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Malnutrition Matters:

Nutritional Management of Malnutrition in Chronic Kidney Disease

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Disclosures

◻ Dietitian Advisory Board, US Renal Care

◻ Honorarium provided by Nutricia North America

Neither pose a conflict of interest for this presentation

The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America

Learning Objectives

Understand clinical characteristics of malnutrition according to published standards & guidelines.

Review biomarkers in identifying and monitoring malnutrition.

Highlight pathophysiology which contributes to protein-energy wasting in chronic kidney disease (CKD).

Differentiate protein-energy malnutrition (PEM) and protein-energy wasting (PEW).

Understanding Malnutrition in CKD

Different authors, multiple different terms

Describe conditions associated with:

- Loss of muscle and fat tissue
- Malnutrition
- Inflammation

What do we call it?

Academy/ASPEN Guideline

Inflammation	Marked Response		Mild to Moderate		Not Present	
	Acute Disease/Injury		Chronic Disease Related		Starvation Related	
Clinical Characteristics	Non-Severe (Moderate) Malnutrition	Severe Malnutrition	Non-Severe (Moderate) Malnutrition	Severe Malnutrition	Non-Severe (Moderate) Malnutrition	Severe Malnutrition
Clinician should work with MD for a bilable diagnosis of malnutrition.						
(1) Energy Intake	<75% for >7 days	<50% for ≥ 5 days	<75% for ≥ 1 month	<75% for ≥ 1	<75% for ≥ 3 months	<50% for ≥ 1
Inadequate food and nutrient intake is a primary criterion for Malnutrition. Clinician must compare recent food intake and compare to estimated needs as a % of requirements over time.						
(2) Interpretation of Weight Loss	1-2% in 1 wk; 5% in 1 mo; 7.5% in 3 mos	>2% in 1 wk; >5% in mo; >7.5 in 3 mos	5% in 1 mo; 7.5% in 3 mos; 10% in 6 mos; 20% in 1 year	>5% in 1 mo; >7.5% in 3 mos; >10% in 6 mos; >20% in 1 year	5% in 1 mo; 7.5% in 3 mos; 10% in 6 mos; 20% in 1 year	>5% in 1 mo; >7.5% in 3 mos; >10% in 6 mos; >20% in 1 year
Clinician to evaluate and assess weight change over time reported as a % of weight lost from baseline. **Including the presence of under- or over- hydration**						
(3) Body Fat Loss	Mild	Moderate	Mild	Severe	Mild	Severe
Loss of subcutaneous fat (orbital, triceps, fat, ribs)						
(4) Muscle Mass Loss	Mild	Moderate	Mild	Severe	Mild	Severe
Muscle loss (temples, clavicles, shoulders, chest muscles, scapula, thigh. calf)						
(5) Fluid Accumulation	Mild	Moderate to Severe	Mild	Severe	Mild	Severe
Clinician to evaluate generalized or localized fluid accumulation (extremities, genetial edema, ascites) **Weight loss is often masked by generalized fluid retention (edema)**						
(6) Reduced Grip Strength	N/A	Measurably Reduced	N/A	Measurably Reduced	N/A	Measurably Reduced
Consult normative standards supplied by the manufacturer of the measurement device.						

Clinical Characteristics of Malnutrition

1) Energy Intake

2) Interpretation of Weight Loss

3) Body Fat Loss

4) Muscle Mass Loss

5) Fluid Accumulation

6) Reduced Grip Strength

Adapted from The Academy of Nutrition & Dietetics/ASPEN: Characteristics Recommended for the Identification of Adult Malnutrition (Undernutrition). JADA. May 2012; 112(5): 730-738.

Background: Malnutrition

Protein-Energy Malnutrition or Protein-Calorie Malnutrition

At least 2 positive criteria

Can Be Moderate or Severe

NFPE

Can be corrected nutritionally.

Review of Top Terms:			
PEM	PEW	Kidney Disease Wasting (KDW)	Cachexia

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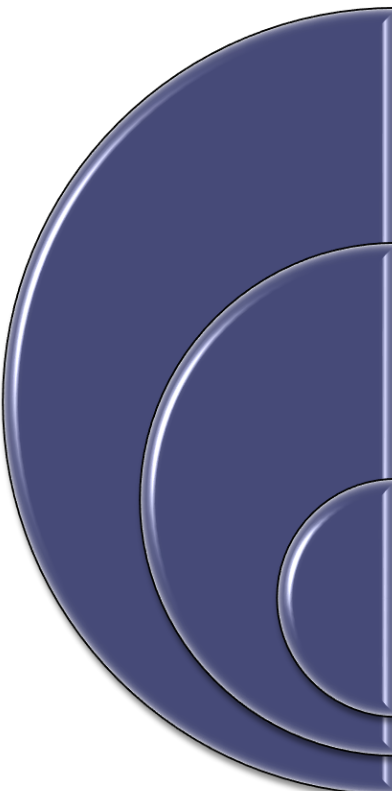NUTRICIA LEARNING CENTER

PEW: Loss of body protein mass and fuel reserves

- 3 characteristics present[1]
  - Low serum albumin, transthyretin, or cholesterol
  - Reduced body mass
  - Reduced muscle mass
- Preferred term of ISRNM[2]

Fouque, Kalantar-Zadeh, et al. Kidney Int. 2008.
International Society of Renal Nutrition and Metabolism (ISRNM)

Kidney-Disease Wasting?

	KDW	• PEW in CKD or AKI • Not a preferred term→ no indication of cause
	Cachexia	• Very severe form of PEW and metabolic depletion ONLY
PEW can also refer to mild degrees of depletion		

Nutrition Assessment in CKD

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Should be multifactorial

- Body Composition
- Biochemical Parameters
- Nutrition Screening and Assessment Tools

Nutrition Assessment: Body Composition

Limitations

Obesity
- Risk factor for HTN and DM
- Independent risk factor– CKD

Paradoxical association between obesity and improved survival, esp maintenance HD
- Reverse epidemiology

Nutrition Assessment: Biochemical Markers

Objective measures

Evaluated as indicators of[1]:

- Normal biological processes
- Pathogenic processes
- Pharmacological responses to therapeutic intervention

Ideal traits of biomarkers

Ikizler TA, Mitch WE (Eds). Handbook of Nutrition and the Kidney. 2010.

Nutrition Assessment: Tools and Instruments

Dietary intake

- FFQ
- 24-hour recall
- Food diaries

PNA

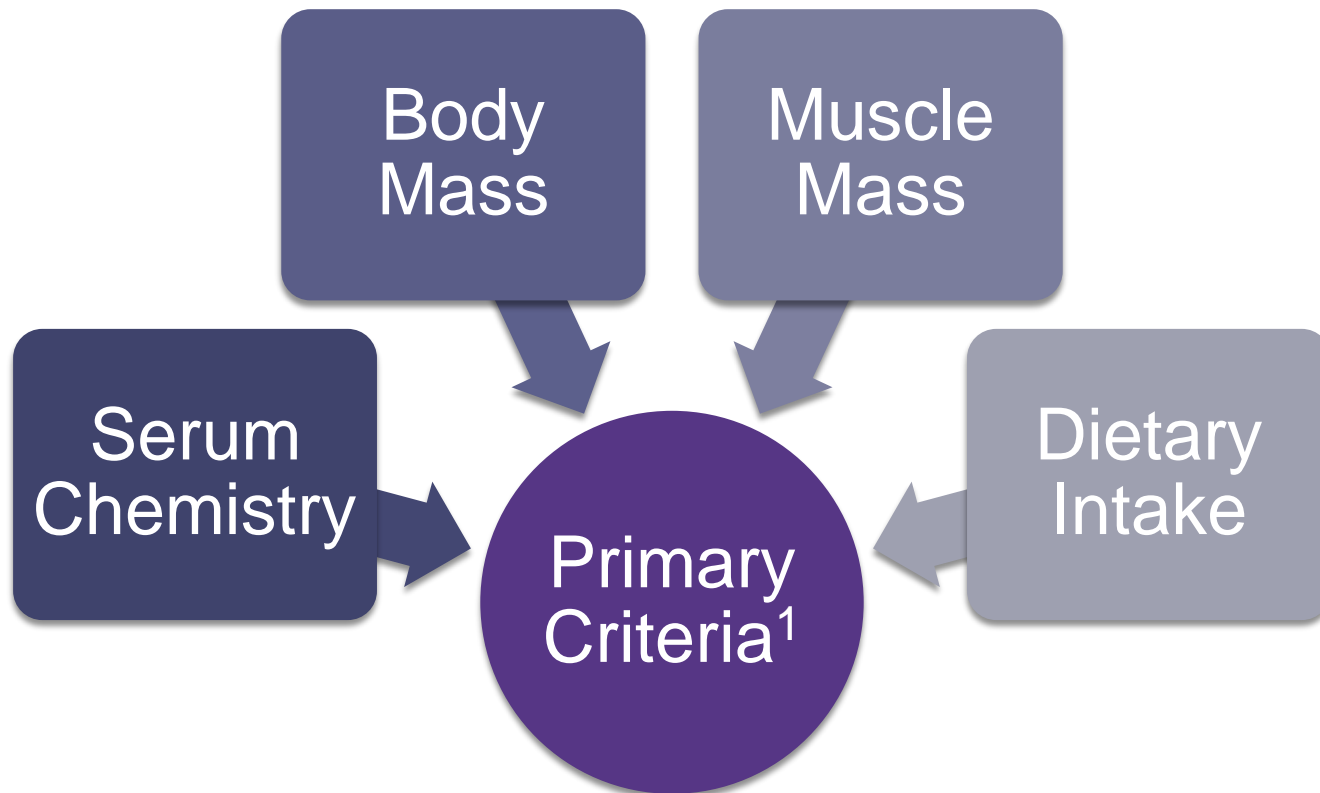## Malnutrition Assessment

- SGA
- MIS
- MNA
- OSND

Identifying Protein-Energy Wasting
And how does malnutrition fit in?

Fouque D, et al. Kidney Int. 2008.

Primary Criteria

Serum Chemistry

- Albumin < 3.8 mg/dL (BCG)
- Serum prealbumin <30 mg/dL (in dialysis Pts)
- Total Cholesterol <100 mg/dL

Body Composition Indices

- BMI<22 (if <65 years old) or BMI<23 (65+ years)
- Unintentional wt loss >5% x 3 mo, or 10% x 6 mo
- Total body fat percentage <10%

Fouque D, et al. Kidney Int. 2008.

Primary Criteria - Muscle Mass

Wasting: reduced muscle mass 5% x 3 mo, 10% x 6 mo

- Difficult to diagnose accurately/reliably

Reduced Mid-Arm Muscle Circumference

- Reduction >10% relative to 50th percentile of reference population
- Creatinine appearance* or net creatinine generation

*this is influenced by muscle mass as well as meat intake

Fouque D, et al. Kidney Int. 2008.

Unintentional decrease in dietary protein intake (DPI)

- <0.80 g/kg/day

Unintentional decrease in dietary energy intake (DEI)

- <25 kcal/kg/day

Fouque D, et al. Kidney Int. 2008.

Recommended Intake by CKD Stage

Dietary Constituent: Protein	Normal Kidney Function	Mild to Moderate CKD	Advanced CKD	Transition to Dialysis	Ongoing Dialysis, or any stage with Existing or Imminent PEW
(g/kg/day)	<1.0	<1.0 (consider 0.6-0.8 if eGFR <45)	0.6-0.8 with 50% HBV protein	0.6-0.8 (non-HD days) and 1.0 on tx days	1.2-1.4; 1.5 in some cases

Adapted from Kalantar-Zadeh K, Fouque D. NEJM. 2017.

Other Tools for Dx of PEW in AKI or CKD

Supportive Criteria[1]

- Appetite, Food Intake, Energy Expenditure
- Body Mass and Composition
- Other Laboratory Markers
- Nutritional Scoring Systems

Fouque D, et al. Kidney Int. 2008.

What Causes Protein-Energy Wasting in CKD?

Review: Functions of the Kidney

Excretion of metabolic waste products

Elimination/detox of drugs and toxins

Volume and ionic composition of fluids

Acid-base regulation

Systemic BP regulation

Production of erythropoietin

Degradation and catabolism of peptide hormones

Regulation of metabolic processes

Causes of PEW in CKD/ESRD

Anorexia

Decreased Nutrient Intake

Endocrine Disorders

Inflammation

Oxidative and carbonyl stress

Metabolic Acidosis
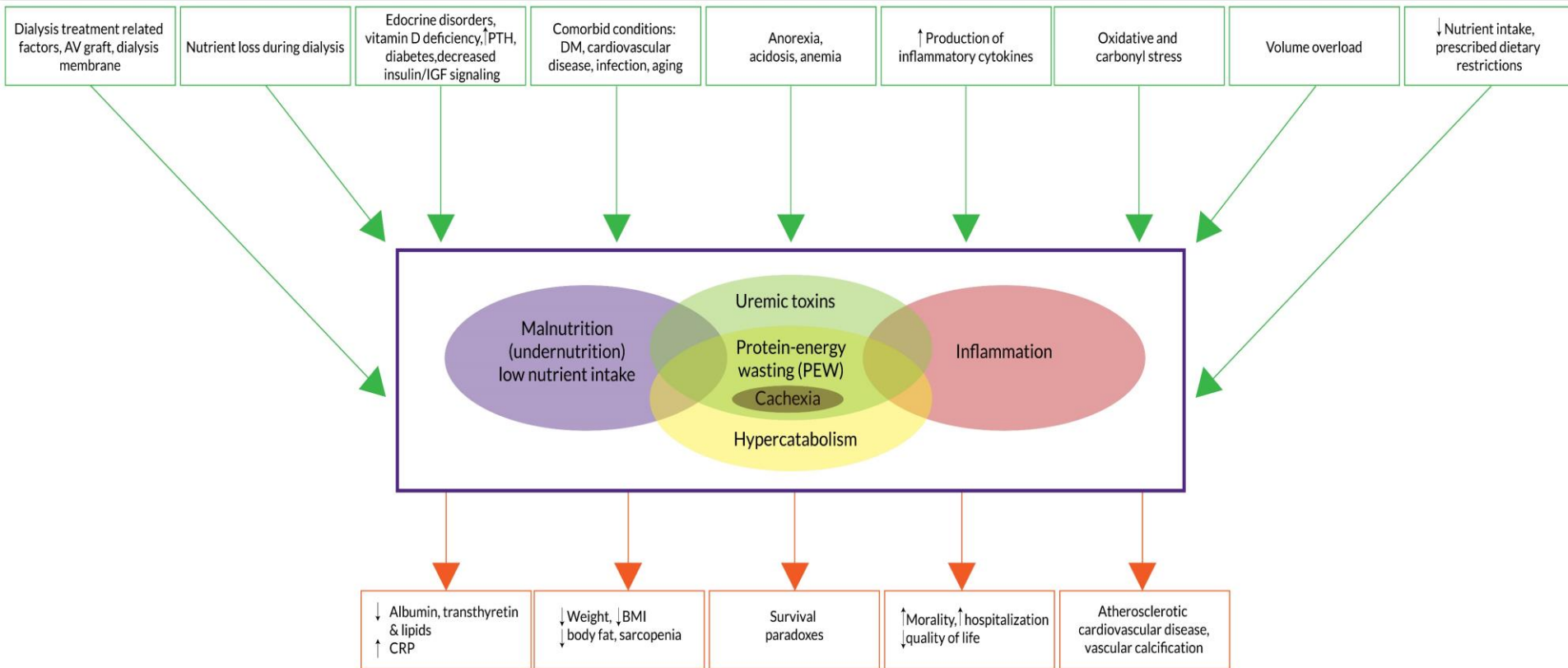
Volume Overload

Co-morbid conditions

Nutrient loss during dialysis treatment

Increased energy utilization

Abnormal protein kinetics

Kopple JD, Massry SG, Kalantar-Zadeh K. Nutritional Management of Renal Nutrition, Third Edition. 2013

Causes and Manifestations of PEW

Dialysis treatment related factors, AV graft, dialysis membrane

Nutrient loss during dialysis

Edocrine disorders, vitamin D deficiency,↑PTH, diabetes,decreased insulin/IGF signaling

Comorbid conditions: DM, cardiovascular disease, infection, aging

Anorexia, acidosis, anemia

↑Production of inflammatory cytokines

Oxidative and carbonyl stress

Volume overload

↓Nutrient intake, prescribed dietary restrictions

Malnutrition (undernutrition) low nutrient intake

Uremic toxins

Protein-energy wasting (PEW)

Cachexia

Hypercatabolism

Inflammation

↓ Albumin, transthyretin & lipids
↑ CRP

↓Weight, ↓BMI ↓body fat, sarcopenia

Survival paradoxes

↑Morality,↑hospitalization ↓quality of life

Atherosclerotic cardiovascular disease, vascular calcification

Image adapted from:
Fouque D et al. Kidney Int. 2007

Anorexia

- Uremic toxins
- Suppress appetite/intake

Decreased Nutrient Intake

- Spontaneous protein intake decreases as renal function declines[1]
- Protein and nutrition status correlate directly with eGFR[2]

Ikizler TA et al. J Am Soc Nephrol. 1995.

Kopple JD et al. Kidney Int- Suppl. 1989.
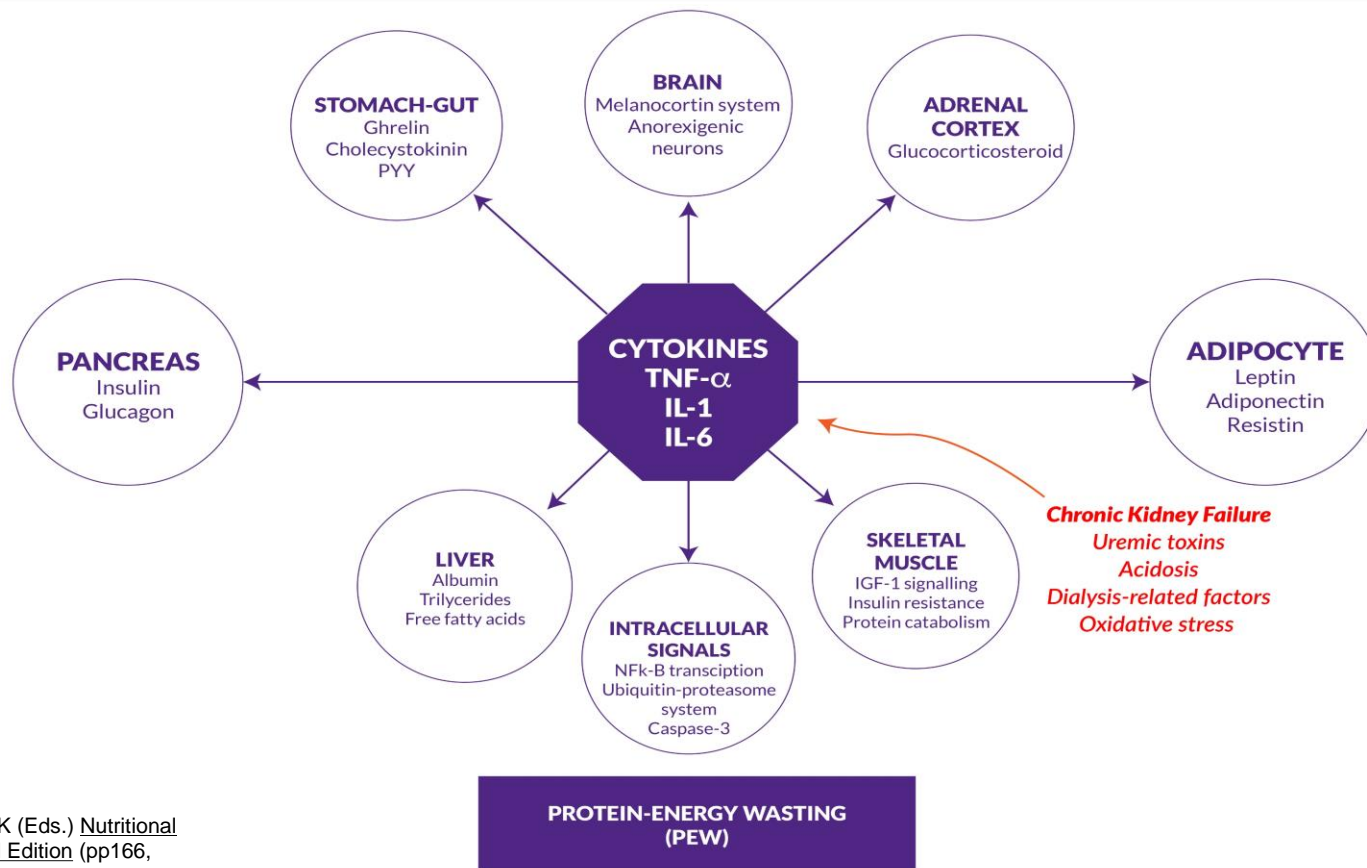
Causes and Manifestations

Endocrine Disorders

- Insulin resistance
- Decreased IGF-I
- Testosterone deficiency
- Vitamin D deficiency
- hyperparathyroidism

Inflammation

- Cytokines: TNF-a, IL-1, IL-6
  - Anorexia
- Facilitate augmented protein catabolism
  - Muscle-derived IL-6 released during tx

Cytokines in Pathophysiology of PEW

Causes and Manifestations

Oxidative and Carbonyl Stress

- Increased oxidative stress during tx→ contribute to muscle wasting
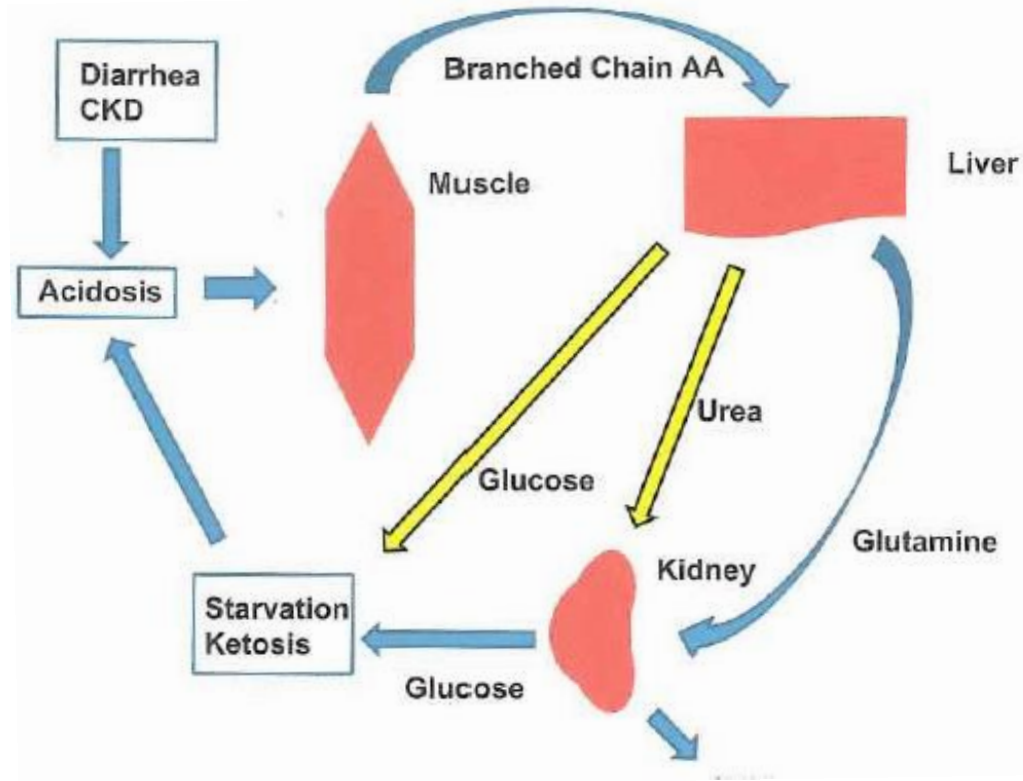- ROS and muscle atrophy

Volume Overload

- Chronic volume overload and concomitant heart failure = frequent complications of CKD
- Correlates to inflammation markers and poor nutrition

KDOQI Guidelines: bicarb at least 22 mEq/L

Observed lower risk of death[1]

Catabolic effects of metabolic acidemia

Diarrhea CKD → Acidosis → Muscle — Branched Chain AA → Liver — Glucose, Urea, Glutamine — Kidney → Glucose → Starvation Ketosis

Wu DY et al. Clin J Am Soc Nephrol. 2006.

Causes and Manifestations

Co-morbid Conditions

- May contribute to PEW in some Pts
- DM, HTN, atherosclerosis, chronic heart failure
- Malnutrition-Inflammation-Atherosclerosis (MIA)
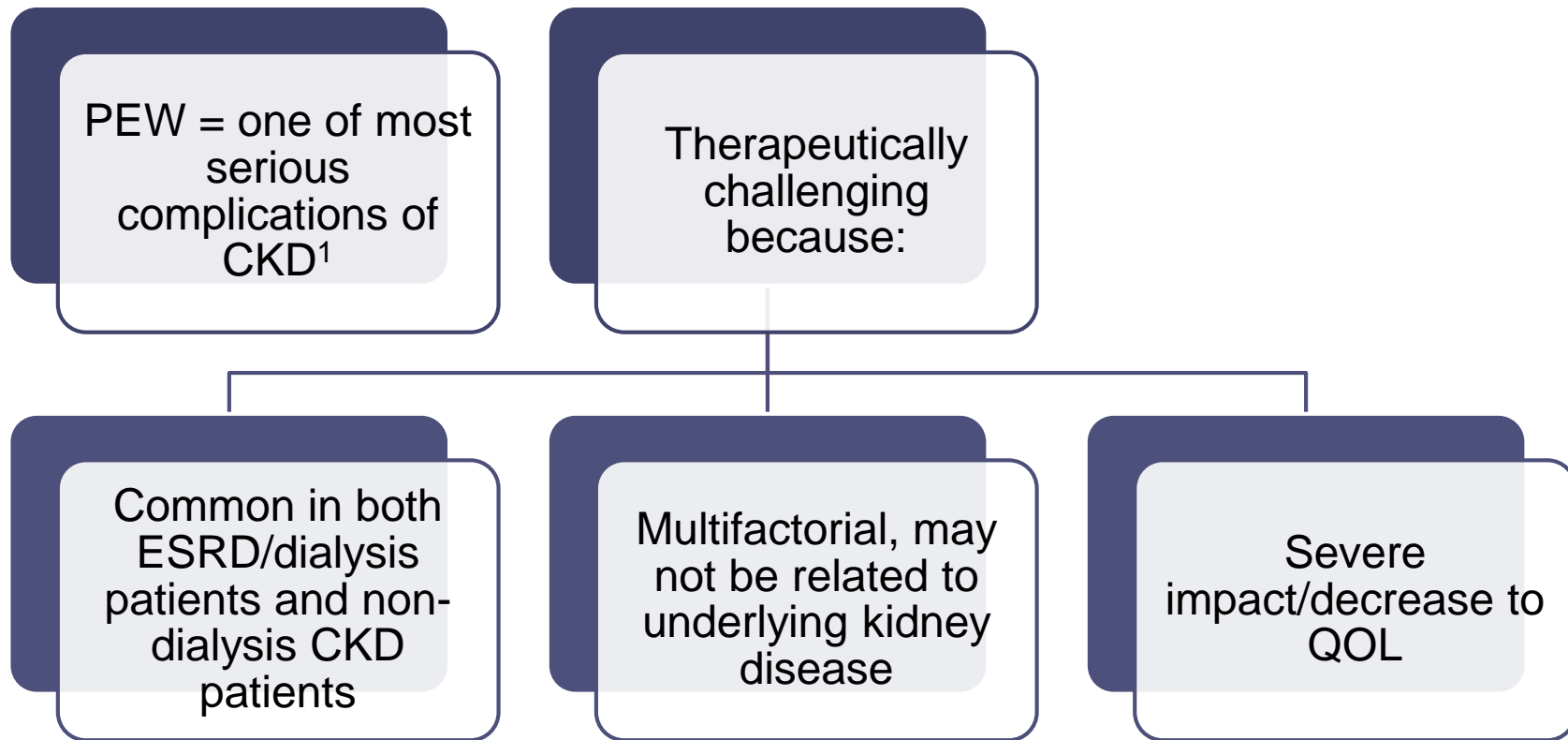
Nutrient Loss During Dialysis Tx

- Glucose, amino acids, peptides, protein
- Water-soluble vitamins
- AA concentration maintained by muscle protein catabolism[1]

Raj DS. Am J Physiol Endocrinol Metab. 2004.

Increased Energy Utilization & Abnormal Protein Kinetics

- Intradialytic increase in catabolism
- Increase in BOTH protein synthesis and catabolism[1]
- Net loss

Raj DS. Am J Physiol Endocrinol Metab. 2004.

Why Does Malnutrition Matter?

Why Does Malnutrition Matter?

PEW = one of most serious complications of CKD[1]

Therapeutically challenging because:

Common in both ESRD/dialysis patients and non-dialysis CKD patients

Multifactorial, may not be related to underlying kidney disease

Severe impact/decrease to QOL

Kopple JD. Am J Clin Nutr. 1997.

PEW worsens in severity over time, increases in prevalence[1]

Data suggest that amelioration of mortality linked to PEW biomarkers (such as increases to serum alb, body fat) over time may mitigate the deleterious complications of PEW[2]

PEW

Significant because it coexists with other comorbid risk factors:

- DM
- Inflammation
- Atherosclerosis

Strong association with all-cause mortality in ESRD population[1]

Strong predictor for high morbidity/mortality[2]

Stenvinkel P. Kidney Int. 1999.   Kopple J. Am Soc for Clin Nutr. 1997.

Is Malnutrition a Frequent Misdiagnosis in HD Patients?

Yes, according to Mitch

"Malnutrition" used to describe/diagnose a multifactorial syndrome of wasting, loss of mass, derangement of serum proteins

- Result of catabolic mechanisms stimulated by renal insufficiency[1]

This opinion pre-dates the ISRNM Consensus Statement (2006) regarding nomenclature

Misdiagnosis? Or failure to tell the whole story?

Mitch W. J Clin Invest. 2002.

Where We Are Now

Waiting for coding to catch up as well

- Malnutrition
- Kwashiorkor (rare in U.S.)
- Marasmus (again, rare)

Just beginning to identify malnutrition broadly in general in-patient population

- Now, moving to LTC
- Eventually expected to move to outpatient chronic clinics such as HD

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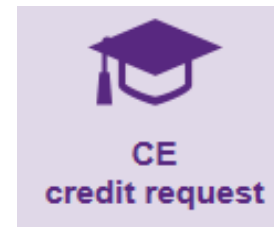
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