Management of Malnutrition in the Hemodialysis Population

Presented by: Christine Nash, MSc (C), RD

## Overview

- Defining Protein-Energy Malnutrition (PEM)
- Contributory Factors
- Methods to Identify PEM
- □ Management of PEM
  - Traditional
  - Non-traditional
- Conclusion

# 

### □ K/DOQI perspective on nutrition:

"Provision of adequate nutrition is a key component of the prevention and treatment of protein-energy malnutrition (PEM) in patients receiving dialysis"

http://www.kidney.org/professionals/kdoqi/guidelines/nut\_intro.html

## Introduction Defining Protein-energy Malnutrition

Protein-energy Malnutrition (PEM)

"The lack of sufficient energy or protein to meet the body's metabolic demands, as a result of inadequate intake, increased demands due to disease, increased nutrient losses...or a combination of these factors."

Kuhlman et al. Nephrol Dial Transplant. 2007;22(Suppl 3):13-19

## Introduction Defining Protein-energy Malnutrition

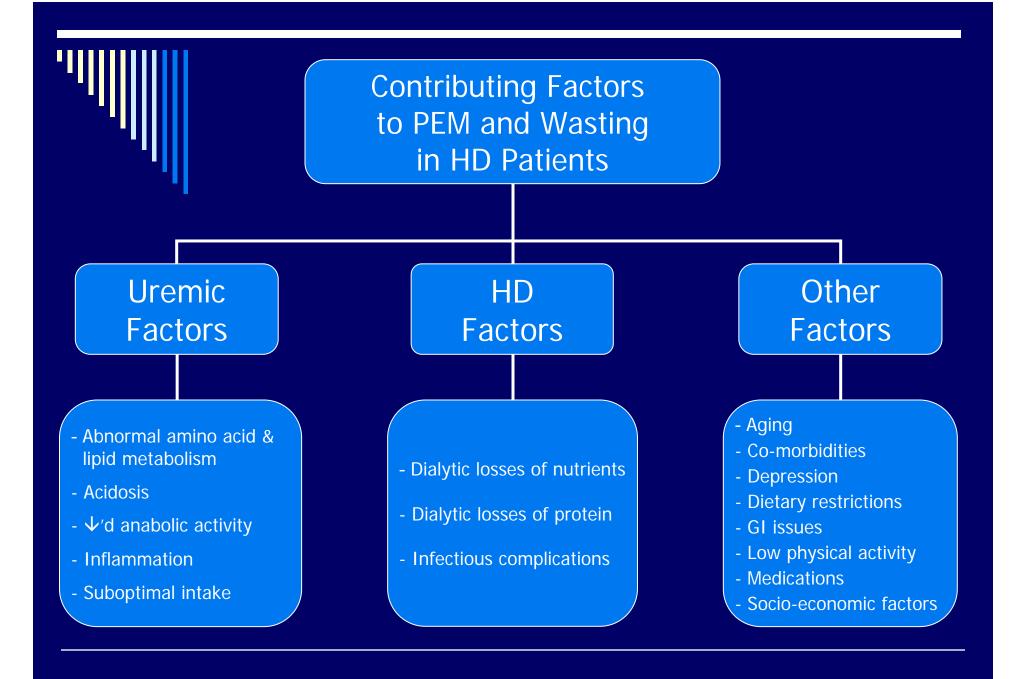
Protein-energy Malnutrition (PEM)

- Powerful predictor of morbidity and mortality
- Prevalence between 18-70%
- Pathogenesis is multi-factorial

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□ Conclusion



Inflammation is thought to play an integral role in the development of PEM:

- Insulin resistance
- Appetite suppression

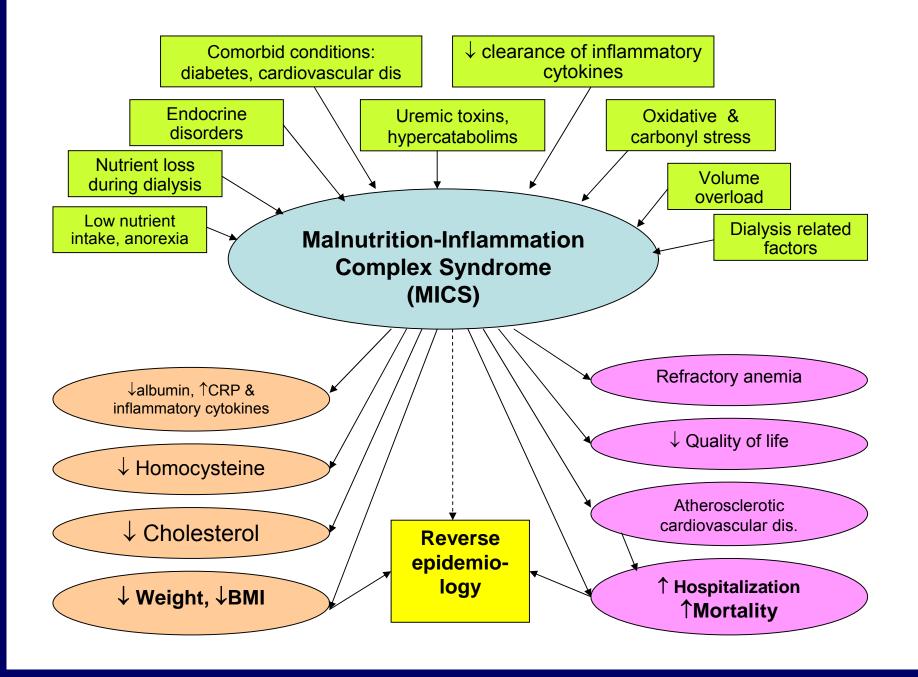
□ ↑'d protein hydrolysis / muscle protein breakdown

- Activation of the ATP-ubiquitin-proteasome proteolytic pathway
- Insulin resistance
  - Mechanisms are not fully understood
  - May ↓ anabolic action of insulin on skeletal muscle

- Resting energy expenditure (REE)
  - Accounts for 60-80% of total energy expenditure
  - Significant correlations found between inflammation, malnutrition, and *\u03c6*'d REE
- Appetite suppression
  - Mechanisms are not well understood
    - Anorexigenic substances can produce disorders of the hunger-satiety cycle

#### PEM and Inflammation

- Studies suggest these 2 factors are:
  - Independent predictors of hospitalization in HD patients
  - Associated with higher CVD mortality rates in HD patients



## Overview

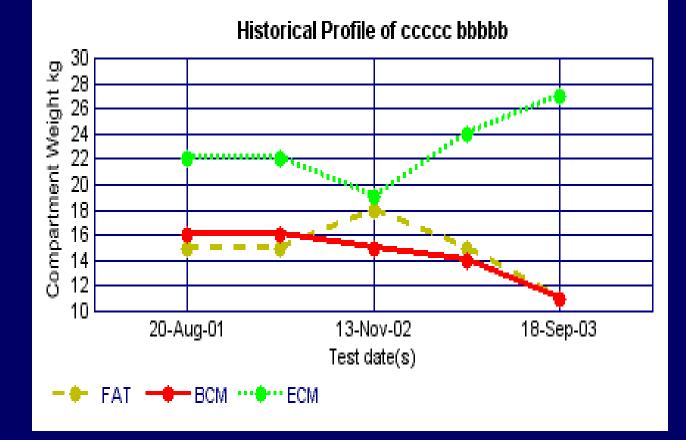
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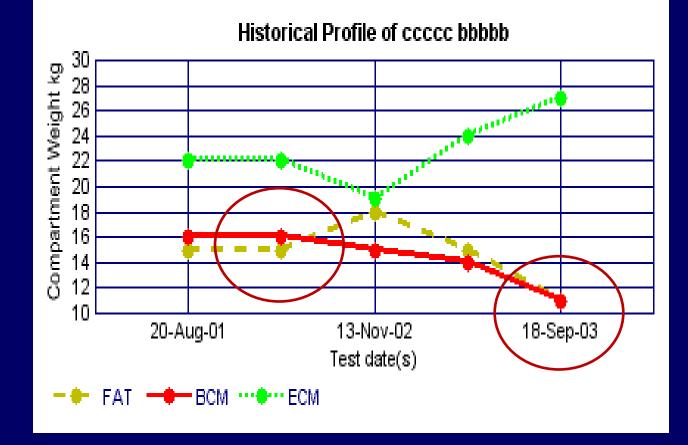
□ Conclusion

- Anthropometrics
- Biochemical markers
- Bioelectrical impedance analysis (BIA)
- Diet history
- Subjective global assessment (SGA)



- Quick, non-invasive, and inexpensive
- Used in the clinical evaluation of patients OVER TIME for assessment of nutritional status
- Taken at baseline & repeated every 6 months in conjunction with SGA





### □ SGA

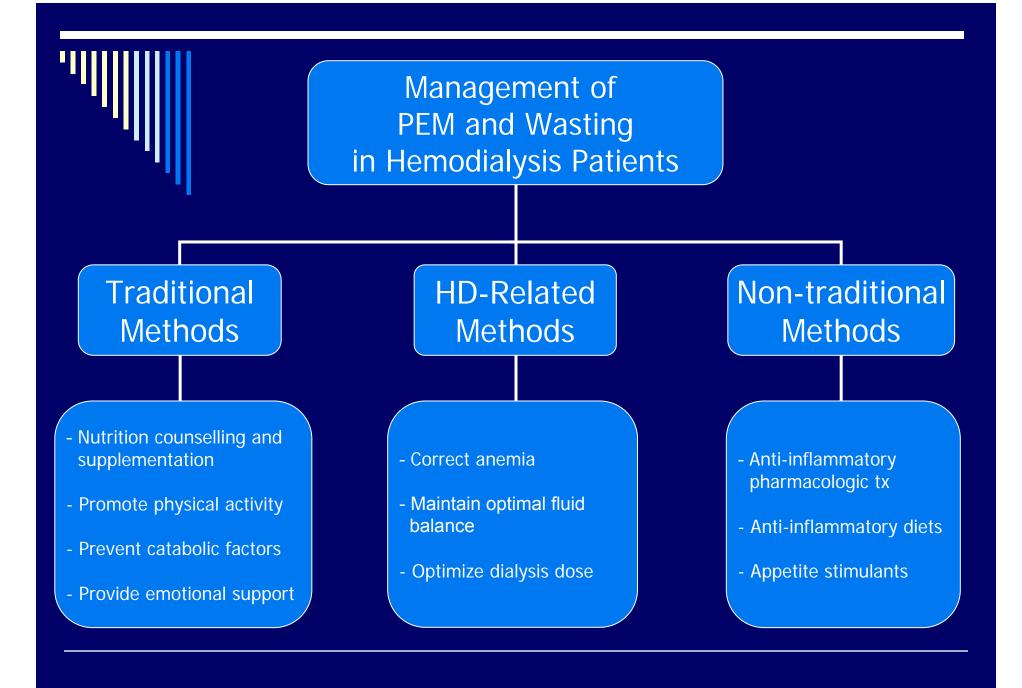
An inexpensive, easy, & reproducible way to assess nutritional status



UHN Subjective Global Assessment Scoring Sheet						
Patient Name:	Patient ID:	Date:				
Part 1: Medical History					A Score	
1. Weight Change				Α	BC	
A. Overall change in past	6 months: kgs. (dry	weight)				
B. Percent change:	gain -< 5% loss					
	5 - 10% loss					
<u></u>	> 10% loss					
C. Change in past 2 week	s: increase					
	no change					
	decrease					
2. Dietary Intake						
A. Overall change:	appetite					
	no change	change				
B. Duration:	weeks					
C. Current intake:	suboptimal solid diet	full li	quid diet			
	hypocaloric liquids	star	vation			
	supplements	how long				
3. Gastrointestinal Symptoms	(persisting for > 2 weeks)					
none; nause	a; vomiting; diarrhe	a; anorexi	a			
swallowing / dental	problems; constipation;	meat aversio	on			
4. Functional Impairment (nut	ritionally related)					
A. Overall impairment:	none					
	moderate					
	severe					
B. Change in past 2 weeks	: improved					
	no change					
	regressed					
			S	GA Score		
Part 2: Physical Examinat 5. Evidence of: Loss of subcut			Normal M	ild Moderate	Severe	
Muscle wasting Edema						
Lucind						
Part 3: SGA Rating (check one) Well-Nourished: Mildly-Moderately Malnourished: Severely Malnourished:						
Well-Nourished:	Mildly-Moderately Malnourished:	□ B-	Severely Malne □ C+	□ C		

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Management of PEM: *Traditional: Supplementation* 

Oral Route

> High protein/high kcal supplements

Enteral Route

- > Nasogastric (NG) tube
- Percutaneous endoscopic gastrostomy (PEG) tube
- Parenteral Route
  - Intradialytic parenteral nutrition (IDPN)

## Management of PEM: High Protein/High Kcal Supplements

Nutritional Composition of Canadian Supplements

PRODUCT	Novasource Renal	Resource 2.0	Boost High Kcal	Boost High Pro	Boost Diabetic	Boost Pudding
Serving Size	237 ml	237 ml	237 ml	237 ml	237 ml	142 g
Energy (kcal)	475	475	360	240	190	240
Protein (g)	17.4	20	14	15	16	7
Fat (g)	24.1	21	14	6	7	9
CHO (g)	47.3	52	45	33	16	33
Sodium	210	190	170	170	180	125
Phosphorus (mg)	154	250	300	300	300	200
Potassium (mg)	192	360	380	380	80	250

Management of PEM: Oral Supplementation

- Bossola et al, 2010 (J Ren Nutr)
  - Reviewed available literature on oral supplementation in the HD population
    - ✓ RCTs
    - Comparative non-randomized clinical trials
    - Single-arm studies
  - Results
    - Improvement in nutritional parameters
    - Insufficient data on clinical outcome

Management of PEM: *High Protein/High Kcal Supplements* 

#### Pros

- Variety of flavours
- Meets high protein/high calorie needs
- Can individualize to meet therapeutic needs

#### Cons

- Palatability
- Nutrient density may impact meal consumption

Management of PEM: Enteral Nutrition

Dialysis-related PEM not an indication for enteral nutrition

Used 1° in patients who have a functioning GI tract and develop concurrent diseases

✓ NG tube <30 days</p>

✓ PEG tube >30 days

### □ Purpose:

Supplemental nutrition for malnourished patients receiving hemodialysis

Indication for use:

Patients receiving hemodialysis who demonstrate poor nutritional status and are at high risk for malnutrition

## Management of PEM:

Intradialytic Parenteral Nutrition (IDPN)

### □ Clinical criteria to indicate IDPN:

- > Weight loss
  - $\checkmark \ge 10\%$  ideal body weight (IBW)
  - $\checkmark \ge 20\%$  usual body weight (UBW)
- Dietary intake
  - ✓ protein < 0.8 g/kg
  - ✓ kcal < 25 kcal/kg</p>

➢ SGA "C"

## Management of PEM:

Intradialytic Parenteral Nutrition (IDPN)

#### □ Clinical criteria to indicate IDPN:

- Nutrition bloodwork
  - ✓ urea < 15 mmol/L</p>
  - $\checkmark$  albumin < 35 g/L
  - ✓ creatinine ↓'ing over 3 month period
- Clinical examination consistent with moderate to severe malnutrition
- > Oral/enteral supplementation is unsuccessful

### Optimal use of IDPN

- > Observed in patients who are able to maintain:
  - ✓ 70-80% kcal requirements
  - 40-50% protein requirements

#### Outcomes:

- >  $\Lambda$ 's in appetite, weight gain, nutrition bloodwork
- Improved nutrition status within 90-180 days

Management of PEM: Intradialytic Parenteral Nutrition (IDPN)
Standard Composition (Canada):

Amino acids 4.25%
Dextrose 10-25%
Amino acids / dextrose solution = 1 litre

3) Lipids:

10% lipid (500 ml) OR 20% lipid (250 ml)

Individualized to the patient and varies between hospital sites

## Management of PEM:

Intradialytic Parenteral Nutrition (IDPN)

#### Sample Calculations

Volume	Concentration	Grams	Calories Provided	
1 litre	10 - 25% Dextrose	100 – 250 g Dextrose	340 – 850 kcal	
	4.25 - 6% Amino acids	42.5 – 60 g Amino acids	170 – 240 kcal	
250 mls	20% Lipid	50 g Lipid	- 500 kcal	
500 mls	10% Lipid	50 g Lipid		
Total volume: 1250 – 1500 mls			Total energy: 1010 – 1590 kcal	

#### Dextrose:

- Serum glucose levels may require monitoring
  - Can add 5 units insulin to 1L IDPN solution as an initial dose
  - Increase by 2 unit increments until target is achieved

#### □ Lipids:

Triglyceride levels should be monitored closely

 50% increase between 1<sup>st</sup> and 2<sup>nd</sup> treatments may indicate lipid intolerance

☐ Vitamins/Minerals/Electrolytes:

- Serum potassium, magnesium, and phosphorus require weekly monitoring
- May cause muscle cramping

Administration and monitoring:

Infusion pump maintained at a constant rate

> IDPN volume / IDWG determines fluid removal

#### □ Advantages:

- No additional vascular access required
- Provides nutrition with little interference to pt's daily activities
- Ability to remove infused liquid during dialysis

#### Disadvantages:

- Unable to provide sole source of nutrition
- Cost of treatment
- Lacks conclusive evidence of efficacy

## Management of PEM:

Intradialytic Parenteral Nutrition (IDPN)

#### □ Majority of studies characterized by $\ge$ 1 limitation:

- Small sample size
- Short study duration
- Retrospective
- No control group
- Criteria for PEM diagnosis not adequately described
- IDPN solutions / doses not standardized
- > Oral intake / supplements not controlled or not monitored
- Dialysis dose not described / standardized
- Comorbid conditions / relevant clinical characteristics not described

## IDPN – Nonrandomized Studies

Study	Design	Duration	Parameters	Outcome
Heidland and Kult, 1975	18 pts: 16.75 g EAA,100 kcal	60 weeks	Albumin; total protein, transferrin	Increase in all parameters after 16 wks in 13 pts Decrease 6 wks post-therapy
Bilbrey and Cohen, 1989 *	20 pts: 50 g of EAA + NEAA, 50 g lipids, 125 g glucose	3 months minimum	Bloodwork, MAMC	Increase in MAMC, no change in bloodwork
Chertow et al, 1994	1679 pts: 1.2 g/kg pro + 15 kcal/kg 22,517 pts: no treatment	12 months or until death	Albumin, URR, odds of death	Decrease in mortality in IDPN pts with alb ≤ 33 g/L
Capelli et al, 1994	50 pts: 50 g EAA, 50 g lipids, 125 g glucose 31 pts: dietary supplements	9 months	Albumin, BW, mortality	32/50 tx pts + 16/31 untx pts survived
Hiroshige et al, 1998 *	10 pts: 200 ml each of 50% gluc, 7% EAA, 20% lipids 18 pts: dietary counselling	12 months	BW, BMI, MAMC, Alb, transferrin, aa, mortality	All IDPN pts survived during study period
Cherry, 2002 *	24 pts: 10% aa, 50% gluc, 20% fat	4.3 months (mean)	Albumin, dry weight	Increase in albumin + dry weight

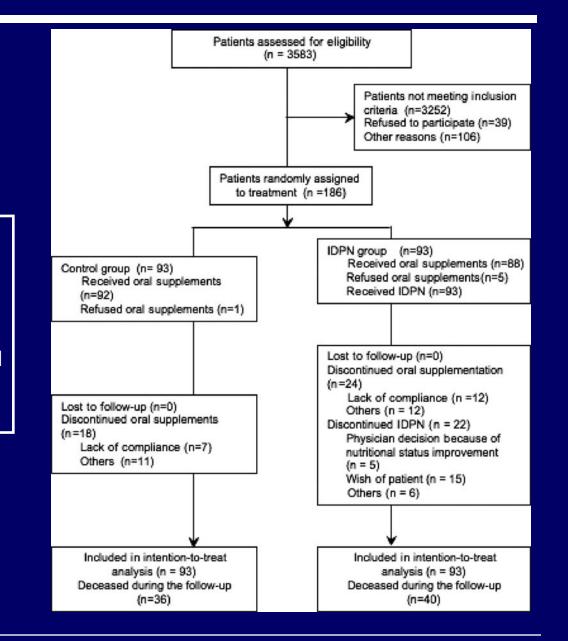
### IDPN – Randomized Studies

Study	Design	Duration	Parameters	Outcome
Toigo et al, 1989	11 pts: 26.5 g modified EAA 10 pts: 24.0 g EAA + NEAA	6 months	Albumin; nerve conduction velocity	Decrease in albumin in both groups
Cano et al, 1990 *	12 pts: 0.08 g of N/kg + 1.6 g/kg lipids per HD session 14 pts: no intervention	3 months	Appetite, MAMC, and bloodwork	Increase in kcal + protein intake in IDPN treated pts
McCann et al, 1999	19 pts: 70% gluc, 15% aa, 20% lipids	11 weeks	Delivered Kt/V and URR	Decrease in delivered Kt/V in pts with aa-containing IDPN
Navarro et al, 2000	17 pts	3 months	aa concentrations, nutrition status	+ net aa balance; increase in PCR, alb, transferrin
Cano et al, 2006	17 pts: olive oil-based lipid 18 pts: soybean-based lipid	5 weeks	Nutrition status, lipid, oxidative + inflammatory meas.	Similar improvement in nutrition, lipid, oxidative + inflammatory measures
Cano et al, 2007 *	89 pts: IDPN 93 pts: control	12 months	All-cause mortality, BW, BMI, hospital admissions	No difference between groups

- "French Intradialytic Nutrition Evaluation Study" (FineS) - Cano et al, 2007
  - Largest and most carefully monitored prospective RCT study of IDPN conducted
  - > 186 HD patients randomly assigned to receive or not receive IDPN for a 1 year period
    - Both groups received oral supplementation
    - ✓ All patients had  $\ge$  2 indicators of PEM

#### Figure 1.

Number of patients who entered the study, were assigned to intradialytic parenteral nutrition (IDPN) or control group, completed the protocol, and were included in intention-to-treat analysis.



Cano, N. J.M. et al. J Am Soc Nephrol 2007;18:2583-2591

"French Intradialytic Nutrition Evaluation Study" (FineS) - Cano et al, 2007

- Patients were followed up for a period of 2 years
- Both groups demonstrated similar improvements in:
  - ✓ PEM indicators
  - Hospitalization rates
  - ✓ Mortality

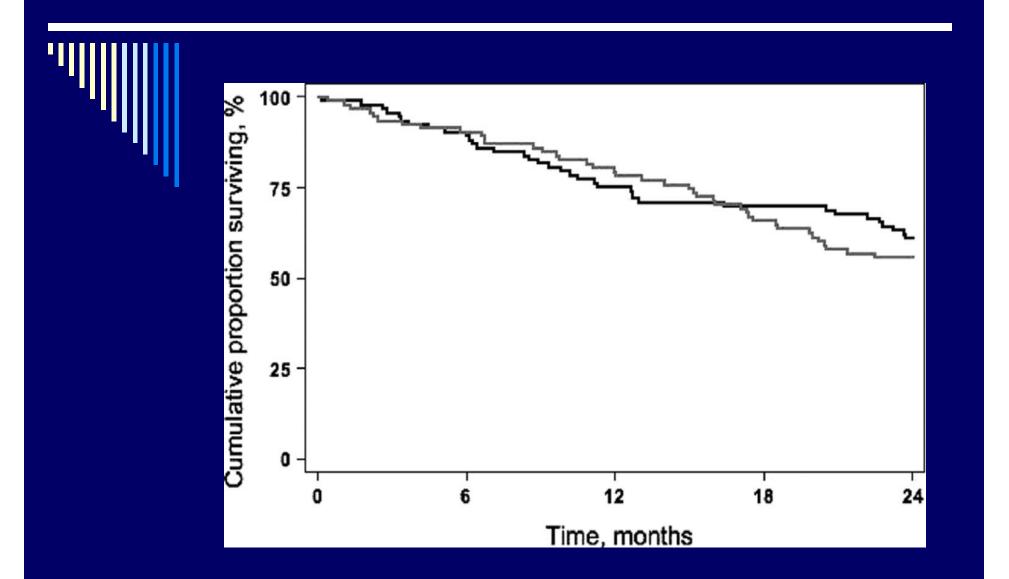
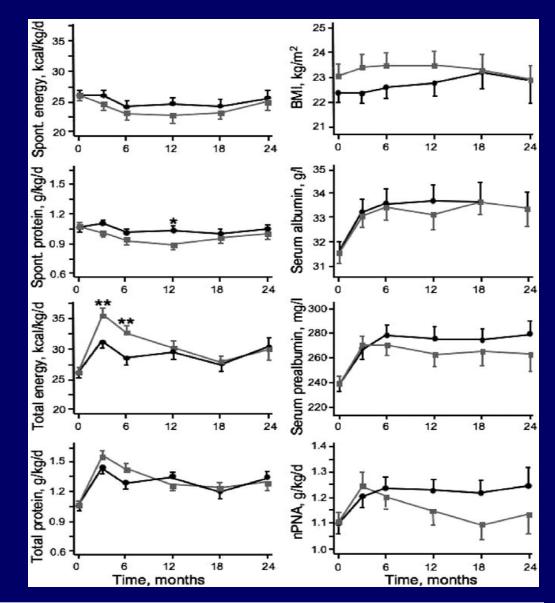


Figure 2. Kaplan-Meier survival analysis in control (black line) and IDPN (gray line) groups (NS)

Cano, N. J.M. et al. J Am Soc Nephrol 2007;18:2583-2591

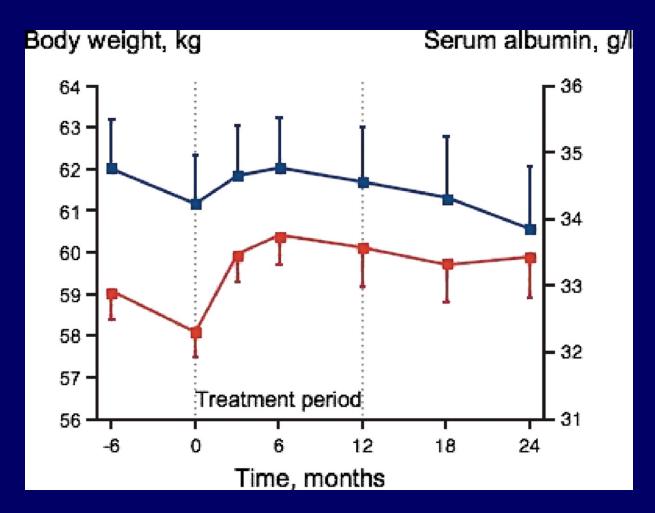
#### Figure 3.

Changes in total energy and protein intakes, body mass index (BMI), serum albumin, prealbumin, and normalized protein nitrogen appearance (nPNA) during the 2-yr follow-up in control (black line) and IDPN (gray line) groups (means {+/-} SEM)



Cano, N. J.M. et al. J Am Soc Nephrol 2007;18:2583-2591

Figure 7. Body weight (blue line) and serum albumin (red line, n = 121) changes before, during, and after nutritional therapies



Cano, N. J.M. et al. J Am Soc Nephrol 2007;18:2583-2591

 "French Intradialytic Nutrition Evaluation Study" (FineS) - Cano et al, 2007

Study Conclusion:

No added benefit of giving IDPN with oral supplements

#### Considerations:

 True impact of IDPN on patient outcomes difficult to assess, as both groups received nutrition intervention

□ IDPN Research Caveats:

- ➤ Lack of uniformity with study designs and patient populations
   → difficult to compare
- Outcomes measured are sensitive to disease process, fluid status, and inflammation (ie. albumin)
- > Total nutrient intake is often not quantified
- Clinical judgement should be based on the individual with scientific literature to guide decision-making

□ Case: Miss JC

> 18 yr old female

> ESRD 2° Schimke Immuno Osseous Dysplasia (SIOD)

✓ Prevalence 1:1 000 000 to 1:3 000 000

++ clinical manifestations (including renal)

"Quite an extensive past medical history, despite her tender young age"

Intradialytic Parenteral Nutrition (IDPN)

#### Medical Timeline (HSC)

Date	Medical Event	Outcome	Dietary Intake	Weight
Jul' 2005	Renal failure	PD initiated	Fair	↓'d to 36.5 kg
Sept' 2006	Kidney transplant	Kidney transplant	Good	个'd to 45 kg
Oct' 2007	Graft failure 2° BK virus	HD initiated	Fair	↓'d to 36 kg
May 2008	Not indicated	Nephrectomy	Poor	↓'d to 34 kg
Oct' 2008	Planned G-tube insertion - PEM	Insertion failed 2° ascites	Poor	$\downarrow$ 'd to 32.5 kg

Intradialytic Parenteral Nutrition (IDPN)

#### Medical Timeline (HSC $\rightarrow$ SMH $\rightarrow$ TGH)

Date	Medical Event	Outcome	Dietary Intake	Weight
Feb' 2009	∱'d PEM	IDPN initiated	Fair	32.5 kg
Mar' 2009	Turned 18 yrs old Pneumonia	Transferred to SMH – IDPN cont.	Fair	32.5 kg
May 2009	C Difficile	Transferred to TGH – IDPN held	Fair	↓'d to 31.5 kg
Jun' 2009 (beginning)	C Difficile	↑'d PEM – IDPN initiated 3/wk	Poor	↓'d to 29.5 kg
Jun' 2009 (end)	Failure to thrive	IDPN ∱'d to 4/wk	Poor	↓'d to 27.5 kg

- Case: Miss JC (June 2009)
  - Medical issues: complex disease manifestation
  - Nutrition issues: severe PEM; had lost 15% of BW in 12 weeks
  - Socioeconomic issues: depression, social/financial difficulties
  - Medication issues: dependency on pain meds
  - <u>Physical issues</u>: no longer able to ambulate independently

Intradialytic Parenteral Nutrition (IDPN)

#### **IDPN** Timeline (TGH)

Date	IDPN Nutrition	Supplement	Intake	Weight
Jun.24/09	130 cc/hr x 3 hrs + 60 cc x ½ hr 844 kcal / 35 g protein	Carnation Instant Breakfast BID	Fair	27.5 kg
Jul.30/09	160 cc/hr x 3 hrs + 80 cc x ½ hr 1051 kcal / 43 g protein	Carnation Instant Breakfast BID	Fair	∱'d to 28.5 kg
Sep.11/09	160 cc/hr x 3 hrs + 80 cc x ½ hr 1051 kcal / 43 g protein	Carnation Instant Breakfast OD	Good	∱'d to 31.8 kg
Sep.25/09	↓'d to 3 x wk	Carnation Instant Breakfast OD	Good	∱'d to 33.5 kg
Oct.14/09	IDPN Discontinued	Carnation Instant Breakfast OD	Good	∱'d to 34.0 kg

Intradialytic Parenteral Nutrition (IDPN)

### Case: Miss JC

- > Outcomes:
  - ✤ 23% increase in body weight
  - Increased appetite; protein and energy intake
  - Improvement in:
    - body image
    - mood
    - \* physical abilities

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Cannabinoids

Corticosteroids

Cyproheptadine

Megestrol acetate

#### Cannabinoids

- Evaluated in patients with cancer, HIV, and Alzheimer's disease
  - $> \uparrow$ 'S appetite and reduces weight loss in cancer patients
  - Promotes weight gain in individuals with HIV and Alzheimer's disease
- Used as a comfort measure in palliative patients

Corticosteroids

Studies have demonstrated improved appetite and well-being in patients with cancer

Does not provide a lasting effect

Cyproheptadine

Primarily been used as treatment for cancerinduced weight loss and anorexia

Megestrol acetate

> Semi-synthetic progestational steroid

#### > Used primarily as an appetite stimulant

 Has been shown to effectively improve appetite and nutrition status in the HIV and cancer population

> Exhibits anti-inflammatory properties

Megestrol acetate

> Appetite-stimulating and anti-inflammatory properties make it a potentially optimal agent for treating "MICS" in dialysis patients

Approximately 0.5-1.5% dialysis patients on Megace in the U.S.

Canadian statistics???

Megestrol acetate

Safety and side-effect profile in the dialysis population a limiting factor

Major route of elimination is urinary excretion

Dialyzability of megace?

Studies in the renal population are limited

Non-traditional – Appetite Stimulants

Reference	# of Pts	Megace Dose	Duration	Effects
Lien et al, 1996	16	40 mg / day	?	1 Arian Arian (sig)
Burrows et al, 1999	1	320 mg to start; ↑'d to 560 mg	24 weeks	Body fat $\uparrow$ 'd 163%, lean mass $\downarrow$ 'd 10.6%; stable albumin; no side effects
Boccanfuso et al, 2000	17	800 mg / day	5-6 months	↑'d wt, stable alb; ++side effects only 3 pts left by end of study
Costero et al, 2004	32	160 mg / day	Mean of 6 months	个'd wt (sig) and 个'd alb (not sig) No side effects
Rammohan and Kalantar, 2005	10	400 mg / day	16 weeks	<ul> <li>↑ in wt, body fat, alb (sig)</li> <li>↓'d CRP; no side effects</li> </ul>
Monfared et al, 2009	11 Megace 11 Controls	80 mg / day	2 months	<ul> <li>↑'d albumin in Megace group</li> <li>↓'d albumin in control group</li> </ul>

"Report of a Pilot, Double-blind, Placebo-controlled study of Megestrol Acetate in Elderly Patients with Cachexia" (Yeh et al, 2010)

- <u>Objective</u>: Examined effects of megestrol acetate versus placebo, and resistance exercise on:
  - ✓ Weight
  - Lean body mass (LBM)
  - Quality of life (QOL)

- ✓ Ability to exercise
- Pro-inflammatory cytokines
- Anti-inflammatory cytokines

- "Report of a Pilot, Double-blind, Placebo-controlled study of Megestrol Acetate in Elderly Patients with Cachexia" (Yeh et al, 2010)
  - <u>Intervention</u>: Megestrol acetate 800 mg/day (or placebo)
     + weight resistance therapy x 20 weeks
  - > 22 HD patients randomly assigned to intervention or control group
    - Source Both groups received weight resistance therapy 2 x wk

"Report of a Pilot, Double-blind, Placebo-controlled study of Megestrol Acetate in Elderly Patients with Cachexia" (Yeh et al, 2010)

<u>Results</u>

Intervention group:

- $\uparrow$ 'd body fat (p=0.018) and total body weight (p=0.044)
- $^{\circ}$   $^{\prime}$ d sense of well-being, appetite, and ability to exercise

✓ Both groups:

No statistical significance in any cytokine measures

#### Table 2.

**Table 2.** Comparison of Outcome Changes FromBaseline to Week 24 in MA Compared WithPlacebo Group

	Mean (SD) Change in Outcome			
Outcome	MA Group	Placebo Group	P	
Weight (pounds)	11.1 (2.8)	-1.5 (2.7)	.02	
Fat (pounds)	6.2 (1.9)	-0.4 (1.7)	.04	
Appetite	1.3 (0.8)	0.5 (0.3)	NS	
Sense of well-being	15.8 (11.4)	3.8 (12.3)	NS	
Borg RPE scale	4.7 (0.7)	0.5 (1.0)	.02	

Comparison of Outcome Changes From Baseline to Week 24 in MA Compared With Placebo Group



- PEM and chronic inflammation are highly prevalent comorbid conditions
- Exact mechanisms of these conditions are not fully understood, but are likely multi-factorial
- Traditional and non-traditional strategies may need to be utilized in combination to target this complex process

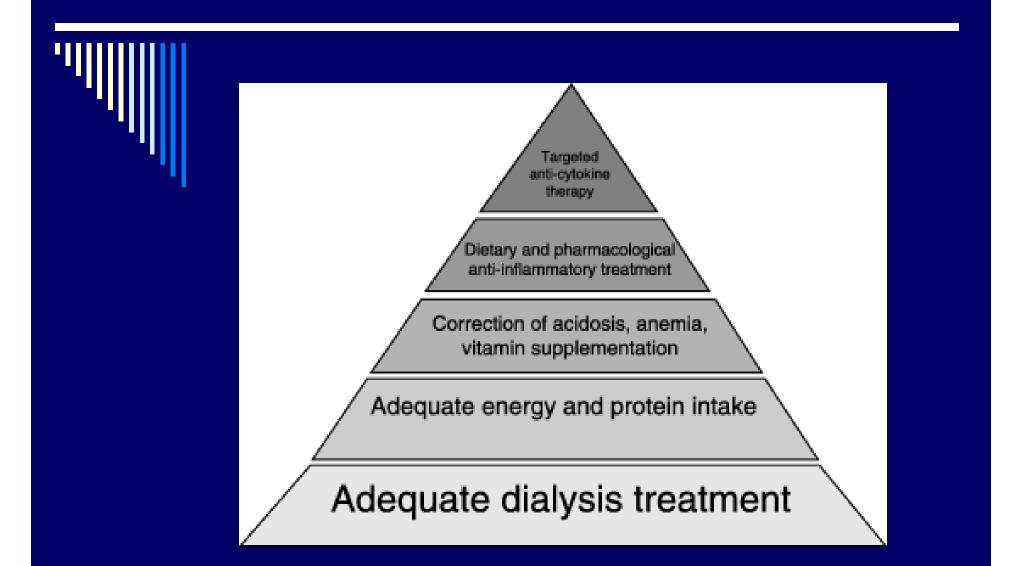


Fig. 1. Integrated therapy of wasting consists of a combination of several treatment components, each of which is necessary, but not in itself sufficient to prevent and treat uremic wasting and malnutrition.

Stenvinkel et al, Semin Dial 2004;17(6):505-15



# Questions or Comments?