

Nutrition and Metabolism in Acute Renal Failure

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Adequate nutritional support is necessary to maintain protein stores and to correct pre-existing or disease-related deficits in lean body mass. The objectives for nutritional support for patients with acute renal failure (ARF) are not much different from those with other catabolic conditions. The principles of nutritional support for ARF, however, differ from those for patients with chronic renal failure (CRF), because diets or infusions that satisfy minimal requirements in CRF are not necessarily sufficient for patients with ARF.

In patients with ARF modern nutritional therapy must include a tailored regimen designed to provide substrate requirements with various degrees of stress and hypercatabolism. If nutrition is provided to a patient with ARF the composition of the dietary program must be specifically designed because there are complex metabolic abnormalities that affect not only water, electrolyte, and acid-base-balance but also carbohydrate, lipid, and protein and amino acid utilization.

In patients with ARF the main determinants of nutrient requirements (and outcome) are not renal dysfunction per se but the degree of hypercatabolism caused by the disease associated with ARF, the nutritional state, and the type and frequency of dialysis therapy. Pre-existing or hospital-acquired malnutrition has been identified as an important contributor to the persisting high mortality in critically ill persons.

Thus, with modern nutritional support requirements must be met for all nutrients necessary for preservation of lean body mass, immunocompetence, and wound healing for a patient who has acquired ARF—in many instances among other complications. At the same time the specific metabolic alterations and demands in ARF and the impaired excretory renal function must be respected to limit uremic toxicity.

In this chapter the multiple metabolic alterations associated with ARF are reviewed, methods for estimating nutrient requirements are discussed and, current concepts for the type and composition of nutritional programs are summarized. This information is relevant for designing nutritional support in an individual patient with ARF.

CHAPTER

18

NUTRITION IN ACUTE RENAL FAILURE

Goals

- Preservation of lean body mass
- Stimulation of wound healing and reparatory functions
- Stimulation of immunocompetence
- Acceleration of renal recovery (?)

But not (in contrast to stable CRF)

- Minimization of uremic toxicity (perform hemodialysis and CRRT as required)
- Retardation of progression of renal failure

Thus, provision of optimal but not minimal amounts of substrates

METABOLIC PERTURBATIONS IN ACUTE RENAL FAILURE

Determined by

- Renal dysfunction (acute uremic state)
- Underlying illness
- The acute disease state, such as systemic inflammatory response syndrome (SIRS)
- Associated complications (such as infections)

Plus

- Specific effects of renal replacement therapy
- Nonspecific effects of extracorporeal circulation (bioincompatibility)

FIGURE 18-1

Nutritional goals in patients with acute renal failure (ARF). The goals of nutritional intervention in ARF differ from those in patients with chronic renal failure (CRF): One should not provide a minimal intake of nutrients (to minimize uremic toxicity or to retard progression of renal failure, as recommended for CRF) but rather an optimal amount of nutrients should be provided for correction and prevention of nutrient deficiencies and for stimulation of immunocompetence and wound healing in the mostly hypercatabolic patients with ARF [1].

FIGURE 18-2

Metabolic perturbations in acute renal failure (ARF). In most instances ARF is a complication of sepsis, trauma, or multiple organ failure, so it is difficult to ascribe specific metabolic alterations to ARF. Metabolic derangements will be determined by the acute uremic state plus the underlying disease process or by complications such as severe infections and organ dysfunctions and, last but not least by the type and frequency of renal replacement therapy [1, 2].

Nevertheless, ARF does not affect only water, electrolyte, and acid base metabolism: it induces a global change of the metabolic environment with specific alterations in protein and amino acid, carbohydrate, and lipid metabolism [2].

Metabolic Alterations in Acute Renal Failure

Energy metabolism

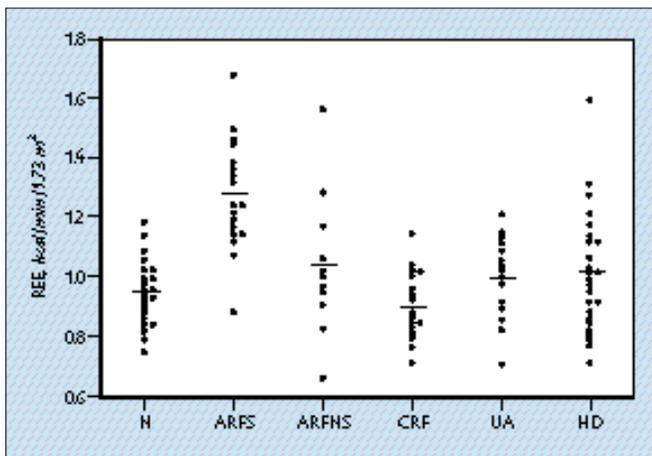


FIGURE 18-3

Energy metabolism in acute renal failure (ARF). In experimental animals ARF decreases oxygen consumption even when hypothermia and acidosis are corrected (uremic hypometabolism) [3]. In contrast, in the clinical setting oxygen consumption of patients with various form of renal failure is remarkably little changed [4]. In subjects with chronic renal failure (CRF), advanced uremia (UA), patients with regular hemodialysis therapy (HD) but also in patients with uncomplicated ARF (ARFNS) resting energy expenditure (REE) was comparable to that seen in controls (N). However, in patients with ARF and sepsis (ARFS) REE is increased by approximately 20%.

Thus, energy expenditure of patients with ARF is more determined by the underlying disease than acute uremic state and taken together these data indicate that when uremia is well-controlled by hemodialysis or hemofiltration there is little if any change in energy metabolism in ARF. In contrast to many other acute disease processes ARF might rather decrease than increase REE because in multiple organ dysfunction syndrome oxygen consumption was significantly higher in patients without impairment of renal function than in those with ARF [5]. (From Schneeweiss [4]; with permission.)

ESTIMATION OF ENERGY REQUIREMENTS

Calculation of resting energy expenditure (REE) (Harris Benedict equation):

Males: $66.47 \div (13.75 \times \text{BW}) \div (5 \times \text{height}) - (6.76 \times \text{age})$

Females: $655.1 \div (9.56 \times \text{BW}) \div (1.85 \times \text{height}) - (4.67 \times \text{age})$

The average REE is approximately 25 kcal/kg BW/day

Stress factors to correct calculated energy requirement for hypermetabolism:

Postoperative (no complications) 1.0

Long bone fracture 1.15–1.30

Cancer 1.10–1.30

Peritonitis/sepsis 1.20–1.30

Severe infection/polytrauma 1.20–1.40

Burns (= approx. REE + % burned body surface area) 1.20–2.00

Corrected energy requirements (kcal/d) = REE \times stress factor

FIGURE 18-4

Estimation of energy requirements. Energy requirements of patients with acute renal failure (ARF) have been grossly overestimated in the past and energy intakes of more than 50 kcal/kg of body weight (BW) per day (*ie*, about 100% above resting energy expenditure (REE) have been advocated [6]. Adverse effects of overfeeding have been extensively documented during the last decades, and it should be noted that energy intake must not exceed the actual energy consumption. Energy requirements can be calculated with sufficient accuracy by standard formulas such as the Harris Benedict equation. Calculated REE should be multiplied with a stress factor to correct for hypermetabolic disease; however, even in hypercatabolic conditions such as sepsis or multiple organ dysfunction syndrome, energy requirements rarely exceed 1.3 times calculated REE [1].

Protein metabolism

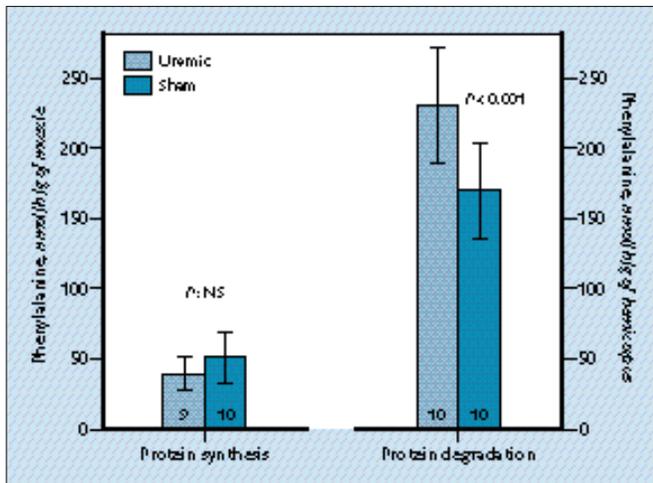


FIGURE 18-5

Protein metabolism in acute renal failure (ARF): activation of protein catabolism. Protein synthesis and degradation rates in acutely uremic and sham-operated rats. The hallmark of metabolic alterations in ARF is activation of protein catabolism with excessive release of amino acids from skeletal muscle and sustained negative nitrogen balance [7, 8]. Not only is protein breakdown accelerated, but there also is defective muscle utilization of amino acids for protein synthesis. In muscle, the maximal rate of insulin-stimulated protein synthesis is depressed by ARF and protein degradation is increased, even in the presence of insulin [9]. (From [8]; with permission.)

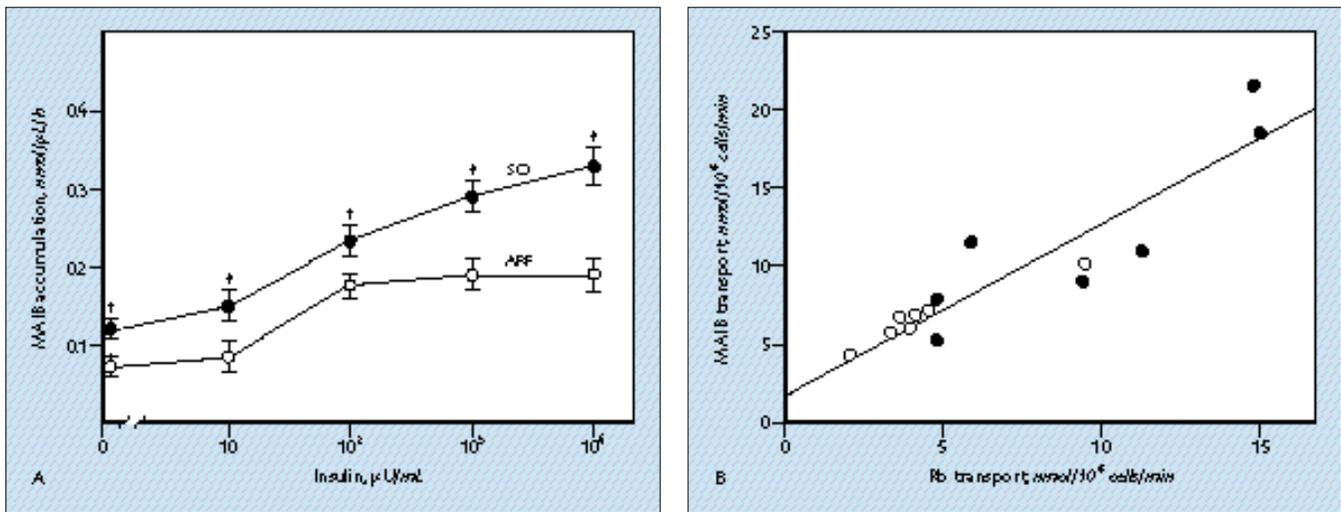


FIGURE 18-6

Protein metabolism in acute renal failure (ARF): impairment of cellular amino acid transport. **A**, Amino acid transport into skeletal muscle is impaired in ARF [10]. Transmembranous uptake of the amino acid analogue methyl-amino-isobutyrate (MAIB) is reduced in uremic tissue in response to insulin (muscle tissue from uremic animals, *black circles*, and from sham-operated animals, *open circles*, respectively). Thus, insulin responsiveness is reduced in ARF tissue, but, as can be seen from the parallel shift

of the curves, insulin sensitivity is maintained (*see also* Fig. 18-14). This abnormality can be linked both to insulin resistance and to a generalized defect in ion transport in uremia; both the activity and receptor density of the sodium pump are abnormal in adipose cells and muscle tissue [11]. **B**, The impairment of rubidium uptake (Rb) as a measure of Na-K-ATPase activity is tightly correlated to the reduction in amino acid transport. (*From* [10,11]; with permission.)

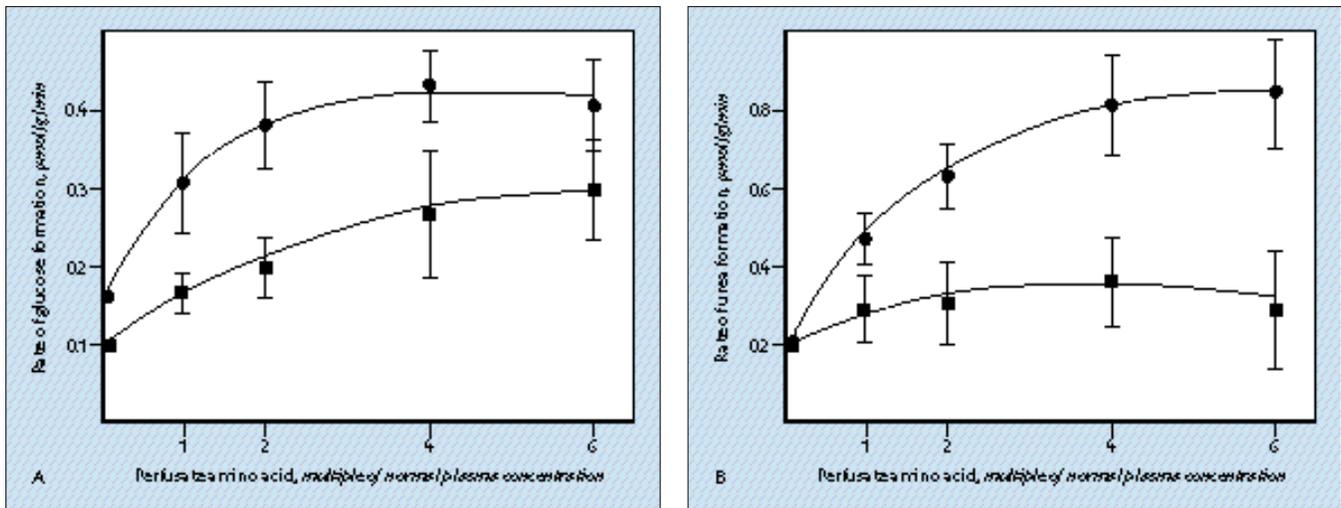


FIGURE 18-7

Protein catabolism in acute renal failure (ARF). Amino acids are redistributed from muscle tissue to the liver. Hepatic extraction of amino acids from the circulation—hepatic gluconeogenesis, **A**, and ureagenesis, **B**, from amino acids all are increased in ARF [12]. The dominant mediator of protein catabolism in ARF is this accel-

erated hepatic gluconeogenesis, which cannot be suppressed by exogenous substrate infusions (*see* Fig. 18-15). In the liver, protein synthesis and secretion of acute phase proteins are also stimulated. *Circles*—livers from acutely uremic rats; *squares*—livers from sham operated rats. (*From* Fröhlich [12]; with permission.)

CONTRIBUTING FACTORS TO PROTEIN CATABOLISM IN ACUTE RENAL FAILURE

Impairment of metabolic functions by uremia toxins

Endocrine factors

- Insulin resistance
- Increased secretion of catabolic hormones (catecholamines, glucagon, glucocorticoids)
- Hyperparathyroidism
- Suppression of release or resistance to growth factors

Acidosis

Systemic inflammatory response syndrome (activation of cytokine network)

Release of proteases

Inadequate supply of nutritional substrates

Loss of nutritional substrates (renal replacement therapy)

FIGURE 18-8

Protein catabolism in acute renal failure (ARF): contributing factors. The causes of hypercatabolism in ARF are complex and multifold and present a combination of nonspecific mechanisms induced by the acute disease process and underlying illness and associated complications, specific effects induced by the acute loss of renal function, and, finally, the type and intensity of renal replacement therapy.

A major stimulus of muscle protein catabolism in ARF is insulin resistance. In muscle, the maximal rate of insulin-stimulated protein synthesis is depressed by ARF and protein degradation is increased even in the presence of insulin [9].

Acidosis was identified as an important factor in muscle protein breakdown. Metabolic acidosis activates the catabolism of protein and oxidation of amino acids independently of azotemia, and nitrogen balance can be improved by correcting the metabolic acidosis [13]. These findings were not uniformly confirmed for ARF in animal experiments [14].

Several additional catabolic factors are operative in ARF. The secretion of catabolic hormones (catecholamines, glucagon, glucocorticoids), hyperparathyroidism which is also present in ARF (see Fig. 18-22), suppression of or decreased sensitivity to growth factors, the release of proteases from activated leukocytes—all can stimulate protein breakdown. Moreover, the release of inflammatory mediators such as tumor necrosis factor and interleukins have been shown to mediate hypercatabolism in acute disease [1, 2].

The type and frequency of renal replacement therapy can also affect protein balance. Aggravation of protein catabolism, certainly, is mediated in part by the loss of nutritional substrates, but some findings suggest that, in addition, both activation of protein breakdown and inhibition of muscular protein synthesis are induced by hemodialysis [15].

Last (but not least), of major relevance for the clinical situation is the fact that inadequate nutrition contributes to the loss of lean body mass in ARF. In experimental animals, starvation potentiates the catabolic response of ARF [7].

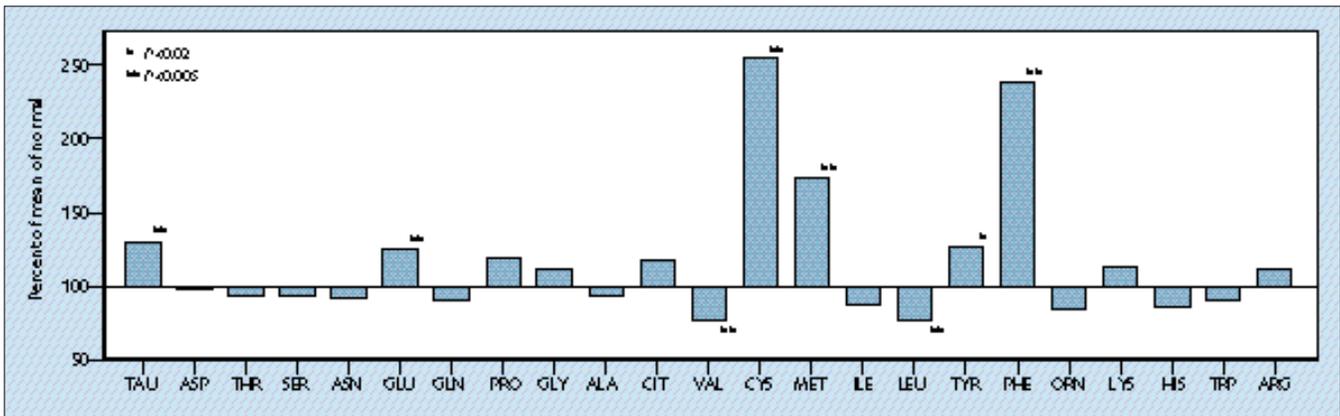


FIGURE 18-9

Amino acid pools and amino acid utilization in acute renal failure (ARF). As a consequence of these metabolic alterations, imbalances in amino acid pools in plasma and in the intracellular compartment occur in ARF. A typical plasma amino acid pattern is seen [16]. Plasma concentrations of cysteine (CYS), taurine (TAU), methionine (MET), and phenylalanine (PHE) are elevated, whereas plasma levels of valine (VAL) and leucine (LEU) are decreased.

Moreover, elimination of amino acids from the intravascular space is altered. As expected from the stimulation of hepatic

extraction of amino acids observed in animal experiments, overall amino acid clearance and clearance of most glucoplastic amino acids is enhanced. In contrast, clearances of PHE, proline (PRO), and, remarkably, VAL are decreased [16, 17]. ALA—alanine; ARG—arginine; ASN—asparagine; ASP—aspartate; CIT—citrulline; GLN—glutamine; GLU—glutamate; GLY—glycine; HIS—histidine; ORN—ornithine; PRO—proline; SER—serine; THR—threonine; TRP—tryptophan; TYR—tyrosine. (From Druml *et al.* [16]; with permission.)

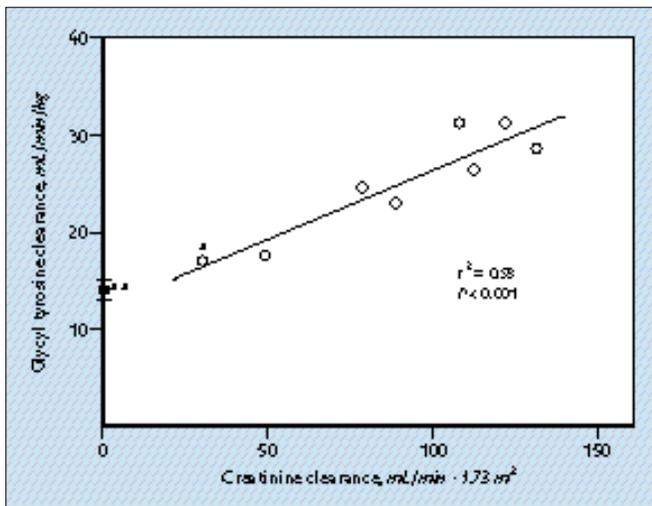


FIGURE 18-10

Metabolic functions of the kidney and protein and amino acid metabolism in acute renal failure (ARF). Protein and amino acid metabolism in ARF are also affected by impairment of the metabolic functions of the kidney itself. Various amino acids are synthe-

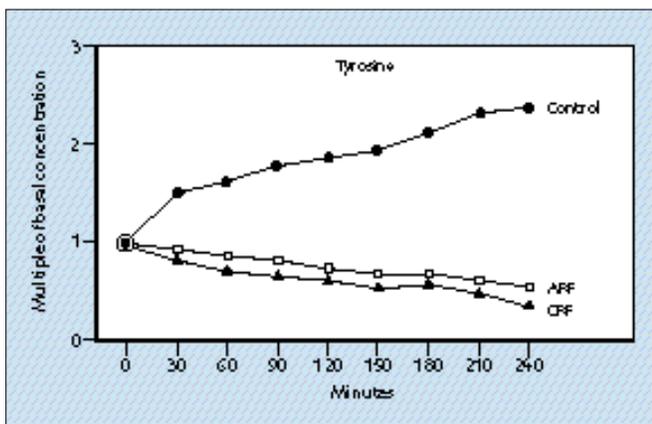


FIGURE 18-11

Amino acids in nutrition of acute renal failure (ARF): Conditionally essential amino acids. Because of the altered metabolic environment of uremic patients certain amino acids designated as nonessential for healthy subjects may become conditionally indispensable to ARF

sized or converted by the kidneys and released into the circulation: cysteine, methionine (from homocysteine), tyrosine, arginine, and serine [18]. Thus, loss of renal function can contribute to the altered amino acid pools in ARF and to the fact that several amino acids, such as arginine or tyrosine, which conventionally are termed nonessential, might become conditionally indispensable in ARF (see Fig. 18-11) [19].

In addition, the kidney is an important organ of protein degradation. Multiple peptides are filtered and catabolized at the tubular brush border, with the constituent amino acids being reabsorbed and recycled into the metabolic pool. In renal failure, catabolism of peptides such as peptide hormones is retarded. This is also true for acute uremia: insulin requirements decrease in diabetic patients who develop of ARF [20].

With the increased use of dipeptides in artificial nutrition as a source of amino acids (such as tyrosine and glutamine) which are not soluble or stable in aqueous solutions, this metabolic function of the kidney may also gain importance for utilization of these novel nutritional substrates. In the case of glycyl-tyrosine, metabolic clearance progressively decreases with falling creatinine clearance (*open circles*, 7 healthy subjects and a patient with unilateral nephrectomy*) but extrarenal clearance in the absence of renal function (*black circles*) is sufficient for rapid utilization of the dipeptide and release of tyrosine [21]. (From Druml *et al.* [21]; with permission.)

patients: histidine, arginine, tyrosine, serine, cysteine [19]. Infusion of arginine-free amino acid solutions can cause life-threatening complications such as hyperammonemia, coma, and acidosis.

Healthy subjects readily form tyrosine from phenylalanine in the liver: During infusion of amino acid solutions containing phenylalanine, plasma tyrosine concentration rises (*circles*) [22]. In contrast, in patients with ARF (*triangles*) and chronic renal failure (CRF, *squares*) phenylalanine infusion does not increase plasma tyrosine, indicating inadequate interconversion.

Recently, it was suggested that glutamine, an amino acid that traditionally was designated non-essential exerts important metabolic functions in regulating nitrogen metabolism, supporting immune functions, and preserving the gastrointestinal barrier. Thus, it can become conditionally indispensable in catabolic illness [23]. Because free glutamine is not stable in aqueous solutions, dipeptides containing glutamine are used as a glutamine source in parenteral nutrition. The utilization of dipeptides in part depends on intact renal function, and renal failure can impair hydrolysis (see Fig. 18-10) [24]. No systematic studies have been published on the use of glutamine in patients with ARF, and it must be noted that glutamine supplementation increases nitrogen intake considerably.

Protein requirements

ESTIMATING THE EXTENT OF PROTEIN CATABOLISM

Urea nitrogen appearance (UNA) (g/d)
 = Urinary urea nitrogen (UUN) excretion
 + Change in urea nitrogen pool
 = $(UUN \times V) + (BUN_2 - BUN_1) \times 0.006 \times BW$
 + $(BW_2 - BW_1) \times BUN_2/100$
 If there are substantial gastrointestinal losses, add urea nitrogen in secretions:
 = volume of secretions \times BUN₂
 Net protein breakdown (g/d) = UNA \times 6.25
 Muscle loss (g/d) = UNA \times 6.25 \times 5
 V is urine volume; BUN₁ and BUN₂ are BUN in mg/dL on days 1 and 2
 BW₁ and BW₂ are body weights in kg on days 1 and 2

FIGURE 18-12

Estimation of protein catabolism and nitrogen balance. The extent of protein catabolism can be assessed by calculating the urea nitrogen appearance rate (UNA), because virtually all nitrogen arising from amino acids liberated during protein degradation is converted to urea. Besides urea in urine (UUN), nitrogen losses in other body fluids (eg, gastrointestinal, choledochal) must be added to any change in the urea pool. When the UNA rate is multiplied by 6.25, it can be converted to protein equivalents. With known nitrogen intake from the parenteral or enteral nutrition, nitrogen balance can be estimated from the UNA calculation.

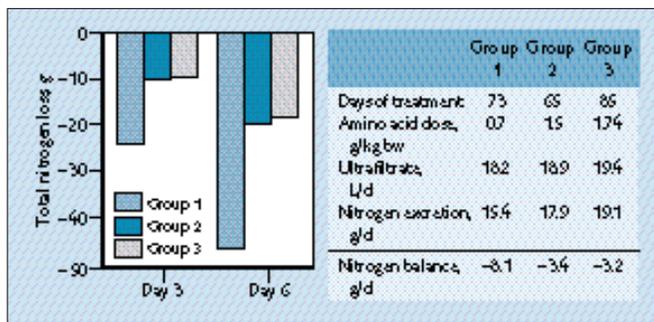


FIGURE 18-13

Amino acid and protein requirements of patients with acute renal failure (ARF). The optimal intake of protein or amino acids is affected more by the nature of the underlying cause of ARF and the extent of protein catabolism and type and frequency of dialysis than by kidney dysfunction per se. Unfortunately, only a few studies have attempted to define the optimal requirements for protein or amino acids in ARF:

In nonhypercatabolic patients, during the polyuric phase of ARF protein intake of 0.97 g/kg body weight per day was required to achieve a positive nitrogen balance [25]. A similar number (1.03g/kg

body weight per day) was derived from a study in which, unfortunately, energy intake was not kept constant [6]. In the polyuric recovery phase in patients with sepsis-induced ARF, a nitrogen intake of 15 g/day (averaging an amino acid intake of 1.3 g/kg body weight per day) as compared to 4.4 g/kg per day (about 0.3 g/kg amino acids) was superior in ameliorating nitrogen balance [26].

Several recent studies have tried to evaluate protein and amino acid requirements of critically ill patients with ARF. Kierdorf and associates found that, in these hypercatabolic patients receiving continuous hemofiltration therapy, the provision of amino acids 1.5 g/kg body weight per day was more effective in reducing nitrogen loss than infusion of 0.7 g (−3.4 versus −8.1 g nitrogen per day) [27]. An increase of amino acid intake to 1.74 g/kg per day did not further ameliorate nitrogen balance.

Chima and coworkers measured a mean PCR of 1.7 g/kg body weight per day in 19 critically ill ARF patients and concluded that protein needs in these patients range between 1.4 and 1.7 g/kg per day [28]. Similarly, Marcias and coworkers have obtained a protein catabolic rate (PCR) of 1.4 g/kg per day and found an inverse relationship between protein and energy provision and PCR and again recommended protein intake of 1.5 to 1.8 g/kg per day [29]. Similar conclusions were drawn by Ikizler in evaluating ARF patients on intermittent hemodialysis therapy [30]. (From Kierdorf *et al.* [27]; with permission.)

Glucose metabolism

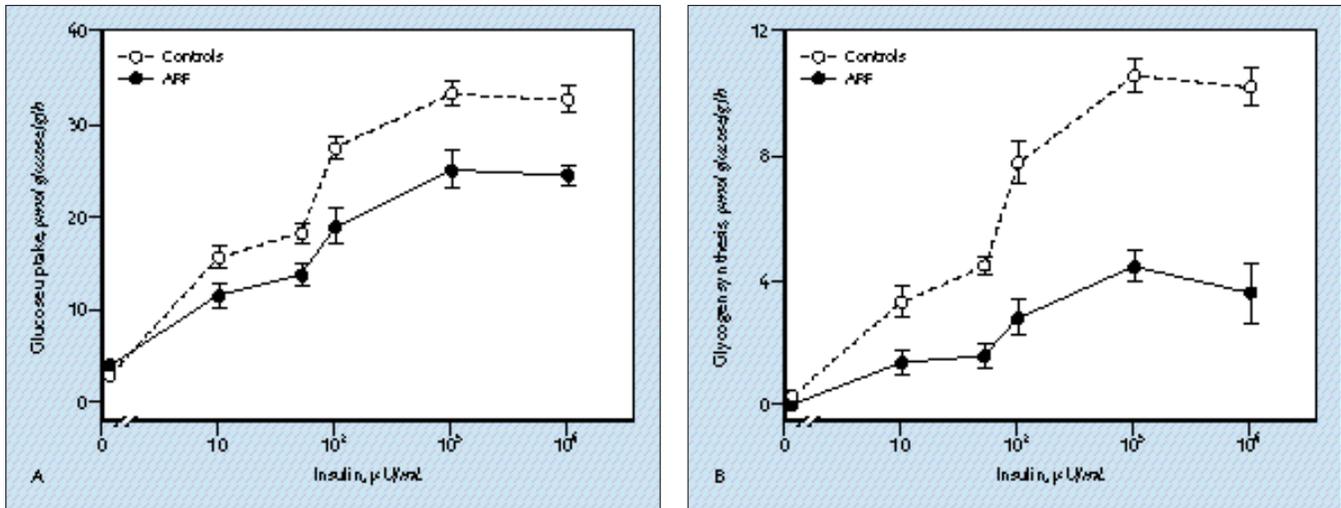


FIGURE 18-14

Glucose metabolism in acute renal failure (ARF): Peripheral insulin resistance. ARF is commonly associated with hyperglycemia. The major cause of elevated blood glucose concentrations is insulin resistance [31]. Plasma insulin concentration is elevated. Maximal insulin-stimulated glucose uptake by skeletal muscle is decreased by 50 %, **A**, and muscular glycogen synthesis is impaired, **B**. However, insulin concentrations that cause half-maximal stimulation of glucose uptake are normal, pointing to a postreceptor defect rather

than impaired insulin sensitivity as the cause of defective glucose metabolism. The factors contributing to insulin resistance are more or less identical to those involved in the stimulation of protein breakdown (see Fig. 18-8). Results from experimental animals suggest a common defect in protein and glucose metabolism: tyrosine release from muscle (as a measure of protein catabolism) is closely correlated with the ratio of lactate release to glucose uptake [9]. (From May *et al.* [31]; with permission.)

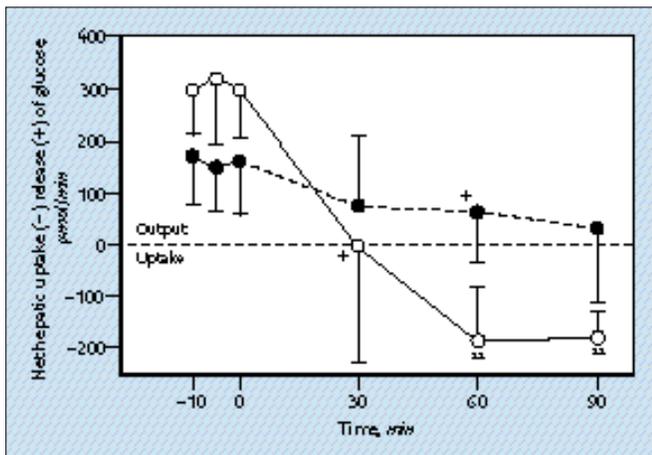


FIGURE 18-15

Glucose metabolism in acute renal failure (ARF): Stimulation of hepatic gluconeogenesis. A second feature of glucose metabolism (and at the same time the dominating mechanism of accelerated protein breakdown) in ARF is accelerated hepatic gluconeogenesis, mainly from conversion of amino acids released during protein catabolism. Hepatic extraction of amino acids, their conversion to glucose, and urea production are all increased in ARF (see Fig. 18-7) [12].

In healthy subjects, but also in patients with chronic renal failure, hepatic gluconeogenesis from amino acids is readily and completely suppressed by exogenous glucose infusion. In contrast, in ARF hepatic glucose formation can only be decreased, but not halted, by substrate supply. As can be seen from this experimental study, even during glucose infusion there is persistent gluconeogenesis from amino acids in acutely uremic dogs (•) as compared with controls dogs (○) whose livers switch from glucose release to glucose uptake [32].

These findings have important implications for nutrition support for patients with ARF: 1) It is impossible to achieve positive nitrogen balance; 2) Protein catabolism cannot be suppressed by providing conventional nutritional substrates alone. Thus, for future advances alternative means must be found to effectively suppress protein catabolism and preserve lean body mass. (From Cianciaruso *et al.* [32]; with permission.)

Lipid metabolism

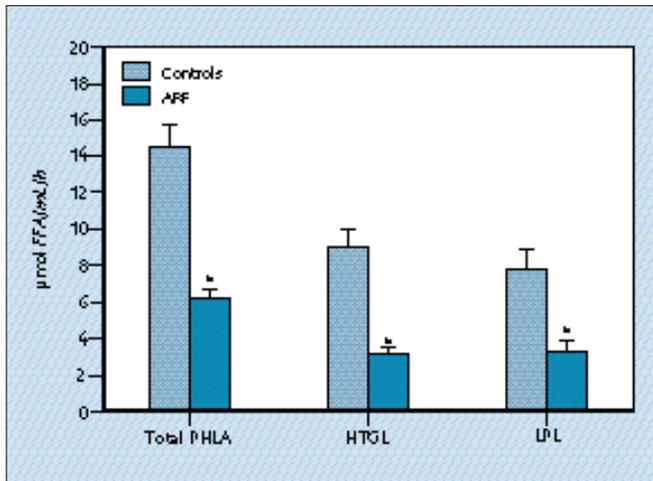


FIGURE 18-16

Lipid metabolism in acute renal failure (ARF). Profound alterations of lipid metabolism occur in patients with ARF. The triglyceride content of plasma lipoproteins, especially very low-density (VLDL) and low-density ones (LDL) is increased, while total cholesterol and in particular high-density lipoprotein (HDL) cholesterol are decreased [33,34]. The major cause of lipid abnormalities in ARF is impairment of lipolysis. The activities of both lipolytic systems, peripheral lipoprotein lipase and hepatic triglyceride lipase are decreased in patients with ARF to less than 50% of normal [35].

Maximal postheparin lipolytic activity (PHLA), hepatic triglyceride lipase (HTGL), and peripheral lipoprotein lipase (LPL) in 10 controls (*open bars*) and eight subjects with ARF (*black bars*). However, in contrast to this impairment of lipolysis, oxidation of fatty acids is not affected by ARF. During infusion of labeled long-chain fatty acids, carbon dioxide production from lipid was comparable between healthy subjects and patients with ARF [36]. FFA—free fatty acids. (*Adapted from Druml et al.* [35]; with permission.)

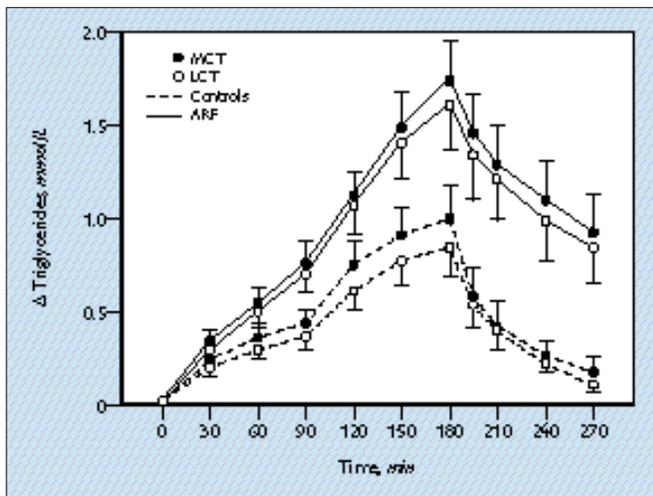


FIGURE 18-17

Impairment of lipolysis and elimination of artificial lipid emulsions in acute renal failure (ARF). Fat particles of artificial fat emulsions for parenteral nutrition are degraded as endogenous very low-density lipoprotein is. Thus, the nutritional consequence of the impaired lipolysis in ARF is delayed elimination of intravenously infused lipid emulsions [33, 34]. The increase in plasma triglycerides during infusion of a lipid emulsion is doubled in patients with ARF (N=7) as compared with healthy subjects (N=6). The clearance of fat emulsions is reduced by more than 50% in ARF. The impairment of lipolysis in ARF cannot be bypassed by using medium-chain triglycerides (MCT); the elimination of fat emulsions containing long chain triglycerides (LCT) or MCT is equally retarded in ARF [34]. Nevertheless, the oxidation of free fatty acid released from triglycerides is not impaired in patients with ARF [36]. (*From Druml et al.* [34]; with permission.)

Electrolytes and micronutrients

CAUSES OF ELECTROLYTE DERANGEMENTS IN ACUTE RENAL FAILURE

Hyperkalemia

Decreased renal elimination
 Increased release during catabolism
 2.38 mEq/g nitrogen
 0.36 mEq/g glycogen
 Decreased cellular uptake/
 increased release
 Metabolic acidosis: 0.6 mmol/L rise/0.1
 decrease in pH

Hyperphosphatemia

Decreased renal elimination
 Increased release from bone
 Increased release during catabolism:
 2 mmol/g nitrogen
 Decreased cellular uptake/utilization
 and/or increased release from cells

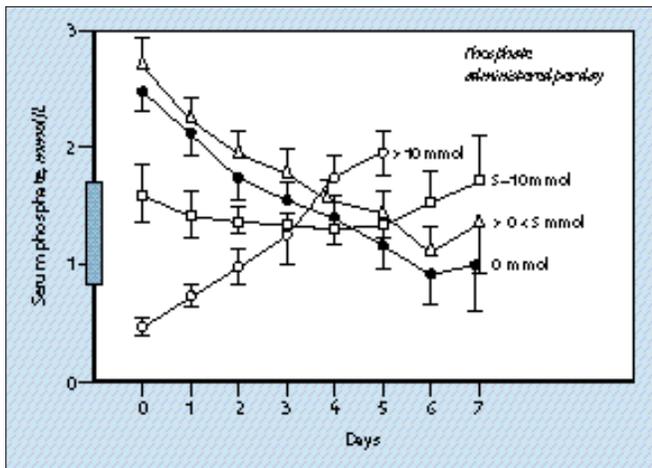


FIGURE 18-19

Electrolytes in acute renal failure (ARF): hypophosphatemia and hypokalemia. It must be noted that a considerable number of patients with ARF do not present with hyperkalemia or hyperphosphatemia, but at least 5% have low serum potassium and more than 12% have decreased plasma phosphate on admission [38]. Nutritional support, especially parenteral nutrition with low electrolyte content, can cause hypophosphatemia and hypokalemia in as many as 50% and 19% of patients respectively [39,40].

In the case of phosphate, phosphate-free artificial nutrition causes hypophosphatemia within a few days, even if the patient was hyperphosphatemic on admission (*black circles*) [41]. Supplementation of 5 mmol per day was effective in maintaining normal plasma phosphate concentrations (*open squares*), whereas infusion of more than 10 mmol per day resulted in hyperphosphatemia, even if the patients had decreased phosphate levels on admission (*open circles*).

Potassium or phosphate depletion increases the risk of developing ARF and retards recovery of renal function. With modern nutritional support, hyperkalemia is the leading indication for initiation of extracorporeal therapy in fewer than 5% of patients [38]. (Adapted from Kleinberger *et al.* [41]; with permission.)

FIGURE 18-18

Electrolytes in acute renal failure (ARF): causes of hyperkalemia and hyperphosphatemia. ARF frequently is associated with hyperkalemia and hyperphosphatemia. Causes are not only impaired renal excretion of electrolytes but release during catabolism, altered distribution in intracellular and extracellular spaces, impaired cellular uptake, and acidosis. Thus, the type of underlying disease and degree of hypercatabolism also determine the occurrence and severity of electrolyte abnormalities. Either hypophosphatemia or hyperphosphatemia can predispose to the development and maintenance of ARF [37].

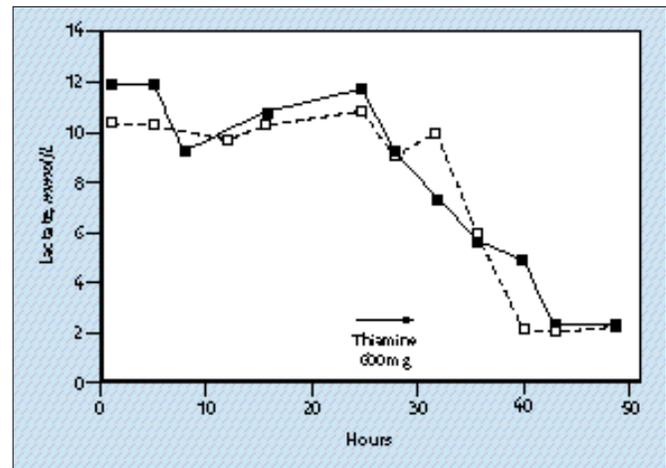


FIGURE 18-20

Micronutrients in acute renal failure (ARF): water-soluble vitamins. Balance studies on micronutrients (vitamins, trace elements) are not available for ARF. Because of losses associated with renal replacement therapy, requirements for water-soluble vitamins are expected to be increased also in patients with ARF. Malnutrition with depletion of vitamin body stores and associated hypercatabolic underlying disease in ARF can further increase the need for vitamins. Depletion of thiamine (vitamin B₁) during continuous hemofiltration and inadequate intake can result in lactic acidosis and heart failure [42]. This figure depicts the evolution of plasma lactate concentration before and after administration of 600 mg thiamine in two patients. Infusion of 600 mg of thiamine reversed the metabolic abnormality within a few hours. An exception to this approach to treatment is ascorbic acid (vitamin C); as a precursor of oxalic acid the intake should be kept below 200 mg per day because any excessive supply may precipitate secondary oxalosis [43]. (From Madl *et al.* [42]; with permission.)

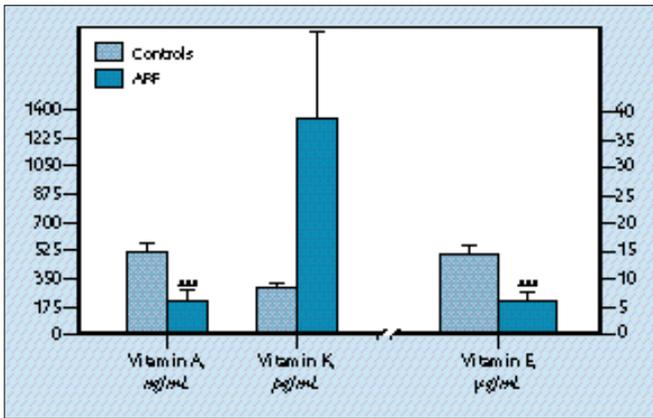


FIGURE 18-21

Micronutrients in acute renal failure (ARF): fat-soluble vitamins (A, E, K). Despite the fact that fat-soluble vitamins are not lost during hemodialysis and hemofiltration, plasma concentrations of vitamins A and E are depressed in patients with ARF and requirements are increased [44]. Plasma concentrations of vitamin K (with broad variations of individual values) are normal in ARF. Most commercial multivitamin preparations for parenteral infusions contain the recommended daily allowances of vitamins and can safely be used in ARF patients. (From Druml *et al.* [44]; with permission.)

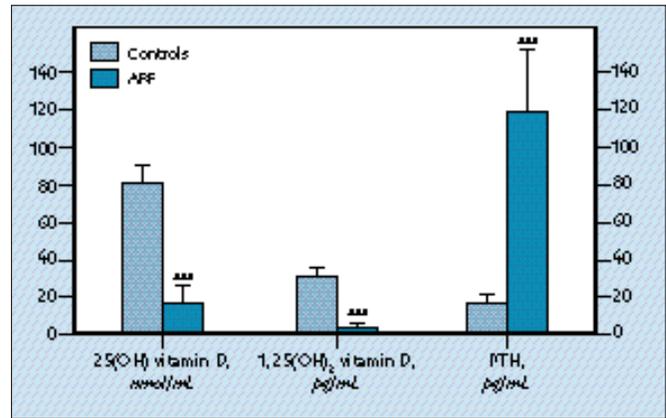


FIGURE 18-22

Hypocalcemia and the vitamin D–parathyroid hormone (PTH) axis in acute renal failure (ARF). ARF is also frequently associated with hypocalcemia secondary to hypoalbuminemia, elevated serum phosphate, plus skeletal resistance to calcemic effect of PTH and impairment of vitamin-D activation. Plasma concentration of PTH is increased. Plasma concentrations of vitamin D metabolites, 25-OH vitamin D₃ and 1,25-(OH)₂ vitamin D₃, are decreased [44]. In ARF caused by rhabdomyolysis rebound hypercalcemia may develop during the diuretic phase. (Adapted from Druml *et al.* [44]; with permission.)

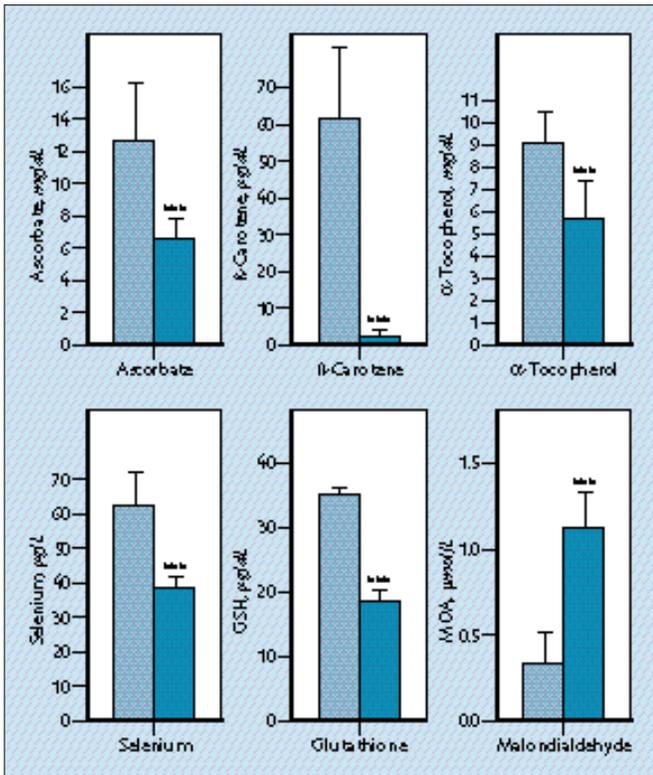


FIGURE 18-23

Micronutrients in acute renal failure (ARF): antioxidative factors. Micronutrients are part of the organism’s defense mechanisms against oxygen free radical induced injury to cellular components. In experimental ARF, antioxidant deficiency of the organism (decreased vitamin E or selenium status) exacerbates ischemic renal injury, worsens the course, and increases mortality, whereas repletion of antioxidant status exerts the opposite effect [45]. These data argue for a crucial role of reactive oxygen species and peroxidation of lipid membrane components in initiating and mediating ischemia or reperfusion injury.

In patients with multiple organ dysfunction syndrome and associated ARF (*lightly shaded bars*) various factors of the oxygen radical scavenger system are profoundly depressed as compared with healthy subjects (*black bars*): plasma concentrations of vitamin C, of β-carotene, vitamin E, selenium, and glutathione all are profoundly depressed, whereas the end-product of lipid peroxidation, malondialdehyde, is increased (double asterisk, P < 0.01; triple asterisk, P < 0.001). This underlines the importance of supplementation of antioxidant micronutrients for patients with ARF. (Adapted from Druml *et al.* [46]; with permission.)

Metabolic Impact of Renal Replacement Therapy

METABOLIC EFFECTS OF CONTINUOUS RENAL REPLACEMENT THERAPY

Amelioration of uremia intoxication (renal replacement)
 Plus
 Heat loss
 Excessive load of substrates (eg, lactate, glucose)
 Loss of nutrients (eg, amino acids, vitamins)
 Elimination of short-chain proteins (hormones, mediators?)
 Induction or activation of mediator cascades
 Stimulation of protein catabolism?

FIGURE 18-24

Metabolic impact of extracorporeal therapy. The impact of hemodialysis therapy on metabolism is multifactorial. Amino acid and protein metabolism are altered not only by substrate losses but also by activation of protein breakdown mediated by release of leukocyte-derived proteases, of inflammatory mediators (interleukins and tumor necrosis factor) induced by blood-membrane interactions or endotoxin. Dialysis can also induce inhibition of muscle protein synthesis [15].

In the management of patients with acute renal failure (ARF), continuous renal replacement therapies (CRRT), such as continuous

(arteriovenous) hemofiltration (CHF) and continuous hemodialysis have gained wide popularity. CRRTs are associated with multiple metabolic effects in addition to “renal replacement” [47].

By cooling of the extracorporeal circuit and infusion of cooled substitution fluids, CHF may induce considerable heat loss (350 to 700 kcal per day). On the other hand, hemofiltration fluids contain lactate as anions, oxidation of which in part compensates for the heat loss. This lactate load can result in hyperlactemia in the presence of liver dysfunction or increased endogenous lactate formation such as in circulatory shock.

Several nutrients with low protein binding and small molecular weight (sieving coefficient 0.8 to 1.0), such as vitamins or amino acids are eliminated during therapy. Amino acid losses can be estimated from the volume of the filtrate and average plasma concentration, and usually this accounts for a loss of approximately 0.2 g/L of filtrate and, depending on the filtered volume, 5 to 10 g of amino acid per day, respectively, representing about 10 % of amino acid input, but it can be even higher during continuous hemodiafiltration [48].

With the large molecular size cut-off of membranes used in hemofiltration, small proteins such as peptide hormones are filtered. In view of their short plasma half-life hormone losses are minimal and probably not of pathophysiologic importance. Quantitatively relevant elimination of mediators by CRRT has not yet been proven. On the other hand, prolonged blood-membrane interactions can induce consequences of bioincompatibility and activation of various endogenous cascade systems.

Nutrition, Renal Function, and Recovery

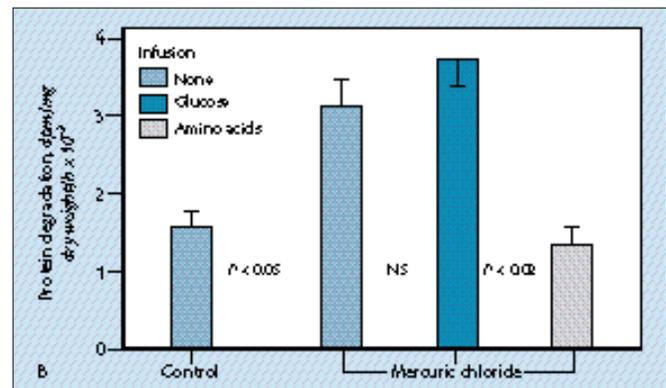
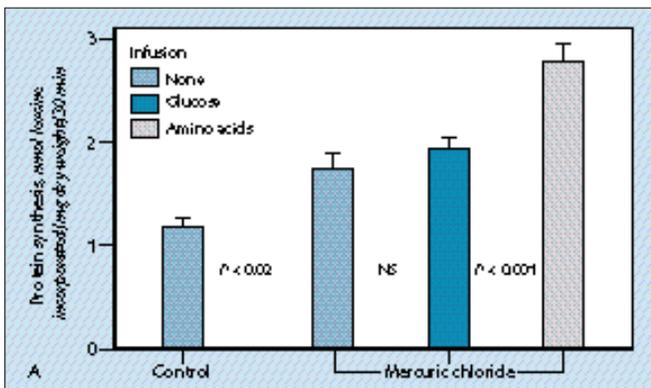


FIGURE 18-25

A, B, Impact of nutritional interventions on renal function and course of acute renal failure (ARF). Starvation accelerates protein breakdown and impairs protein synthesis in the kidney, whereas refeeding exerts the opposite effects [49]. In experimental animals, provision of amino acids or total parenteral nutrition accelerates tissue repair and recovery of renal function [50]. In patients, however, this has been much more difficult to prove, and only one study has reported on a positive effect of TPN on the resolution of ARF [51].

Infusion of amino acids raised renal cortical protein synthesis as evaluated by ^{14}C -leucine incorporation and depressed protein breakdown in rats with mercuric chloride-induced ARF [49]. On the other hand, in a similar model of ARF, infusions of varying quantities of essential amino acids (EAA) and nonessential amino acids (NEAA) did not provide any protection of renal function and in fact increased mortality [52]. However, in balance available evidence suggests that provision of substrates may enhance tissue regeneration and wound healing, and potentially, also renal tubular repair [49]. (From Toback *et al.* [50]; with permission.)

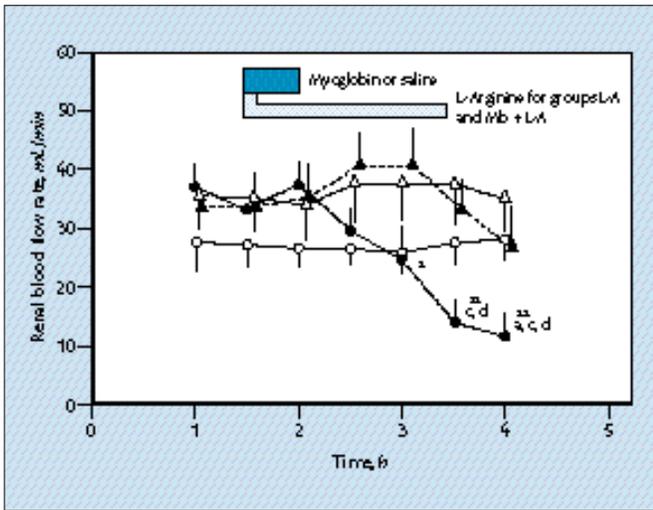


FIGURE 18-26

Impact of nutritional interventions on renal function in acute renal failure (ARF). Amino acid infused before or during ischemia or nephrotoxicity may enhance tubule damage and accelerate loss of renal function in rat models of ARF. In part, this therapeutic paradox [53] from amino acid alimentation in ARF is related to the increase in metabolic work for transport processes when oxygen supply is limited, which may aggravate ischemic injury [54]. Similar observations have been made with excess glucose infusion during renal ischemia. Amino acids may as well exert a protective effect on renal function. Glycine, and to a lesser degree alanine, limit tubular injury in ischemic and nephrotoxic models of ARF [55]. Arginine (possibly by producing nitric oxide) reportedly acts to preserve renal perfusion and tubular function in both nephrotoxic and ischemic models of ARF, whereas inhibitors of nitric oxide synthase exert an opposite effect [56,57]. In myoglobin-induced ARF the drop in renal blood flow (*black circles*, ARF controls) is prevented by L-arginine infusion (*black triangles*) [57]. (From Wakabayashi *et al.* [57]; with permission.)

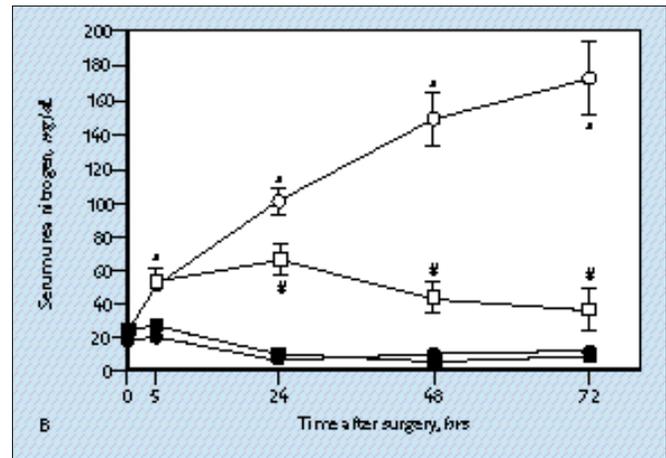
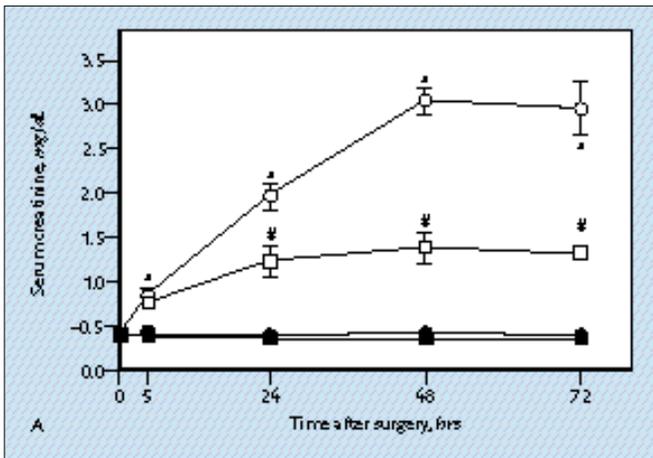


FIGURE 18-27

Impact of endocrine-metabolic interventions on renal function and course of acute renal failure (ARF). Various other endocrine-metabolic interventions (eg, thyroxine, human growth hormone [HGH], epidermal growth factor, insulin-like growth factor 1 [IGF-1]) have been shown to accelerate regeneration after experimental ARF [51]. In a rat model of postischemic ARF, treatment with IGF-1 starting 5 hours after induction of ARF accelerates recovery from

ischemic ARF, **A**, but also reduces the increase in BUN and improves nitrogen balance, **B**, [58]. (*open circles*) ARF plus vehicle; (*black circles*, sham-operated rats plus vehicle; *open squares*, ARF plus rhIGF-I; *black squares*, sham operated rats plus rhIGF-I.) Unfortunately, efficacy of these interventions was not uniformly confirmed in clinical studies [59, 60]. (From Ding *et al.* [58]; with permission.)

Decision Making, Patient Classification, and Nutritional Requirements

DECISIONS FOR NUTRITION IN PATIENTS WITH ACUTE RENAL FAILURE

Decisions dependent on

Patients ability to resume oral diet (within 5 days?)

Nutritional status

Underlying illness/degree of associated hypercatabolism

1. What patient with acute renal failure needs nutritional support?
2. When should nutritional support be initiated?
3. At what degree of impairment in renal function should the nutritional regimen be adapted for renal failure?
4. In a patient with multiple organ dysfunction, which organ determines the type of nutritional support?
5. Is enteral or parenteral nutrition the most appropriate method for providing nutritional support?

FIGURE 18-28

Nutrition in patients with acute renal failure (ARF): decision making. Not every patient with ARF requires nutritional support. It is important to identify those who will benefit and to define the optimal time to initiate therapy [1].

The decision to initiate nutritional support is influenced by the patient's ability to cover nutritional requirements by eating, in addition to the nutritional status of the patient as well as the type of

underlying illness involved. In any patient with evidence of malnourishment, nutritional therapy should be instituted regardless of whether the patient will be likely to eat. If a well-nourished patient can resume a normal diet within 5 days, no specific nutritional support is necessary. The degree of accompanying catabolism is also a factor. For patients with underlying diseases associated with excess protein catabolism, nutritional support should be initiated early.

If there is evidence of malnourishment or hypercatabolism, nutritional therapy should be initiated early, even if the patient is likely to eat before 5 days. Modern nutritional strategies should be aimed at avoiding the development of deficiency states and of "hospital-acquired malnutrition." During the acute phase of ARF (the first 24 hours after trauma or surgery) nutritional support should be withheld because nutrients infused during this "ebb phase" are not utilized, could increase oxygen requirements, and aggravate tissue injury and renal dysfunction.

The nutritional regimen should be adapted for renal failure when renal function is impaired. The multiple metabolic alterations characteristic of ARF occur when kidney function is below 30% of normal. Thus, when creatinine clearance falls below 50 to 30 mL per minute/1.73 m² (or serum creatinine rises above 2.5 to 3.0 mg/dL) the nutritional regimen should be adapted to ARF.

With the exception of severe hepatic failure and massively deranged amino acid metabolism (hyperammonemia) or protein synthesis (depletion of coagulation factors) renal failure is the major determinant of the nutritional regimen in patients with multiple organ dysfunction.

Enteral feeding is preferred for all patients, including those with ARF. Nevertheless, for a large portion of patients, parenteral nutrition—total or partial—will be necessary to meet nutritional requirements.

PATIENT CLASSIFICATION AND SUBSTRATE REQUIREMENTS IN PATIENTS WITH ACUTE RENAL FAILURE

	Extent of Catabolism		
	Mild	Moderate	Severe
Excess urea appearance (above nitrogen intake)	>6 g	6–12 g	>12 g
Clinical setting (examples)	Drug toxicity	Elective surgery ± infection	Severe injury or sepsis
Mortality	20 %	60%	>80%
Dialysis or hemofiltration frequency	Rare	As needed	Frequent
Route of nutrient administration	Oral	Enteral or parenteral	Enteral or parenteral
Energy recommendations (kcal/kg BW/d)	25	25–30	25–35
Energy substrates	Glucose	Glucose + fat	Glucose + fat
Glucose (g/kg BW/d)	3.0–5.0	3.0–5.0	3.0–5.0 (max. 7.0)
Fat (g/kg BW/d)		0.5–1.0	0.8–1.5
Amino acids/protein (g/kg/d)	0.6–1.0	0.8–1.2	1.0–1.5
	EAA (+NEAA)	EAA + NEAA	EAA + NEAA
Nutrients used	Foods	Enteral formulas Glucose 50%–70% + fat emulsions 10% or 20%	Enteral formulas Glucose 50%–70% + fat emulsions 10% or 20%
	EAA + specific NEAA solutions (general or “nephro”) Multivitamin and multitrace element preparations		

BW—body weight; EAA—essential amino acids; NEAA—nonessential amino acids.

FIGURE 18-29

Patient classification: substrate requirements. Ideally, a nutritional program should be designed for each individual acute renal failure (ARF) patient. In clinical practice, it has proved useful to distinguish three groups of patients based on the extent of protein catabolism associated with the underlying disease and resulting levels of dietary requirements.

Group I includes patients without excess catabolism and a UNA of less than 6 g of nitrogen above nitrogen intake per day. ARF is usually caused by nephrotoxins (aminoglycosides, contrast media, mismatched blood transfusion). In most cases, these patients are fed orally and the prognosis for recovery of renal function and survival is excellent.

Group II consists of patients with moderate hypercatabolism and a UNA exceeding nitrogen intake 6 to 12 g of nitrogen per day. Affected patients frequently suffer from complicating infections, peritonitis, or moderate injury in association with ARF. Tube feeding or intravenous nutritional support is generally required, and dialysis or hemofiltration often becomes necessary to limit waste product accumulation.

Group III are patients who develop ARF in association with severe trauma, burns, or overwhelming infection. UNA is markedly elevated (more than 12 g of nitrogen above nitrogen intake). Treatment strategies are usually complex and include parenteral nutrition, hemodialysis or continuous hemofiltration plus blood pressure and ventilatory support. To reduce catabolism and avoid protein depletion nutrient requirements are high and dialysis is used to maintain fluid balance and blood urea nitrogen below 100 mg/dL. Mortality in this group of patients exceeds 60% to 80%, but it is not the loss of renal function that accounts for the poor prognosis. It is superimposed hypercatabolism and the severity of the underlying illness. (Adapted from Druml [1]; with permission.)

Enteral Nutrition

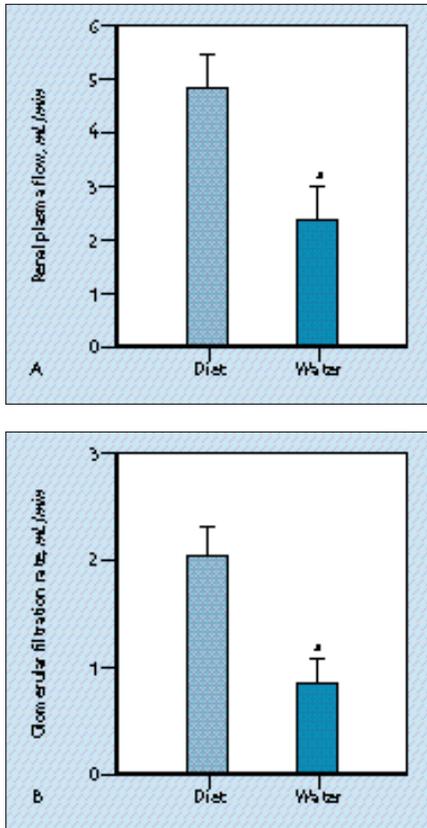


FIGURE 18-30

Enteral nutrition (tube feeding). The gastrointestinal tract should be used whenever possible because enteral nutrients may help to maintain gastrointestinal function and the mucosal barrier and thus prevent translocation of bacteria and systemic infection [61]. Even small amounts of enteral diets exert a protective effect on the intestinal mucosa. Recent animal experiments suggest that enteral feeds may exert additional advantages in acute renal failure (ARF) patients [63]: in glycerol-induced ARF in rats enteral feeding improved renal perfusion, **A**, and preserved renal function, **B**. For patients with ARF who are unable to eat because of cerebral impairment, anorexia, or nausea, enteral nutrition should be provided through small, soft feeding tubes with the tip positioned in the stomach or jejunum [61]. Feeding solutions can be administered by pump intermittently or continuously. If given continuously, the stomach should be aspirated every 2 to 4 hours until adequate gastric emptying and intestinal peristalsis are established. To avoid diarrhea, the amount and concentration of the solution should be increased gradually over several days until nutritional requirements are met. Undesired, but potentially treatable side effects include nausea, vomiting, abdominal distension and cramping and diarrhea. (From Roberts *et al.* [62]; with permission.)

SPECIFIC ENTERAL FORMULAS FOR NUTRITIONAL SUPPORT OF PATIENTS WITH RENAL FAILURE

	Amin-Aid	Travasorb renal*	Salvi peptide nephro†	Survimed renal‡	Suplena§	Nepro§
Volume (mL)	750	1050	500	1000	500	500
Calories (kcal)	1467	1400	1000	1320	1000	1000
(cal/mL)	1.96	1.35	2.00	1.32	2.00	2.00
Energy distribution						
Protein:fat:carbohydrates (%)	4:21:75	7:12:81	8:22:70	6:10:84	6:43:51	14:43:43
kcal/g N	832:1	389:1	313:1	398:1	418:1	179:1
Proteins (g)	14.6	24.0	20.0	20.8	15.0	35
EAA (%)	100	60	23			
NEAA (%)	—	30	20			
Hydrolysate (%)	—	—	23	100		
Full protein (%)	—	—	34	—	100	100
Nitrogen (g)	1.76	3.6	3.2	3.32	2.4	5.6
Carbohydrates (g)	274	284	175	276	128	108
Monodisaccharides (%)	100	100	3		10	12
Oligosaccharides (%)	—	—	28			
Polysaccharides (%)	—	—	69	88		90
Fat (g)	34.6	18.6	24	15.2	48	47.8
LCT (%)		30	50		100	100
Essential GA (%)		18	31	52	22	
MCT (%)		70	50	30	0	0
Nonprotein (cal/g N)	502	363	288	374	393	154
Osmol (mOsm/kg)	1095	590	507	600	635	615
Sodium (mmol/L)	11	—	7.2	15.2	32	34.0
Potassium (mmol/L)	—	—	1.5	8	27.0	28.5
Phosphate (mmol)	—	16.1	6.13	6.4	11.0	11.0
Vitamins	b	a	a	a	a	a
Minerals	b	b	a	a	a	a

* 3 bags + 810 mL = 1050 mL

† component I + component II + 350 mL = 500 mL

‡ 4 bags + 800 mL = 1000 mL

§ Liquid formula, cans 8 fl oz (=237.5 mL), supplemented with carnitine, taurine with a low-protein (Suplena) or moderate-protein content (Nepro)

a 2000 kcal/d meets RDA for most vitamins/trace elements

b Must be added

EAA—essential amino acids; FA—fatty acids; LCT—long-chain triglycerides; MCT—medium-chain triglycerides; N—nitrogen; NEAA—non-essential amino acids.

FIGURE 18-31

Enteral feeding formulas. There are standardized tube feeding formulas designed for subjects with normal renal function that can also be given to patients with acute renal failure (ARF).

Unfortunately, the fixed composition of nutrients, including proteins and high content of electrolytes (especially potassium and phosphate) often limits their use for ARF.

Alternatively, enteral feeding formulas designed for nutritional therapy of patients with chronic renal failure (CRF) can be used. The preparations listed here may have advantages also for patients

with ARF. The protein content is lower and is confined to high-quality proteins (in part as oligopeptides and free amino acids), the electrolyte concentrations are restricted. Most formulations contain recommended allowances of vitamins and minerals.

In part, these enteral formulas are made up of components that increase the flexibility in nutritional prescription and enable adaptation to individual needs. The diets can be supplemented with additional electrolytes, protein, and lipids as required. Recently, ready-to-use liquid diets have also become available for renal failure patients.

Parenteral Nutrition

RENAL FAILURE FLUID—ALL-IN-ONE SOLUTION

Component	Quantity	Remarks
Glucose 40%–70%	500 mL	In the presence of severe insulin resistance switch to D30W
Fat emulsion 10%–20%	500 mL	Start with 10%, switch to 20% if triglycerides are < 350 mg/dL
Amino acids 6.5%–10%	500 mL	General or special “nephro” amino acid solutions, including EAA and NEAA
Water-soluble vitamins	Daily	Limit vitamin C intake < 200 mg/d
Fat-soluble vitamins*	Daily	
Trace elements*	Twice weekly	Caveats: toxic effects
Electrolytes	As required	Caveats: hypophosphatemia or hypokalemia after initiation of TPN
Insulin	As required	Added directly to the solution or given separately

* Combination products containing the recommended daily allowances.

FIGURE 18-32

Parenteral solutions. Standard solutions are available with amino acids, glucose, and lipids plus added vitamins, trace elements, and electrolytes contained in a single bag (“total admixture” solutions, “all-in-one” solutions). The stability of fat emulsions in such mixtures should be tested. If hyperglycemia is present, insulin can be added to the solution or administered separately.

To ensure maximal nutrient utilization and avoid metabolic derangements as mineral imbalance, hyperglycemia or blood urea nitrogen rise, the infusion should be started at a slow rate (providing about 50% of requirements) and gradually increased over several days. Optimally, the solution should be infused continuously over 24 hours to avoid marked derangements in substrate concentrations in the presence of impaired utilization for several nutritional substrates in patients with acute renal failure. EAA, NEAA—essential and nonessential amino acids; TPN—total parenteral nutrition.

AMINO ACID SOLUTIONS FOR THE TREATMENT OF ACUTE RENAL FAILURE (“NEPHRO” SOLUTIONS)

	Rose-Requirements	RenAmin (Clintec)	Aminess (Clintec)	Aminosyn RF (Abbott)	NephroAmine (McGaw)	Nephroject (Fresenius)
Amino acids (g/L)		65	52	52	54	100
(= g/%)		6.5	5.2	5.2	5.4	10
Volume (mL)		500	400	1000	1000	500
(mOsm/L)		600	416	475	435	908
Nitrogen (g/L)		10	8.3	8.3	6.5	16.3
Essential amino acids (g/L)						
Isoleucine	1.40	5.00	5.25	4.62	5.60	5.80
Leucine	2.20	6.00	8.25	7.26	8.80	12.80
Lysine acetate/HCl	1.60	4.50	6.00	5.35	6.40	12.00
Methionine	2.20	5.00	8.25	7.26	8.80	2.00
Phenylalanine	2.20	4.90	8.25	7.26	8.80	3.50
Threonine	1.00	3.80	3.75	3.30	4.00	8.20
Tryptophan	0.50	1.60	1.88	1.60	2.00	3.00
Valine	1.60	8.20		5.20	6.40	8.70
Nonessential amino acids (g/L)						
Alanine		5.60				6.20
Arginine		6.30	6.00	6.00		8.20
Glycine		3.00				6.30*
Histidine		4.20	4.12	4.29	2.50	9.80
Proline		3.50				3.00
Serine		3.00				7.60
Tyrosine		0.40				3.00†
Cysteine					0.20	0.40

* Glycine is a component of the dipeptide.

† Tyrosine is included as dipeptide (glycyl-L-tyrosine).

FIGURE 18-33

Amino acid (AA) solutions for parenteral nutrition in acute renal failure (ARF). The most controversial choice regards the type of amino acid solution to be used: either essential amino acids (EAAs) exclusively, solutions of EAA plus nonessential amino acids (NEAAs), or specially designed “nephro” solutions of different proportions of EAA and specific NEAA that might become “conditionally essential” for ARF (see Fig. 18-11).

Use of solutions of EAA alone is based on principles established for treating chronic renal failure (CRF) with a low-protein diet and an EAA supplement. This may be inappropriate as the metabolic adaptations to low-protein diets in response to CRF may not have occurred in patients with ARF. Plus, there are fundamental differences in the goals of nutritional therapy in the two groups of patients, and consequently, infusion solutions of EAA may be sub-optimal.

Thus, a solution should be chosen that includes both essential and nonessential amino acids (EAA, NEAA) in standard propor-

tions or in special proportions designed to counteract the metabolic changes of renal failure (“nephro” solutions), including the amino acids that might become conditionally essential in ARF.

Because of the relative insolubility of tyrosine in water, dipeptides containing tyrosine (such as glycyl-tyrosine) are contained in modern nephro solutions as the tyrosine source [22, 23]. One should be aware of the fact that the amino acid analogue *N*-acetyl tyrosine, which previously was used frequently as a tyrosine source, cannot be converted into tyrosine in humans and might even stimulate protein catabolism [21].

Despite considerable investigation, there is no persuasive evidence that amino acid solutions enriched in branched-chain amino acids exert a clinically significant anticatabolic effect. Systematic studies using glutamine supplementation for patients with ARF are lacking (see Fig. 18-11).

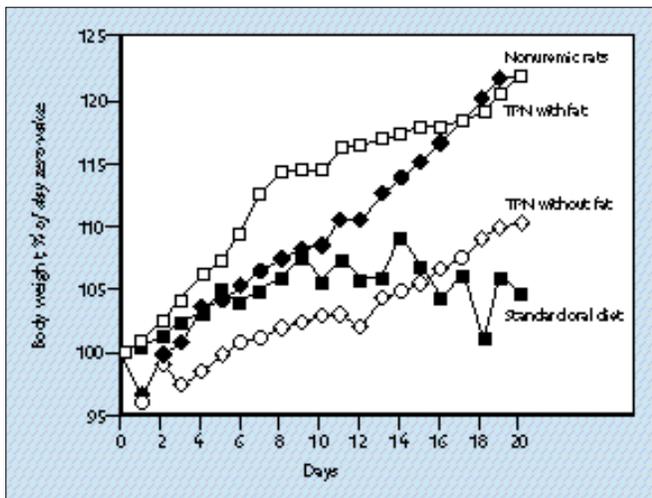


FIGURE 18-34

Energy substrates in total parenteral nutrition (TPN) in acute renal failure (ARF): glucose and lipids. Because of the well-documented effects of overfeeding, energy intake of patients with ARF must not exceed their actual energy expenditure (*ie*, in most cases 100% to 130% of resting energy expenditure [REE]; see Figs. 18-3 and 18-4) [2].

Glucose should be the principal energy substrate because it can be utilized by all organs, even under hypoxic conditions, and has the potential for nitrogen sparing. Since ARF impairs glucose tolerance, insulin is frequently necessary to maintain normoglycemia. Any hyperglycemia must be avoided because of the untoward associated side effects—such as aggravation of tissue injury, glycation of proteins, activation of protein catabolism, among others [2]. When intake is increased above 5 g/kg of body weight per day infused glucose will not be oxidized but will promote lipogenesis with fatty infiltration of the liver and excessive carbon dioxide production and hypercarbia. Often, energy requirements cannot be met by glucose infusion without adding large amounts of insulin, so a portion of the energy should be supplied by lipid emulsions [2].

The most suitable means of providing the energy substrates for parenteral nutrition for patients with ARF is not glucose or lipids, but glucose *and* lipids [2]. In experimental uremia in rats, TPN with 30% of nonprotein energy as fat promoted weight gain and ameliorated the uremic state and survival [63]. (*From Wennberg et al.* [63]; with permission.)

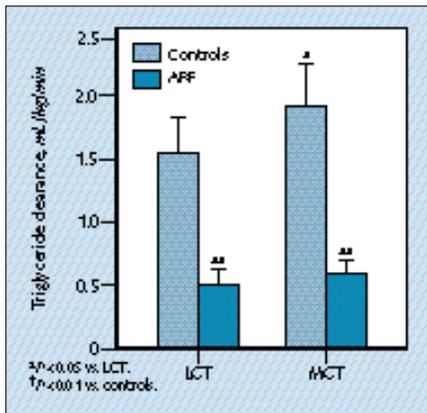


FIGURE 18-35

Energy substrates in parenteral nutrition: lipid emulsions. Advantages of intravenous lipids include high specific energy content, low osmolality, provision of essential fatty acids and phospholipids to prevent deficiency syndromes, fewer hepatic side effects (such as steatosis, hyperbilirubinemia), and reduced carbon dioxide production, especially relevant for patients with respiratory failure.

Changes in lipid metabolism associated with acute renal failure (ARF) should not prevent the use of lipid emulsions. Instead, the amount infused should be adjusted to meet the patient's capacity to utilize lipids. Usually, 1 g/kg of body weight per day of fat will not increase plasma triglycerides substantially, so about 20% to 25% of energy requirements can be met [1]. Lipids should not be administered to patients with hyperlipidemia (*ie*, plasma triglycerides above 350 mg/dL) activated intravascular coagulation, acidosis (pH below 7.25), impaired circulation or hypoxemia.

Parenteral lipid emulsions usually contain long-chain triglycerides (LCT), most derived from soybean oil. Recently, fat emulsions containing a mixture of LCT and medium-chain triglycerides (MCT) have been introduced for intravenous use. Proposed advantages include faster elimination from the plasma owing to higher affinity to the lipoprotein lipase enzyme, complete, rapid, and carnitine-independent metabolism, and a triglyceride-lowering effect; however, use of MCT does not promote lipolysis, and elimination of triglycerides of both types of fat emulsions is equally retarded in ARF [34]. (*Adapted from* [34]; with permission.)

SUGGESTED SCHEDULE FOR MINIMAL MONITORING OF PARENTERAL NUTRITION

Variables	Metabolic Status	
	Unstable	Stable
Blood glucose	1–6 × daily	Daily
Osmolality	Daily	2 × weekly
Electrolytes (Na ⁺ , K ⁺ , Cl ⁻)	Daily	Daily
Calcium, phosphate, magnesium	Daily	3 × weekly
Daily BUN increment	Daily	Daily
Urea nitrogen appearance rate	Daily	2 × weekly
Triglycerides	Daily	2 × weekly
Blood gas analysis, pH	Daily	1 × weekly
Ammonia	2 × weekly	1 × weekly
Transaminases + bilirubin	2 × weekly	1 × weekly

FIGURE 18-36

Complications and monitoring of nutritional support in acute renal failure (ARF).

Complications: Technical problems and infectious complications originating from the central venous catheter, chemical incompatibilities, and metabolic complications of parenteral nutrition are similar in ARF patients and in nonuremic subjects. However, tolerance to volume load is limited, electrolyte derangements can develop rapidly, exaggerated protein or amino acid intake stimulates excessive blood urea nitrogen (BUN) and waste product accumulation and glucose intolerance, and decreased fat clearance can cause hyperglycemia and hypertriglyceridemia. Thus, nutritional therapy for ARF patients requires more frequent monitoring than it does for other patient groups, to avoid metabolic complications.

Monitoring: This table summarizes laboratory tests that monitor parenteral nutrition and avoid metabolic complications. The frequency of testing depends on the metabolic stability of the patient. In particular, plasma glucose, potassium, and phosphate should be monitored repeatedly after the start of parenteral nutrition.

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