

## 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

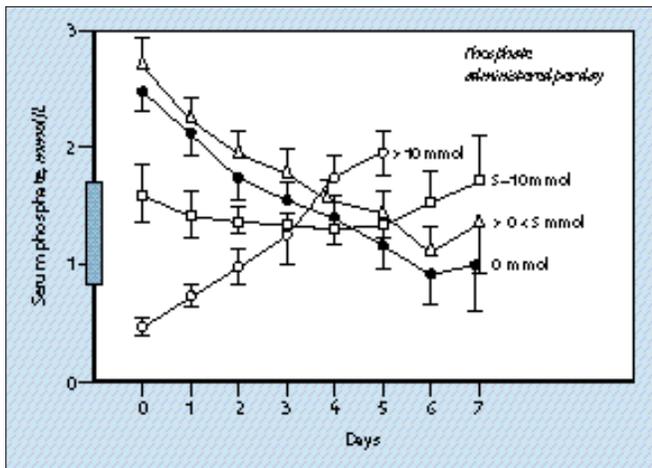


FIGURE 18-19

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].

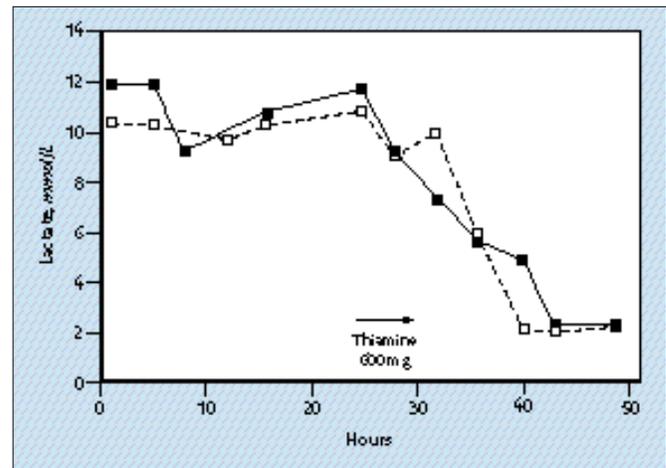
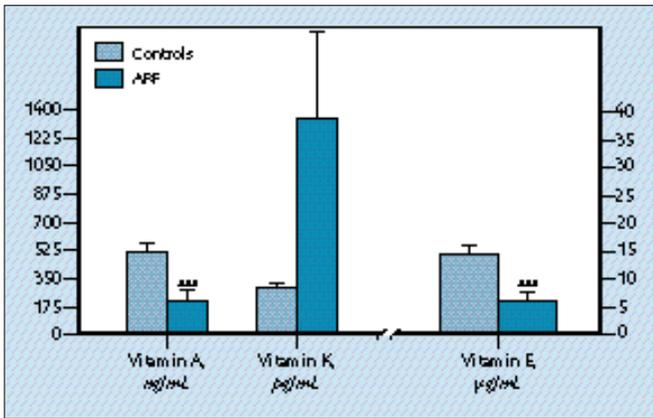


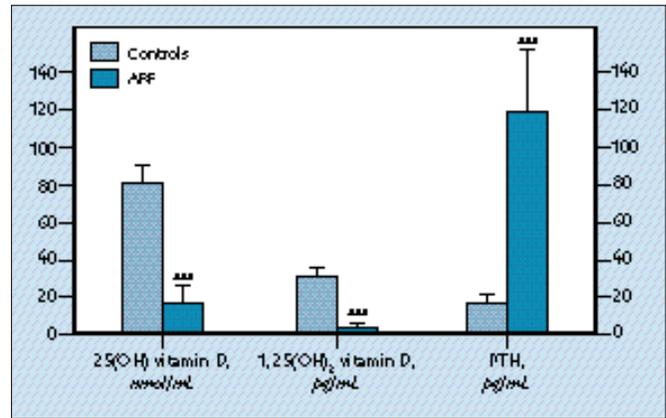
FIGURE 18-20

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 B<sub>1</sub>) 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.)



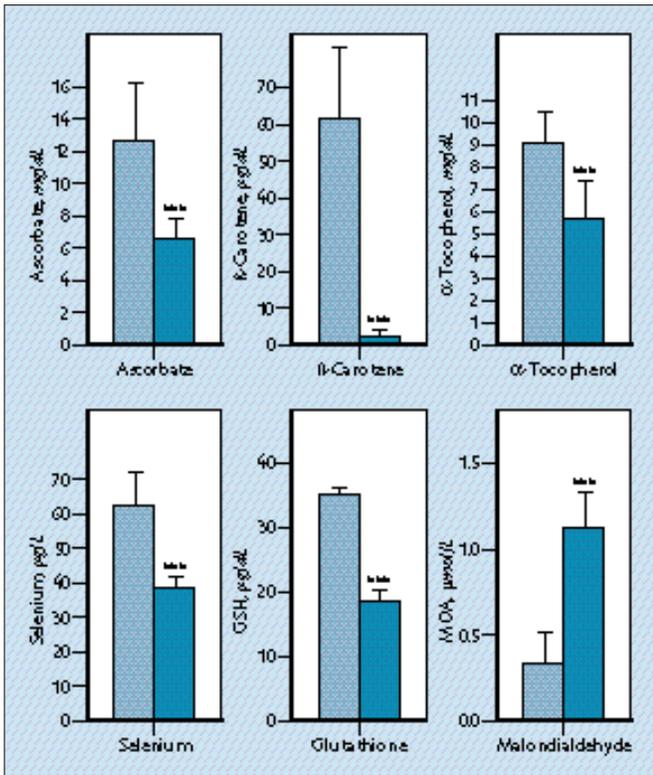
**FIGURE 18-21**

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 D<sub>3</sub> and 1,25-(OH)<sub>2</sub> vitamin D<sub>3</sub>, 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

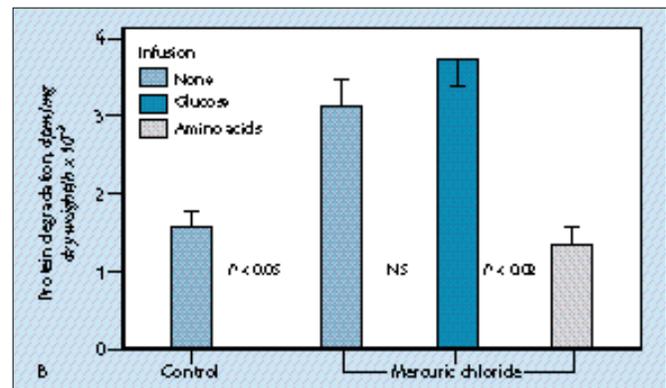
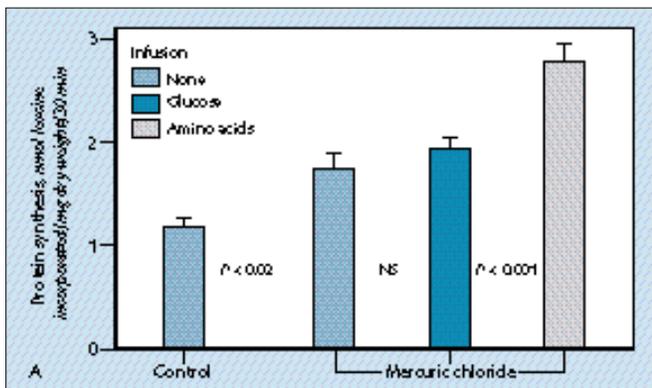
(arteriovenous) hemofiltration (CHF) and continuous hemodialysis have gained wide popularity. CRRTs are associated with multiple metabolic effects in addition to “renal replacement” [47].

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  $^{14}\text{C}$ -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.)