

# Basics of Parenteral Nutrition



# Basics of Parenteral Nutrition

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## I. General background

Eating and drinking supplies in the form of foodstuffs chemically defined substances called nutrients. They are needed for growth and for the maintenance of body functionality. Nutrients are classified into two main groups:

- Nutrients without calories: Water, electrolytes, vitamins and trace elements.
- Nutrients with calories: Proteins, carbohydrates and lipids.

Nutrients are often essential which means that the body needs them but cannot synthesize them or cannot synthesize them in sufficient quantities to meet the daily requirements even under the best circumstances. Essential nutrients hence need to be supplied in adequate quantities.

Some nutrients can be essential under certain circumstances, e.g. during growth or in disease, though in other circumstances they are not. These nutrients are referred to as conditionally essential (sometimes also as semi-essential).

Proteins have an average calorific value of 4 kcal/g and are the only nutrients with a substantial amount of nitrogen, on average 16 g N per 100 g of dry weight. They contain up to 20 different amino acids, 8 of which are essential. Also the nitrogen as such is essential.

Carbohydrates have an average calorific value of 4 kcal/g and are not essential in the specified sense of the word. However, because the body has a very limited reserve of glucose in the form of glycogen

and because once consumed the only major precursor for glucose in the body is protein, a sufficient amount of carbohydrate is normally part of the diet.

Lipids (more precisely triglycerides) have an average calorific value of 9 kcal/g if they are long-chain triglycerides (LCT), and 8.3 kcal/g if they are medium-chain triglycerides (MCT). Two fatty acids are known to be essential, linoleic acid ( $\omega 6$ ) and  $\alpha$ -linolenic acid ( $\omega 3$ ).

After a normal meal the gut breaks down the foodstuffs to nutrients and these are absorbed. The body receives here a lot more nutrients than it actually would need to cover its basal needs over the period of absorption. Hence, most of the nutrients are put into stores. The underlying processes are called anabolic and the main hormone of anabolism is insulin.

Glucose is converted to its reserve form, glycogen, in the liver and in muscle. Triglycerides end up in the adipose tissue, the main energy store of the body. Amino acids are used for protein synthesis.

Once absorption is finished, the body starts to reverse the anabolic processes in a situation referred to as catabolism. The main hormone of catabolism is glucagon. The result is a release of glucose from the glycogen stores, of fatty acids and glycerol from the triglyceride stores and of amino acids from protein breakdown. In catabolism the bulk of these amino acids are used to synthesize glucose (gluconeogenesis).

In a normal human being, a prolonged starvation will lead to metabolic changes with the aim to reduce the consumption of calories and especially the breakdown of protein, which is always functional.

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Because protein is the only major glucose precursor (liver glycogen constitutes a very small glucose reserve that is exhausted after one day) and because the brain consumes about 150 g/day oxidatively, the mechanism for protein-sparing is by offering the brain alternative energy substrates. In a prolonged starvation these alternative energy substrates are produced from fatty acids in the liver, the so-called ketone bodies. They can largely, but not completely, substitute for glucose in the brain.

In injury and infection the catabolism that ensues is totally different in nature. There is a hypercatabolic state with increased energy expenditure and a specially pronounced increase of the gluconeogenesis (1). This leads to a rapid deterioration of the body's protein status and hence functional mass. The consequences are lowered resistance to infections, impaired wound healing and deterioration of organ functions.

In clinical settings where normal oral food and fluid intake is not possible clinical nutrition must be implemented. This can be achieved either enterally with formula diets or parenterally with nutrient solutions and lipid emulsions.

The general aim of clinical nutrition is to avoid nutrient deficiencies and their related complications. In detail there are some additional objectives. In children the aim is to achieve normal growth and development. In an adult with a good nutritional status and no hypercatabolism the aim is to maintain this condition. In hypercatabolic patients the aim is to minimize the protein losses in

order to avoid their deleterious effects, though protein equilibrium cannot be achieved during the acute phase of hypercatabolic states. Enteral nutrition is the preferred form of clinical nutrition, as it maintains the functionality of the gut. For it to be feasible the intestine must be working appropriately so that nutrient demands can be met. If nutrient demands cannot be met by the enteral route alone a parenteral supplement must be given. When the gut is not working or the tolerance to enteral nutrition is very poor the only viable route of administration is parenteral. In this situation it may still often be possible to give a minimum of nutrients enterally. This is important in order to stimulate the gut and maintain its integrity. Some 10-20 ml/h of a formula diet are enough (2).

It is beyond the scope of a booklet on parenteral nutrition to go into the details of enteral nutrition and in the following only parenteral nutrition will be considered.

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## II. Nutrient requirements in parenteral nutrition

This section summarizes current standard nutrient intake recommendations for adult and pediatric patients receiving parenteral nutrition. In practice an adaptation of the intakes to the clinical conditions of the specific patient will be necessary.

### II.1. Water and electrolyte requirements in parenteral nutrition

The normal requirements for adults and children are shown in tables 1a-c.

**Table 1a: Maintenance requirements for water and electrolytes in the parenteral nutrition of adults (3)**

Nutrient	Requirement per kg body weight per day unless stated otherwise	
Water	20-40 ml	
Sodium	1-2 mmol	
Potassium	1-2 mmol	
Magnesium	4-10 mmol/day	0.1-0.2 mmol <sup>a)</sup>
Calcium	5-7.5 mmol/day	0.05-0.15 mmol <sup>a)</sup>
Phosphate	20-40 mmol/day	0.2-0.5 mmol <sup>a)</sup>
Chloride/Acetate	So as to maintain acid-base balance	

<sup>a)</sup> Recommendations from other sources.

**Table 1b: Basal water requirements in children**

Body weight	Daily water requirements
< 1500 g	120-150 ml/kg bw
1500-2000 g	110-130 ml/kg bw
2.5-10 kg	100 ml/kg bw
> 10 and up to 20 kg	1000 ml for 10 kg + 50 ml/kg bw for each kg > 10 kg
> 20 kg	1500 ml for 20 kg + 20 ml for each kg > 20 kg

**Table 1c: Basal electrolyte requirements in children (mmol per kg body weight per day if not stated otherwise):**

Age	Na <sup>+</sup>	K <sup>+</sup>	Mg <sup>2+</sup>	Ca <sup>2+</sup>	P <sup>-</sup>	Cl <sup>-</sup>
Neonates	2-5	1-4	0.15-0.25	1.5-2.0	1.0-2.0	1-5
Infants/Children	2-6	2-3	0.15-0.25	0.5-1.25	0.5-1.0	2-5
Adolescents	<sup>a)</sup>	<sup>a)</sup>	10-15 mmol/d	5-10 mmol/d	10-40 mmol/d	<sup>a)</sup>

<sup>a)</sup> Individualized

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## II.2 Vitamins and trace element requirements in parenteral nutrition

Vitamins and trace elements are essential and their inclusion in parenteral nutrition is necessary to avoid deficiencies (tables 2 and 3). Administration is according to daily maintenance requirements and follows recommendations shown in tables 4-6

**Table 2: Typical signs of vitamin deficiencies**

Vitamin	Signs of deficiency
<b>Fat-soluble:</b>	
Retinol (A)	Night blindness, xerophthalmia, keratomalacia
Calciferol (D)	Rickets, hypocalcaemia
Tocopherol (E)	Hemolytic anemia (children), reduced red cell life (adults), oxidative damage
Phylloquinone	Decreased prothrombin time
<b>Water-soluble:</b>	
Thiamine (B1)	Beri-beri, neurological symptoms, reduced appetite, cardiomyopathy, lactic acidosis
Riboflavin (B2)	Cheilosis, bleeding gums, magenta-colored tongue, seborrheic dermatitis
Pyridoxine (B6)	Depression, seborrheic dermatitis, hypochromic anemia, peripheral neuritis
Cyanocobalamin (B12)	Pernicious anemia, neurological symptoms
Ascorbic acid	Poor wound healing, reduced resistance to infections, scurvy, Möller-Barlow-syndrome
Biotin	Dermatitis, hypocholesterolemia
Folic acid	Megaloblastic anemia
Niacin	Pellagra, dermatitis, diarrhea, dementia
Pantothenic acid	Nausea, fatigue, reduced antibody production

**Table 3: Typical signs of trace element deficiencies**

Trace element	Signs of deficiency
Iron	Anaemia, RBC microcytosis and hypochromia
Zinc	Growth disturbances, delayed wound healing, loss of hair, acrodermatitis enteropathica
Copper	Anemia, neutropenia, bone demineralisation, slowing of growth
Chromium	Reduced glucose tolerance
Manganese	Growth disturbances, ataxia, convulsions, disorders of fat metabolism
Selenium	Muscular weakness, cardiomyopathy, neuropathy
Iodide	Hypothyroidism, mental retardation, goiter
Fluoride	Dental caries

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**Table 4: Recommendations of the American Medical Association Department of Foods and Nutrition (4)**

Vitamin	Children 0–10 years	Children from 11 years on and adults
	per kg body weight per day <sup>a)</sup>	per day
Retinol (IU) <sup>c)</sup>	230	3330
Calciferol (IU) <sup>d)</sup>	40	200
Tocopherol (IU) <sup>e)</sup>	0.7	10
Phylloquinone (mg)	0.02	<sup>b)</sup>
Ascorbic acid (mg)	8	100
Folic acid (µg)	14	400
Niacin (mg)	1.7	40
Riboflavin (mg)	0.14	3.6
Thiamine (mg)	0.12	3.0
Pyridoxine (mg)	0.1	4.0
Cyanocobalamin (µg)	0.1	5.0
Pantothenic acid (mg)	0.5	15
Biotin (µg)	2	60

<sup>a)</sup> For a body weight more than 10 kg the dose is as for 10 kg.

<sup>b)</sup> 2–4 mg, once per week, if not anticoagulated with coumarin derivatives

<sup>c)</sup> 1 IU = 0.3 µg retinol

<sup>d)</sup> 40 IU = 1 µg calciferol

<sup>e)</sup> 1 IU = 1 mg D,L- $\alpha$ -tocopherylacetate = 0.67 mg D- $\alpha$ -tocopherol.

The recommended intakes of  $\alpha$ -tocopherol vary with the intake of polyunsaturated fatty acids and disease and may be higher than shown in the table

**Table 5: Estimated trace element requirements in the parenteral nutrition of adults (5, 6)**

Trace element	Estimated requirements per day
Iron	1-2 mg/day
Zinc	2.5-4 mg/day
Copper	0.5-1.5 mg/day
Chromium	10-15 µg/day
Manganese	0.15-0.8 mg/day
Molybdenum	50-400 µg/day
Selenium	20-50 µg/day
Iodide	0.15 mg/day <sup>a)</sup>
Fluoride	1 mg/day <sup>a)</sup>

<sup>a)</sup> These oral recommendations are also adequate for parenteral nutrition

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**Table 6: Estimated trace element requirements in the parenteral nutrition of children (5, 7)<sup>a)</sup>**

Trace element	Estimated daily requirements for:			
	Preterm infants ( $\mu\text{g}/\text{kg bw}$ )	Term infants ( $\mu\text{g}/\text{kg bw}$ )	Children ( $\mu\text{g}/\text{kg bw}$ )    max. ( $\mu\text{g}/\text{day}$ )	
Iron	200 <sup>b)</sup>	100 <sup>c)</sup>	No data	No data
Zinc	400	250 <sup>d)</sup> /100 <sup>e)</sup>	20	300
Copper	20	20	0.2	5
Chromium	0.2	0.2	0.2	5
Manganese	1.0	1.0	1	50
Molybdenum	0.25	0.25	0.25	5
Selenium	2.0	2.0	2	30
Iodide	1.0	1.0	1	150
Fluoride	f)	f)	f)	e)

<sup>a)</sup> Conversion factors: Iron (1 mg  $\rightarrow$  0.0179 mmol), Zinc (1 mg  $\rightarrow$  0.0153 mmol), Copper (1 mg  $\rightarrow$  0.0157 mmol), Chromium (1 mg  $\rightarrow$  0.0192 mmol), Manganese (1 mg  $\rightarrow$  0.0182 mmol), Molybdenum (1 mg  $\rightarrow$  0.0104 mmol), Selenium (1 mg  $\rightarrow$  0.0127 mmol), Iodide (1 mg  $\rightarrow$  0.0079 mmol), Fluoride (1 mg  $\rightarrow$  0.0526 mmol)

<sup>b)</sup> Starting 2<sup>nd</sup> month or after reaching 2000 g body weight

<sup>c)</sup> Not in the first three months

<sup>d)</sup> For age up to three months

<sup>e)</sup> If older than three months

<sup>f)</sup> Oral recommendations are adequate

### II.3 Amino acid, glucose, and lipid requirements in parenteral nutrition

The intake of water and electrolytes is relatively easy to calculate and the appropriateness of the calculation can be checked through the calculation of the corresponding balances and the measurements of the electrolytes in serum.

In respect of the nutrients with calories, it is possible to measure the real energy expenditure with indirect calorimetry and to calculate the oxidation of amino acids, carbohydrates and lipids from oxygen consumption, carbon dioxide production and urinary nitrogen. However, the technical possibility to do so often does not exist in a hospital, as an indirect calorimeter is required. It follows that energy expenditure and the distribution between amino acids, glucose and lipids has to be estimated. This can be done by several methods; only three of these will be shown in the following:

- The estimation of actual energy expenditure from **basal metabolic rate** and the calculation of the intakes for amino acids, glucose, and lipids.
- The use of **standard situation-specific intakes** of amino acids, glucose, and lipids.
- The use of a defined amount of **non-protein calories per grams of nitrogen** administered.

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## Basal metabolic rate

Several possibilities for the calculation of basal metabolic rate exist. The most commonly known are the Harris and Benedict equations (8), which correlate a person's basal metabolic rate (BMR) with body weight (bw in kg), height (ht in cm) and age (a in years).

$$\text{BMR}_{\text{men}} = 66 + (13.7 \times \text{bw}) + (5 \times \text{ht}) - (6.8 \times \text{a})$$

$$\text{BMR}_{\text{women}} = 655 + (9.6 \times \text{bw}) + (1.8 \times \text{ht}) - (4.7 \times \text{a})$$

Once basal metabolic rate is calculated the next step is to estimate actual energy expenditure ( $\text{AEE}_{\text{est.}}$ ). It is assumed today that in patients without stress actual energy expenditure is just 10 % higher than basal metabolic rate. Factors of up to twice basal metabolic rate were used in the past for patients in hypercatabolic states. Reassessments of the real requirements and the notion that overfeeding may cause harm have led to revised intakes. Today, a factor of more than 1.3 is seldom used.

$$\text{AEE}_{\text{est.}} = \text{BMR} \times \text{Factor}$$

$$\text{Factor} = 1.1 - 1.3$$

As the estimated actual energy expenditure includes calories from the oxidation of protein, carbohydrate and lipids, the next steps deal with finding the right ratio between them.

In this context a reasonably accurate estimation of protein oxidation is possible. Protein losses due to oxidation of amino acids appear in urine mainly as urea but also as creatinine. Creatinine in urine is fairly constant and depends mainly on muscle mass. It accounts for not more than 5–10 % of the normal urinary nitrogen losses and the relative amount is further diminished when there is an increase of amino acid oxidation in hypercatabolic states related to the stress response.

As long as the kidneys work, urinary nitrogen (UN) will correlate with amino acid oxidation and urinary urea nitrogen (UUN) as the measured parameter will be good enough from a practical point of view for calculations. The corresponding equations are:

$$\text{Amino acid oxidation (g/d)} = \text{U(U)N (g/day)} \times 6.25$$

$$\text{Amino acid oxidation (kcal/d)} = \text{U(U)N (g/day)} \times 6.25 \times 4$$

$$\text{U(U)N} = \text{Urinary nitrogen or urinary urea nitrogen}$$

When the kidneys are not working properly a quantitatively important portion of urea will remain in the blood increasing blood urea nitrogen (BUN). A correction for this portion of the urea nitrogen should then be introduced into the equations as follows:

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$$U(U)N_{\text{corr.}} \text{ (g/d)} = U(U)N \text{ (g/d)} + \frac{(BUN_E - BUN_S)}{100} \times bw \times F_{\text{tbw}}$$

$U(U)N_{\text{corr.}}$  = Corrected urinary (urea) nitrogen

$BUN_S$  = Blood urea nitrogen (mg/dl) at the beginning of a time period

$BUN_E$  = Blood urea nitrogen (mg/dl) 24 hours later

$Bw$  = Body weight (kg)

$F_{\text{tbw}}$  = Factor for total body water (0.6 in adult men, 0.55 in adult women)

While urinary (urea) nitrogen is a good indicator of the degree of protein breakdown, it is not necessarily very useful for the calculation of the amino acid intake in parenteral nutrition, as many patients have nitrogen losses which would correspond to amino acid intakes that surpass the highest allowed dosage recommendations. The general rule here is to use an amino acid dose of  $\sim 1.0$  g/kg bw per day in patients without hypercatabolism and an amino acid intake of  $\sim 1.5$  g/kg bw per day in hypercatabolic patients, irrespective of the real nitrogen losses. On this basis what is taken into account in the calculation of a regimen for parenteral nutrition is not the true amino acid oxidation, but the calories corresponding to the amino acid quantity administered on the basis of the equation:

$$\text{Protein calories (kcal/d)} = \text{Amino acid intake (g/d)} \times 4$$

It is now easy to calculate the non-protein calories according to the equation:

$$\text{Non-protein calories (kcal/d)} = \text{AEE}_{\text{est.}} - \text{protein calories}$$

In the last step the non-protein calories are now divided between glucose and lipids. Ratios used are:

$$\text{GLC : LIP} = 7 : 3 \text{ kcal/kcal in patients without hypercatabolism}$$

$$\text{GLC : LIP} = 5 : 5 \text{ kcal/kcal in patients with hypercatabolism}$$

### Example

Imagine a hypercatabolic 45 year old male patient with 85 kg body weight and 185 cm height suffering from acute pancreatitis and in need of parenteral nutrition.

$$\begin{aligned} \text{BMR} &= 66 + (13.7 \times \text{bw}) + (5 \times \text{ht}) - (6.8 \times \text{a}) \\ &= 66 + (13.7 \times 85) + (5 \times 185) - (6.8 \times 45) \\ &= 66 + 1165 + 925 - 306 \\ &\sim 1850 \text{ kcal/d} \end{aligned}$$

$$\text{AEE}_{\text{est.}} = 1850 \times 1.3 \sim 2400 \text{ kcal/d}$$

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Amino acid intake	= 1.5 x 85	= 127.5 g/d
Calorific equivalent	= 127.5 x 4	= 510 kcal/d
Non-protein calories	= 2400-510	= 1890 kcal
Glucose/lipid calories	= 1890 : 2	= 945 kcal/d
Glucose equivalent	= 995 : 4	~ 235 g/d
Lipid equivalent	= 995 : 10 <sup>a)</sup>	~ 95 g/d

<sup>a)</sup> Though lipids have a calorific value of ~ 9 kcal/g in lipid emulsions the value per 1 g of lipid is about 10 kcal, due to the contents of glycerol and phospholipids

The Harris and Benedict equations will overestimate basal metabolic rate in obese patients. On the other hand the use of ideal instead of actual body weight will very significantly underestimate the calorific needs in these patients and the use of actual body weight is preferable. The more marked the obesity is, the more difficult it becomes to estimate metabolic rate (for a review on this topic see 9).

### Standard situation-specific intakes

This approach assumes that adult patients can be classified into two different groups as shown in table 7. The approach is easier than the one that uses the Harris and Benedict equations and quite accurate in the resulting estimations for amino acids, glucose and lipids.

**Table 7: Daily situation-specific standard intakes for parenteral nutrition of the adult**

Patients	Total calories (kcal/kg bw)	Amino acids (g/kg bw)	Glucose (g/kg bw)	Lipids (kcal/kg bw)
Basal requirements (good nutritional status, no hypercatabolism)	25	1.0-1.2	3-4	0.7-1.0
Increased requirements (signs of malnutrition and/or hypercatabolism)	30	1.2-1.5	3-4	1.0-1.5

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## Example

Taking the patient from above (hypercatabolic 45 year old male patient with 85 kg body weight and 185 cm height suffering from acute pancreatitis and in need of parenteral nutrition) the calculation would now be:

Amino acids	=	1.5 x 85	=	127.5 g/day
Glucose	=	3.0 x 85	=	255 g/day
Lipids	=	1.2 x 85	~	100 g/d

Recommended standard intakes for the administration of amino acids, glucose and lipids have been published for adults and children (table 7). The basis for the recommendations is normal body weight, which means that over-estimations of real needs are probable in obese patients, specially the severely obese ones. As mentioned in the preceding section, ideal body weight will underestimate the requirements substantially. There is so far no well-documented and feasible approach to solve this problem.

### Non-protein calories per grams of nitrogen

This method defines an intake of amino acids assuming that 1 g nitrogen corresponds to 6.25 g amino acids, and adapts the amount of non-protein calories to the nitrogen intake in a way that the ratio between the non-protein calories and the grams of nitrogen is between 100-150.

$$\frac{\text{Non-protein calories (kcal/d)}}{\text{Nitrogen intake (g)}} = 100\text{-}150 \text{ kcal/g N} \times \text{d}$$

It is therefore important to note that while in the natural proteins there is a fair correlation between the dry weight of the protein and its nitrogen content (1 g N = 6.25 g protein, 16 g N = 100 g protein), in amino acid solutions this ratio can vary substantially (~ 14-18 g N per 100 g amino acids). When using this calculation in connection with regimen standardization, where 9 g N constitute a basal and 14 g N an increased intake, the variation in the resulting amino acid is not trivial. An intake of 9 g N can be equivalent to an amino acid intake of ~50-70 g. Only the upper value would constitute an appropriate basal amino acid intake. Likewise, 14 g N can be equivalent to 80-100 g amino acids and, again, the higher value would better meet increased requirements.

Another difficulty with this method is that the ratio between non-protein calories and grams of nitrogen (100-150) is rather wide.

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## Example

Taking the patient from the above (hypercatabolic 45 year old male patient with 85 kg body weight and 185 cm height suffering from acute pancreatitis and in need of parenteral nutrition) the calculation would now be:

Amino acid intake	= 14 g N	~ 80-100 g amino acids
Non-protein calories (kcal/d)	= 14 x 150	= 2100 kcal/d
Glucose/lipid calories	= 2100 : 2	= 1050 kcal/d
Glucose equivalent	= 1050 : 4	~ 260 g/d
Lipid equivalent	= 1050 : 10 <sup>a)</sup>	~ 100 g/d

## Published general dosage guidelines

There are recommended general dosage guidelines in the literature (one example is shown in table 8).

**Table 8: Recommended daily standard intakes for amino acids, non-protein calories, glucose and lipids in parenteral nutrition (3)**

Patients	Amino acids	Glucose	Lipids	Non-protein calories
	(g/kg bw)	(g/kg bw)	(g/kg bw)	(kcal/kg bw)
Neonates	2.5-3.0	120-140	≤ 4 <sup>a)</sup>	-
Infants	2.0-2.5	No data	≤ 4	-
Children	1.5-2.0	No data	No data	-
Adolescents	0.8-2.0	No data	No data	-
Adults (Maintenance)	0.8-1.0	< 7.0 <sup>b)</sup>	< 2.5 <sup>c)</sup>	d)
(Catabolic patients)	1.2-2.0			
Preterm neonates	-	-	-	120-140
< 6 months	-	-	-	90-120
6-12 months	-	-	-	80-100
1-7 years	-	-	-	75-90
7-12 years	-	-	-	60-75
> 12-18 years	-	-	-	30-60

<sup>a)</sup> ≤ 3 g/kg bw per day for small-for-gestational-age neonates and for preterm neonates less than 32 weeks of gestational age.

<sup>b)</sup> Absolute upper limit. Usually 3.0-5.0 g/kg bw per day (see text below).

<sup>c)</sup> Absolute upper limit. At least enough to cover essential fatty acid requirements. Most prescribing instructions set an upper dose limit of 2.0 g/kg bw per day.

<sup>d)</sup> Data are given only for total calories. The recommendation is 25-30 kcal/kg bw per day.

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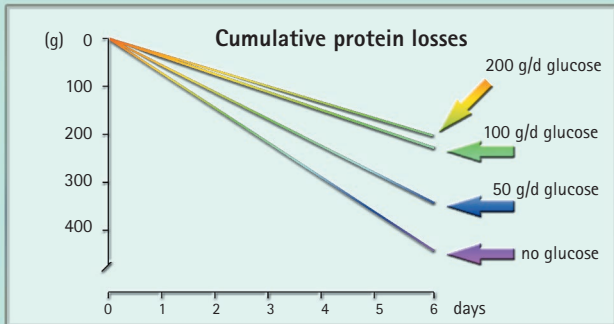
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Such tables try to cover wide ranges of dosages and, therefore, need additional information. They should not be used without the corresponding text of the publication and a good knowledge on the topic.

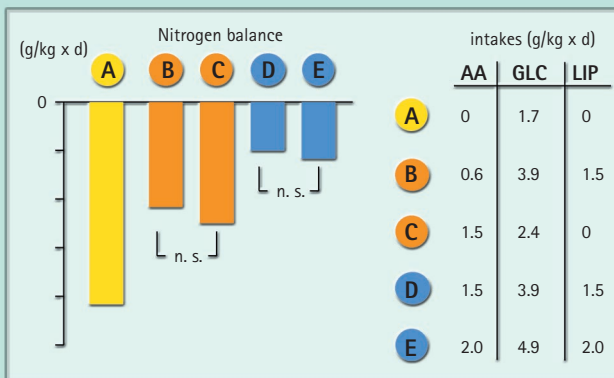
In respect of dosages for amino acids, glucose and lipids the following remarks are meant to help understand where sensible lower and upper limits of intake are.

The aim of glucose administration in parenteral nutrition is not only to supply carbohydrate calories but to take advantage of the protein-sparing effect of glucose. In healthy adults as little as 100g/day glucose have already a substantial protein-sparing effect that cannot be increased much further by giving 200 g/day (10) (fig. 1).

In hypercatabolic patients a substantial protein sparing can be achieved at a glucose intake of 2.4 g/kg bw per day. This can be improved further by increasing it to 3.9 g/kg bw per day, while a further increase to 4.9 g/kg bw per day does not have an additional effect (11) (fig. 2). In neonates the minimum glucose intake to achieve an appropriate protein gain seems to be ~ 8-10 g/kg bw per day (12, 13), while less (e.g. 6 g/kg bw per day) is insufficient (14).



**Figure 1** Influence of different glucose intakes as compared to starvation on nitrogen balance. Modified from (10).



**Figure 2** Influence of different calorific nutrient intakes on nitrogen balance in patients with trauma and sepsis. Modified from (11).

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On the other hand excessive glucose administration should be avoided. At blood glucose levels of  $> 10.0$ - $11.1$  mmol/l (180-200 mg/dl) the renal threshold for glucose re-absorption is surpassed and there is an onset of osmotic diuresis, which can dehydrate the patients severely. An increase of septic complications has been described in patients when the blood glucose values exceed 12.1 mmol/l (220 mg/dl) (15), and one paper describes a reduction of morbidity and mortality in critically ill patients when the blood glucose levels are maintained within the normal range (4.4-6.1 mmol/l or 80-110 mg/dl) rather than allowing them to increase to values of 10.1-11.1 mmol/l (180-200 mg/dl) (16). Excessive administration of glucose has also been associated with a fatty infiltration of the liver, increased minute ventilation and problems to wean patients from respirators (17).

The respiratory quotient (RQ), which is defined as the volume of carbon dioxide produced, divided by the volume of oxygen consumed over the same period of time depends on the fuel mix utilized by the body. A predominant energy gaining from glucose leads to an RQ of 1.0, while a predominant energy gaining from triglycerides leads to an RQ of 0.7. As excess glucose is converted into triglycerides in the so-called liponeogenesis and is accompanied by a massively increased production of carbon dioxide and the RQ goes above 1.0. This effect has been used to determine the upper value for the administration of glucose. A study in burn patients has shown that RQ remains fairly constant with glucose intakes of up to  $\sim 5$  g/kg bw per day and starts to increase substantially at higher intakes (18) (fig. 3). A study in

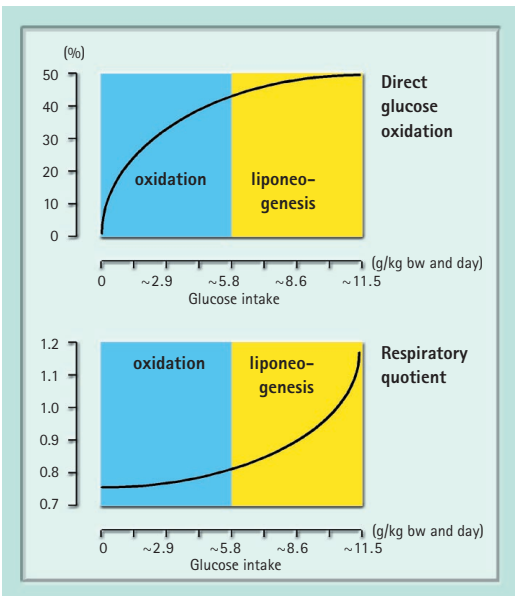
neonates demonstrates that the onset of significant liponeogenesis is at glucose intakes  $> 18$  g/kg bw per day in these patients (19).

In respect of lipid administration the minimum that should be administered must cover the daily requirements of essential fatty acids. Linoleic acid requirements in adults have been met by administering soya oil lipid emulsions at lipid intakes of 1.2–2.4 g/kg bw every two weeks (20). This would correspond to a daily administration of 0.043–0.086 g/kg bw. In neonates and infants an intake of 2–4 % of the total calories ( $\sim 0.5$  g/kg bw per day lipids) as soya oil emulsion lipids would cover the daily requirements (21). The requirements of  $\alpha$ -linolenic acid of an adult are not known. In children the estimated needs of  $\sim 0.5$  % of the total calories ( $\sim 0.044$  g/kg bw per day) are based on a case report (22). An amount of soya oil lipids covering the daily requirements of linoleic acid would also cover those for  $\alpha$ -linolenic acid.

It is more difficult to say where the upper limit of lipid administration should be. With recommended total calorific intakes of no more than 30 kcal/kg bw per day in an adult (3) more than 1.5 g/kg bw per day lipids is probably unjustified in most cases and prescribing instructions for lipid emulsions normally limit the intake to no more than 2 g/kg bw per day in an adult. The nitrogen-sparing effect of 2 g/kg bw per day is also not superior to that of 1.5 g/kg bw per day (10) (fig.2).

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In neonates and infants assuming an intake of 2.5–3.0 g/kg bw per day amino acids and 18–20 g/kg bw per day glucose, the administration of 3 g/kg bw per day lipids would put the total calorific intake at ~ 110–120 kcal/kg bw per day. This would cover the needs in most cases. In order to achieve a total calorific intake of 140 kcal/kg bw per day and assuming an administration of 3.0 g/kg bw per day amino acids, there would be a need to give 3–4 g/kg bw per day lipids with 24.5–22 g/kg bw per day glucose.



**Figure 3**  
Glucose oxidation and respiratory quotient in burn patients at different glucose intakes. Modified from (18).

### III. Indications of clinical nutrition

All the situations leading to an indication for clinical nutrition have in common that normal oral food and fluid intake is not possible for an unacceptably long period of time. Conditions in which this can happen are listed in table 10.

**Table 10: Examples of conditions with potential indication for clinical nutrition**

Malnutrition	Intractable diarrhoea
Anorexia	Pancreatitis
Cancer	Peritonitis
Oropharyngeal trauma	Renal failure
Esophageal strictures	Hepatic failure and liver transplantation
Gastrointestinal stenoses	Bone marrow transplantation
Operations of the digestive tract	Multiple trauma
Bowel fistulae	Head injuries, neurosurgery, strokes
Inflammatory bowel disease	Severe burns
Radiation enteritis	SIRS <sup>a)</sup> and sepsis
Short bowel	AIDS <sup>b)</sup>
Ileus and chronic pseudo-obstruction	Neonatology

<sup>a)</sup> SIRS = Systemic inflammatory response syndrome

<sup>b)</sup> Acquired immunodeficiency syndrome

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Guidelines for the use of parenteral and enteral nutrition have been published (23).

In general terms, as the body gets depleted quickly of water and electrolytes an adequate intake of these nutrients must be undertaken as soon as possible. Together with water and electrolytes a minimum of glucose (100–150 g/d in an adult) should be administered in order to reduce protein losses. In patients with no malnutrition and no hypercatabolism such an incomplete regimen can be given for a few days. If the expected period of starvation is longer a basal regimen should be given. In such a case clinical nutrition should start as soon as possible.

Malnourished patients and patients with hypercatabolism (or patients suffering from both conditions) should receive a regimen that covers their increased requirements, and clinical nutrition should be started at the earliest possible.

The following sections will cover the important indications for clinical nutrition in greater detail.

### III.1 Malnutrition

Malnutrition in hospitals is an old problem and has been linked to an increased risk of morbidity and mortality (24, 25, 26). Early reports put the incidence of malnutrition in hospitalized patients at around 40–50% (27, 28) and more recent investigations (29, 30) have come to similar conclusions. The potential to save costs in hospitalized patients by giving them nutritional support has been calculated and is substantial (31). Therefore methods should be implemented that allow the identification of the malnourished patients by simple means and with acceptable accuracy. Patients should be checked for malnutrition on admission but also in the hospital at regular intervals, especially when they are at increased risk of developing malnutrition in the hospital (e.g. periods of starvation, hospital stays of more than 10 days, hypercatabolism). A screening for malnutrition should include questioning about a patient's nutritional habits, changes in these habits over the last three months because of such conditions as anorexia, gastrointestinal pains or chewing problems, and involuntary weight loss of more than 10% of the body weight over the last 3–6 months. Albumin levels  $< 35$  g/l and total lymphocyte counts  $< 1500/\text{mm}^3$  are indicative of protein malnutrition and correlate with morbidity and mortality (32). A good parameter for the evaluation of general nutritional status is the body mass index (BMI, table 11), though it should be kept in mind that in patients with protein malnutrition the index may make them appear to be better nourished than they actually are. A combination with

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anthropometric measurements like triceps skinfold thickness and upper arm muscle circumference improves the picture but has to be performed by experienced persons (33).

**Table 11: Body mass index (BMI) and nutritional status**

Value	Nutritional status
> 30	Obese
25-30	Overweight
20-25	Normal
18-20	Slim
15-18	Moderate malnutrition
< 15	Severe malnutrition

$$\text{BMI} = \frac{\text{Body weight (kg)}}{[\text{Height (m)}]^2}$$

It is also important to look for physical signs of malnutrition, e.g. fine and brittle hair, weak limbs, edema, etc. A method for subjective global assessment of nutritional status has been described (34).

The regimens for patients with malnutrition should cover increased requirements (see section II.3). Special care must be taken in the nutritional support of malnourished patients to provide enough potassium, magnesium and phosphate, all of which are essential ions with high intracellular concentrations. The dosage of these electrolytes

cannot be calculated on the basis of maintenance requirements but must include a very substantial extra intake for the build-up of body cell mass. Insufficient intakes will lead to the refeeding syndrome which can result in death if not recognized and treated appropriately. The topic has been reviewed (35).

### III.2 Cancer

The prevalence of malnutrition in cancer patients is high and may be related to the effects of the malignancy on appetite and metabolism or to the toxicity of the cancer treatment. The response of nutritional parameters to clinical nutrition, however, is much less pronounced than in malnourished non-cancer patients, but at least it is possible to prevent a further deterioration of the nutritional status.

For malnourished cancer patients two meta-analyses suggest a statistically significant decrease in the rate of major postoperative complications if the patients received preoperative parenteral nutrition (36, 37). One prospective randomized study shows reduction of septic complications and abdominal abscess formation in malnourished cancer patients with preoperative parenteral or enteral nutrition as compared to malnourished cancer patients without preoperative nutritional support (38).

While controversial in the past, there are meanwhile sufficient data available to show that clinical nutrition does not have deleterious effects in respect of tumor growth (39).

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Guidelines on clinical nutrition versus hydration in terminal cancer patients have been proposed (40).

The regimens used in cancer patients should cover increased requirements (see section II.3).

## III.3 Severe burns

Thermal full-thickness burns of large parts of the body surface area lead to severe hypercatabolism that correlates with the percentage of body surface area burned. The body surface area can be calculated from the rule of nines (fig. 4).

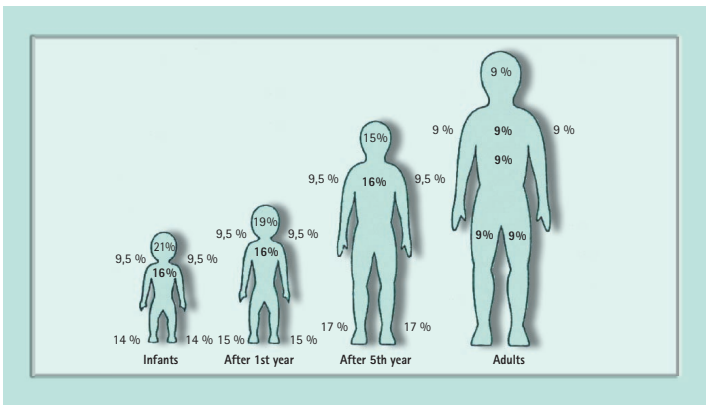


Figure 4 The rule of nines

The most accurate estimation of actual energy expenditure in burns is obtained by using the Toronto equation (41):

$$\text{AEE}_{\text{est.}} = -4343 + (10.5 \times \text{BBSA}) + (0.84 \times \text{BMR}) \\ + (0.23 \text{ TCI}) + (+114 \times \text{BT}) - (4.5 \times \text{PBD})$$

$\text{AEE}_{\text{est.}}$  = Estimated actual energy expenditure (kcal/d)

$\text{BBSA}$  = Burned body surface area (% of total BSA)

$\text{BMR}$  = Basal metabolic rate (kcal/d) (Harris and Benedict)

$\text{TCI}$  = Total calorific intake (kcal/d) (= BMR on day 1)

$\text{BT}$  = Body temperature ( $^{\circ}\text{C}$ )

$\text{PBD}$  = Post burn day

Severe burns are accompanied by huge nitrogen losses (1) which cannot be covered with clinical nutrition. Optimal protein or amino acid intakes have not been studied systematically, though  $\sim 1.5$  g/kg bw per day seem to be adequate (42). Non-protein calories can be easily calculated from the estimated actual energy expenditure by subtracting the calories provided as amino acids (1 g amino acids are equivalent to 4 kcal). Enteral nutrition can start early in most patients but to cover the needs by enteral nutrition alone may not be possible due to problems with tolerance. In these cases parenteral supplements should be administered.

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## III.4 Inflammatory bowel disease and radiation enteritis

Inflammatory bowel disease (Crohn's disease and ulcerative colitis) are inflammations of the small and large bowel respectively. Their etiology is unknown.

Patients with Crohn's disease are very often severely malnourished. Among the reasons for the development of malnutrition are inadequate intake because of chronic abdominal pains, bowel obstruction, or inadequate absorption from the gut due to diarrhea and damages of the mucosa. Malnutrition can be exacerbated by multiple surgical interventions and the development of complications like bowel fistulae or abscess formation, especially if insufficient care is taken with clinical nutrition. The chronic steroid therapy often used is a known reason for muscle wasting.

A number of studies suggest that in Crohn's disease clinical nutrition (enteral or parenteral) leads to an improvement of the inflammation in a majority of cases. On the other hand, studies comparing drugs (steroids, sulfasalazine) with clinical nutrition have shown remissions to occur in a higher number of patients and also more quickly (43). Clinical nutrition can, therefore, be considered as adjunct treatment for drug therapy, facilitating remission and helping to maintain or improve nutritional status.

Ulcerative colitis does not profit from clinical nutrition in terms of remission, so clinical nutrition is useful only as an adjunct for nutritional interventions that become necessary.

There is little information on the use of clinical nutrition in radiation enteritis. In severe radiation enteritis it is probably difficult to give enteral nutrition. One study on parenteral nutrition in these patients shows that maintenance of nutritional status can be achieved but that the situation as such is not improved (44).

The regimens for all these patients should cover increased requirements (see chapter II.3).

### **III.5 Short bowel syndrome**

The term short bowel syndrome is used to characterize the clinical effects of large resections of the small bowel. The clinical picture of short bowel syndrome varies depending on which part or parts of the small bowel were resected and how much of the bowel is left.

Patients with large resections of the jejunum and anastomosis of what remains of the jejunum with the ileum have a good chance to be able to feed themselves with normal foodstuffs eventually.

Patients with partial resections of the jejunum in combination with total resections of the ileum and anastomosis of the jejunum to the colon will often not need iv nutrient supplementation if the remaining length of the jejunum is  $> 100$  cm, while oral supplements of water and sodium will become necessary if the length of the remaining jejunum is less, and increasing requirements of iv nutrients will be needed with decreasing length of the jejunum. With lengths of the remaining jejunum  $< 50$  cm most nutrient intake will have to be

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parenteral. As vitamin B12 is absorbed in the terminal ileum, a resection there will make it necessary to administer vitamin B12 intravenously.

If part of the jejunum, all of the ileum and additionally the colon are resected the problem of water and sodium absorption is exacerbated considerably and also the amount of nutrients administered intravenously will have to be increased.

Typical problems related to resections of the short bowel are diarrhea, steatorrhea, hypomagnesaemia, hypocalcaemia, oxalosis and gall stone formation.

Parenteral nutrition will be essential to provide all the nutrients needed and avoid deficiencies. However, because the remaining small bowel reacts to enteral nutrition with hyperplasia and improved nutrient absorption, enteral nutrition should be started as early as possible and be gradually increased according to tolerance and improving absorption capacity.

For a detailed review of the short bowel syndrome see (45). General recommendations for clinical nutrition are available (23).

The regimens for these patients should cover increased requirements (see section II.3) if in bed. Additional requirements are necessary if the patient is not in bed and has physical activity. In such cases, 1.5 times basal metabolic rates seems appropriate.

### III.6 Bowel fistulae

Gastrointestinal cutaneous fistulae arise mostly as a complication after surgery with an incidence of 2–5 % following surgeries of the gastrointestinal tract. They lead to significant morbidity and the mortality is ~ 30–40 %. The most important factors in respect of morbidity and mortality are fluid and electrolyte imbalances, abscess formation, wound infections, septic complications and malnutrition. The management of the gastrointestinal cutaneous fistulae aims to close the fistula and to re-establish intestinal continuity and comprises a stabilization phase (24–48 hours), an investigation phase (up to 10 days) and the definitive therapy (several weeks). Clinical nutrition plays a role in the maintenance of nutritional status during this period and may help to achieve a spontaneous closure of the fistula (i.e. without further surgical intervention). If the fistula has not closed within 4 weeks a surgical intervention is necessary. The topic has been reviewed (2).

Patients with gastrointestinal cutaneous fistulae need regimens supplying increased requirements (see section II.3).

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## III.7 Acute pancreatitis

Pancreatitis refers to a range of pancreatic inflammations of a not well understood etiology. Risk factors for its development are biliary diseases like sludge formation or gallstones, alcohol abuse and hypertriglyceridemia.

In most patients with acute pancreatitis the prevalent form is the relatively mild edematous pancreatitis which resolves within a few days of conservative treatment.

Especially the alcohol-related pancreatitis has a tendency to become chronic and even though conservative treatment is often effective too, alcoholism as such bears a high risk of significant protein-calorie malnutrition. Nutritional support may be indicated in these patients.

In 5-15 % of the patients with acute pancreatitis a severe necrotizing form develops. It is accompanied by significant hypercatabolism and is often complicated by the development of fistulae, pancreatic abscess, intraabdominal sepsis and ileus. The treatment lasts weeks to months and nutritional support is mandatory.

While in the past the severe forms of pancreatitis were an absolute indication for parenteral nutrition, there is meanwhile evidence from studies that enteral nutrition is feasible if administered into the jejunum (46, 47). Parenteral nutrition will still often be indicated because of the mentioned complications.

There is sufficient evidence that lipid emulsions can be used safely in parenteral nutrition on patients with severe acute pancreatitis (48).

In a number of patients severe acute pancreatitis is accompanied by strong triglyceridemia. This constitutes a contraindication as long as the triglyceride levels remain high ( e.g.  $> 400$  mg/dl). Patients with severe acute pancreatitis may have a reduced lipid clearance and the dose must be adapted accordingly. Triglyceridemia should hence be monitored at regular intervals.

In respect of electrolytes, special attention should be paid to calcium, as hypocalcaemia is very frequent in these patients. When the origin of the pancreatitis is alcohol abuse hypomagnesaemia is also often observed.

Patients with severe forms of acute pancreatitis need regimens supplying increased requirements (see section II.3).

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## III.8 Systemic inflammatory response syndrome

The systemic inflammatory response syndrome (SIRS) is characterized by the presence of two or more of the following conditions (49):

Body temperature  $> 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$

Heart rate  $> 90$  beats/min

Respiratory rate  $> 20$  breaths/min or  $\text{PaCO}_2 < 32$  mm Hg ( $< 4.3$  kPa)

WBC  $> 12,000$  cells/ $\text{mm}^3$  or  $< 4000$  cells/ $\text{mm}^3$  or  $> 10\%$  immature neutrophils ("bands")

SIRS develops as a response of the body to injury, infection or inflammation and can hence be observed as a common feature in critically ill patients with severe trauma, head injuries, burns, sepsis, pancreatitis, delayed treatment of hypovolemic shock, etc. Without successful treatment SIRS progresses to multiple organ dysfunction syndrome with coagulation disorders, dysfunction of lungs, kidneys, liver, and heart. Finally shock develops and death occurs. For the estimation of the risk of death the use of the APACHE II scoring index (50) has been proposed (49).

SIRS leads to hypercatabolism with a particularly pronounced increase of the nitrogen losses. Blood glucose levels are high due to ongoing gluconeogenesis and insulin resistance. Lipid oxidation is increased, though triglyceride clearance may be impaired in advanced SIRS.

Nutritional support is mandatory. The patients with SIRS need regimens supplying increased requirements (see section II.3).

### III.9 Acute renal dysfunction and chronic renal failure

Acute renal dysfunction can develop secondary to a primary condition like hypovolemia, SIRS, etc. which means that it is accompanied by hypercatabolism. The patients are in need of nutritional support and the appropriate regimens are those described for increased requirements in section II.3. Because of the kidney dysfunction, however, there are limitations in respect of the daily fluid, electrolyte and protein intake as long as dialytic procedures (e.g. hemodialysis, hemofiltration) are not used concomitantly. Here the aim is to give the basal requirements (see section II.3) with 1.0–1.5 l of fluid. Electrolyte intakes are met individually and must be monitored closely.

When parenteral nutrition is used, amino acid intakes of  $< 0.8$  g/kg bw per day are insufficient to cover even the basal requirements (3). The practice to give 0.2–0.5 g/kg bw per day amino acids in the form of solutions of the eight essential amino acids plus histidine should be abandoned (23). The original concept assumes a substantial recycling of urea nitrogen for the synthesis of nonessential amino acids (51) which has been shown not to occur (52). A superiority of special amino acid solutions for renal failure over well-balanced standard amino acid solutions has not been shown either (53).

Patients with acute renal dysfunction often have reduced capacity to clear lipids and care should be taken that triglyceride levels do not exceed acceptable limits (e.g. 400 mg/dl).

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Chronic renal failure is a progressive deterioration of the kidney function leading to total failure and the need for chronic use of dialytic procedures or kidney transplantation. Chronic renal failure is often accompanied by malnutrition. One reason is anorexia leading to insufficient nutrient intakes. In patients with chronic hemodialysis a protein intake of at least 0.75 g/kg bw per day is needed in order to maintain nitrogen balance, and an intake of 1.2 g/kg bw per day should be the aim (54). Patients with chronic renal failure have protein intakes which are often below the minimum. Some losses of amino acids and protein are the consequence of the dialytic procedure. In hemodialysis, losses of amino acids are 2-8 g per treatment and losses of protein 2-5 g per treatment (54). When malnutrition is diagnosed measures must be taken to treat it. Within this setting intradialytic parenteral nutrient supplementation is a possibility. Mixtures of amino acids (45-60 g per session) and non-protein calories ( 500-1750 kcal per session as glucose and lipids) are typically administered (54). It is obvious that no special amino acid solutions are needed for this procedure.

### III.10 Hepatic failure

Patients with severe liver disease have a very high incidence of malnutrition with a specially pronounced protein malnutrition and reduced immune defenses that correlate with the protein malnutrition and mortality (55). Especially in the cirrhotics there is a reduced production of those coagulation factors synthesized in the liver and as a consequence a tendency to suffer from severe bleedings, particularly of the gastrointestinal tract. Problems with the digestion of lipids may lead to steatorrhea and deficiencies of lipid-soluble vitamins may develop. Other nutrient deficiencies (vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, folic acid and zinc) may develop as a result of inadequate intakes or changed storage, especially in alcoholic liver disease.

Portal hypertension leads to a partial shunting of portal blood around the liver and toxins of gut origin contained in it can affect now the brain causing hepatic encephalopathy. The standard treatment of hepatic encephalopathy aims to reduce ammonia uptake from the gut and includes intestinal lavage, nil per os, and the administration of neomycin or lactulose.

Patients with severe liver disease have significant amino acid imbalances in the blood. Of special importance are the lower than normal values for the branched-chain amino acids (isoleucine, leucine, and valine) and the higher than normal values for two of the aromatic amino acids (phenylalanine and tyrosine). A study published in 1976 showed a correlation between the severity of these imbalances and the hepatic encephalopathy score (56). A specially composed amino

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acid solution that would correct these imbalances was infused in combination with glucose and an improvement of the hepatic encephalopathy score was achieved (56). Solutions of this type have higher concentrations of the branched-chain amino acids and lower concentrations of phenylalanine and tyrosine as compared to normal amino acid solutions. They contain all the essential and a more or less wide range of the nonessential amino acids. They can be used not only for the treatment of hepatic encephalopathy but also for the parenteral nutrition of patients with severe liver disease and a tendency to develop hepatic encephalopathy.

There has been some controversy as to whether these so-called "Hepa" solutions are superior to the treatment of hepatic encephalopathy or not. Studies comparing the treatments have generally shown a superiority of the "Hepa" solutions over neomycin or lactulose with regard to ammonia level reduction in blood and the time needed for the improvement of the hepatic encephalopathy (57, 58, 59).

The amino acid dose administered for the treatment of hepatic encephalopathy can be 1.2-1.5 g/kg bw per day in combination with ~ 5 g/kg bw per day glucose. The infusion rate of the amino acids should be higher than normal (~ 0.2 g/ kg bw per hour) in the first two hours of the treatment. It can be reduced to ~ 0.1 g/kg bw per hour for the next two hours and be put at 0.07 g/kg bw per hour thereafter. This will lead to a more rapid correction of the amino acid imbalances than if infusion rates typical for parenteral nutrition are used from the beginning of the treatment.

In the parenteral nutrition of patients with severe liver disease regimens for increased requirements (see section II.3) are used, though amino acid intakes tend to be in the range of 1.1-1.2 g/kg bw per day. Lower amino acid intakes are insufficient (23). The non-protein calories are distributed between glucose and lipids in the usual ratios.

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## IV. Organ functions and parenteral nutrition

Organs that may be influenced by parenteral nutrition are mainly the lungs and the liver.

For the effects of excessive glucose administration see chapter II.3. Lipid emulsions are widely used in parenteral nutrition and they are very safe and well tolerated. Side effects are mostly the consequence of excessive doses or infusion rates.

In the adult reductions of  $\text{PaO}_2$  have been observed with lipid administration and it seems that the effect can be explained by the influence of too rapid administration of lipid emulsions on eicosanoid metabolism (63). Hence, infusion rates of no more than 0.11 g/kg bw and hour have been recommended (64).

In the infant, especially the preterm infant, there are concerns about potential effects of lipid emulsions on the lungs. The topic has been reviewed (65). An early onset of lipid administration has been correlated with an increased incidence of chronic lung disease, though a meta-analysis has concluded that there is no such link. Reductions of  $\text{PaO}_2$  have been observed and seem to be related to a too high infusion rate. Another concern is the formation of lipid peroxides in lipid emulsions, especially under the influence of the intensive light exposure with phototherapy. This can be overcome by protecting the lipid emulsion from light with an aluminium cover. An adequate content of vitamin E in the lipid emulsion will also help.

Hepatobiliary dysfunction is a major complication of parenteral nutrition of poorly understood origin (66, 67). With short-term parenteral nutrition (a few weeks) the hepatobiliary abnormalities are mainly intrahepatic cholestasis and periportal inflammation. The patients may develop hepatomegaly and jaundice. When oral food intake is resumed the symptoms disappear and the liver normally recovers fully. With long-term parenteral nutrition severe irreversible liver damage often develops. Inflammatory bowel disease and short bowel increase the risk. Children are more susceptible than adults.

Among the measures to reduce incidence and severity of hepatobiliary dysfunction are the reduction of non-protein calorie intake (both glucose and lipids), the use of MCT-containing lipid emulsions, and partial enteral feeding. A prospective randomised study in patients on home parenteral nutrition suggests that lipid administration should be  $< 1.0$  g/kg bw per day when emulsions based only on soya oil are used.

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## **V. Practical aspects of parenteral nutrition**

This chapter will very briefly summarize aspects of "all-in-one" mixtures for parenteral nutrition, venous access, infusion rates and clinical monitoring.

### **V.1 "All-in-one" mixtures for parenteral nutrition**

The presentations of products for parenteral nutrition are often modular. Amino acid solutions, concentrated glucose solutions, or oil-in-water emulsions are supplied in single dose containers and the same is true for concentrates of electrolytes, vitamins, and trace elements. These components have to be administered to the patients in appropriate quantities.

From a practical point of view it is easiest and safest to administer a regimen to a patient from one container and through one infusion line. It has hence become routine to put all the nutrients into one bag via compounding. The resulting regimens are referred to as "all-in-one" mixtures or "total nutrient admixtures" for TPN. The practice is safe if strict aseptic technique is followed, incompatibilities are avoided and appropriate shelf lives for the resulting regimens are defined. These nutrient mixtures are very complex physicochemically and chemically and there is a virtually unlimited number of them. It is obvious that not all the potentially possible TPN mixtures can be tested in the laboratory for compatibility and shelf life. On the other hand there is no theoretical way to predict the compatibility and

shelf life of such mixtures. As a consequence over the years there has been a trend towards the use of standardized TPN regimens of known compatibility and shelf life. These regimens are either compounded from the modules for parenteral nutrition or they are available as convenience systems in two and three-chamber bags.

When compounding "all-in-one" mixtures for parenteral nutrition it is important, to follow the right mixing sequence, as a wrong mixing sequence can render a compatible regimen incompatible. The general rules to be followed are that the pH of what will be the final mixture is achieved during the mixing process at the earliest possible stage and that additions of calcium gluconate 10 % are done at a maximum dilution of the mixture but when it can still be inspected visually (i.e. prior to adding the lipid emulsion). The resulting sequence for the filling of a mixing bag is:

- Begin with the amino acid solutions, continue with the glucose solutions and mix thoroughly.
- Add the inorganic or organic phosphates and mix thoroughly.
- Add the sodium and potassium chloride and the magnesium sulphate and mix thoroughly.
- Add the calcium gluconate 10 % and mix thoroughly.

The next steps depend on whether the regimen will be administered immediately after preparation or shall be stored for later use.

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In case the regimen is going to be administered immediately after preparation:

- Continue by adding the trace elements and mix thoroughly.
- Add the lipid emulsion.
- Add dissolved and appropriate vitamin preparations following the manufacturer's recommendations for dissolution.

In case the regimen is going to be stored for later use

- Add the lipid emulsion and store at 2-8 °C for the shortest possible time, maximum for as long as the shelf life of the regimen allows.
- Add the vitamins and trace elements only prior to infusing the regimen.

## V.2 Venous access in parenteral nutrition

Parenteral nutrition can be administered through peripheral or central veins.

The use of peripheral veins bears the risk of development of thrombophlebitis for various reasons (60). Among the most important are a too high osmolarity of the solutions infused and a prolonged duration of the infusion. In order to reduce the rate of thrombophlebitis, osmolarity should not be higher than  $\sim 900$  mOsm/l which means that only regimens covering basal requirements (see chapter II.3) can be administered peripherally. When Teflon cannulas are used the site of infusion should not be near to a joint, and the cannula should be fixed appropriately and covered daily with a fresh sterile, dry, air-permeable dressing. The cannula and the site of infusion should be changed every 2-3 days.

The introduction of short fine-bore catheters about 15 cm into a peripheral vein makes it possible to infuse solutions with osmolarities of up to 1100 mOsm/l with a low incidence of thrombophlebitis. Changes of the infusion site have to be done only every 4-5 days (60).

Central venous catheters can be inserted peripherally, a practice that has gained some popularity. It is more common, however, to insert central catheters through the subclavian vein or the internal or external jugular vein. The tip of the catheter is placed in any case in the superior vena cava near the entry into the right atrium. Among the more serious complications of central venous catheters are

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malpositions, perforations of vessels, lesions of the pleura with the potential of consecutive development of pneumo, hydro or hemothorax and septic complications. To keep them at a minimum insertion of central venous catheters should be done by experienced personnel following strict aseptic technique. The dressing must be changed every 1-2 days respecting the strictest rules of hygiene. Manipulations of lines for parenteral nutrition should be kept to a minimum and the lines should not be used for any other purpose but nutrition.

### V.3 Infusion rates in parenteral nutrition

Most of the complications of clinical nutrition are related to wrong dosages of nutrients or wrong rates of infusion. In order to achieve the best nutritional results and the best tolerance the right amount of nutrients has to be administered in a simultaneous fashion and at a slow and constant rate (61, 62). Today parenteral nutrition is most commonly administered with the "all-in-one" system, where all nutrients are mixed in one container, normally a bag, and infused over a 24 hour period. The maximum recommended infusion rates of amino acids, glucose and lipids are given in table 12.

**Table 12: Maximum recommended infusion rates for amino acids, glucose and lipids in g/kg bw per hour**

Nutrient	Adults	Neonates and infants
Amino acids	0.1	0.125
Glucose	0.25	0.9
Lipids	0.15	0.15

The patient must be gradually adapted to the situation of parenteral nutrition. In adults water and electrolytes requirements should be covered fully from the beginning but only 50 % of the calculated amount of amino acids, glucose and lipids should be given on the first day and increased to the calculated daily intake on the second day. In neonates and infants the parenteral nutrition intake has to be increased even more slowly. An example is given in table 13.

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**Table 13: Example for the gradual increase of the parenteral nutrition intake in neonates and infants (% of calculated final intake)**

Nutrient	Day 1	Day 2	Day 3	Day 4	Day 5
Fluid and electrolytes	70	85	100	100	100
Amino acids	30	50	70	85	100
Glucose	50	60	70	85	100
Lipids <sup>a)</sup>	20	30	50	75	100

<sup>a)</sup> Often no lipids are administered on the first 3 days of life and then lipid intake is started with 0.5 g/kg bw and day and increased by 0.5 g/kg bw and day until the final intake of 2.5-3.0 g/kg bw and day is achieved.

#### V.4 Patient monitoring in parenteral nutrition

In order to be able to correct dosages early and to minimize complications like fluid and electrolyte imbalances, disturbances of acid-base balance, hyperglycemia and hypertriglyceridemia, a clinical and laboratory monitoring of the patients receiving parenteral nutrition is mandatory. Suggestions for hospitalized patients are made in tables 14–16. For patients on parenteral nutrition at home a monthly monitoring is normally sufficient.

**Table 14: Clinical monitoring of hospitalized adult patients on parenteral nutrition**

Parameter	Unstable patient	Stable patient
Patient examination	Once per day	Once per day
Temperature	Every 4 hours	Once per day
Pulse, blood pressure	Every 4 hours	Once per day
Respiration	Every 4 hours	Once per day
Ward urine analysis	Every 6 hours	Once per day
Fluid balance	Once per day	Once per day
Nutrient intake	Once per day	Once per day
Body weight	Once per day	Once per day

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**Table 15: Laboratory monitoring of hospitalized adult patients on parenteral nutrition <sup>a)</sup>**

Parameter	Unstable patient	Stable patient
<b>In blood:</b>		
Glucose	Every 4 hours	Once per day
Hemoglobin	Once per day	Twice per week
Packed cell volume	Once per day	Twice per week
WBC	Once per day	Twice per week
Platelets	Once per day	Twice per week
Prothrombin time	Once per day	Twice per week
Acid-base balance	Once per day	Not needed
<b>In serum:</b>		
Sodium, potassium, chloride	Once per day	Once per day
Magnesium, calcium, phosphate	Twice per week	Twice per week
Urea, creatinine	Once per day	Once per day
Albumin	Three times per week	Twice per week
Triglycerides	Once per day	Three times per week
ASAT, ALAT, $\gamma$ -GT, bilirubin	Three times per week	Twice per week
Osmolality	Once per day	Three times per week
<b>In urine:</b>		
Glucose	Once per day	Once per day
Sodium, potassium, chloride	Once per day	Once per day
Urea, creatinine	Once per day	Once per day
Osmolality	Once per day	Three times per week

<sup>a)</sup> Electrolyte and fluid losses with drainages, diarrhea etc. must be calculated separately as required.

**Table 16: Laboratory monitoring of neonates and infants on parenteral nutrition <sup>a)</sup>**

Parameter	Unstable patient <sup>a)</sup>	Stable patient
Weight	Once per day	Once per day
Length	Once per week	Once per week
Head circumference	Once per week	Once per week
<b>In blood:</b>		
Glucose	As required	As required
Hemoglobin	Twice per week	Once per week
Packed cell volume	Twice per week	Once per week
WBC	Once per week	Once per week
Platelets	Twice per week	Once per week
<b>In serum:</b>		
Sodium, potassium, chloride	Three times per week	Once per week
Magnesium, calcium, phosphate	Twice per week	Once per week
Urea, ammonia	Twice per week	Once per week
Triglycerides	Twice per week	Once per week
Total serum protein, albumin	Once per week	Once per week
AP, ASAT, ALAT, $\gamma$ -GT, bilirubin	Once per week	Once per week
<b>In urine:</b>		
Glucose	Two to six times per day	Once per day

<sup>a)</sup> This refers also to the initial period with the gradual increase of intakes.

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