Total parenteral nutrition in children

C. Ricour
Unité de réanimation digestive et d'assistance nutritive
Hôpital des enfants malades, 149, rue de Sèvres, 75743 Paris, Cedex 15, France

The last twenty years have seen a revolution in the nutritional management of severely-ill children. The clinical course of many conditions which were usually lethal, both medical and surgical, has been radically changed. Gastrointestinal diseases were the first to benefit, especially those in which either the surface area or the absorptive function of the intestinal mucosa was reduced for any reason, whether primarily, or secondarily to protein-energy malnutrition. More recently, the application of parenteral nutrition has been extended to all those conditions of severe malnutrition in haematology, oncology, nephrology, and especially neonatology.

Results have been remarkable, and iatrogenic complications, whether due to technique or metabolic, most of which occurred in the early years, can now be largely foreseen and prevented, thanks to technical improvements and standardisation of methods. However, when digestive function continues to be insufficient for independent existence, it becomes necessary to plan a long-term parenteral nutrition. Results are equally spectacular in such cases, but new constraints then arise which may be technical, but are largely metabolic. Management of long-term programmes can only be undertaken by specialist teams.

After discussing intravascular routes for parenteral nutrition, we will deal with the regulation of supplies of macro- and micronutrients, the practical management of these, firstly in the acute phase of undernutrition and stress, and then when nutritional stability is achieved. We will then consider the prevention of complications and, finally, the place of short and long term parenteral nutrition.

Intravascular routes
Intravascular parenteral nutrition may involve the superficial veins, the superior vena cava or the creation of arteriovenous fistulae.

Superficial veins [1-4]
Micro-catheters or small cranial catheters are used. This approach is, of course, reserved for short-duration parenteral nutrition. The technique is very simple, and in most cases carries the least iatrogenic risk, mainly because the risk of infection is small. At the same time, there must be meticulous asepsis of the cutaneous route of entry and of the perfusion line because of the high risk of septicaemia in the malnourished child. Only isosmolar solutions can be used, because of the calibre of the veins and the rate of flow through them, and it is this which makes the use of lipid emulsions necessary to assure an appropriate supply of energy. Thus there are two factors which in practice limit the use of the intravascular route: reduction, or even disappearance of the capacity of the superficial veins; and the degree of malnutrition and/or the severity of the condition which, at the outset, may dictate that the use of artificial emulsions is contra-indicated, or, above all, may require that parenteral nutrition be prolonged for several weeks.

Superior vena cava [5-7]
In most cases this is the only accessible vessel. Because of the particular risks of this method, it should only be undertaken in centres specializing
in neonatology or in nutritional resuscitation. Success depends on close cooperation between physicians, surgeons, clinical pathologists, pharmacists and specially trained nurses.

Only a silicone catheter may be used. It must occupy the superior vena cava, and not the right auricle, and its calibre must be appropriate for the age and weight of the child. It can be inserted transcutaneously into a superficial cranial vein or into an arm vein, especially in a premature infant. In an older child, especially when long-term parenteral nutrition is envisaged, the catheter must be inserted in the operating theater by means of surgical exposure of the vessels in the jugular or humero-axillary region, using local or general anaesthesia. If angiography shows that it has not reached the superior vena cava, the inferior vena cava may be tried, inserting the catheter into the femoral vein and placing the tip in the region of the diaphragm.

It is essential that the entry points in the skin and in the vein be separated by a subcutaneous track measuring 5 to 10 cm. This will fix the catheter, which has a bio-adhesive dacron sleeve, and this in addition plays an important part in preventing infection. Afterwards the skin entry point should receive meticulous daily care, using iodinized disinfectants.

An anti-bacterial filter (0.22 μ) is inserted in the tip of the catheter, isolating it from the infusion line and the perfusion bag.

A pump is essential to ensure a constant flow of perfusion fluid. The choice of pump is important according to three criteria: reliability at slow flow rates, ease of use, and a safety alarm capable of signalling a change in flow rate, an air bubble or a blockage leading to increased pressure.

*Perfusion in a region of high rate of venous flow* [8, 9]

This is reserved only for long-term parenteral nutrition.

A silicone arterio-venous shunt may be used, which has the advantage of being available for immediate use. It is in general limited to a period of a few months. Perfusion into an arterialized venous pathway fashioned in the upper limb or Scarpa's triangle, supported by an arterio-venous fistula, is much more satisfactory. Such a technique cannot be used in an infant, but it is unquestionably better from the technical and psychological point of view in an older child or adolescent, since it does away with permanently implanted material. It is therefore ideal for long-term, intermittent, nocturnal, parenteral nutrition.

**Solutions for perfusion**

*Basic solutions*

These comprise a 50% solution of glucose, an amino acid solution, whose composition must be appropriate for the age or degree of maturity of the child, and which must supply 19 amino acids, of which 13 are essential or semi-essential; electrolyte solutions containing sodium, potassium, magnesium, calcium and phosphorus in the form of mono- and dipotassium phosphates; and solutions of vitamins and trace elements appropriate to the age, body weight and energy intake of the child.

*Mixing of solutions* [10]

This is done each day in the hospital pharmacy under the most rigorous aseptic conditions (laminar-flux hood, filtration sterile blister or even sterile room).

The physico-chemical limitations of solubility of the nutriments and mineral salts necessitate their successive and controlled introduction, especially in relation to the pH of the solution. Thus it is scarcely possible to dissolve more than 300 mg calcium and 400 mg phosphorus in a litre of solution. The final mixture may be a double one of glucose and amino acids, or triple, with an admixture of a lipid emulsion, the latter demanding an especially rigorous technique. The final mixture should preferably be dispensed in silicone bags rather than in glass.
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**Essential fatty acids** [11, 12]

An adequate supply can be ensured in the premature infant by the cutaneous application of polyunsaturated vegetable oil several times a day. The needs of the older child can only be met by the use of injectable lipid emulsions. Those most commonly used to-day contain 54% of their fatty acids in the form of linoleic acid, whose recommended dose is 450 mg/100 kcal (107 mg/100 kJ).

**Types of parenteral nutrition**

Because of the severity of the stress and/or the malnutrition which calls for parenteral re-feeding, practical methods differ according to whether it is being applied to the initial, acute phase of resuscitation, or to the later stage of actual nutrition. The composition of the solution must be adapted, according to the developing situation as monitored by clinical and biological examination and laboratory surveillance, if serious iatrogenic accidents are to be avoided. Three chronological stages may be distinguished: the first days, a stage of nutritional stability, and the stage of intermittent supply.

**The first days** [13]

These are dominated by risks which it is important to evaluate with a view to planning a strategy of anticipation rather than of treatment. Such risks are haemodynamic, metabolic and infective, and they also concern water and electrolytes.

**The first hours are dominated by emergency measures**

The risk of water and sodium intoxication, increased by an inappropriate secretion of vasopressin and by hyper-aldosteronism, requires a reduction in supplies of water and sodium, except in acute dehydration. This reduction aims particularly to compensate for insensible losses and those from the gastrointestinal tract. However, it must be remembered how difficult it is to estimate a third intraperitoneal or intestinal compartment which is not exteriorized.

Correction of potassium depletion is essential, but must be achieved very gradually, with strict measurement of urinary excretion and heart monitoring. It would indeed be dangerous to try to correct the deficit in one step when the capacity for fixing potassium is much more reduced than is the deficit in protein. Excessive administration runs the risk of hyperkalaemia [14].

The re-establishment or maintenance of an effective circulation may require plasma albumin or blood transfusion, depending on the haematocrit, with monitoring of the central venous pressure. Circulatory failure is a particular risk in the first 12 hours. There may be a need for assisted ventilation with intubation of the trachea if cardiopulmonary function is impaired.

Maintenance of a steady blood sugar requires continuous intravenous administration of glucose. On the other hand, the risk of hyperglycaemia with osmotic diuresis and hyperosmolar coma, as part of the hormonal picture of stress, involves limiting the supply of glucose according to the blood sugar level and the plasma and urinary osmolality. The supply of energy at this stage can only at the most cover that required for maintenance, and can only be met by glucose because of the limited clearance of plasma triglycerides [7, 15].

In these conditions of stress and energy shortage, it is both futile and dangerous to try to avoid protein breakdown. Indeed, supplying too much protein at this stage can result in hyperammonaemia and especially acidosis, by exceeding the capacity of the kidneys to clear hydrogen ions and phosphates. However by supplying 0.5 to 1.0 g/kg amino acids parenterally, one can help maintain the plasma amino acid pool by compensating for the losses from digestion.

The risk of infection, due to the depression of specific and non-specific immunity in malnutrition, can always threaten survival and aggravate the nutritional problem. Infection of the respiratory, gastrointestinal and urinary tracts, of the bones and joints, and septicemia, must be repeatedly looked for, both clinically and by laboratory investiga-
tions. As soon as a localized or generalized infection is identified, specific treatment with antibiotics is urgent. However systematic antibiotic therapy in an undernourished child is not recommended in the absence of bacteriological evidence; although it can be indicated if there is a body of indirect evidence suggesting that infection is likely [16].

In considering these emergency measures in children, we cannot exaggerate the importance of the quality of the nursing: the maintenance of a body temperature between 36.5 and 37°C by warming where necessary, the prevention of sores at all the pressure points and by commencing physiotherapy to prevent musculo-tendinous contraction in the limbs.

**Correction of the protein-energy deficiency**

When the initial stress phase is under control this is a primary objective. Restoration to normal levels must be gradual, and the greater the severity and duration of the malnutrition, the more carefully one must proceed. Excessive, unbalanced and, especially, too rapid treatment can threaten life.

It is therefore important to give nitrogen and calories together and in a proper ratio (160 to 400 mg/kg/24 h, and 200 to 500 kJ/kg/24 h respectively for 8 days). If too much nitrogen is given to an undernourished child, especially in the form of branched amino acids, a risk of hyperammonaemia may be added to one of hyperazotaemia and acidosis [17]. From the point of view of energy, it is sometimes necessary to give more, and there may be too much, especially when given parenterally at a constant rate for 24 h. There may then be a constant insulin stimulus which will result in excess triglycerides and glycogen in the liver, and above all a change of nitrogen anabolism, which preferentially facilitates protein synthesis in muscle. Such a distortion of metabolic function can be prevented by avoiding an excess of glucose and lipid, and especially by imposing alternating feeding and fasting, as described below, as soon as possible.

By very gradually increasing the energy supply in steps of 41 kJ/kg, beginning with 332 kJ/kg/24 h, one can avoid acute accidents associated with abnormal water and sodium retention with oliguria and a fall in urinary sodium and potassium excretion. It is likely that changes in the supply of glucose, and even of lipid, play a part in causing such accidents. Indeed it has been clearly shown that the sudden onset of such accidents, as well as their equally sudden reversibility, is closely associated with changes in the energy supply, and specifically that of glucose. This action of glucose may be similar to the nitrogen retention which is seen during the correction of experimental undernutrition. The insulin secreted in these circumstances seems to produce a reabsorption of sodium in the distal tubule; and the alkalosis, which is usually reported at this time, may represent the reabsorption of bicarbonate [14, 18, 19].

The resurgence of anabolism produced in this way requires that the interrelations between nutrients, electrolytes, vitamins and trace elements be taken into account. If their supply is not simultaneously regulated, it is during this phase that clinical and/or biological pathological disorders will manifest themselves to a greater or lesser degree. Their deficiency can usually be prevented by administering them in the following proportions: for each gram of nitrogen, it is suggested that there should be 1045 kJ energy, 3.2 mmol calcium, 2 mmol phosphorus, 1 mmol magnesium, 10 mmol potassium, 7 mmol sodium and chloride, and 1.2 mg zinc. At the same time, one must regulate the dose of copper, manganese, chromium, iron, iodine, selenium, cobalt and fluorine, as well as vitamins, especially those of the B group. Finally, there must be a close correlation with the supply of essential fatty acids, tocopherols and selenium, in a proportion of 100 mg, 0.6 mg and 3 μg respectively.

**The stage of nutritional stability**

**Nitrogen** [1, 20, 21]

Nitrogen requirement is, of course, very dependent on the age and the degree of undernutrition. In the premature it varies, depending on the author,
between 400 and 650 mg/kg/24 h. In the infant it varies from 400 to 800 mg/kg/24 h when losses are large. In the older child 300 mg/kg/24 h are usually enough. Such doses, exceeding the needs for growth, cover metabolism and nitrogen lack. Beyond that more is not required, since there is a negative correlation between nitrogen supply and its percentage retention. More would actually be dangerous and, particularly in the premature, would cause hyperaminoacidaemia, metabolic acidosis and iso-osmolar coma. Finally, it is likely that such doses would account for the anomalies of phosphorus and calcium metabolism which have been reported in these conditions [22, 23].

From the qualitative point of view, although the composition of the available amino acid solutions has been progressively changed in regard to their essentiality or otherwise, none of them is perfect for the premature infant, the infant or the older child, especially when they are malnourished. Indeed, because of the disordered function of certain enzyme systems in undernutrition, or of their immaturity in the premature, it may be necessary to reduce, increase or add certain amino acids when using solutions in children in these high risk groups. Threonine, as well as phenylalanine and methionine, must be reduced in this way. In contrast, cystine, taurine, histidine, proline and lysine must be added or increased. Finally, it has been suggested that the proportion of essential to total amino acids should be increased from 0.45 to 0.53 [21].

**Energy**

Energy supply is closely related to that of nitrogen. In the premature infant, it is recommended that there should be from 418 to 527 kJ/kg/24 h, and the same is true for the infant. In contrast, in the older child it is reduced to a mean of 325 kJ/kg/24 h [24].

In parenteral nutrition, glucose is the only carbohydrate source which can be used. Others are not advisable in the infant. Fructose, whose use has been recommended because its cellular metabolism is not insulin-dependent, in fact induces a lactic acidosis when it is supplied at an hourly rate of more than 0.3 g/kg [2].

In practice, in parenteral nutrition using the superficial veins, glucose at a rate of more than 15 g/kg/24 h is not possible because of its osmolarity. Using a central catheter, on the other hand, it is sometimes possible to administer from 1.5 times to twice this amount. Such amounts are usually well tolerated, to judge by the normality of plasma levels of glucose, glycosylated haemoglobin, growth hormone, glucagon and insulin. However, such tolerance is only possible when the osmotic load of glucose is increased in stages and does not exceed 100 mosmol/100 ml. At the same time it is essential, of course, that the perfusion flow rate should be absolutely constant, and should not exceed 1.5 g/kg/h of glucose. Glycosuria in such conditions indicates an error of perfusion technique, or even stress due to infection [25-27].

As we have seen, the use of lipid emulsions takes care of essential fatty acid requirements. From the point of view of energy they have undoubted advantages: they make good peripheral parenteral nutrition possible, because of their high energy and low osmolarity. From the metabolic viewpoint, non-protein energy requirements can be met by a mixture of 70% glucose and 30% lipid without a build-up of excess glucose in the form of fats and/or an iatrogenic accumulation of exogenous lipids. Thus a supply of lipids of between 2 and 4 g/kg/24 h is recommended, if possible as a continuous perfusion in the course of 24 h, either as a single ternary mixture, or a binary mixture with a lipid perfusion in parallel. As we have seen above, it is necessary to add tocopherol and selenium in balanced proportions in order to avoid peroxidation of the fatty acids. Some believe that a carnitine supplement should be added so as to facilitate intracellular fatty acid oxidation. Finally, it is suggested that 25 to 50 IU/kg heparin should be added to the lipid emulsion according to the plasma lipid concentration and the turbidity index [28-33].

However great the advantages of lipid emulsions in parenteral nutrition, they are contra-
indicated in certain pathological conditions. An example is infection with septicaemia and thrombocytopenia, because of a reduced post-heparin lipoprotein lipase activity. The possibility that free fatty acids may displace unconjugated bilirubin from the plasma proteins prevents their use in cases of neonatal jaundice or of serious hepatic dysfunction. The metabolism of phospholipids, which assures the stability of the lipid emulsion, also produces H⁺ ions (37 mEq/litre of 10% intravenous fat emulsion [Intralipid®]), and this makes its use dangerous when there is metabolic acidosis, and especially when there is renal insufficiency. If respiratory distress should arise, especially in the infant, this will constitute a temporary contra-indication to the use of lipid emulsions because of the increased risk of troubles in the alveolocapillary diffusion. Finally, all disturbances of lipoprotein metabolism are contra-indications to the use of lipid emulsions [34-38].

Water and electrolytes

Water balance is usually achieved by supplying the following amounts: 150 to 250 ml/kg/24 h in the premature [39]; 120 to 140 ml/kg/24 h in the infant; and 80 to 100 ml/kg/24 h in the older child, to which is added 3 to 5 mEq/kg/24 h each of chloride, sodium and potassium. These approximate quantities must, of course, be adjusted when there are losses from the digestive tract. Thus, when these are due to vomiting or gastric aspiration, a loss of 100 ml water implies a mean loss of 8 mEq sodium, 1 mEq potassium, 6 mEq H⁺ ions and 12 mEq chloride. When there is an enterostomy, a loss of 100 ml water corresponds to a depletion of 14 mEq sodium, 1 mEq potassium, 10 mEq chloride and 5 mEq bicarbonate. Finally, in severe colitis, a loss of 100 ml water corresponds to 5 mEq sodium, 10 mEq potassium and 12 mEq chloride.

Phosphorus requirements, due to accretion of calcium and phosphorus in bone and to protein anabolism, carry a requirement for 1.5 mmol phosphorus/kg/24 h for every 400 mg nitrogen/kg/24 h and 0.8 mmol calcium/kg/24 h. If less phosphorus is supplied, or if the supply of nitrogen and/or calcium is greater, a severe depletion of phosphorus may occur, accompanied by neurological signs, hypophosphataemia and hypercalciuria with acidosis, due to a reduced secretion of H⁺ ions by the kidney. Magnesium requirements are usually met by 0.4 mmol/kg/24 h [22, 40].

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<thead>
<tr>
<th>mineral salts</th>
<th>trace elements</th>
<th>vitamins</th>
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<tbody>
<tr>
<td>sodium 3 mmol</td>
<td>iodine 5 µg</td>
<td>vitamin A 250 IU</td>
</tr>
<tr>
<td>potassium 4 mmol</td>
<td>copper 20 µg</td>
<td>vitamin D 50 IU</td>
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<tr>
<td>phosphorus 1.3 mmol</td>
<td>zinc 200 µg</td>
<td>vitamin E 0.7 mg/g EFA*</td>
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<tr>
<td>calcium 0.8 mmol</td>
<td>manganese 5 µg</td>
<td>vitamin K 10 µg</td>
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<tr>
<td>magnesium 0.4 mmol</td>
<td>fluorine 30 µg</td>
<td>vitamin C 10 mg</td>
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<tr>
<td>iron 50 µg</td>
<td>vitamin B₁ 100 µg</td>
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</tr>
<tr>
<td>selenium 3 µg</td>
<td>vitamin B₂ 100 µg</td>
<td></td>
</tr>
<tr>
<td>chromium 2 µg</td>
<td>vitamin B₆ 80 µg</td>
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</tr>
<tr>
<td>niacin 250 µg</td>
<td>vitamin B₁₂ 0.1 µg</td>
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<tr>
<td>folic acid 10 µg</td>
<td>pantothenic acid 400 µg</td>
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<td>biotin 5 µg</td>
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* EFA: essential fatty acids
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Vitamins and trace elements

These must be calculated in relation to the supply of the respective nutrients, the losses from the digestive tract, or supervening stress (surgical or infective), and above all to the age of the child. The recommendations set out in the table will usually prevent either deficiency or excess [41-46].

Intermittent administration

As soon as the nutritional supply has been established, it becomes necessary to modify the rhythm of administration, and this is usually from the third week. During a period of about 10 days this should be changed from continuous perfusion throughout the 24 h to intermittent nocturnal perfusion of 12 to 18 h duration. This new rhythm must be achieved gradually in steps of 30 min at the beginning and the end of the daily (by preference nocturnal) perfusion. An intermittent regime has both a metabolic and psychological advantage. Thus alternating periods of feeding and fasting induce a more normal rhythmic behaviour of insulin and glucagon. In this way, they prevent the hyperinsulinism which is responsible for fatty liver, and encouraged muscle synthesis in preference to that in the liver. Finally, it transforms the quality of life of the children, especially of older children, by allowing them to undertake their normal physical activity whose importance during recuperation from undernutrition is well-known [47, 48].

Prevention of complications

Technique

Infection is the greatest problem with long-term intravascular therapy in high-risk children. Prevention involves scrupulous asepsis when setting up, as well as during the course of perfusion using the superficial veins. This is too often neglected, due to the very widespread use of this route.

Implanting a central venous catheter certainly increases the risk of infection. Preventive measures in specialist centres have reduced the frequency of such complications remarkably, to from 5 to 10% of vena cava catheterizations, depending on the pathology and the centre. They depend on controlled, permanent and comprehensive asepsis, with regular follow-up inspection, not only at the place of introduction of the catheter, but also at all points of the infusion line from the antibacterial filter to its entry point in the skin. Doctors and nurses in charge of these children must be well-trained and made responsible for this technique [49].

It should be noted that the use of an arteriovenous fistula spectacularly reduces the risk of infection, which makes this the method of choice when a prolonged programme of parenteral nutrition is decided upon.

In practice, the appearance of fever or of any other clinical sign suggesting infection must lead to a search, both inside and outside the digestive tract, while awaiting the results of the blood pictures. Blood culture, both of peripheral blood and of blood from the catheter must be performed. It is recommended that the lumen of the catheter be washed out with a heparin solution and the infusion bag replaced as well as the line and the filter. If the temperature remains elevated in spite of these measures, antibiotics should be added to the infusion until the results of the blood cultures are known, which should be at the most 4 days later. Obviously a collection of pus in the subcutaneous track of the catheter, or at its point of entry, must be carefully looked for, a measure which allows it to be left in place in most instances. The catheter should be removed without delay if the clinical situation gets worse in spite of antibiotics in the ensuing 12 to 24 h, providing, of course, that no other cause is discovered [50].

Nevertheless, an infective focus and/or septicaemia in a child with serious malnutrition, is not only not a contra-indication to parenteral nutrition: it even constitutes an additional and immediate indication if the digestive tract cannot be used.

Antibiotic therapy will, of course, be part of the parenteral nutrition in these cases.
Thanks to the meticulous observance of all these rules, displacement or obstruction of the catheter or thrombosis of the vena cava has become very rare. Similar care when using superficial veins should also avoid thrombophlebitis or septic embolism [51].

Prevention of metabolic complications

Most metabolic complications can be prevented by meticulous monitoring of the course of re-feeding and by appropriately formulated solutions. In this way it is essential, especially in the first few days, to monitor the following: infusion rate, temperature, cardiac and respiratory rhythm, 3-hourly blood pressure, 6-hourly urinary or gastrointestinal losses, and 12-hourly body weight. During the first 5 days, and whenever the osmolar load is increased, it is necessary to measure the pH and the osmolality of the urine at each micturition, and to look for glycosuria and/or proteinuria. Plasma and urinary ionic concentration and haematocrit must be regularly estimated, as must be coagulatory proteins, plasma albumin, bilirubin, transaminases and alkaline phosphatases. Progressive adjustment of the constituents of the solutions according to these results, and in relation to the aetiology, the age of the child, the nutritional state, should make deficiency or overload exceptional. In practice, the criteria of adequate nutrition are: steady, but not excessive weight gain, gradual correction of the lean body mass and of body fat using anthropometric indices such as skinfold thickness and arm circumference, a retention of 50 to 70% of the infused nitrogen, normal blood levels of pre-albumin, transferrin, coagulatory proteins and haemoglobin, the absence of proteinuria or glycosuria, balanced urinary excretion of sodium and potassium, and urinary calcium not exceeding 5 mg/kg/24 h while keeping a “safe” level of phosphaturia.

Three kinds of complications in practice threaten parenteral nutrition when it continues for several months: hepato-biliary complications, gastrointestinal tract dysfunction and disorders of calcium and phosphorus regulation.

Hepato-biliary complications such as cholestasis, fatty liver or even portal fibrosis, are risks which it is still difficult to prevent during the course of parenteral nutrition, especially when it is prolonged; and this may be due to several factors. One should be alerted and take appropriate measures as soon as there is any elevation of any of the following blood constituents: bilirubin, transaminases, or alkaline phosphatases. These manifestations may be caused by an essential fatty acid deficiency and/or factors interfering with their metabolism such as tocopherol, selenium or carnitine; an excessive supply of energy in the form of glucose, or an inappropriate administration of lipid emulsion must be detected and quickly dealt with. Finally stimulation of the entero-biliary system might be considered, either by the ingestion of a mixture of peptides and long-chain triglycerides, or by the subcutaneous injection of cholecystokinin or of cerulein. The intraluminal development of an intestinal bacterial flora has been put forward to account for this liver disorder, and oral metronidazole might be used to prevent such an anomaly of intestinal colonization. Finally, the institution of intermittent parenteral nutrition might, as we have seen, induce a return of hepatic function to normality [52-58].

Dysfunction of the gastrointestinal tract during exclusive parenteral nutrition might be responsible for such complications as gastric intolerance and diarrhoea when enteral feeding is resumed. Several factors are responsible: reduction of gastric and biliary-pancreatic secretions, diminution of the enzymatic activity of the intestinal brush border, alteration of the luminal flora, and slowing of gastric emptying and reduction of intestinal motility. The prevention of poor intraluminal digestion and of intestinal malabsorption in this situation depends on the gradual substitution of parenteral feeding for enteral, semi-elementary feeding by constant-rate infusion over 24 h. This will allow a return of secretory, motor and enzymatic function [59, 60].

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Disorders of calcium and phosphorus regulation are an important metabolic risk whatever the age of the child. This so-called “bone disease” resembles rickets, with fractures of the limbs which are sometimes asymptomatic and are only discovered on routine X-rays. In the laboratory, a rise in alkaline phosphatases and hypercalciuria are the most constant features, contrasting with normal, or sub-normal levels of vitamin D metabolites and of parathyroid hormone. Bone histology shows the changes of osteomalacia, associated with faulty mineralization and an excess of osteoid tissue. The aetiology of these bony lesions is probably multifactorial: excessive vitamin D, or disorders of its metabolism mean that it must be given very prudently in prolonged parenteral nutrition. In addition, it is possible to reduce the hypercalciuria by seeing that the supply of phosphorus, nitrogen and energy is properly balanced, while reducing the supply especially of amino acids, and above all of sulphates. Finally, in the long-term, it is necessary to be sure that there is no contamination of the solutions with aluminium. The prevention of this “bone disease” rests on regular estimation of alkaline phosphatases, and above all of the urinary calcium, which must not exceed 5 mg/kg/24 h [61-65].

Indications for parenteral nutrition

Parenteral nutrition is indicated in all malnourished children, for whatever cause, as soon as it becomes impossible to use the enteral route. Such indications, originating in the gastrointestinal tract and outside it have very greatly increased in recent years. However, taking into account the iatrogenic risks of the technique, especially when it is used for several weeks, it must only be performed in specialist units.

The choice between superficial and deep veins is, of course, a function of the degree of malnutrition, the possibility or otherwise of using an artificial emulsion intended for energy, the state of the superficial veins, and above all the foreseeable duration of the programme. Indications may be divided into long term and short term.

Short term indications

This means a duration of about one month, which is most often the case both in gastrointestinal and non-gastrointestinal pathology.

Gastrointestinal pathology

The commonest indications are severe, intractable diarrhoea in infants, and untreatable diarrhoea in older children, whatever the aetiology. In such cases, parenteral nutrition is inescapable when elementary enteral nutrition has failed [66].

Whatever the age of the child, parenteral nutrition, together with enteral nutrition, is indicated as a setting for all gastrointestinal surgery in which there is extensive resection of the small intestine, an enterocutaneous fistula or a proximal enterostomy [67, 68].

In the case of gastrointestinal malformations present at birth, parenteral nutrition is begun as soon as the corrective surgical treatment has allowed a critical few weeks to pass, during which enteral nutrition has seen to be either impossible of insufficient to provide the needs for growth. Examples are omphalocoele laparoschisis, Hirschsprung’s disease, and “adynamic” small intestine, whether primary, or secondary to peritoneal adhesions [69, 70].

In other situations, parenteral nutrition cannot only play a symptomatic role in correcting a protein energy deficit, but can also constitute specific therapy. Thus it can inhibit the production of digestive hormones which stimulate intestinal motility and gastric and bilo-pancreatic secretion; it can reduce the abnormal proliferation of intestinal flora; it can allow the total exclusion of highly antigenic dietary proteins; and, finally, it affects the intestinal circulation of blood and lymph. It is probably because of these multiple factors that parenteral nutrition has produced remarkable results in in-
flammatory diseases of the gastrointestinal tract, especially in Crohn's disease and in certain cases of unidentified colitis. The same is true in acute pancreatitis and severe ulcerative diseases, as well as for the consequences of abdominal radiotherapy, with or without chemotherapy. Equally spectacular are the results obtained in vascular enteropathies, whether necrotizing enterocolitis in the infant or that complicating Hirschsprung's disease. The same is true of the severe capillitis or arteriolitis occurring in certain forms of rheumatoid purpura or periarteritis [71-73].

Non-gastrointestinal indications

Certain congenital or acquired metabolic diseases, such as severe hepatic or renal failure with gastrointestinal complications, can benefit from appropriate amino acid solutions. Parenteral nutrition can also be necessary where there is increased nitrogen catabolism or excessive nitrogen loss, as in multiple trauma or extensive burns. Finally, parenteral nutrition has revolutionized the management of oncological chemotherapy protocols. The same is true of the future development of combined enteral and parenteral feeding of very low-birthweight premature patients.

Long-term indications

Compared with the indications mentioned above, these are, of course, much less common. They need to be completely managed by a specialist centre, from which a programme of domiciliary parenteral nutrition can be organized. Such nutrition can be exclusively parenteral for months or years, or is more often mixed. Some indications are: total or subtotal excision of the small intestine; syndromes of chronic pseudo-obstruction of the intestine; refractory atrophies of the intestinal mucosa with severe, persistent malabsorption, either alone, or associated with immune deficiency; and certain cases of Crohn's disease which are extensive and/or have received multiple surgery, with growth restriction and following other therapeutic failure [74-76].

The objective of prolonged parenteral nutrition in these cases is to ensure normal growth of the child, while offering him a quality of life as close as possible to that of other children or adolescents of the same age, while waiting for an inflammatory syndrome to subside, or for residual intestine to adapt, or pending an intestinal transplant.

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