BMI
Cause of death available from USRDS data
Creatinine levels were averaged quarterly

The association of baseline serum Cr level and Δ during first 3 months after enrollment with all-cause mortality examined.

**Creatinine levels divided into seven categories**

- <4.0
- 4.0–5.9
- 6.0–7.9
- 8.0–9.9
- 10.0–11.9
- 12.0–13.9
- ≥14.0 mg/dL

**Δ Cr levels were divided into:**

- < -1.0
- -1.0 to 1.0
- > 1.0 mg/dL

For the stratified analyses, PD duration was divided into:

- <3 months
- 3 to <12 months
- ≥12 months
RESULTS:

Compared with patients with creatinine: 8.0–9.9 mg/dL
- Patients with creatinine <4.0 mg/dL and 4.0–5.9 mg/dL had ↑ risk of death
- Patients with creatinine categories of 10.0–11.9 mg/dL & higher had ↓ risk of death.

The creatinine–mortality association was robust in patients with PD treatment duration of ≥ 12 months, but was not observed in those with PD duration of <3 months.

CONCLUSIONS:
Muscle mass reflected in serum Cr level may be associated with survival even in PD patients. However, the creatinine–mortality association is attenuated in the early period of PD treatment, suggesting competing effect of muscle mass versus residual RRF on mortality.
Incidence of Malnutrition in PD


**SGA used in 6 Centers EU and N. America 224 pts 41% malnourished**


**SGA used 224 CAPD & 263 MHD 42.3% PD malnourished (HD 30.8%)**

Peritoneal Dialysis Serum Albumin Findings for October 2006-March 2007 ESRD CPM Project

**37% of US Adult PD albumin of < 3.5 g/dL**


CROWNWeb lab values for May 2016

**42.8% PD alb <3.5g/dL (17.7% of HD)**
How to Address Factors Contributing to PEW?

- Nutritional Interventions: What the Experts Say
- Potential Role of Alternative PD Solutions
**Figure 5** | Proposed algorithm for enteral nutritional support in patients with CKD. The target of total protein intake should be a DPI of ≥1.2 g/kg per day for patients on dialysis.

**Periodic nutritional assessment & dietary counseling of patients with CKD:**
EDW, albumin, pre-albumin, muscle mass, nutritional scores (SGA, MIS), appetite, diet (DPI, DEI, K, P, Fluid, Na, vitamins, other micronutrients)

**Indications for nutritional interventions:**
Poor appetite and/or poor oral intake
Unintentional loss of dry weight, sarcopenia
Albumin <4.0 g/dL or pre-albumin <300 mg/l
MIS 5 or SGA malnourished range DPI <1.0

**Start CKD-specific oral nutritional supplementation 1–2 servings per day**
CKD stage 5D:
DPI target of >1.2 g/kg per day using oral supplements at home and in-center meals & oral supplements during dialysis treatment
Proposed algorithm cont’d

**Monthly assessment** Monitor nutritional status for changes in appetite, food intake, weight status, serum albumin and pre-albumin concentration, MIS and SGA

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**Improvement**

- Maintenance oral therapy if albumin reaches 4.0 g/dL.
- Continue in-center meals & oral suppl’ts to target DPI 1.2 g/kg & DEI 30–35 kcal/kg/d
- Consider liquid oral supplement with pill intake

**No Improvement or Deterioration**

- Adjunct pharmacological and Dialysis therapies
  - Appetite stimulators
  - Antidepressant
  - Anti-inflammatory and/or Antioxidative
  - Anabolic and/or muscle enhancing
  - Dialysis treatment alterations

- Intensify enteral therapy or add’l interventions
  - Increase quantity of oral therapy;
  - **Tube feeding** (including PEG);
  - **Parenteral interventions:** IDPN (especially if enteral feeding not possible)
  - IPN
In this latest consensus, it is stated:

“Oral or parenteral nutrition supplementation should be prescribed when dialysis patients exhibit signs of malnutrition despite standard preventive measures.

Several studies have demonstrated that these interventions improve nutritional parameters such as lean body mass or serum albumin concentrations.
Algorithm ONS Intervention:

ONS can provide an additional 7–10 kcal/kg per day of energy and 0.3–0.4 g/kg per day of protein (1)

Studies show positive results on nutritional parameters and metrics:
* ↑ Kcal & protein intake
* ↑ nPNA and albumin (some studies)
* ↑ body weight and anthropometrics

Several studies noting negative results:
* Albumin trend inconsistent and often does not change or improve
* Non-compliance and intolerance is common

Barriers that may influence response to ONS: abdominal distention; early satiety, delayed gastric emptying, appetite suppression, volume overload

Study Shortcomings: Limited Data, small sample size, ONS variability

<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Study Components</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eustace JA et al. <em>Kidney Int.</em> 2000;57:2527-2538</td>
<td>47: 29HD 18PD 4 PD alb &lt;3.8g/dL; 14 PD alb &lt;3.5g/dL</td>
<td>Received 3.6g EAA or placebo 3X daily for 3 months</td>
<td>Compliance by month 3 dropped to 50%. No significant ↑ in alb. in PD patients. Higher hospitalization in group with alb. &lt;3.5g/dL.</td>
</tr>
<tr>
<td>Boudville N et al <em>Am J Kid Dis</em> 41: 658, 2003</td>
<td>13</td>
<td>Cross over design. 3 visits with placebo or ONS 30 min before or 2 hrs. before lunch (self selected buffet). Food intake measured Mean BMI 27.5</td>
<td>ONS 2 hrs before lunch significant ↑ compared with placebo + lunch in total caloric and protein intake. No significant difference in taking ONS 30 min before or 2 hr. before lunch.</td>
</tr>
<tr>
<td>Gonzalez Espinoza L, et al. <em>Perit Dial Int</em> 2005;25:173-80</td>
<td>28</td>
<td>6 mo. flu monthly clinical &amp; biochemical evals ; quarterly assessments of dialysis adequacy and nutrition 15 counsel only and 13 counsel &amp; egg albumin based ONS</td>
<td>Baseline vs. 6 mo., significant improvement in alb. in ONS group but not controls. Kcal/pro intake ↑ more in ONS group &amp; nPNA ↑ significantly more in ONS group vs. control. At study end, 6% ↓ in moderate or severe nutrition in control and 28% in ONS</td>
</tr>
<tr>
<td>Texido-P et al <em>Perit Dial Int</em> 2005;25:163-72</td>
<td>65</td>
<td>Prophylactic evaluation of ONS on baseline, 6 &amp; 12 mo. nutr’l parameters 65 patients 35 receive ONS (pro/kcal) 30 control.</td>
<td>29 completed study(9 ONS and 20 Control) Significant noncompliance &amp; intolerance (15/65) Significant improvement in BW, TSF,AMC, LBM.</td>
</tr>
<tr>
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<td>Results</td>
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<tr>
<td>Ray C J Ren Nutr 2005;15:260-4</td>
<td>22&lt;br&gt;Mean alb at start 3.7g/dL</td>
<td>Intent was to observe, quantitatively report, and discuss nutr’l status, alb &amp; life quality of patients using whey protein suppl’t (Procel). Supp’t was individualized to meet pt. needs. At study start and end, CMIS and KDQOL-SF were obtained.</td>
<td>11 patients completed the study. Pts w/multiple co-morbid conditions, hospitalization and/or infections had an average ↓ in alb. (3.5g/dL) &amp; KDQOL–SF score yet improved CMIS score. Remaining pts. had an avg. ↑ in alb. KDQOL-SF, CMIS remained same. 10/11 high avg. transporters.</td>
</tr>
<tr>
<td>Poole R et al Renal Nutrition Forum 2006; Vol 25 Number 4 Fall</td>
<td>130: 99 HD 31PD&lt;br&gt;Alb. &lt;3.5g/dL for 2 of 3 month or &gt;5% wt loss 1 mo. or &gt;10% 6 mo.</td>
<td>Malnourished pts qualified through ONS grant program (annual income &lt;$24K.) 3 mo. ONS and 3 mo. after ONS cessation. Info tracked on alb., DW, phos., hospitalization or infection</td>
<td>Statistically significant ↑ in alb. level starting in first mo. of ONS and persisted throughout the 3 months. Improvement of alb. persisted (significant increase) even after ONS was stopped during the 3 mo. observation.</td>
</tr>
<tr>
<td>Poole R et al Adv in Perit Dialysis 2008;24:118-124</td>
<td>190 PD: 157 HD 33PD&lt;br&gt;Same criteria as above</td>
<td>Same as above.</td>
<td>Alb significantly ↑ in HD vs. PD pts for all study periods. Albumin levels did not change in PD patients. PD had no significant ↑ in wt. nor alb. during or after ONS period. No drop in albumin levels in the flu period. 18% PD patients had 1 or more episodes peritonitis. Non-adherence to ONS: 5/33 PD &amp; 13/157 HD</td>
</tr>
<tr>
<td>Study</td>
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<td>Study Components</td>
<td>Results</td>
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<tr>
<td>Moretti HD et al J Ren Nutr 2009;19:298-303</td>
<td>49 HD &amp; PD</td>
<td>1 yr. randomized cross over study comparing albumin, nPCR, total hospitalizations, and LOS in pts who received ONS (Proteinex:15g pro 7 days/week) and those who did not</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; 6 months: In ONS group, significant ↑ nPCR by mo. 4 &amp; control significant ↓ nPCR no improvement in alb. 2&lt;sup&gt;nd&lt;/sup&gt; 6 mo.: ONS group ↑ alb. Significant ↓ control group and nPCR did not ∆ but ↑ trend ONS group. When ONS ended, pts with BMI &lt;20 had significant ↓ wt. No significant differences in hosp. but ONS trend toward ↓ LOS</td>
</tr>
<tr>
<td>Dharmatti G et al Indian Journal of Nephrology 2013 23: 1-4</td>
<td>34 HD&amp; 16 PD</td>
<td>Baseline and 6 mo. of albumin and BIA of 25 pts receiving whey protein (46g pro, 230 kcal) and 25 egg albumin (70gm pro 316 kcal per 100gm). Amt. as per deficit per K/DOQI guidelines.</td>
<td>Mean initial intake of pro in whey &amp; egg alb group 0.74±0.3 vs. 0.69±0.2 and kcal intake: 20±5.6 vs 20±5.1 respectively. 2 died 28% dropped out w/in 1 mo. due to side effects (N &amp; V). Of remaining 34 who completed the study, 80% could not consume &gt;50% of suppl’t. Pro &amp; kcal intake remained similar at baseline and 6mo in both groups. No ↑ in TP or kcals; no difference in alb or BIA</td>
</tr>
<tr>
<td>Unverdi S et al. Ren Fail. 2014;36: 1416-9</td>
<td>44 PD All with alb. &lt;3.5g/dL</td>
<td>Baseline &amp; 6 mo. comparison/analysis labs &amp; demographics 31 pts. oral EAA suppl’t: 5 pills 3x/day. 14 pts. used 2L 1.1%AA daily (ACD).</td>
<td>Significant ↑ BMI, albumin and protein in both groups. Mean alb ↑ significantly in ACD (.54g/dL) and .49 g/dL in EAS group following 6 months.</td>
</tr>
<tr>
<td>Satirapoi B et al Int J Nephrol Renovasc Dis 2017;10:145-151</td>
<td>30 PD. All alb. &lt;3.8g/dL, Pro &lt;1g/kg/d &amp; Kcal 20-5kcal/d</td>
<td>Observe albumin, pre-albumin &amp; inflammatory stress in pts receiving daily oral ONS for 15 days.</td>
<td>Significant ↑ Pro and Kcal intake, BW and BUN intake during the study. Higher pre-albumin at study end as compared to baseline. Improvement in SGA , higher</td>
</tr>
</tbody>
</table>

- 2 started PEG feeding before starting PD: no complications
- 2 already on PD cont’d with long-term PD after PEG was placed
- 2 of the 8 patients whose PD was not interrupted at the time of PEG placement immediately developed peritonitis.
- 6 maintained on HD: 2 developed peritonitis within 1 wk. of starting PEG
- 3 had no complications
- 1 developed peritonitis when PD resumed.

Authors stated that PEG placement prior to PD initiation appears to be safe. Maintaining patients on HD for at least 6 wks. appears to ↓ incidence of peritonitis. Use of antifungal prophylaxis and maintenance of the patient on HD for longer than 6 wks. may produce better results.
Algorithm Interventions:
Intra-peritoneal Nutrition (IPN)

IPN is a solution of amino acids and dextrose solution placed directly into the peritoneal cavity

History of the use of the peritoneal cavity for nutrition
Gjessing J., Addition of amino acids to peritoneal-dialysis fluid. 1968 Lancet 2:812

Very first use of AA was reported in 1968.
Gjessing demonstrated that substantial amounts of AA could be absorbed through the peritoneal cavity

Very first use of the peritoneal cavity for providing Glucose, AA and lipids was reported in 1980. Substrates were provided intraperitoneally for 9 days (2000kcals/day).
BUN stabilized and 3 methyl histidine losses were reduced.

Authors indicated that administration of AA through the peritoneum may reduce muscle catabolism & therefore improve nutritional status
IPAA and IPN Products as Dialysate: ‘Glucose Sparing’

ADVANTAGES:

- Good osmotic agents providing ~ twice osmotic load of glucose per gm
- Using an AA based solution provides a means to replace & minimize loss of AA from the patient during PD
- Reduces glucose load thereby ↓potential metabolic & physical effects of standard solutions.

PRODUCTS:

Nutrineal 1.1% AA 2L and 2.5 L bags (contain amino acids ONLY)
Not available in the U.S. and used in European studies in PD

Intraperitoneal Nutrition: IPN
Compounded product utilizing the PD dialysate bag where dextrose is removed and AA’s are added.
Nutritional Advantages IPAA/IPN Studies and Shortcomings

Majority of studies with positive results on nutrition parameters & metrics:

* Improvement in serum proteins
* Normalized AA plasma patterns
* Improved N2 balance
* Improved MAMC/LBM
* Advantage in nutritional response when kcals are provided at the same time
* Improvement in lipid profile

Few studies showing no change in nutritional parameters

Study Shortcomings

Subjects sometimes not malnourished
Studies using various concentrations, volumes & products for AA
Subjects given AA with no calories and some with calories
Subjects provided AA at different times of the daily prescription
Short study period, small numbers of subjects (IPN study one of the largest)
High technique failure rate complicates conducting LT studies
Large IPN Study in Malnourished PD Patients

**STUDY PURPOSE:**
Determine whether IPN dialysate is associated with longitudinal trends in lab surrogates of nutritional status

**CRITERIA:** Must have at least 2 alb. Levels recorded during IPN therapy.

**METHOD:** Data extracted from NMC database from Jan 1993-June 1994

**RESULTS:** 183 CAPD patients received 1% AA 2L exΔ for a mean of 6.6 mo
Mean baseline albumin (2.65 ± 0.49 g/dl) strongest predictor: hosp. & death
Reduced baseline alb & obesity; ↑ hosp.& death
Statistically significant ↑ in alb over time: 9 mo. treatment: ↑ 0.4g/dL
Slight ↓ TG levels. No metabolic acidosis

**CONCLUSIONS:** A small but clinically important ↑ albumin observed over time
Low alb. and ↑ obesity were associated with hospitalization or death over a maximum 9 mo. treatment time.
Benefits of Additional Calories with IPAA: Isotope Methodology


STUDY PURPOSE: Assess effects of IPAA with or w/out oral energy intake.

METHODS: 6 stable, non-DM patients receiving 1.1%AA
1 session without a meal & 1 session with meal (600 kcal: CHO & lipid)

RESULTS/CONCLUSIONS:

1.1% AA solution efficaciously utilized for protein synthesis. *Ingestion of a CHO-Lipid meal during a cycle with 1.1%AA inhibited protein breakdown & reinforces a positive effect of the AA solution on protein balance*


STUDY PURPOSE: Compare AAG vs. G in the fed state

METHODS: 12 CAPD patients compare 2 7 day periods each of:
1% AA + G (AAG) vs (G) as control dialysate fed identical Q hr. liquid meals.

RESULTS/CONCLUSIONS:

*Rates of protein synthesis significantly in AAG group compared to G. Dialysate that contains AA plus G also improves pro synthesis in fed CAPD patients.*
<table>
<thead>
<tr>
<th>Authors</th>
<th>Number</th>
<th>Duration and Intervention</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Williams, P et al.</td>
<td>6 Non-DM patients</td>
<td>Studied after glucose dialysate overnight. (AM dwell)</td>
<td>Ultrafiltration similar to 4.25% glu; effective removal urea, creat., K+. Well tolerated <strong>90% absorption AA in 6 hrs</strong> ↑ plasma AA corresponded to AA in dialysate. Between groups, no significant Δ’s in urea in dialysate suggesting AA incorporated into pro rather than degraded for energy</td>
</tr>
<tr>
<td>Oren A et al.</td>
<td>6 malnourished</td>
<td>4 wk. study of 2 -1L 1%AA exchanges alternated with 2 Glu</td>
<td>In 4 wks., significant ↑ BUN, body N2, transferrin (improved nutritional status). No Δ in fasting alb. (alb. half-life ~ 21 days). IPAA well tolerated; no adverse effects on fasting or post-infusion plasma AA concentration.</td>
</tr>
<tr>
<td>Bruno M et al.</td>
<td>6 patients, 3 with RRF, 3 anuric</td>
<td>Studied 6 months 1 exchange 2L of 1% AA per day <strong>just before lunch</strong></td>
<td>N2 balance (-1.3) before → significantly positive AA (+3.1) after, no Δ in alb.; ↑ wt. &amp; LBM in all patients. Significant ↑ in MAMC; AA profile improved toward normal. Chol, TG significantly ↓; ↑ urea &amp; pH; slight ↓ HCO3 Study demonstrated safety/efficacy of long term use of AA. Did not induce toxic effects nor impair membrane function.</td>
</tr>
<tr>
<td>Dibble NV et al</td>
<td>8 patients Alb &lt;3.5g/dL</td>
<td>12 wk study of 1 exchange 2L of 1%AA (AM dwell)</td>
<td>Chol &amp; LDL ↓ at 8 &amp; 12 wks. except ↑ in 1 patient. No Δ in wt, AMC, TG or HDL, growth hormone, fasting plasma glucose</td>
</tr>
<tr>
<td>Dombros NV et al</td>
<td>5 Patients Pro &lt;.8g/Kg and/or Albumin &lt;3.5g/dL</td>
<td>Studied 6 months 1 exchange 2L 1% AA (Travesol) <strong>8 hr overnight dwell</strong> plus Glu for other exchanges</td>
<td>BUN ↑ first mo. No Δ in: avg. oral p.o, BW, creat., chol., TG, TP, alb., TB K+, transferrin, TSF, &amp; plasma AA levels. Total body N2 ↓. Authors stated: reason for no improvement in nutr’l status may be due to: timing of administration, AA composition, or low kcal intake and/or that patients weren’t severely malnourished</td>
</tr>
<tr>
<td>Study</td>
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<tr>
<td>Arfeen S et al. <em>Clinical Nephrology</em> 1990;33:192-199</td>
<td>7 non-DM patients Alb 3.6-3.8g/dL</td>
<td>8 wk study of 2 exchanges of 1%AA and 2 Glu plus standardized meals.</td>
<td>Improved plasma AA (↑BCAA) and albumin concentration but mild metabolic acidosis (lactate 35mmol/L). No Δ TG, insulin, glucose, transferring</td>
</tr>
<tr>
<td>Musk M et al. <em>Adv Perit Dial.</em> 1992;8:153-156</td>
<td>16 patients Non-malnourished, Non DM</td>
<td>4 wk. crossover study with 1%AA replacing first glucose bag or Glu only</td>
<td>No effects on hunger/satiety, food appeal, lunch time food intake or 3 day food intake. Feelings of fullness ↓ with AA. AA do not affect subjective appetite for food intake in PD</td>
</tr>
<tr>
<td>Kopple, J et al. <em>Kidney Int.</em> 1995;47: 11481157</td>
<td>19 patients with: Muscle wasting; Pro &lt;1.0g/kg/d; Alb ≤4g/dL in men &amp; ≤3.7g/dL woman OR &lt;90% BW</td>
<td>20 day hospital study, Diet: .8g pro/kg 28 + 3 kcal/kg 1-2 exchanges/day of 1.1% (1.5 to 2L bag) AA instead of glu exchanges in amount to bring pro intake up to 1.1-1.3g/kg</td>
<td>N2 balance significantly (+) during treatment periods (+1.71 ± 2.4g/day). ↑ in net protein anabolism. Isotope studies: More nl fasting plasma AA pattern. Significant ↑ TP &amp; transferrin. Alb ↑ approached significance (3.18g/dL to 3.34g/dL) Well tolerated; mild metabolic acidosis in some</td>
</tr>
<tr>
<td>Chertow G et al. <em>J Ren Nutr</em> 1995; 5: 116-123</td>
<td>183 patients Mean baseline alb: 2.65 ± 0.49 g/dl</td>
<td>2-9 mo. study period 1% AA 2L exchange daily (IPN)</td>
<td>Baseline alb strongest predictor: hosp &amp; death Reduced baseline alb &amp; obesity; ↑ hosp.&amp; death Statistically significant ↑ in alb: ~0.05 g/dl per month. Slight ↓ TG levels. No metabolic acidosis.</td>
</tr>
<tr>
<td>Faller B et al. <em>Nephrol Dial Transplant</em> 1995; 10: 1432-5</td>
<td>15 non-DM pts</td>
<td>3 month study 1 exchange/day of 2L 1.1% AA as the second exchange of the day</td>
<td>Significant increase in albumin (3.27 ± 2.3 to 3.51 ± 2.2 g/l) and transferrin</td>
</tr>
<tr>
<td>Misra M et al Adv Perit Dial. 1996;12:311-4</td>
<td>18 nutritionally unselected group of patients</td>
<td>6 month cross over study; 10 received 2L 1.1%AA initial 6 mo. (Group A), and 8 received second 6 mo. (Group B).</td>
<td>Patients in group A w/albumin &lt;3.0g/dL showed significant ↑ at 2 mo. &amp; persisted at 6 mo. AA showed a trend toward improvement in MAMC in both groups. Nutrition score (combined albumin, anthropometry, TLC) improved in both groups; significant increase in FDRP.</td>
</tr>
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<tr>
<td>Maurer O et al.</td>
<td>19 patients</td>
<td>Assigned to receive overnight 1% AA or Glu solution.</td>
<td><strong>Glucose group</strong>: Total body fat mass ↑ but ↓ in AA group. Lean mass similar in both groups; no Δ alb &amp; transferrin either group. nPCR ↑ in AA group. Authors state: overnight PD with AA offers minor advantages to protein malnourished PD patients</td>
</tr>
<tr>
<td>Optatrna S et al</td>
<td>8 patients</td>
<td>4 wk. study using 1.1%AA</td>
<td>As compared with baseline, significant ↑ PCR and urea concentration. Phos ↓ significantly. No difference in anthropometrics, albumin, TP, transferrin or AA. Authors state that administration of AA by raising PCR maybe indirect evidence of an anabolic effect. Long term and controlled studies needed</td>
</tr>
<tr>
<td>Jones M et al.</td>
<td>20 pts from 5 centers</td>
<td>Research center 4 day study of 2L 1.1% AA first exchange</td>
<td>Mean absorption of amino acids was 80%. Gain of AA was 17.6 ± 2.6 g Gains were unrelated to membrane transport characteristics. Net gain of AA seen in all patients.</td>
</tr>
<tr>
<td>Asola M, et al.</td>
<td>13 non-DM</td>
<td>Cross over study where each patient studied twice: fasting state &amp; during euglycemic insulin stimulation &amp; positron emission tomography. Compared AA to Glucose based PD solution on skeletal muscle AA uptake.</td>
<td>In PD treatment w/ AA solution: significant ↑ in skeletal muscle AA uptake both in fasting state (2.18 ± 0.34 to 3.08 ± 0.55) and insulin stimulation (1.88 ± 0.15 to 2.42 ± 0.30). Compared to PD using glucose, skeletal muscle AA uptake was significantly ↑ during AA both in fasting (15.2 ± 5.8 vs. 20.0 ± 5.6) and insulin stimulation (16.8 ± 4.5 vs. 21.1 ± 4.9) respectively</td>
</tr>
</tbody>
</table>
## IPAA/IPN Isotope Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Duration &amp; Intervention</th>
<th>Results</th>
</tr>
</thead>
</table>
Protocol 1 – Dextrose dialysate (8 pts)  
Protocol 2 – Dex & 1.1%AA 2L (5 pts)  
Protocol 3 - Control saline (5 pts) | Protocol 1: Insulin ↑ after infusion  
↓ in forearm proteolysis and ↓ in forearm protein synthesis. Anabolic effect of insulin is tempered by unavailability of AA (EAA/BCAA)  
Protocol 2: Insulin ↑ after infusion  
↓ in forearm proteolysis ↑ in forearm protein synthesis |
Measured whole body protein turnover (labeled Leucine) and N2 balance studied in the fasting state.  
Isonitrogenous, isocaloric diet provided  
7 nights: One 2.5L bag 1.1%AA (27 g) + Four 2.5L bags glu AAG  
7 nights: Glu alone G | Net AA absorption from dialysate was 47%  
Net protein synthesis ↑ and breakdown ↓ during AAG.  
Net pro balance in AAG compared to G improved in all patients (not statistically significant) Supply of AAs probably not high enough.  
Plasma and dialysate urea levels were similar in both study periods suggesting AA were used for pro anabolism and not energy. CO2 slightly lower in AA group, but still within nl. |
| Tjong HL et al *J Am Soc Nephrol* 2007 | 12 PD | Crossover study to compare daytime with 7 d intervals of 1.1% AA plus G (AAG) vs G in fed state. Whole-body protein turnover studied (labeled leucine) during the daytime. A mixture AAG vs. G fed-state conditions created by identical liquid hourly meals. | Rates of protein synthesis increased significantly in the AAG as compared to the G  
Dialysate that contains AA plus G also improves protein synthesis in fed CAPD patients. |
<table>
<thead>
<tr>
<th>Study</th>
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<th>Duration &amp; Intervention</th>
<th>Results</th>
</tr>
</thead>
</table>
| Li, FK et al. AJKD 2003      | 60 patients 24 in study at end | 30 received one 2L 1.1% AAs 30 usual dextrose                                         | Similar mortality, hospitalization duration, CRP and drop out rate (~40% in 2 yr)  
Dextrose group: Significant drop in alb at 36 mo (3.4 → 3.1)  
AA group: Alb better maintained; Pro intake sustained  
Pro intake g/kg Dex. Group: 1.08 → .99  
AA Group: 1.02 → 1.15) |
| Taylor GS et al AJKD 2002    | 22 patients 19/22 taking ONS | All received one exchange of 2L 1.1% AAs  
Mean 13.6 mo                                                                 | IPAA associated with low peritonitis rate and mortality  
(1 episode of peritonitis per 23 treatment months & 1 pt died)  
Significant increase in albumin (2.24 → 2.56)  
& nPCR (.89 → 1.08)  
Kt/V & creat clearance ↓ significantly but remained within adequate range in >80% |
**IPN : Absorption in PD vs. Cycler Bag**

CAPD IPN: Research indicates ~ 80-90% of AA absorbed in 6 hrs.
Cycler IPN: Research indicates ~ 50% of AA absorbed 5-6 hrs.

*Absorption will be dependent on dwell time and transporter type.*

<table>
<thead>
<tr>
<th>IPN CAPD Options using a 2L bag</th>
<th>6 hr dwell</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amino Acid (g)</td>
</tr>
<tr>
<td>Regimen 1 1%</td>
<td>20</td>
</tr>
<tr>
<td>Regimen 2 1.5%</td>
<td>30</td>
</tr>
<tr>
<td>Regimen 3 2%</td>
<td>40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IPN for CYCLER Options using a 6L bag</th>
<th>6 hr dwell</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Regimen 1 1%</td>
<td>60</td>
</tr>
<tr>
<td>Regimen 2 1.5%</td>
<td>90</td>
</tr>
<tr>
<td>Regimen 3 2%</td>
<td>120</td>
</tr>
</tbody>
</table>
Neutral pH-low GPD Solutions (‘Biocompatible Solutions’)  

PD solutions stored within multi-chamber bag systems. Glucose component is separated (in one or more chambers) from other electrolytes under acidic conditions to minimize the formation of GDP’s during heat sterilization and storage.

Patient breaks the seal immediately before use and the final solution has a neutral pH and either a low or ultra low GPD content.

Delflex Neutral pH (Fresenius Medical Care North America, Waltham, MA, USA), the first neutral-pH PDF to be approved by the US FDA
Clinical Benefits Reported with ‘Biocompatible Solutions’

Szeto C, Johnson D. 2017 Seminars in Nephrology 37;30-42

5 systematic reviews and meta-analyses have concluded:
Better preservation of RRF as compared to conventional PD solutions
Consistent and higher urine volumes

Further study needed to clarify effects on:

Ultrafiltration
Fluid status
Inflow pain
Peritonitis
Solute transport rate
Technique survival and patient survival
Extraneal:

PD solution containing icodextrin which is a starch derived, water soluble glucose polymer

- Used as a single long dwelling (8-16 hr.) exchange
- Rate of absorption much slower than glucose

IPN is not compatible with icodextrin and is NOT a substitute for icodextrin. *IPN could be used before or after icodextrin with consideration of PD regimen and ultrafiltration needs/hydration status.*
Clinical Benefits Reported with Icodextrin

* Increased ultrafiltration (especially in high peritoneal transporters)
* Improved glycemic control and insulin sensitivity
* Improved lipid profiles in diabetic patients
* Enhanced phosphate removal
* Some evidence that using icodextrin solutions is associated with better technique survival in PD patients

Further study needed to clarify effects on:
* Peritoneal membrane function
* Inflammatory marker elevations ? Subclinical inflammation
* Technique survival and patient survival
<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient population</th>
<th>Prescription</th>
<th>Results with Icodextrin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sisca S, et al.</td>
<td>PD with Hypertriglyceridemia</td>
<td>Icodextrin vs. Glucose</td>
<td>Significant ↓ in TG</td>
</tr>
<tr>
<td>Van V, Schoonjans RS, et al.</td>
<td>PD</td>
<td>Icodextrin vs. Glucose</td>
<td>Gastric emptying time significantly shorter</td>
</tr>
<tr>
<td>Konings CJ et al.</td>
<td>PD</td>
<td>Icodextrin vs. Glucose</td>
<td>Significant ↑ in daily ultrafiltration volume and ↓ in extracellular (ECW) water. Significant ↓ left ventricular mass</td>
</tr>
<tr>
<td>Davies SJ, et al.</td>
<td>PD</td>
<td>Icodextrin vs. Glucose</td>
<td>No ↑ in non-fluid weight gain in icodextrin group unlike glucose group</td>
</tr>
<tr>
<td>Dallas et al Perit Dial Int. 2004;24:542-6</td>
<td>PD</td>
<td>Icodextrin</td>
<td>33% ↑ long dwell ultrafiltration and 29% ↑ 24 hr ultrafiltration</td>
</tr>
<tr>
<td>Martikainen T, et al.</td>
<td>PD</td>
<td>Icodextrin and AA vs, Glucose</td>
<td>Improved glucose and lipid metabolism (↑Glucose oxidation, ↓ lipid oxidation)</td>
</tr>
<tr>
<td>Furuya R, et al.</td>
<td>Non-DM PD</td>
<td>Icodextrin vs. Glucose</td>
<td>↓ leptin, insulin, and TG; ↑ adiponectin &amp; HDL. Improved insulin sensitivity</td>
</tr>
<tr>
<td>Authors</td>
<td>Patient population</td>
<td>Prescription</td>
<td>Results with Icodexin</td>
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<tr>
<td>Paniagua R, et al. <em>Perit Dial Int.</em> 2009;29:422-432</td>
<td>DM PD High, High Average Transport</td>
<td>Icodexin vs. Glucose</td>
<td>Better metabolic control; required less insulin and had better glycemic control. Also better BP control and reduction in total body water and ECF volume</td>
</tr>
<tr>
<td>Dousdampanis P et al. <em>Int Urol Nephrol.</em> 2011;43:203-9</td>
<td>9 PD with poor UF</td>
<td>2 Icodexin exchanges per day</td>
<td>Reduced body wt. in 6 of 9 patients. Mean BP was reduced. Mean creatinine ↑slightly. Serum Na+ ↓ from baseline at 3 &amp; 6 mo. In patients with DM, avg. daily insulin req’t were reduced after 6 mo</td>
</tr>
<tr>
<td>Gobin J et al. <em>Blood Purif.</em> 2008;26:279-83</td>
<td>PD High, High Average Transporters</td>
<td>2 Icodexin/day</td>
<td>Reduction in mean glucose exposure from baseline and 3 and 6 months.</td>
</tr>
<tr>
<td>Sav T et al <em>Perit Dial Int.</em> 2009;29:443-9</td>
<td>PD</td>
<td>2 Icodexin/day</td>
<td>Significant reduction in left ventricular mass by end of 3rd month. Mean BP significantly reduced. No ↓ in dialysis adequacy or any side effects.</td>
</tr>
<tr>
<td>Sav T et al <em>Nephrology</em> 2010;15:307-213</td>
<td>28 High or High Average Transporters</td>
<td>One or twice daily Icodexin</td>
<td>Both groups significant ↓ brain natriuretic peptide, LV dysfunction, &amp; cardiothoracic index. Improvement in ejection fraction. The percentage of Δ significantly better in the twice daily group.</td>
</tr>
<tr>
<td>Authors</td>
<td>Patient population</td>
<td>Prescription</td>
<td>Results with Icodextrin</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Takatori Y, et al. Clin J Am Soc Nephrol. 2011;6:1337-44.</td>
<td>DM PD</td>
<td>Icodextrin vs. Glucose</td>
<td>After 2 yrs follow-up eval, technique survival was 71.4% for Icodextrin group &amp; 45.0% Glu group. 3 patients in Icodextrin and 9 in Glu group withdrew due to uncontrolled fluid volume excess caused by insufficient UF.</td>
</tr>
<tr>
<td>Hiramatsu T et al Adv Perit Dial 2013;29:9-13</td>
<td>DM PD</td>
<td>Icodextrin vs. Glucose</td>
<td>Left ventricular mass index (LVMI) and aortic valve calcification (AVC) score significantly ↓ &amp; daily phos elimination was significantly ↑ in Ico group. Mean daily phos. elimination significantly and negatively correlated with the amelioration in LVMI and AVD score.</td>
</tr>
<tr>
<td>Martikainen TA Perit Dial Int. 2005;25:453-60</td>
<td>PD</td>
<td>Icodextrin or AA vs. Glucose</td>
<td>Icodextrin and especially AA may lead to preservation of mesothelial cell mass &amp; host defense. However activation of systemic and peritoneal inflammation may appear during use of Icodextrin and to a lesser extent during use of AA.</td>
</tr>
<tr>
<td>Moriishi M et al. Perit Dial Int. 2008;28 Suppl: S96-100</td>
<td>PD</td>
<td>Icodextrin vs. Glu</td>
<td>Among other data, markers of inflammation measured were markedly elevated after switching from Glu to Icodextrin &amp; remained high after switch back to Glu. Icodextrin may induce an inflammatory reaction in peritoneum.</td>
</tr>
</tbody>
</table>
Hypoalbuminemia & creatinine (pts on PD ≥ 12 months) are strongly predictive of poor outcomes in PD patients as well as presence of malnutrition.

Factors unique to PD patients influence potential for PEW: albumin losses and turnover; RRF; prevalent GI issues, glucose absorption; incompatibility of IPN solutions to the peritoneal membrane; transporter type; and peritonitis.

Expert renal nutrition researchers provide an algorithm for malnourished patients inclusive of ONS, enteral feeding via PEG, and IPN.

Consistent favorable response to ONS in PD is challenging due to noncompliance and/or intolerance. Limited information exists on tube feeding.

IPN is a safe & effective dialysate for hypoalbuminemic PD patients who fail to respond to oral/enteral interventions. Studies have found improvements in serum proteins, normalized plasma AA patterns, improved N2 balance & MAMC/LBM.

Alternative dialysate solution Extraneal has demonstrated clinical benefits and can be considered for inclusion in the PD prescription per discretion of the nephrologist. Long term studies are needed to fully assess impact on peritoneum.
ANY QUESTIONS?