CORE CURRICULUM IN NEPHROLOGY

Nutritional Considerations in Kidney Disease: Core Curriculum 2010

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INTRODUCTION

Nutritional considerations form an integral part in the care of a patient with kidney disease because of the kidney's central role in dietary metabolism. Not only can dietary manipulations ameliorate the signs and symptoms of kidney disease, but they also form an important adjunct of therapy regardless of the degree of decrease in kidney function. Whether the patient has chronic kidney disease (CKD) not yet requiring dialysis therapy, is undergoing renal replacement therapy, or has received a kidney transplant, timely and appropriate nutritional intervention can optimize patient care and outcomes. Last, nutritional markers, such as serum albumin, are highly predictive of morbidity and mortality and further emphasize the importance of nutritional concerns in the management of patients with kidney disease.

NUTRITIONAL REQUIREMENTS

Definition of a Nutrient

- Chemical substance in food that serves as a metabolic fuel, a substrate for tissue growth or maintenance, or regulates normal cellular and metabolic processes
- Indispensable nutrients are essential

Classes of Nutrients

- Organic compounds that serve as sources of fuels for energy requirements
  - Carbohydrates
  - Fats
  - Proteins
- Vitamins
  - Organic compounds, necessary in small amounts for normal growth, maintenance of health, and reproduction
- Minerals
  - Macroinorganic elements (eg, sodium, chlorine, calcium, magnesium, phosphorus)
- Water

Recommended Dietary Allowances

- Amount considered sufficient for the maintenance of health in nearly all adults
- Recommendations are concerned with health maintenance and are not intended to be sufficient for therapeutic purposes

Dietary Guidelines

- Amounts considered optimal for promotion of health
- Amounts vary for individuals of different risk and may be intended for therapeutic purposes in those with certain diseases

Factors Affecting Nutrient Requirements

- Dietary factors
  - Chemical form of nutrient
  - Energy intake
  - Food processing and preparation
  - Effect of other dietary constituents
- Host factors
  - Age
  - Sex
  - Genetic makeup
  - Pathologic states

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ENERGY

- Healthy patients with CKD and transplant recipients may have normal or slightly decreased basal energy requirements
- Caloric intake should be based on energy needs
- Inflammatory diseases and dialysis increase basal energy expenditure
- Dietary energy intake of about 30-35 kcal/kg/d is more likely to maintain or increase body mass, maintain neutral or positive nitrogen balance, and decrease urinary nitrogen appearance for CKD and dialysis patients
- Sedentary individuals older than 60 years may be prescribed 30 kcal/kg/d, as well as patients who are obese with edema-free body weight >120% of desirable body weight for CKD and dialysis patients

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CARBOHYDRATES

In patients with CKD, patients with end-stage renal disease (ESRD), and transplant patients, metabolism is impaired, leading to glucose intolerance, insulin resistance, and impaired insulin secretion.

Resistance to the Peripheral Action of Insulin

- Skeletal muscle is the major site for decreased sensitivity to insulin action
- Other defects in glucose metabolism exist at steps in the glycolytic pathway before the production of glyceraldehyde-3-phosphate
- Hepatic glucose production and suppression of its production by insulin occur normally
- A postreceptor defect (impairment of IRS-1 [insulin receptor substrate 1]) is responsible for resistance to the peripheral action of insulin in uremia
  - Occurs early in the course of CKD and is observed in most patients with advanced CKD (stages 4 and 5) and those treated with hemodialysis
  - Defect is markedly improved with hemodialysis, continuous ambulatory peritoneal dialysis (CAPD), or dietary protein restriction, suggesting that a dialyzable compound may be involved
- Glucocorticoids (eg, prednisone), obesity, and calcineurin inhibitors further exacerbate insulin resistance

Impaired Insulin Secretion

- In response to hyperglycemia, blood insulin levels may be decreased, normal, or increased
- Both the initial and late phases of insulin secretion are impaired in CKD
- Response to L-leucine and potassium (insulin secretagogues) is impaired
- Excess parathyroid hormone (PTH) inhibits insulin secretion independent of CKD
  - Caused by an increase in basal calcium levels in pancreatic islets, impairing activities of the calcium-transporting adenosine triphosphatase (Ca^{2+}-ATPase) and adenosine triphosphatase sodium-potassium pump (Na^{+}-K^{+}-ATPase)
  - Insulin secretion is markedly improved in children with ESRD after normalization of blood PTH levels by treatment with vitamin D
- The metabolic clearance rate of insulin also varies because insulin is metabolized and cleared by the kidney
  - Daily renal clearance of insulin (6-8 units) is impaired when glomerular filtration rate (GFR) decreases to <40 mL/min, markedly prolonging the half-life
  - Fasting blood glucose levels are normal, but spontaneous hypoglycemia occurs
  - Fasting and postprandial hyperinsulinemia
    - Proinsulin, C-peptide, glucagon, and growth hormone levels also are increased

- The metabolic clearance rate of insulin is improved with dialysis, most likely by increasing its degradation in peripheral tissues

Dietary Implications

- A diet moderate to rich (depending on caloric needs) in complex carbohydrates is advised
  - Lower glycemic index carbohydrates (complex carbohydrates) are preferred carbohydrate sources to prevent hyperglycemia due to insulin resistance
  - The high phosphorus and/or potassium content of many complex carbohydrates (legumes, whole grains, fruit) creates difficulties in those with stages 3-5 CKD and ESRD
  - Other strategies to control phosphorus and potassium levels may allow greater consumption of complex carbohydrates
- Very low-carbohydrate diets may be tolerated poorly because of the long insulin half-life

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LIPID METABOLISM

Lipid abnormalities are common in kidney disease, including CKD, nephrotic syndrome, and dialysis dependence.

Chronic Kidney Disease

- Two causes of moderate plasma hypertriglyceridemia
  - Augmented synthesis by intestine or liver
  - Impaired triglyceride removal from plasma
- Hepatic triglyceride lipase and lipoprotein lipase (LPL) activities are decreased
  - Gemfibrozil, which activates both hepatic triglyceride lipase and LPL, can normalize the hypertriglyceridemia of CKD
  - Metabolism of newly secreted chylomicrons and very low-density lipoprotein (VLDL) particles is delayed by diminished LPL activity
  - Clearance of partially metabolized lipoproteins and chylomicron remnants is delayed by decreased hepatic triglyceride lipase activity
- Plasma apolipoprotein profiles are highly abnormal
  - Apolipoprotein AI (Apo-AI), Apo-AII, and Apo-E concentrations are decreased
  - Apo-B level is slightly increased
  - Apo-CIII levels are significantly increased, whereas Apo-CI and Apo-CII are slightly increased
  - Apo-CIII ratio is abnormally low
    - Equal to ratio of Apo-CIII in heparin-treated plasma supernatant to that present in precipitate
    - Correlates with the efficacy of processes responsible for the degradation of triglyceride-rich particles

Nephrotic Syndrome

- Dyslipidemia is present in 70%-100% of patients
  - Most often appears as combined hyperlipidemia, with increased total serum cholesterol, low-density lipoprotein (LDL) cholesterol, VLDL cholesterol, and intermediate-density lipoprotein (IDL) cholesterol, accompanied by increased serum triglyceride levels
  - Types of hyperlipidemia (see Box 1 for characteristics)
    - Type IIa is present in 33%
    - Type IIb is present in 50%
    - Type IV (hypertriglyceridemia) is present in 4%

Box 1. Types of Dyslipidemia

Type IIa
↔ Triglycerides
↑ ↑ ↑ Cholesterol
↑ LDL cholesterol
↑ HDL cholesterol
Type IIb
↑ VLDL cholesterol
↑ ↑ Triglycerides
↑ ↑ or ↑ ↑ ↑ Cholesterol
↑ LDL cholesterol
↑ ↑ HDL cholesterol
Type IV
↑ VLDL cholesterol
↑ ↑ Triglycerides
↓ or ↑ Cholesterol
↓ LDL cholesterol
↑ ↑ HDL cholesterol

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

- High-density lipoprotein (HDL) cholesterol levels can be low, normal, or high
- Increased hepatic synthesis and decreased lipid and lipoprotein catabolism contribute to the hyperlipidemia, with various mechanisms proposed

- Changes in plasma apolipoprotein concentrations parallel changes in lipoproteins
  - Apo-B and Apo-E levels are increased
  - Apo-AI reflects HDL cholesterol levels
  - Apo-CI, Apo-CII, and Apo-CIII levels are increased, but there is no change in Apo-CII:Apo-CIII ratio
  - Levels of lipoprotein(a) (Lp[a]), a powerful atherosclerotic risk factor, are increased

Hemodialysis

- Typical pattern is hypertriglyceridemia in combination with low HDL cholesterol level

Peritoneal Dialysis

- Lipoprotein abnormalities similar to those found in hemodialysis patients
- However, plasma cholesterol, triglyceride, LDL cholesterol, and Apo-B levels are higher because of:
  - Loss of considerable amounts of protein into peritoneal dialysate (7-14 g/d)
  - Excessive absorption of glucose (150-200 g/d)

Kidney Transplant

- Increased cholesterol and triglyceride levels
- Type of dyslipidemia and prevalence vary considerably
- Influencing factors
  - Concomitant drug treatment for hypertension (β-blockers and diuretics) or immunosuppression
  - Insulin resistance
  - Obesity
  - Transplant dysfunction

Dietary Implications

- Diets to improve lipid abnormalities in patients with kidney diseases have not been well studied
- Although lipid patterns represent a highly atherogenic condition, the degree to which diets may modify lipid levels or affect the risk of coronary heart disease is unknown
- Lipid-lowering drugs have not been very effective in causing regression of coronary artery disease in patients with nephrotic syndrome, on hemodialysis or CAPD therapy, or after kidney transplant
- Hypertriglyceridemia increases insulin resistance, with effects on carbohydrate and protein metabolism
- There are few data for the relation of dyslipidemia to progression of kidney disease
- Increased serum lipid levels parallel lipid deposits and lipoprotein components in human glomerular disease (focal segmental glomerulosclerosis [FSGS])
- In patients with type 1 diabetic nephropathy, cholesterol levels are an independent risk factor for progression after blood pressure and glycemic control are considered

Treatment Guidelines

General Aspects

- Bases for decision to modify lipid content
  - Extrapolation from epidemiologic and clinical studies in nonrenal conditions
  - Conventional individual assessment of the patient's lipid profile, risk profile, and prognosis

- Treatment recommended for subsets of patients
  - Established coronary artery disease and hyperlipidemia
  - Diabetes with high risk of cardiovascular event
  - Nephrotic syndrome or early-stage CKD
  - High LDL cholesterol level (>160 mg/dL [>4.14 mmol/L])
  - High serum triglyceride level (>100-500 mg/dL [>1.54-5.65 mmol/L])
  - Marked hyperlipidemia in a young or middle-aged man facing decades of renal replacement therapy

How to Treat

- Serum total cholesterol and triglyceride levels should be monitored every 3-6 months, and serum LDL and HDL cholesterol levels should be monitored annually
- Body weight should be maintained near desirable weight in early CKD and transplant patients
- In patients with significant comorbid conditions, stage 5 CKD, or ESRD, body weight goals are controversial because of the risk of protein-energy wasting (PEW; discussed later)
  - Weight reduction should be avoided in patients with PEW
  - Resistive exercise is still strongly recommended in these groups
- In patients with nephrotic syndrome in early stages of CKD, stringent diet modification (eg, reduced meat and/or soy-based vegetarian diets with fish oil) significantly decreased total cholesterol, LDL cholesterol, and triglyceride levels and proteinuria
  - Fat restriction and the quality of fats and proteins in manipulated diets may be important for correction of hypercholesterolemia and urinary protein loss
- Strategies for lipid modification of the diet appropriate for the high-risk general population may be appropriate in all kidney patients unless the change in lipid sources adds nutritional difficulties that prevent adequate protein and calorie intake
- Diets rich in polyunsaturated fatty acids of both vegetable origin (omega 6) and fish, nut, or vegetable origin (omega 3) have increased the removal of triglyceride-rich lipoprotein remnants and dramatically decreased postprandial lipoprotein levels in plasma of nonrenal patients
- Exercise training may improve dyslipidemia and glucose tolerance
- Avoiding excessive weight gain after kidney transplant appears to be important
- Cholesterol- and triglyceride-lowering drugs have effects on serum lipid levels quantitatively similar in kidney patients and the healthy population

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PROTEIN METABOLISM

CKD (especially ESRD) causes abnormal protein metabolism.

Amino Acid Concentrations

- Stages 4 and 5 CKD may cause striking abnormalities in free amino acid concentrations in muscle and plasma
  - Essential amino acid levels are lower in plasma secondary to augmented peripheral tissue metabolism
  - Levels of plasma branched-chain amino acids (BCAAs; valine, leucine, and isoleucine, as well as threonine and tryptophan) are especially low
    - Acidosis and glucocorticoids worsen these changes

        - Plasma and muscle BCAA concentrations, depressed in patients with uremia, are corrected by supplementing the diet with sodium bicarbonate
- Acidosis-stimulated muscle proteolysis and total-body leucine oxidation require glucocorticoids
- Because leucine has an anabolic effect on muscle, low levels could drive muscle wasting
- Histidine and serine become essential amino acids in patients with ESRD because of decreased synthesis
- Lower ratio of tyrosine to phenylalanine is caused by depressed liver tyrosine hydroxylase activity
- In patients with ESRD, losses of amino acids in dialysate decrease plasma levels

Nitrogen Handling

- Altered by CKD and nutritional status
- Nonurea nitrogen metabolism is the difference between total nitrogen excretion and urea nitrogen appearance and represents fecal and nonurea nitrogen appearance
    - Urea excreted into the gut is degraded by bacterial urease to ammonia and carbon dioxide, which returns to the liver through the portal circulation
        - This extrarenal clearance of nitrogen increases in CKD, but does not significantly decrease the quantity of retained waste products (most are simply converted to another form of nitrogen)
        - The difference between urea production and that recycled by the gut is termed "urea nitrogen appearance," which represents urea that appears in body water and urine
    - Fecal nitrogen excretion does not increase significantly in patients with uremia unless there is compromise in gut or liver function
- As urinary function decreases, renal ammonia production decreases, which decreases the proportion of urinary nitrogen presenting as ammonia

Clinical Effects of Protein Intake

- Dietary protein in excess of daily requirements is degraded to urea, other nitrogenous waste, acid, phosphate, and sulfate
    - These waste products accumulate in patients with uremia, leading to muscle catabolism, bone loss, and vascular calcification
    - Correction of acidosis slows loss of kidney function
- Dietary protein restriction slows progression of CKD
    - Protein or amino acid loads:
        - Acutely alter renal hemodynamics
        - Increase proteinuria
    - Decreases acid, uric acid, and nitrogenous waste generation
    - Clinical results of protein restriction vary due to primary diagnosis and variability in achieving goal protein intakes
- In response to catabolic stimulus or inadequate protein or caloric intake, endogenous protein stores also are degraded
    - Protein synthesis and protein catabolism are normal in patients with CKD unless a second process is present
    - Inability to adapt to a low-protein diet may be due to inadequate caloric intake
        - Anorexia is a common symptom of both uremia and comorbid conditions
        - Caloric requirements are higher in patients with ESRD (up to 35-40 kcal/kg) due to an increased basal metabolic rate, which is driven by high sympathetic nervous system activity
    - When calories are inadequate, dietary amino acids are used for energy, increasing the need for muscle stores to supplement visceral protein synthesis

Catabolism

- Inflammation is a major catabolic stimulus
    - Acute-phase reactants are made instead of albumin, and albumin catabolism increases
    - Insulin resistance drives loss of muscle protein
        - Glucocorticoids and inflammatory cytokines have major roles
    - Inflammation often is caused by comorbid conditions rather than CKD
        - Chronic comorbid conditions (diabetes mellitus, lupus erythematosus, heart failure, nephrotic syndrome, emphysema)

    - Acute intercurrent illnesses
- Altered hormonal milieu promotes catabolism by:
  - Resistance to the anabolic hormones (insulin, growth hormone, insulin-like growth factor 1 [IGF-1])
  - Increased levels of catabolic hormones (glucagon, PTH, corticosteroids)
- Other catabolic stimuli
  - Accumulation of toxic uremic metabolites
  - Loss of the kidney's metabolic activity
  - Metabolic acidosis
    - Acidosis decreases amino acid levels
    - Acidosis blocks insulin-stimulated muscle protein synthesis
  - ESRD is always associated with protein catabolism
    - Inflammation from the dialysis procedure
    - Amino acid loss during dialysis

Dietary Implications

- Neutral nitrogen balance can be achieved in patients with nondialysis CKD with a minimum of 0.6 g/kg/d of high-biological-value protein in stable nonacidotic patients when adequate calories are given
  - High-biological-value protein contains a high fraction of the essential amino acids proportioned approximately according to daily dietary requirements for humans
    - At least 0.35 g/kg/d should be high-biological-value protein
    - Essential amino acids may be supplemented or administered as their keto-analogues
  - If achieved, such diets slow progression, decrease acid and phosphorus loads
- Low-protein diets have been proved safe in individuals with strict monitoring of nutritional status
  - Many individuals are unwilling or unable to comply with such diets or monitoring
    - Diets higher in protein (0.75 g/kg/d) are recommended for such patients with predialysis CKD
    - At least 0.35 g/kg/d should be high-biological-value protein
- Patients with active comorbid conditions may not tolerate protein-restricted diets (see PEW section)
  - Evidence of deterioration should lead to a diagnostic workup for comorbid conditions
  - Dietary protein intake should be liberalized during acute illnesses
- Patients with ESRD will not tolerate low-protein diets
  - Recommended protein intakes
    - 1.0-1.2 g/kg/d (hemodialysis)
    - 1.2-1.4 g/kg/d (peritoneal dialysis)
  - Higher protein and amino acid losses in peritoneal fluid account for the differences
- Transplant patients on steroid therapy will not tolerate the lowest protein diets

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VITAMIN METABOLISM

- Intestinal absorption of riboflavin, folate, and vitamin D_3 decreases with decreasing GFR
- Patients with CKD, acute kidney injury (AKI), and ESRD may have a higher incidence of vitamin deficiencies
  - 1,25-Dihydroxycholecalciferol production is decreased

- Vitamin intake is decreased because of anorexia and decreased food intake
  - The prescribed diet frequently contains less than the recommended daily allowances for certain water-soluble vitamins
- Kidney injury alters the absorption, metabolism, or activity of some vitamins
  - Riboflavin, folate, and vitamin D_3 absorption is impaired
  - Folate and pyridoxine metabolism is impaired
- Certain medicines may interfere with the intestinal absorption, metabolism, or actions of vitamins
- Nutritional requirements for most vitamins are not well defined in patients with CKD, but there is some evidence that daily supplements of the following vitamins will prevent or correct vitamin deficiencies:
  - Pyridoxine hydrochloride, 5 mg
  - Folic acid, 1 mg
  - Recommended daily allowances for healthy individuals for other water-soluble vitamins
    - Vitamin C, 60 mg; higher doses have been associated with increased plasma oxalate levels
    - Supplemental vitamin A is not recommended
    - Vitamin K often is not needed
    - Vitamin D should be supplemented to a plasma level >30 pg/mL
- These deficiencies are severe after institution of dialysis therapy because of the loss of water-soluble vitamins in dialysate on a thrice-weekly regimen
  - Replacement is similar to CKD, except 75-90 mg/d of vitamin C, 10-50 mg/d of pyridoxine, and 1-5 mg/d of folate should be prescribed

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PROTEIN-ENERGY WASTING

Background

- PEW occurs when mechanisms to compensate for decreased protein intake fail (see previous Protein Metabolism section)
  - PEW occurs frequently in patients with stages 4 and 5 CKD and established hemodialysis or peritoneal dialysis patients
  - Dietary protein and energy intake and the parameters of nutritional status (including serum albumin, transferrin, body weight, midarm muscle circumference, and percentage of body fat) decrease as GFR decreases toward 10 mL/min/1.73 m^2 (0.167 mL/s/1.73 m^2)

Morbidity and Mortality

- Nutritional status of patients undergoing maintenance hemodialysis or peritoneal dialysis is a powerful predictor of morbidity and mortality
  - Serum albumin, weight, muscle mass, and changes in body weight are associated with morbidity and mortality
  - Comorbid conditions often account for both the PEW and increased mortality
  - Individuals with lower muscle mass may be less likely to survive acute intercurrent illnesses
  - The term "reverse epidemiology" describes lower mortality with higher body weight, cholesterol level, and other traditional

Table 1. Liquid Protein Supplements

Product	Amount	Calories	Protein (g)	Calcium (mg)	Potassium (mg)	Phosphorus (mg)	Sodium (mg)
Boost	8 fl oz	240	10	330	400	310	130
Boost High Protein	8 fl oz	240	15	330	380	310	170
Boost Plus	8 fl oz	360	14	330	380	310	170
Boost Diabetic	237 mL	250	13.8	276	260	220	260
Ensure	8 fl oz	250	8.8	300	370	300	200
Ensure High Protein	8 fl oz	230	12	300	500	250	290
Ensure Plus	8 fl oz	350	13	300	500	300	240
Glucerna	8 fl oz	237	9.9	170	370	170	220
Nepro Carb Steady[a]	8 fl oz	425	19.1	250	250	165	250
Novasource Renal[a]	8 fl oz	475	17.4	308	192	154	210
Promote	8 fl oz	237	14.8	285	470	285	240
Suplena Carb Steady	8 fl oz	425	10.6	250	265	165	185
Resources Shake Plus	8 fl oz	480	15	350	250	350	200
Nutren Renal	8 fl oz	500	17.5	350	314	175	185
Re/Gen HP/HC[a]	4 fl oz	250	10	15	25	45	90

Note: Boost, Novasource Renal, Resources Shake Plus, and Nutren Renal products are manufactured by Nestle (www.nestle-nutrition.com); Ensure, Glucerna, Nepro Carbo Steady, Promote, Suplena Carb Steady, by Abbott Laboratories (www.abbott.com); Re/Gen HP/HC by Nutra/Balance Products (www.nutra-balance-products.com).

[a]Indicated for dialysis patients.

cardiac risk factors that is believed to be caused by PEW

Treatment

- Treatment of PEW depends on reversing the acute illness, providing adequate protein and calories, and muscle loading to rebuild muscle mass
  - In patients with CKD, dietary protein intake should be liberalized
  - Reduction of inflammation portends a good prognosis
  - Dietary supplements are helpful in restoring albumin levels in patients with low spontaneous protein and/or calorie intake (Table 1)
    - Intradialytic parenteral nutrition appears effective, but not superior to oral feeding
  - Dietary supplements are not effective in restoring muscle mass without muscle loading
    - Feeding can increase muscle protein synthesis, but this is matched by increased breakdown in individuals at rest
  - The role of spontaneous versus prescribed exercise has not been determined
    - Exercise programs have been recommended in analogy to exercise use in patients with cancer, heart failure, and lung disease muscle wasting
    - No protocol has been successfully developed specifically for kidney patients
  - Anabolic agents (eg, growth hormone, IGF-1, anabolic steroids) and appetite stimulants (eg, progesterones) are under active investigation for PEW
    - Many anabolic agents have had successful small-scale trials
    - Optimal regimens have not been established
    - The role of carnitine, used in the transport of fatty acids, and its supplementation has been debated

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ASSESSMENT OF NUTRITIONAL STATUS IN KIDNEY DISEASE

Approach to Screening

Level 1 Screen

- Identifies risk factors that increase chances of PEW
  - Diseases or conditions that have nutritional implications
  - Excessive or inadequate intakes
  - Dentition
  - Reduced social contact
  - Behavioral
    - Depression
    - Cognitive impairment
  - Multiple medications
    - Complex regimens and adherence difficulties
    - Alteration of taste and nutrient metabolism
    - Inappropriate medications or procedures
  - Involuntary weight loss or gain
  - Need assistance with self-care
  - Function-related problems and sensory and activity limitations

Level 2 Screen

- For individuals with suspected PEW who have identifiable risk factors identified by a level 1 screen
  - Anthropometric and other body composition measurements
    - Patient's height, weight, and trends in weight over time are the simplest and most useful anthropometric measurements
  - Lean body mass (consists of fat-free body mass or body weight minus the weight of the body fat)
    - Midarm muscle circumference; simple to do but only grossly abnormal with far advanced protein-calorie malnutrition
    - Bioelectrical impedance is less reliable when edema is present
  - Other anthropometric measurements (eg, skin folds at the triceps) may be used with proper training

Biochemical Assessment

- Serum cholesterol level very low in PEW
- Biochemical tests of protein stores
  - No valid or reliable somatic (muscle) protein marker
  - Albumin, transferrin, prealbumin, and methylhistidine are used for visceral proteins
    - Albumin level is a nonspecific indicator of disease because it decreases with inflammation and has a long half-life
    - Prealbumin and transferrin levels may more accurately reflect the current nutritional state, but also increase with inflammation
    - Creatinine level reflects muscle mass, but variability in excretion/clearance and change with meat intake decreases utility

Biochemical Estimates of Protein Intake for Determining Dietary Adherence

- In predialysis patients with CKD, 24-hour urine urea nitrogen excretion is used to estimate protein intake

- Estimated protein intake (g protein/kg/d) = 6.25 × [UUN + (0.031 × weight in kg)], where UUN is urine urea nitrogen excretion in grams of nitrogen per kilogram per day
- The same formula can be used to estimate nondialysis clearance from residual kidney function

- In hemodialysis, urea kinetics are used to calculate protein equivalent of total nitrogen appearance (PNA)
- In peritoneal dialysis, PNA (g/24 h) =
  - 13 + 0.261 × urea appearance (in mmol/24 h) + protein losses (g/24 h)
  - 19 + 0.272 × urea appearance (in mmol/24 h), in absence of excessive protein losses in dialysate and urine

Dietary Assessment

- Methods include
  - 24-Hour recall
  - Food-frequency questionnaires
  - Dietary history food diary or record
- Useful clinically, but less accurate than in general population

Subjective Global Assessment and Similar Combined Scoring Tools

- More powerful than individual tools
- Subjective Global Assessment accurately predicts mortality, especially in combination with a biochemical marker

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SPECIAL CONSIDERATIONS: HYPERTENSION

- Although the pathophysiologic process of essential hypertension is complex and multifactorial, a variety of dietary factors contribute to the increase in blood pressure above normal, especially when combined with a genetic predisposition to hypertension
- Obesity and especially abdominal fat distribution have a significant influence on blood pressure
- Most, but not all, studies have shown a positive and significant relationship between dietary salt (sodium chloride) and systolic blood pressure
- Differences among studies suggest that the degree of sensitivity of blood pressure to sodium chloride varies widely in different groups of patients with essential hypertension
  - 50% of patients with essential hypertension may be salt sensitive (defined as blood pressure increase of at least 10 mm Hg when sodium intake increases from 20 to 200 mEq/d (20 to 200 mmol/L/d) for 1 week)
  - Higher salt intake results in a greater number of individuals with hypertension being salt sensitive
  - Salt sensitivity appears to be greater in African Americans, obese patients, patients with diabetes, and older patients
- The chloride ion appears to be important because sodium chloride and not sodium citrate or bicarbonate increases blood pressure
  - Sodium chloride increases blood volume to a greater extent
  - Bicarbonate drag increases renal sodium excretion
- Short- and long-term trials have shown that a decrease in sodium intake results in decreases in both systolic and diastolic blood pressure
  - Dietary sodium intake may be an independent determinant of left ventricular hypertrophy
- Salt-sensitive groups, such as blacks, the elderly, and diabetic individuals, are more likely to develop kidney failure as a consequence of hypertension

- Individuals with salt-sensitive hypertension show a decrease in renal blood flow and increases in filtration fraction and intraglomerular pressure
- Salt-sensitive patients with essential hypertension manifest a greater amount of urinary albumin excretion than salt-resistant patients

- Dietary potassium, calcium, and magnesium intakes are related inversely to blood pressure
  - Dietary potassium restriction causes a substantial increase in blood pressure in both normotensive and hypertensive individuals, whereas the converse appears to be true for dietary potassium administration
    - Potassium increases sodium excretion and decreases urinary calcium excretion and renin and aldosterone secretion
  - Low calcium intake is associated with higher blood pressure and increased prevalence of hypertension; however, the decrease in blood pressure with the use of calcium supplements has been modest
  - Serum magnesium concentrations more often are lower in hypertensive than normotensive individuals and adequate intake may decrease blood pressure
- Studies have shown that blood pressure is largely independent of protein, carbohydrate, and fat content of isocaloric diets
  - Complex sugars may have an antihypertensive effect due to decreased intestinal absorption, decreased insulin secretion, and improvement in insulin resistance
  - Adequate intake of omega-3 fatty acids can decrease blood pressure depending on initial blood pressure levels
- Alcohol consumption can increase blood pressure
  - A decrease in alcohol consumption and calorie restriction reduces blood pressure by as much as twice the effect of each modality given individually
  - A decrease in alcohol results in a significant decrease in systolic more than diastolic blood pressure

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SPECIAL CONSIDERATIONS: HEMODIALYSIS

- Nutrient losses
  - Amino acid losses are approximately 8-10 g during dialysis, depending on the type of dialyzer used
  - About 25 g of glucose are removed during a hemodialysis session with a glucose-free dialysate and 30 g of glucose are absorbed when dialysate containing glucose of 180 mg/dL (9.99 mmol/L) is used
  - Vitamins B_1, B_2, and B_6; ascorbic acid; and folic acid are prone to be lost with dialysis, whereas loss of vitamin B_{12}, which is protein bound, is negligible
- Sodium and water must be tightly restricted
  - Patients should be counseled against ingesting high-sodium diets
    - Excessive sodium intake may lead to large interdialytic weight gains, hypertension, edema, congestive heart failure, and increased risk of death
    - Restriction of sodium intake and glucose control will reduce water intake to appropriate level
- Potassium, magnesium, and phosphate are poorly cleared by hemodialysis
  - Dietary intake not $>$70 mEq (70 mmol/L) or 2 g of potassium per day for patients
  - If 1.0 mEq/L (0.5 mmol/L) of magnesium is in dialysate, magnesium intake should be 200-300 mg/d
  - Maintenance hemodialysis patients should be prescribed 8-17 mg/kg/d of phosphorus

        - Because very low-phosphorus diets (<800 mg/d) are unpalatable, phosphorus binders usually are required
- Midweek predialysis serum bicarbonate level should be 20-22 mEq/L
    - Supplementation should be given if lower and consideration of increased protein intake if higher
- Patients using alternate hemodialysis modalities (nocturnal, daily) have increased potassium, magnesium, and phosphate clearance
    - Diet should be liberalized and supplements given if needed
        - Monitoring protein intake
    - Coupling between Kt/V urea and normalized protein catabolic rate (nPCR) occurs because both are calculated from pre- and postdialysis urea measurements
        - Any confounding factor of serum urea or Kt/V will affect nPCR

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SPECIAL CONSIDERATIONS: NOCTURNAL HEMODIALYSIS

- Nutrient losses
    - Amino acid losses during dialysis are offset by increases in total-body nitrogen
    - Essential, nonessential, and BCAAs all increase within a year of treatment
    - A significant increase in appetite and striking weight gains are noted within 6 months of treatment
    - Average weight gains are about 1 kg after 1 year
- Sodium, potassium, and water are unrestricted
- In most instances, antihypertensive medications can be discontinued
- Exquisite phosphorus control is achieved within the first week of treatment
    - Phosphate binders can be discontinued
    - An unrestricted diet is recommended
        - Calcium adjustments in the dialysis bath must be individualized based on bone density and pre-/postdialysis calcium and PTH levels
        - For some individuals, phosphorus must be added to the dialysate

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SPECIAL CONSIDERATIONS: SHORT DAILY HEMODIALYSIS

- Protein intake
    - Dietary protein intake tends to increase
    - Albumin levels and dry weight reportedly increase
    - Overall changes in nutritional parameters tend to be modest in comparison to nocturnal hemodialysis
- Sodium, potassium, and water intake may be slightly liberalized
- Improved blood pressure control has been reported with discontinuation of some, but not all, blood pressure medications
- Because phosphorus control is dependent on time on dialysis, dietary phosphorus restrictions and phosphate binders must still be used

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SPECIAL CONSIDERATIONS: PERITONEAL DIALYSIS

- Nutrient losses

- Phosphorus and potassium have increased clearance with peritoneal dialysis relative to hemodialysis
  - Potassium intake can be liberalized to 4 g in many peritoneal dialysis patients
  - Phosphorus intake can be increased
- Because of sodium sieving, water may be lost preferentially to sodium
  - Very tight sodium restriction is essential and positive sodium balance correlates closely with mortality
- Protein losses in peritoneal dialysate vary from 5-15 g/24 h, with albumin as the major constituent
- Protein intake should be 1.2-1.4 g/kg (with 50% of high biological value)
- Protein losses may indirectly contribute to various nutritional and metabolic disturbances:
  - Low HDL cholesterol levels correlate with apolipoprotein losses in dialysate
  - Metabolic bone disease due to loss of vitamin D–binding protein
  - Protein losses mirror peritoneal transport characteristics in CAPD patients
- Average dialysate losses of free amino acids into dialysate during CAPD vary from 1.2-3.4 g/24 h
  - Amino acid–based dialysis fluids may supplement daily losses of amino acids during dialysis with glucose-based solutions

- Absorption of glucose from dialysate (glucose, 100-200 g/24 h, averaging 8 kcal/kg body weight daily)
  - The high calorie load from dialysate makes it easier to obtain calorie goals, making protein goals more critical in planning the diet
    - High sugar load contributes to the feeling of satiety
    - Abdominal distention from dialysate is not a significant contributor to satiety in most patients
  - Increased insulin resistance from high sugar loads

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SPECIAL CONSIDERATIONS: NEPHROTIC SYNDROME

- Protein restriction decreases urinary protein excretion and may have a beneficial effect on the rate of kidney disease progression
  - Composition of dietary protein may be important
    - BCAAs, arginine, proline, glutamine, glutamate, aspartate, or asparagine do not greatly worsen proteinuria (soy diets)
- Fractional rate of albumin catabolism increases in nephrotic patients fed a high-protein diet so that albumin levels decrease
  - Dietary protein should not be restricted to <0.8 g/kg/d in nephrotic patients
  - Additional protein up to 10 g can be added to the diet to account for protein losses in urine
- American Heart Association (AHA) lipid recommendations should be followed for hyperlipidemia

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SPECIAL CONSIDERATIONS: KIDNEY TRANSPLANT

Early Posttransplant Recommendations

- Most patients will require high protein intake to maintain a positive nitrogen balance

- Protein of 1.4-2 g/kg when patients are receiving high corticosteroid doses
- Cyclosporine has a steroid-sparing effect and has been associated with lower protein requirements

- Corticosteroids cause abnormalities in carbohydrate metabolism, including glucose intolerance and relative insulin resistance
  - Concentrated sugars should be limited
  - Allocate 50% of total caloric intake to carbohydrate (30-35 kcal/kg)
- More liberal salt intake may be needed to avoid volume depletion
- Phosphate may need to be supplemented because of increased serum PTH levels, 1,25-dihydroxyvitamin D deficiency, and high glucocorticoid doses
- Magnesium may need to be supplemented when using cyclosporine

Late Posttransplant Recommendations

- Low-dose maintenance corticosteroid therapy increases protein catabolism and muscle wasting
  - Protein, 0.8-1 g/kg/d, should address concerns for maintaining lean muscle mass without compromising transplant function
- Exercise with physical training may reverse muscle atrophy and prevent excessive weight gain and obesity
  - A calorie-controlled diet may be needed
- American Diabetes Association diet is recommended for hyperglycemia associated with corticosteroid and other immunosuppressive medications
- AHA diets are recommended for hyperlipidemia in patients without hyperglycemia
- Minerals are adjusted according to transplant function

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SPECIAL CONSIDERATIONS: AKI

- Accelerated increase in plasma concentrations of potassium, nitrogenous metabolites, and hydrogen ion occurs in patients with AKI
- Protein losses secondary to degradation (catabolism) can be massive, especially in setting of shock, sepsis, and rhabdomyolysis; as much as 200-250 g/d
- Gastrointestinal motility is impaired due to medications, glucose and electrolyte disorders, diabetes, or mechanical ventilation
- AKI is a highly catabolic state, and mean nPCR of 1.5 g/kg of body weight daily (range, 1.4-1.8) have been reported
- Macronutrient requirements are determined more by the severity of the underlying disease, type and intensity of extracorporeal renal replacement therapy, and nutritional status than by the AKI
  - Protein restriction should be used in patients with AKI only when there is no underlying inflammatory disease
  - Catabolic patients should receive protein of 1-1.2 g/kg of ideal body weight daily, and dialysis should be performed as needed for clearance
  - Higher protein intake may be needed in continuous renal replacement therapy (CRRT) because of amino acid losses

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SPECIAL CONSIDERATIONS: KIDNEY STONES

Inadequate water, potassium, calcium, and magnesium and excess sodium, oxalate, and net acid load contribute to stone formation.

Urinary Volume

- Increasing urinary volume is the single most important dietary intervention
- Randomized trial shows the effectiveness of monitoring urine volume for prevention of recurrent stones

Dietary Influences

- A randomized trial shows that a low-sodium, adequate-calcium, low-protein diet is superior to a low-calcium diet for prevention of stones
- Excess animal protein intake and insufficient fruit and vegetable intake are associated with stone formation
- Hypercalciuric stone formers may have low bone density
- Dietary Approaches to Stop Hypertension (DASH)-style diets are associated with decreased stone formation
- Dietary oxalate does increase the risk of stones
  - Dietary oxalate is difficult to restrict tightly without eliminating many fruits and vegetables
  - Adequate calcium intake reduces urinary oxalate
- Vitamin B deficiency (especially B_6) and excess vitamin C supplementation increase the risk of stones
- Obesity and diabetes increase the risk of calcium and uric acid stones
  - Insulin resistance is associated with uric acid stones
  - Urine pH decreases with insulin resistance

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