ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure

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Summary

Enteral nutrition (EN) by means of oral nutritional supplements (ONS) and tube feeding (TF) offers the possibility of increasing or ensuring nutrient intake in cases where normal food intake is inadequate. These guidelines are intended to give evidence-based recommendations for the use of ONS and TF in nephrology patients. They were developed by an interdisciplinary expert group in accordance with officially accepted standards and are based on all relevant publications since 1985. They were discussed and accepted in a consensus conference.

Because of the nutritional impact of renal diseases, EN is widely used in nephrology practice. Patients with acute renal failure (ARF) and critical illness are characterized by a highly catabolic state and need depurative techniques inducing massive nutrient loss. EN by TF is the preferred route for nutritional support in these patients. EN by means of ONS is the preferred way of refeeding for depleted conservatively treated chronic renal failure patients and dialysis patients. Undernutrition is an independent

KEYWORDS
Guideline; Clinical practice; Evidence based; Enteral nutrition (EN); Oral nutritional supplements (ONS); Tube feeding; Acute renal failure; Chronic renal failure;

Abbreviations: EN, enteral nutrition. This is used as a general term to include both ONS and tube feeding. When either of these modalities is being discussed separately this is specified in the text; Normal food/normal nutrition, normal diet of an individual as offered by the catering system of a hospital including special diets, e.g. gluten-free; lactose-free, etc. diets; ONS, oral nutritional supplements; TF, tube feeding; ARF, acute renal failure; CRF, chronic renal failure; CVVH, continuous veno-venous haemofiltration; CRRT, continuous renal replacement therapies; CAPD, continuous ambulatory peritoneal dialysis; RRT, renal replacement therapy; RDT, regular haemodialysis treatment

For further information on methodology see Schütz et al. For further information on definition of terms see Lochs et al. Corresponding author. Tel.: +33 4918 38835; fax: +33 4918 38838.
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factor of survival in dialysis patients. ONS was shown to improve nutritional status in this setting. An increase in survival has been recently reported when nutritional status was improved by ONS.

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### Summary of statements: Acute renal failure (ARF)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Recommendations</th>
<th>Grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>Macronutrient requirements are not so much determined by acute renal failure (ARF) as by the severity of the underlying disease, the type and intensity of extracorporeal renal replacement therapy, and by nutritional status and associated complications: Table 1</td>
<td></td>
<td>1.7</td>
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<tr>
<td></td>
<td>Extracorporeal treatment induces increased losses of micronutrients which should be supplemented.</td>
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<td></td>
<td>Monitor micronutrient status because excessive supplementation may result in toxicity.</td>
<td>C</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>In ICU patients with ARF, the electrolyte content of most 1500–2000 kcal enteral formulae is usually adequate. However, requirements can differ and have to be assessed individually. Plasma electrolyte monitoring should avoid hypokalaemia and/or hypophosphataemia after initiation of enteral nutrition (EN) (refeeding syndrome).</td>
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<td>1.7</td>
</tr>
<tr>
<td><strong>Indications</strong></td>
<td>Undernutrition is the main but not the only indication for EN.</td>
<td>1.6</td>
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<tr>
<td></td>
<td>In uncomplicated ARF use tube feeding (TF) if normal nutrition and oral nutritional supplements (ONS) are not sufficient to meet estimated requirements.</td>
<td>C</td>
<td>1.6</td>
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<tr>
<td></td>
<td>In severe ARF, the recommendations for TF are the same as for other ICU patients (see guideline “Intensive Care”). If possible initiate EN within 24 h.</td>
<td>C</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>In uncomplicated ARF, when spontaneous alimentation is insufficient, ONS may be useful to meet estimated requirements.</td>
<td>C</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Use nasogastric tube as the standard access for the administration of EN. Jejunal tube placement may be indicated in the presence of severe impairment of gastrointestinal motility.</td>
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<tr>
<td></td>
<td>In some cases where requirements cannot be met via the enteral route, supplementary parenteral nutrition may be needed.</td>
<td>C</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>Type of formula</strong></td>
<td>Standard formulae are adequate for the majority of patients.</td>
<td>C</td>
<td>1.8</td>
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<tr>
<td></td>
<td>In case of electrolyte derangements formulae specific for chronic renal failure can be advantageous.</td>
<td>C</td>
<td>1.8</td>
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</tbody>
</table>

Grade: Grade of recommendation; Number: refers to statement number within the text.
### Summary of statements: Conservatively treated chronic renal failure (CRF)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Recommendations</th>
<th>Grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>An energy intake of 35 kcal/kgBW/day is associated with better nitrogen balance and is recommended in stable CRF patients in the range of ideal body weight ± 10%. Overweight or undernourished patients may need adjustments of energy supply.</td>
<td>A</td>
<td>2.3</td>
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<tr>
<td></td>
<td>Recommendations for protein intakes of metabolically stable patients: Table 3</td>
<td>B</td>
<td>2.3</td>
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<tr>
<td></td>
<td>Recommendations for mineral requirements of metabolically stable patients: Table 4</td>
<td>B</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>Indications</strong></td>
<td>Use TF when adequate oral intake is not possible despite nutritional counselling and ONS. Consider EN in:</td>
<td>C</td>
<td>2.4</td>
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<td></td>
<td>● Patients with CRF and other catabolic intercurrent acute conditions in whom oral feeding is not possible. Treat these patients metabolically and nutritionally like ARF patients.</td>
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<td></td>
<td>● CRF patients in whom adequate oral intake cannot be achieved. Consider overnight TF in order to optimize nutrient intake.</td>
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<td>● Elderly patients with CRF may require special attention. The nutrient requirements and the need for nutritional support in elderly patients with renal failure have not been studied, although the prevalence of uraemic patients older than 75 years is increasing.</td>
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<tr>
<td><strong>Type of formula</strong></td>
<td>Use standard formulae for short-term EN in undernourished CRF patients. For EN &gt; 5 days use special or disease-specific formulae (protein-restricted formulae with reduced electrolyte content). Essential amino acids and ketoanalogues, in association with very low protein formulae, are proposed to preserve renal function.</td>
<td>C</td>
<td>2.6</td>
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Grade: Grade of recommendation; Number: refers to statement number within the text.

### Summary of statements: Patients on maintenance haemodialysis therapy (HD)

<table>
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<tr>
<th>Subject</th>
<th>Recommendations</th>
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<th>Number</th>
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</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>In acutely ill HD patients, the nutritional requirements are the same as in ARF patients.</td>
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<td>3.4</td>
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<td>Macronutrient requirements of metabolically stable patients: Table 5</td>
<td>B</td>
<td>3.4</td>
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<tr>
<td></td>
<td>Mineral requirements of metabolically stable patients: Table 6</td>
<td>B</td>
<td>3.4</td>
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<td></td>
<td>Due to dialysis-induced losses, water-soluble vitamins should be supplied: folic acid (1 mg/day), pyridoxin (10–20 mg/day) and vitamin C</td>
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Grade: Grade of recommendation; Number: refers to statement number within the text.
Vitamin D should be given according to serum calcium, phosphorus and parathyroid hormone levels.

Routine haemodialysis does not induce significant trace-element losses. However, in depleted patients, zinc (15 mg/day) and selenium (50–70 µg/day) supplementation may be useful.

**Indications**

Nutritional support is indicated in undernourished HD patients as defined by low nutritional indices, mainly BMI < 20 kg/m², body weight loss more than 10% over 6 months, serum albumin less than 35 g/l and serum prealbumin less than 300 mg/l.

Consider EN in:
- HD patients with intercurrent catabolic acute conditions in whom normal nutrition is not possible. Treat these patients metabolically and nutritionally like ARF patients.
- HD patients in whom adequate oral intake cannot be achieved. Consider TF to optimize nutrient intake. Unconscious patients on HD, e.g. in neurology, patients in nursing homes in need of EN. Administer TF adapted to the metabolic changes associated with HD.
- In undernourished HD patients with poor compliance to ONS and not requiring daily EN by TF, intradialytic parenteral nutrition can be proposed.

**Route**

Use ONS to improve nutritional status. Use TF if nutritional counselling and ONS are unsuccessful. ONS should be the preferred route in conscious HD patients.

TF through a nasogastric tube should be used when ONS is unsuccessful or inadequate to reach the recommended intakes.

In patients with gastroparesis, unresponsive to prokinetic treatment, nasojejunal TF is preferable. Consider placement of percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ) for long-term TF in selected cases.

**Type of formula**

Treat acutely ill patients with CRF on dialysis in a similar manner to those with ARF.

Use standard ONS. For TF prefer HD-specific formulae. The formula content in phosphorus and potassium should be checked.
Introduction

Patients with renal failure represent an extremely heterogeneous group, whose nutritional requirements can therefore differ widely. Even though the evidence supports the use of the enteral instead of the parenteral route, the optimal method of nutritional support remains controversial, especially in acute renal failure (ARF). Moreover, only a few enteral formulae have been developed addressing the specific needs of the various different groups. Finally, few systematic investigations have been performed, and controlled trials with an acceptable study design are rare. As the development of guidelines using the criteria of evidence-based medicine is rarely possible for this patient group, the following recommendations should be regarded as expert opinion only.

Literature review

In developing recommendations, the keywords "enteral feeding"; "nutrition"; "feeding tube"; "ARF"; "chronic renal failure (CRF)"; "haemodialysis therapy"; "peritoneal dialysis" were used for literature research.

Most studies of enteral nutrition (EN) in renal failure have only investigated feasibility and tolerance, rather than the impact on metabolic parameters and nutritional status. There are no studies with "hard" end points such as outcome, hospital stay, incidence of complications, etc. Studies comparing different enteral formulae are few.

1. EN in patients with ARF

Among patients with renal failure, those with ARF and critical illness represent by far the largest group receiving EN. ARF, especially in the ICU, seldom occurs as isolated organ failure but is usually one component of more complex metabolic changes, in the setting of multiple organ failure. Nutritional programs for ARF patients must not only consider the particular metabolic derangements associated with renal failure and with the underlying disease process and its associated complications, but also the derangements in nutrient balances due to renal replacement therapies (RRTs). This is especially true when higher efficiency depurative techniques are used (continuous therapies such as continuous veno-venous haemofiltration (CVVH), or prolonged intermittent modalities such as sustained low-efficiency dialysis. Finally, it should be remembered that nutrient requirements can change considerably during the course of the underlying illness itself (see also guidelines "Intensive care").

From a metabolic point of view, patients with CRF or on HD who develop acute intercurrent disease are similar to patients with ARF and should therefore receive similar nutritional therapy. Recommendations made for ARF apply also to these patient groups.

1.1. Does ARF exert a major impact on metabolism which is relevant to nutritional therapy?

ARF not only affects water, electrolyte and acid-base metabolism but also induces a global change of the "milieu interieur", with specific alterations in protein and amino acid, carbohydrate and lipid metabolism. Additionally, it exerts a pro-inflammatory reaction and has a profound effect on the antioxidative system. ARF, especially in the ICU setting, rarely represents an isolated disease process: in fact, metabolic changes in these patients are also determined by the underlying disease process and/or co-morbidities, by the different organ dysfunctions, and by the method and intensity of RRT.

Comment: Protein catabolism is the metabolic hallmark of ARF. The metabolism of various amino acids is abnormal, several non-essential amino acids (e.g. tyrosine) become conditionally essential, and there are alterations in the intra- and extracellular amino acid pools as well as in the utilization of exogenously infused amino acids.

There is hyperglycaemia, caused both by peripheral insulin resistance and the activation of hepatic gluconeogenesis. In contrast to patients with CRF and healthy subjects, this increased glucose formation cannot be suppressed by exogenous nutrient supply. Insulin resistance as defined by hyperglycaemia in the setting of higher insulin concentrations may be associated with mortality in critically ill patients with ARF.

Alterations in lipid metabolism are characterized by hypertriglyceridaemia due to an inhibition of lipolysis; exogenous fat clearance after (enteral or parenteral) delivery of lipids can therefore be reduced. Additional features include: depletion of antioxidants, induction of a pro-inflammatory state and impaired immunocompetence.

Plasma concentration of water-soluble vitamins is reduced. Activation of vitamin D3 is impaired, resulting in secondary hyperparathyroidism. Vitamins E and A and selenium levels are low and there is a profound depression of the antioxidant system.
1.2. Does continuous RRT alter metabolism?

**RRTs result in:**
- increased proteolysis,
- water and electrolyte disturbances.

**Comment:** Continuous renal replacement therapies (CRRT), and especially CVVH and veno-venous haemodi-afiltration (CVVHD-F), have become the treatment modality of choice in the critically ill patients with ARF. Because of their continuous nature and the high filtra-tion rates (fluid turnover), these therapies may exert a negative influence on electrolyte and nutrient balance.4

CRRT causes a significant loss of water-soluble, small molecular weight substances including sev-eral nutrients. There is a loss of about 0.2 g amino acids/l filtrate, giving a total daily loss of 10–15 g amino acids, to which (depending on the type of therapy and the membrane material used) a protein loss of 5 g and 10 g/day has to be added. Water-soluble substances such as vitamins are also lost in significant amounts.5

The administration of large amounts of lactate as substitution fluid, or citrate as anticoagulant, can cause complications such as hyperlactacidaemia or metabolic alkalosis. CRRT also frequently induces electrolyte derangements, e.g. hypophosphataemia, hypomagnesaemia and or hyponatraemia.

1.3. Does ARF affect gastrointestinal function?

**Gastrointestinal function (e.g. motility and/or absorption) can be impaired in critically ill ARF patients; the risk of gastrointestinal haemorrhage is also increased.**

**Comment** The influence of ARF on gastrointestinal function remains poorly understood. A positive correlation between impaired gastrointestinal motil-ity and the presence of renal failure has been documented.6 Moreover, multiple factors are known to negatively affect gastrointestinal function in critically ill patients, e.g. medications (sedatives, opiates, catecholamines, etc.), glucose and electrolyte disorders, diabetes or mechanical ventilation.

ARF is a well-defined major risk factor for gastrointestinal haemorrhage, especially in the upper-gastrointestinal tract.7 EN could exert pro-ective effects on the risk of stress ulcers/bleeding.

1.4. Does nutritional status influence outcome in ARF patients?

**Nutritional status is one of the main factors determining outcome.**

**Comment:** A prospective cohort study in 309 patients showed that severe malnutrition, as evaluated at admission by subjective global assessment (SGA), was present in 42% of patients with ARF8 (B). In this study, in-hospital length of stay and mortality were increased in undernourished pa-tients. Moreover, malnutrition appeared to be a predictor of in-hospital mortality independently of complications and co-morbidities.

1.5. Does EN influence renal function, recovery of renal function or patient outcome?

**Several nutrients have an impact on renal function. Both intravenously and enterally administered amino acids increase renal plasma flow and creatinine clearance (renal reserve).9 There are indications that tube feeding (TF) is associated with an improvement in survival in ICU patients with ARF.**

**Comment:** Experimental studies have reported accelerated recovery of renal function in tube-fed rats. EN was superior to parenteral nutrition in this respect.10,11 Two clinical studies have suggested that TF is associated with improved outcome in ICU patients.12,13 The effect of oral nutritional supple-ments (ONS) on renal function in uncomplicated ARF is not documented.

1.6. When is EN indicated in ARF?

**Undernutrition is the main but not the only indication for EN.**

In uncomplicated ARF, TF is indicated if normal nutrition and oral supplements are not sufficient to meet estimated requirements (C). In severe ARF, the recommendations for TF are the same as for other ICU patients (see guidelines "Intensive care"). If possible, EN should be started within 24 h (C).

1.7. Are substrate requirements altered in patients with ARF?

**Macronutrients: Macronutrient requirements are not so much determined by ARF as by the severity of the underlying disease, the type and intensity of extracorporeal RRT, and by nutritional status and associated complications (Table 1).**

**Micronutrients:** Extracorporeal treatment causes increased losses of micronutrients which should be supplemented. Excessive supplementation may result in toxicity. Micronutrient status should therefore be monitored (C).

**Electrolytes:** In ICU patients with ARF, the electrolyte content of most 1500–2000 kcal enteral formulae is usually adequate. However,
requirements can differ and have to be assessed individually. Plasma electrolyte monitoring should aim to avoid hypokalaemia and/or hypophosphataemia after initiation of EN (refeeding syndrome).

Comment: Since renal regulatory functions are impaired, there is intolerance of excessive substrate delivery (amino acids, trace elements, vitamins, etc.) (C).14–17

**Macronutrients:** No major modifications of energy metabolism are associated with ARF per se, as the more relevant effects on energy expenditure are usually due to acute co-morbidities and complications [18]. Even in multiple organ failure, the energy expenditure of critically ill patients amounts to only 130% of predicted energy expenditure (see guidelines ”intensive care”).

The optimal amount of protein supplementation in ARF patients is unknown. ARF is a highly catabolic state, and mean normalized protein catabolic rates (nPCR) of 1.5 g/kgBW/day (range 1.4 to 1.8) have been reported.19–22 Few data are currently available on the effects of high protein intakes on nitrogen balance in ARF patients on CRRT: in an un-controlled study, only 35% of patients achieved a positive N balance with nutrient intakes of 2.5 g/kgBW/day of protein and 35 kcal/kgBW/day of energy,23 while in a cross-over study of ARF patients receiving an isocaloric regimen, nitrogen balance was related to protein intake, and was more likely to be positive with intakes larger than 2 g/kgBW/day.24 However, no data are currently available concerning the clinical efficacy and the safety of such high protein intakes. Finally, it should be emphasized that hypercatabolism cannot be simply overcome by increasing protein or amino acid intake.

The optimal energy to nitrogen ratio has not been clearly determined during ARF, although, in a retrospective study of ARF patients undergoing CVVH, a linear-regression analysis was able to predict less negative or weakly positive nitrogen balance values at protein intakes of 1.5 g/kgBW/day if non-protein energy intake was set at about 25 kcal/kgBW/day.19 Increasing calorie to nitrogen ratio is not associated with better nitrogen balance: a nitrogen intake of 0.25 g/kg/day, an energy provision of 40 kcal/kg/day does not improve nitrogen balance estimates compared with a 30 kcal/kg/day intake; instead, more severe metabolic complications of artificial nutrition (hyperglycaemia, hypertrygliceridaemia) and more positive fluid balance can be observed.25

**Micronutrients:** Experimental ARF is associated with an increase in plasma retinol.26 Although retinol intoxication has not been reported in ARF patients, signs of vitamin A toxicity should be carefully monitored during supplementation.14 Similarly, it has been recommended that vitamin C intake should not exceed 30–50 mg/day, because inappropriate supplementation may result in secondary oxalosis,27 although supplies higher than 50 mg/day may be necessary in ICU patients. Bellomo et al. reported vitamin C (600 μmol/d, i.e. 100 mg/day) and folate (600 nmol/d, i.e. 265 μg/d) losses in ultrafiltrate during CRRT. Trace elements, which circulate mainly in a protein-bounded form, appeared to be poorly affected by ultrafiltration.28 Klein et al.29 reported significant losses of magnesium and calcium, necessitating higher supplies than were provided in standard parenteral nutrition formulae. Additional zinc was not required. Recent data from Berger et al.15 argue strongly for an increase in selenium and thiamine intake to at least double the recommended dietary allowances during prolonged CRRT. Increased requirements have to be substituted parenterally (C).

### 1.8. Are disease-specific formulae required in ARF patients?

*Standard formulae are adequate for the majority of patients (C). However, requirements can differ and have to be assessed individually. When there are electrolyte derangements, formulae specific for CRF patients can be advantageous (C).*

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**Table 1** Nutritional requirements in patients with ARF (nonprotein calories).

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Energy</th>
<th>Carbohydrates</th>
<th>Fat</th>
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<tr>
<td></td>
<td>20–30 kcal/kgBW/d*</td>
<td>3–5 (max. 7) g/kgBW/d</td>
<td>0.8–1.2 (max. 1.5) g/kgBW/d</td>
</tr>
<tr>
<td><strong>Protein (essential and non-essential amino acids)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conservative therapy</td>
<td>0.6–0.8 (max. 1.0) g/kgBW/d</td>
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<td></td>
</tr>
<tr>
<td>Extracorporeal therapy</td>
<td>1.0–1.5 g/kgBW/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCRT, in hypercatabolism</td>
<td>Up to maximum 1.7 g/kgBW/d</td>
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*Adapted to individual needs in case of underweight or obesity.
Comment: Whether disease-specific formulae (ONS, TF formulae) should be used in ARF patients, remains unsettled although they seem justified because of the particular metabolic changes in ARF, especially during exclusively EN. The difficulty in developing a disease-specific formula for ARF patients is related to the wide variation in metabolic changes and the differing individual requirements.1

(a) Free amino acid or peptide-based powder formula: The concept of a low protein diet supplemented with essential amino acids in the normal food of patients with CRF was extended to EN in ARF patients. Some of these formulae contain the eight essential amino acids plus histidine and must therefore be supplemented with energy substrates, vitamins and trace elements. Major disadvantages are the limited spectrum of nutrients, but also the high osmolality of the nutrient solution and potential problems associated with administrating powder formulae. These formulae should be replaced by “ready-to-use” liquid products.

(b) Whole protein formulae designed for non-uraemic patients: In many critically ill patients with ARF, standard formulae are used. Disadvantages with these formulae are the amount and type of protein and their high content of electrolytes that cause problems (e.g. potassium and phosphate). It is not known if formulae enriched in specific substrates such as glutamine, arginine, nucleotides or omega-3-fatty acids (immune-modulating formulae) might exert beneficial effects in ARF patients.

(c) Disease-specific formulae for “renal” patients: One type of these newer ready-to-use liquid formulae has been designed for patients with compensated CRF. It is characterized by reduced protein content and low electrolyte concentrations. A second type of enteral formula was created to meet the nutrient requirements of haemodialysis and contains a higher protein component with reduced electrolyte content and a high specific energy content of 1.5–2.0 kcal/ml. For the time being, these formulae represent the most reasonable approach to the EN of hypercatabolic intensive care patients with ARF.

1.9. What is the preferred route of feeding for ARF patients?

A nasogastric tube is the standard method of access for administration of EN. Jejunal tube placement may be indicated in the presence of severe impairment of gastrointestinal motility. In some cases where requirements cannot be met via the enteral route supplementary parenteral nutrition may be needed (C). In uncomplicated ARF, when spontaneous alimentation is insufficient, ONS may be useful to meet estimated requirements (C).

Comment: TF represents the first and most important measure in order to support and restore gastrointestinal function in the critically ill. However, it is frequently impossible to meet the nutrient requirements exclusively by EN, making supplementation of one or more nutrient by the parenteral route necessary. TF should start at low rates (25–50% of the scheduled calculated intake), and should be increased slowly (over days) until requirements are met. Clear evidence concerning the incidence and severity of refeeding syndrome in ARF patients is not available at present: however, plasma electrolyte and phosphorus levels must be strictly monitored.

Studies of EN in ARF: Few systematic clinical trials of TF in ARF are available. In the largest study to date, Fiaccadori and coworkers evaluated the safety and efficacy of nutritional support administered solely via nasogastric tubes in 182 patients with ARF, using either a standard formula or a disease-specific formula for patients with renal failure on haemodialysis. No evidence was found that ARF is associated with a serious increase of either gastrointestinal, mechanical, or metabolic complications when EN was chosen. High gastric residuals were more frequent in patients with ARF compared to those with normal renal function, but in general TF was safe and effective.30 Underdelivery of enteral formulae due to TF-related complications was a minor problem. However, with use of the enteral formulae currently available on the market, it may be difficult to achieve the protein intake usually recommended in ARF patients. Parenteral amino acid supplementation may therefore be required, especially in patients with ARF on RRT.

2. EN in conservatively treated patients with CRF

In contrast to paediatric nephrology where EN is standard care since it is the only means of providing an adequate nutritional intake in many patients, TF and ONS have rarely been used in adult CRF patients and systematic trials are not therefore available. Recommendations are therefore based on expert opinion only.

2.1. Does CRF have an influence on nutritional status and are there any metabolic alterations that influence nutritional therapy?
The uraemic syndrome leads to undernutrition. The causes are summarized in Table 2. Nutritional intervention strategy in CRF patients is determined by specific metabolic alterations:

- insulin resistance,
- abnormal plasma lipid clearance,
- metabolic acidosis,
- secondary hyperparathyroidism, uraemic bone disease,
- impairments of vitamin D3 activation,
- hyperkalaemia, hyperphosphataemia,
- chronic inflammatory reaction,
- activation of protein catabolism due to enhanced catabolism in intercurrent acute illness, acidosis and inflammation.

Comment: The uraemic syndrome is associated with loss of appetite and a variety of gastrointestinal adverse effects, which result in reduced nutritional intake. There is a direct correlation between renal insufficiency and reduced intake of normal food. Moreover, protein-restricted diets can result in undernutrition, if not closely monitored.

Metabolic acidosis in uraemia is an important factor in the activation of protein catabolism. Alkalization therapy is therefore standard in the treatment of CRF patients.

Intercurrent acute illnesses and/or the chronic inflammatory state also augment protein catabolism and can compromise the efficacy of nutritional support (type 2 malnutrition: "MIA syndrome = malnutrition – inflammation – atherosclerosis").

Note: Nutritional therapy cannot be considered in isolation from other metabolic interventions, such as the therapy of secondary hyperparathyroidism or correction of metabolic acidosis. In diabetic patients, accurate management of glucose metabolism and of hypertension is mandatory. Intercurrent disease (e.g. infections) must be treated.

2.2. Does CRF have an influence on gastrointestinal tract?

Nearly all gastrointestinal functions, mainly gastric emptying, can be compromised in CRF patients.

Comment: Impaired gastric emptying, impaired intestinal motility and disturbances of digestive and absorptive functions, of biliary and pancreatic secretions, and alterations in intestinal bacterial flora can occur in CRF patients. Intestinal fat absorption is delayed. Disturbed intestinal motility is of particular importance clinically. Gastro-paresis is most pronounced in patients with diabetic nephropathy. Gastric prokinetic agents (metoclopramide), control of diabetes and treatment of diabetic neuropathy can improve tolerance to EN.

2.3. What are the nutritional requirements of CRF patients?

An energy intake of 35 kcal/kgBW/day is associated with better nitrogen balance (A) and is recommended in stable CRF patients in the range of ideal body weight ± 10%. Overweight or undernourished patients may need adjustments of energy supply. Recommendations for protein intakes are given in Table 3 and mineral requirements of metabolically stable patients are summarized in Table 4 (B). (Nutritional requirements of acutely ill CRF patients: see ARF.)

2.4. Which CRF patients might need ONS or TF?

In undernourished CRF patients, ONS can be provided in order to optimize nutrient intake. TF is indicated when adequate oral intake is not possible despite dietary counselling and ONS (C).

Comment: Patient groups with CRF in whom TF should be considered are:

(a) Patients with CRF and other catabolic intercurrent acute conditions in whom oral feeding is not possible. These patients should be treated metabolically and nutritionally like ARF patients.

(b) CRF patients in whom adequate oral intake cannot be achieved, overnight TF can be considered in order to optimize nutrient intake.

(c) Elderly patients with CRF may require special attention. The nutrient requirements and the need for nutritional support in elderly patients with renal failure have not been studied, although the prevalence of uraemic patients older than 75 years is increasing.

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Table 2 Causes of undernutrition in patients with CRF.

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced oral intake</td>
</tr>
<tr>
<td>Restrictive dietary regimen</td>
</tr>
<tr>
<td>Uraemic toxicity</td>
</tr>
<tr>
<td>Microinflammation (MIA syndrome)</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Endocrine factors (insulin resistance, hyperparathyroidism, elevated plasma leptin, etc.)</td>
</tr>
<tr>
<td>Gastrointestinal factors (gastroparesis, impaired absorption, etc.)</td>
</tr>
</tbody>
</table>

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2.5. What are the goals of EN in patients with CRF?

When adequate normal food is impossible, the goals of EN are (C):
- Prevention and treatment of undernutrition,
- Correction of uraemic metabolic disturbances,
- Prevention of electrolyte disturbances (e.g. hyperkalaemia),
- Attenuation of disease (CRF) progression through protein or phosphate restriction,
- Preservation of intestinal mucosal integrity and function.

Low-protein diets should be associated with a strict monitoring of energy intake and of nutritional status, in order to prevent undernutrition in patients entering dialysis.

2.6. Which feeding formulae should be used in CRF patients?

Standard formulae can be used for short-term EN in undernourished CRF patients but, for EN for more than 5 days, special or disease-specific formulae (protein-restricted formulae with reduced electrolyte content) should be used (C).

Essential amino acids and ketoanalogues are proposed, in association with very low protein formulae, to preserve renal function in conservatively treated CRF patients (Table 3) (B).

Comment:

(a) Free amino acid or peptide-based formulae for patients with CRF:

The concept of a low protein diet supplemented with essential amino acids designed in the 60s for normal food of patients with CRF has been extended to EN. These earlier formulae containing the eight classic essential amino acids plus histidine were often incomplete, needing supplementation with energy substrates, vitamins and trace elements. Major disadvantages of these formulae are not only the limited spectrum of nutrients, but also the high osmolality of the nutrient solution and the associated problems of a powder formula. They can be used as an ONS in advanced CRF but if total EN becomes necessary, these formulae should be replaced by more complete ones.

Newer types of peptide/amino-acid-based formulae for patients with CRF are modular, integrating a protein and an energy component. The main disadvantages of these powder formulae again are the time-consuming preparation and the risk of contamination. Peptide/amino-acid-based formulae powder formulae have therefore been replaced by ready-to-use whole protein formulae.

(b) Ready-to-use whole protein formulae for stable patients with CRF:

Ready-to-use formulae have been developed for EN in stable patients with compensated CRF. These products have a reduced protein content, are electrolyte-restricted and have a high energy density (1.5–2.0 kcal/ml). Some contain other nutrients, such as histidine, carnitine, and tyrosine Addition of flavours improves palatability so they can be given as ONS.

Clinical studies: Abras and Walser carried out a study on the applicability and feasibility of a disease-specific formula (enriched with nitrogen free amino acid analogues) and showed that EN with a specially adapted formula is feasible in CRF patients. Such studies have also been carried out by Gretz in 1989 (B). The results of several studies
of EN in children with ARF are available. Studies of ready-to-use formulae have been carried out recently, one of which investigated protein-restricted ONS in 18 CRF patients over 4 weeks. Patients consumed normal food and additional ONS (Dosage: 10 kcal/kgBW/d). This improved energy and protein intake and prevented metabolic complications.41 (B).

### 3. EN in patients on maintenance haemodialysis therapy (HD patients)

Despite the increasing number of patients on intermittent HD and the high incidence of undernutrition prevailing in this patient group, experience with EN is limited and only few systematic studies have been performed.

#### 3.1. Are HD patients at risk of developing malnutrition?

**HD patients have a high risk of developing undernutrition. Malnutrition has been reported in 10–70% of HD patients.**31 *Moderate to severe undernutrition, which can compromise survival, has been reported in more than 20%.*

**The prognostic impact of undernutrition implies a monitoring of dietary intakes and of nutritional indices.**31,42

**Comment:** Several large series in the literature demonstrated the high prevalence of malnutrition in HD patients as well as its impact on survival (see ref.13,29 for review). In a recent European series of more than 7000 patients, albumin, transthyretin (prealbumin) and normalized protein nitrogen appearance (nPNA) were below the high-risk thresholds of 35 g/l, 300 mg/l and 1g/kg/day in 20%, 36% and 35%, respectively.43

The following simplified nutritional monitoring can be proposed, based on the ESPEN and the US National Kidney Foundation recommendations31,42: dietary interviews every 6 months; body mass index and nPNA monthly; SGA every 3 months; serum albumin and transthyretin every 1–3 months according to nutritional status.

#### 3.2. Does HD in addition to CRF have effects on nutritional status?

**Several dialysis-specific factors further aggravate the impairment of subjective well being, loss of nutrients, and induction of protein catabolism, thereby contributing to the high incidence of undernutrition.**

**Comment:** In addition to the above-mentioned factors seen in CRF, anorexia is a major cause for the development of undernutrition in HD.44 Most HD patients eat much less than they should. A further factor is inadequate dialysis prescription. Moreover, uraemic syndrome, as well as HD per se, has to be perceived as microinflammatory conditions that induce persistent activation of protein catabolism. Intercurrent disease processes such as infections enhance catabolism and must be treated consistently. Other “treatable” causes of undernutrition are acidosis, hyperparathyroidism and gastroparesis.45

#### 3.3. Does HD have an additional impact on metabolism or substrate requirements?

**The metabolic alterations due to CRF are not completely compensated by HD therapy, fluid and electrolyte problems are aggravated and several dialysis-associated factors become relevant.**

**Comment:** Metabolic alterations associated with HD include loss of nutrients (amino acids, vitamins and carnitine), the induction of dialysis-related catabolism, an increase in susceptibility to intercurrent acute conditions (infections) and potentially dialysis-induced amyloidosis as well as aluminium overload. Because of dialysis-induced catabolism, nitrogen balance is usually negative on HD days.

#### 3.4. What are the nutritional requirements in HD patients?

**In acutely ill HD patients the requirements are the same as in ARF patients. Macronutrient requirements of metabolically stable patients are summarized in Table 5 (B).**

**Mineral requirements are given in Table 6 (B).**

**Due to dialysis-induced losses, water-soluble vitamins should be supplied: folic acid (1 mg/day), pyridoxine (10–20 mg/day) and vitamin C (30–60 mg /day) (C, 13). Vitamin D should be given according to serum calcium, phosphorus and parathyroid hormone levels.**

**Routine haemodialysis does not induce significant trace-element losses. However, in depleted patients, zinc (15 mg/day) and selenium (50–70 μg/day) supplementation may be useful.**

#### 3.5. Does undernutrition in patients on HD have an impact on morbidity and mortality?

**Undernutrition is recognized as an independent determinant of morbidity and mortality in HD patients (IIb).**

**Comment:** Nutritional status at the beginning of dialysis predicts mortality after 1 year of
substitutive treatment. Several parameters of nutritional state like albumin, transthyretin, cholinesterase, creatinine, cholesterol, or weight/height index have a close association with survival in HD patients, albumin and transthyretin showing the strongest predictive value.

It should be noted that the concentration of plasma proteins is also influenced by the inflammatory state of the organism.

3.6. Is EN indicated in HD patients?

Nutritional support is indicated in undernourished HD patients as defined by low nutritional indices, mainly BMI less than 20 kg/m², body weight loss more than 10% over 6 months, serum albumin less than 35 g/l and serum prealbumin less than 300 mg/l (C). ONS improve nutritional status in undernourished HD patients (A). If nutritional counselling and ONS are unsuccessful, TF should be proposed (C).

Comment: A recent systematic review with meta-analysis has shown that ONS and EN increased serum albumin by 2.3 g/l (95% confidence interval, 0.37–4.18) in maintenance HD patients.

In recent randomized controlled trial in 182 undernourished HD patients, standard ONS induced a sustained improvement of serum albumin and transthyretin independently from inflammatory status. The increase in transthyretin during ONS was associated with a better survival.

Some patient groups in whom EN should be considered are:

(a) HD patients with intercurrent catabolic acute conditions in whom normal nutrition is not possible. These patients should be treated metabolically and nutritionally like ARF patients.
(b) HD patients in whom adequate oral intake cannot be achieved. TF may be considered in order to optimize nutrient intake.
(c) Unconscious patients on HD, e.g. in neurology, patients in nursing homes in need of EN. In this group TF adapted to the metabolic changes associated with HD should be administered.

In undernourished HD patients with poor compliance to ONS and not requiring daily EN by TF, intradialytic parenteral nutrition can be proposed.

3.7. Which formulae should be used in HD patients?

Acutely ill patients with CRF on dialysis should be treated in a similar manner to those with ARF (C). Standard ONS can be used (C). HD-specific formulae should be preferred for TF (C). The formula content in phosphorus and potassium should be checked.

Comment: Enteral formulae (ONS and TF formulae) designed for patients with CRF on conservative treatment should not be used in acutely ill patients with CRF on dialysis, as protein content is too low and nutritional requirements of patients are not met.

Several ready-to-use formulae adapted to the nutrient requirements of patients on regular...
haemodialysis treatment (RDT)/continuous ambulatory peritoneal dialysis (CAPD) are available. These have a higher protein content (of high biologic value partly in forms of oligopeptides and free amino acids), but reduced potassium and phosphate concentrations with a high specific energy content of 1.5–2.0 kcal/ml to limit volume intake. They are variably supplemented with histidine, taurine, tyrosine and carnitine. Originally designed for ONS, these formulae, which are available with different flavours, can be used as sole source of EN.

The benefits of disease-specific formulae require further evaluation.

3.8. What is the preferred route for EN in HD patients?

ONS should be the preferred route in conscious HD patients. TF through a nasogastric tube should be used when ONS is unsuccessful or inadequate to reach the recommended intakes (c). In patients with gastroparesis (occurring especially in patients with diabetic nephropathy), unresponsive to prokinetic treatment, nasojejunal TF is preferable (c). Placement of percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ) should be considered for long-term TF in selected cases.54

Comment: In order to avoid a nutritional substitution, ONS should be given after usual meals (2–3 h). The intradialytic delivery of ONS was reported to be associated with a better compliance. Late evening ONS reduces the overnight fast and may be of interest in these patients characterized by an accelerated starvation-induced catabolism.

Clinical studies: Oral nutritional supplementation (ONS): Six controlled studies, in undernourished HD patients, showed a positive effect of ONS on nutritional parameters (see below).55–60 Interestingly, an improvement in Karnofsky scale58 and normal food intake during oral supplementation was reported.60 In some series, however, compliance was reported to be only 50% after a 2–3 months of ONS.59

Intradialytic oral nutrition: In undernourished haemodialysis patients with reduced intake of normal nutrition, when nutritional state cannot be improved by dietary counselling, it is often possible to motivate patients to drink an enteral formula during haemodialysis. Daily ONS of one unit (237 ml) containing 16.6 g protein, 22.7 g fat and 53 g carbohydrates in 85 RDT patients for 6 months improved serum protein concentrations (albumin, transthyretin), SGA score, and to a minor extent BMI.61 However, 20% of the patients dropped out because of non-compliance. Similarly, Sharma and coworkers compared, a home-made preparation and a commercially available ONS (500 kcal, 15 g protein) after each haemodialysis session with a control group without supplement for 1 month.62 Both supplemented groups showed an improvement in dry body weight, BMI, serum albumin and functional scoring. Data from Sharma et al.60 and from Veeneman et al.62 support the use of intradialytic ONS. Other metabolic studies suggest that a late evening ONS may reduce overnight starvation and its consequent catabolism18,63 without reducing normal food consumption by day.

Tube feeding: In contrast to paediatric nephrology, experience with TF in adult patients on chronic RRT is limited. Douglas et al.64 performed nasogastric feeding using standard formulae providing 44 g of protein and 2060 kcal in undernourished patients on routine dialysis treatment. Some of the patients were fed for only 8 hours overnight, providing 55 g of protein and 1450 calories. Nutritional indices (plasma proteins) improved. Cockram et al.41, in 79 haemodialysis patients, compared three different enteral formulae; a standard formula; a disease-specific formula; and a disease-specific formula supplemented with dietary fibre (fructooligosaccharides). They were administered at a level of approximate 35 kcal/kgBW/d and 1.25 g protein kgBW/d, as a sole source of nutrition for at least 10 days. The disease-specific formula improved serum electrolyte concentrations (phosphorus, potassium, calcium). Holley and Kirk retrospectively analysed TF in ten adults on RDT (using a PEG in eight) and noted an improvement in serum albumin.65 However, eight of ten patients developed hypophosphataemia during TF using an electrolyte-restricted formula, emphasising the need for phosphorus monitoring during refeeding.

4. EN in patients on CAPD

Studies of EN in CAPD patients have been carried out almost exclusively in paediatric patients. Experience in adult patients derives mostly from case studies, many published in the form of abstracts.66,67

4.1. Do CAPD patients have specific metabolic characteristics?

Since CAPD patients usually have better residual renal function, metabolic abnormalities are less pronounced than in patients on HD therapy.
However, peritoneal losses of proteins, amino acids and micronutrients are relevant and absorption of glucose is increased.

Comment: Protein losses during CAPD are higher than in HD (5–15 g/day), as are losses of protein-bound substances, such as trace elements. This is further exacerbated by peritonitis. Elimination of amino acids and other water-soluble substances is lower than in HD.

Because peritoneal solutions with a high glucose content are standard, CAPD is associated with a high glucose uptake. Total energy intake is therefore normal or even enhanced. The high glucose intake can cause obesity, hypertriglyceridaemia, hyperglycaemia, induction or aggravation of diabetes.

4.2. How is body composition/nutritional state affected in CAPD patients?

In CAPD patients, body composition is characterized by fluid overload, low fat-free mass and low serum albumin and prealbumin. A normalization or an increase in body fat can be observed during CAPD without concomitant improvement of body cell mass.

Comment: Protein-energy malnutrition is present in a significant proportion of incident and prevalent patients undergoing chronic peritoneal dialysis (for review, see Mehrotra and Kopple68). In a cross-sectional CAPD, patients were found to be more severely undernourished than MHD patients (42% versus 30%). In CAPD versus MHD patients, serum total protein and albumin tended to be lower, midarm muscle circumference were similar, and relative body weight, skinfold thickness, and estimated percent body fat tended to be greater.69 Fluid overload is associated with a reduction of nutrient intake.70 As a consequence of the excess of energy over protein net balance can ensue, and fat mass increase can develop that can conceal a kwashiorkor-like protein malnutrition. Chronic or acute peritoneal inflammation is per se a catabolic stimulus, at the level of body protein mass. The loss of lean body mass is further increased by physical inactivity related to the time-consuming dialysis procedures.31

4.3. What are the nutritional requirements of CAPD patients?

Acutely ill CAPD patients have the same nutritional requirements as ARF patients. The energy, protein and minerals requirements of metabolically stable patients are summarized in Tables 5 and 6 (C). Vitamins, pyridoxine (10 mg) and vitamin C (100 mg) supplements are recommended (C).31

4.4. Are ONS and TF indicated in CAPD patients?

Nutritional support is indicated in undernourished CAPD patients, based on the same nutritional indices as in HD patients (C). In patients on CAPD with insufficient oral intake, ONS can help to optimize nutrient intake. TF is indicated when adequate normal nutrition and ONS are insufficient (C).

Some selected patient groups in whom TF should be considered are:

(a) CAPD patients in whom adequate oral intake despite nutritional counselling and ONS cannot be achieved: TF may be needed in order to optimize nutrient intake.
(b) CAPD patients with intercurrent catabolic acute conditions in whom an adequate oral intake is not possible. These patients should be treated metabolically and nutritionally like ARF patients.
(c) Unconscious CAPD patients, e.g. in neurology wards or nursing homes in need of EN. In this group TF—adapted to the metabolic changes associated with CAPD—should be administered.

4.5. Which feeding formulae should be used in CAPD patients?

Formulae with a higher protein but lower carbohydrate content are to be preferred. Products rich in proteins should be used as ONS (C).

4.6. Is PEG/PEJ placement contraindicated in CAPD patients?

Due to an increased incidence of peritonitis, PEG/PEJ is contraindicated in adult CAPD patients but is standard in children (C).

Clinical studies: Again, in contrast to paediatric nephrology where small infants on CAPD are routinely tube fed, information concerning EN in adult CAPD patients is very limited and usually relates to ONS and normal food. In a study comparing one group who received a low phosphate protein concentrate ONS with another group who received no supplements, an improvement in nutritional parameters (weight, anthropometry and lymphocyte count) was found in the supplemented group. However, 31% of patients abandoned the treatment due to low compliance or adverse side effects.66

References


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