Requirements and Utilization of Macronutrients in Enteral and Parenteral Nutrition in Acute and Chronic Diarrhea

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In most infants and children, the symptoms of acute diarrhea resolve over the course of a few days, but in a small proportion, diarrhea persists and becomes protracted. Protracted diarrhea has been defined as more than four watery stools per day for longer than 2 weeks. The definition of chronic diarrhea is a little controversial. Most experts find this diagnosis appropriate when the infant or child has had diarrhea for 1 month or more.

Whatever is the cause and pathomechanism of acute, protracted, and chronic diarrhea, the long-term consequences of the latter two diseases are the inadequate nutrition and impaired growth and organ development of the digestive organs, liver, circulatory organs, and brain. These perils have become more and more obvious in recent years and have led the medical world to focus particular attention on the availability, transport, and utilization of principal nutrients in diarrheal disease of developing human subjects.

The aim of this short chapter is to discuss the theoretical and practical aspects of nutritional support to patients with acute and chronic diarrhea with particular emphasis on protein, energy, and macronutrient requirements.

Scientific Foundations of Nutrient Requirements

Complete nutritional support for patients is based on the concept that exogenous energy sources should be supplied at levels greater than endogenous energy expenditure. If intake is inadequate, the patient will lose, first, the readily available energy stores such as glycogen and fat, and then, in a second phase, the protein components of the body cell mass.

Whatever route of alimentation seems to be necessary the aim is to meet the special energy and nutrient requirements of an infant and child, which thoroughly differ from those of adults. The adult, from an energetic point of view, is in a steady state, and in providing enough energy and nutrients for his/her maintenance metabolism and external work satisfies the primary aims of nutritional management. In simple words, maintenance metabolism is the complex of total physiological and biochemical mechanisms aimed at keeping the body in a healthy state (1,2).
The infant or child, however, is supposed to grow steadily and increase his/her body weight at a considerable rate, thus changing the energy stores and equilibrium constantly (1–15). Therefore, well-balanced nutritional support is especially important in prolonged gastrointestinal illness of infants and children because they not only need to be provided with enough food to cover maintenance metabolism but also have to be supplied with a variety of nutrients to secure normal growth and development.

In a resting state, essentially all of the energy transferred within the body is dissipated as heat. Thus, for determination of energy needs at a steady state, either the direct measurement of heat loss from the body or calculation of heat production from gaseous exchange (oxygen consumed and carbon dioxide expired) are well-accepted methods. The major problem is that the infant and child are rarely in a steady state from an energetic point of view. We expect them to grow steadily and increase their body weight at a rate of approximately 10 to 15 g/kg per day.

Therefore, in the growing infant and child the calorimetric measurements will provide information only on energy requirements for maintenance (Fig. 1). The other, equally important component of the total energy need is the energy requirement for growth, comprising energy for new tissue synthesis and the energy stored in new tissue. Maintenance metabolism and the process of energy deposition are competitive to a certain extent: in case of an energy supply that is little more than sufficient for maintenance, energy deposition is considerably reduced. In order to derive scientifically sound and clinically useful data, the pediatric researcher must, therefore, learn a lot more about the biochemical aspects of energy metabolism than the clinical investigator dealing with human adults (2).

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**FIG. 1.** Partition of energy metabolism in the infant and child. (From Heim et al., ref. 2, with permission.)
In order to establish data on all components of energy metabolism, such as maintenance, tissue synthesis, stored energy, and energetics of growth, the following measurements can be employed: (a) balance studies, such as energy balance or chemical balance or both, (b) biochemical measurements of nutrients, nutrient metabolites, or related functional and structural components in urine and blood, and, finally, (c) clinical evaluation and performance tests, such as anthropometric measurements, determination of growth velocity, psychomotor performance, etc.

Other techniques such as those involving isotope tracers or tissue biopsy are essentially variations of points (a) and (b). We in the Hospital for Sick Children of Toronto have applied the techniques summarized in point (a) using both energy and chemical balance, including long-term measurement of energy expenditure by computerized indirect calorimetry (9).

**EVALUATION OF THE NUTRITIONAL STATUS**

In order to identify patients who would benefit from nutritional support and to appropriately select the therapy, subjective and objective assessment of the patient's nutritional status should be performed. Ideally, nutritional assessments should be made available on admission and periodically during hospitalization to identify potential nutritional problems. Figure 2 demonstrates the flow chart

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**FIG. 2.** Flow chart for the nutritional assessment of a patient with diarrhea on admission and periodically during hospitalization. Selection of appropriate nutritional management. (From Martin, ref. 16, with permission.)
of nutritional assessment and evaluation of gastrointestinal function in selecting the appropriate enteral or parenteral nutrition (16).

At first examination of a patient in the office or the outpatient department of the hospital, a simple nutritional screening, marked as preliminary assessment, can identify patients requiring more complete nutritional assessment. If not, one can admit and treat the patient immediately.

If in the course of the preliminary assessment some nutritional problem is suspected, one should not hesitate to ask for a complete nutritional assessment or for nutritional support. In cases of severe inflammatory lesions or short bowel syndrome, parenteral nutrition is indicated. In mild undernutrition, peripheral parenteral nutrition (PPN) or protein sparing (PS) therapy, and in moderate malnutrition, peripheral parenteral nutrition or central parenteral nutrition (CPN), may be indicated. Currently, patients with severe undernutrition can best meet their nutritional needs with central parenteral nutrition.

Proper formulation of parenteral feeding regimens is dictated by the clinical situation. Formulation of a feeding regimen for a severely depleted patient will obviously be different from one applied in a moderately depleted case. Alternatively, the specific nutritional recommendations will differ in diarrhea coupled with kwashiorkor from that of the diarrhea developed in a marasmic child.

The nutritional status, based on percentage of ideal body weight, can be classified into four categories: 90% and above, not depleted; 89 to 90%, mildly depleted; 60 to 80%, moderately depleted; and <60%, severely depleted.

The body’s fat stores can be estimated by determining the triceps skinfold thickness using skinfold calipers. The actual measurement on a patient can then be compared with the results obtained on healthy population and classified as the percentage of normal, i.e., not depleted (90%), mildly depleted (80%), moderately depleted (70%), severely depleted (<60%).

The lean body mass or skeletal muscle mass can be estimated by measuring the arm circumference and the nutritional state can then similarly be classified. Visceral proteins are estimated by the serum albumin, serum transferrin, rapid-turnover proteins such as the retinol binding protein, serum and urinary creatinine, urinary 3-methylhistidine excretion, etc.

If any enteropathy is combined with malnutrition, it is worthwhile to classify the latter as precisely as possible in order to be able to design a specific nutritional therapy. The first type, kwashiorkor-like malnutrition, is a result of normal energy intake but deficient protein intake. The second type of protein–calorie malnutrition is marasmus, which is generally associated with long periods of decreased intake of both energy and protein, leading to cachexia. The third type is a combination of kwashiorkor and marasmus. This group represents patients who present with marasmus and are then acutely deprived of protein; e.g., diarrhea treatment with 5% glucose infusion (D5W) intravenously can result in kwashiorkor superimposed on marasmus. These patients have inadequate fat and protein “reserves” and are classified as high risk.

Differentiation among the three types of protein–calorie malnutrition (PCM)
can be made by measurements of body weight, skinfold thickness, arm muscle circumference, and serum albumin levels.

Kwashiorkor-like PCM is characterized by normal body weight, normal skinfold thickness, normal arm muscle circumference, but decreased serum albumin, indicating the acute visceral attrition and protein undernutrition. In marasmus, the body weight is decreased, as are the skinfold thickness and arm muscle circumference, all characteristic signs of cachexia; serum albumin is normal. When kwashiorkor is mixed with marasmus, all four parameters are diminished, indicating that acute visceral attrition is superimposed on marasmus.

It is interesting to note at this point that the incidence of malnutrition on admission to the hospital in the North American continent is less than 10%. The prevalence of protein-calorie malnutrition or undernutrition (PCU) in hospitalized patients, however, increases to 40 to 50%, indicating that nutritional assessment and therapy should be integrated into the concurrent care of each patient.

NUTRITIONAL MANAGEMENT OF ACUTE DIARRHEA

We are all aware of the vigorous campaign to popularize oral rehydration and oral maintenance therapy in lesser developed countries, where diarrheal disease is the leading cause of mortality in infancy. No one can seriously doubt the significant benefits of this approach. The primary emphasis in this management is on rehydration and restoration of electrolyte and acid-base balance, not on nutritional rehabilitation. The World Health Organization (WHO) has recommended a single oral rehydration formula for the management of deficits in water, base, sodium, and potassium. The formula contains, in millimoles per liter, 90 of sodium, 25 of potassium, 80 of chloride, 30 of bicarbonate, and 110 of glucose. Since glucose is relatively expensive, in some parts of the world it has been replaced by the cheaper sucrose.

Palmer and his co-workers (17) compared sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrhea (Fig. 3) and found no major difference in the success or failure rate applying either the mono- or the disaccharide-containing solution (17). However, since only the glucose fraction of sucrose is active in intestinal transport, twice as much sucrose (by weight) must be used.

The recommended oral rehydration solutions contain 110 mM glucose. This is equivalent of an approximately 2% glucose solution, thus containing about 8 kcal/dl energy. Even if the infant consumes 250 to 300 ml of this solution per kilogram body weight per day, and the carbohydrate loss in the stool is disregarded, the energy supply is only 20 to 24 kcal/kg per day, hardly enough to cover one-third of the maintenance requirement of a young infant. Our results illustrate this point.

Under hypocaloric glucose nutrition, the infant must rely on his/her endogenous fat stores to cover maintenance metabolism. In Fig. 4, calorie intake is
plotted against the percentage of calories produced by oxidation of endogenous fat. A highly significant inverse relationship was found between calorie intake and endogenous fat oxidation, with a correlation coefficient of 0.91; thus, the human infant relies on the oxidation of endogenous fatty acids during hypocaloric fat-free TPN. For instance, at 20 kcal/kg per day intake, more than 75% of the energy metabolism is derived from endogenous fat, i.e., approximately 4.5 g/day. With increasing calorie intake, fat oxidation is gradually diminished, and above 70 to 80 kcal/kg per day intake, no endogenous fat was oxidized.

Classical physiology associates increased fat oxidation with starvation or at least with stagnation of body weight; thus, our results imply that the minimal caloric requirements to cover basal energy metabolism and muscular activity of infants receiving TPN are around 70 kcal/kg per day. This calorie intake is the turning point at which endogenous fat oxidation concludes and the infant is in energy equilibrium. Growth, however, cannot be expected. It is obvious that a malnourished baby is lacking the amount of fat stores that could provide 4.5 g/kg per day triglyceride to support maintenance metabolism. If such an
infant contracts diarrhea, he/she will run into negative energy balance rapidly, and severe protein catabolism ensues well before the oral rehydration therapy can be replaced by oral maintenance therapy.

Therefore, with the WHO-recommended oral rehydration formula, restoration of nutritional balance cannot be expected. Supplementation of other substrates such as amino acids has proven to be very effective in controlled balance studies, but there have so far been no large-scale clinical trials. The starches in rice, too, are very effective as substrates in the oral therapy mixture. There are advocates of early introduction of fat into the diet who claim beneficial effect of fat ingestion because a fat-rich diet stimulates the secretion of gastric inhibitory polypeptide (GIP) and thus diminishes the motility of the gastrointestinal tract (18).

Despite the benefits of oral rehydration therapy in acute diarrhea, several countries have shown little enthusiasm for oral rehydration therapy. Pediatricians in Europe and the United States generally adopt a more traditional approach to diarrhea, such as (a) oral replacement of stool loss with low-sodium fluids, (b) limited food intake during diarrhea, and (c) more reliance on intravenous fluid, even in the moderately dehydrated child.

Their cautious approach toward oral rehabilitation of acute diarrhea seems to be substantiated by the kind of results depicted on Fig. 5. A dramatic increase
in the stool output could be observed in 25 patients with cholera receiving intravenous fluid replacement as the only treatment (groups I and II in Fig. 5). However, when the gastrointestinal tract was simultaneously perfused with glucose-containing solutions (groups III–VII), the stool output rate became greatly diminished, indicating a beneficial effect of glucose on overproduction or underabsorption of fluid by the intestine or a combination of both processes (19).

**ENERGY AND MACRONUTRIENT SUPPLY IN PROTRACTED AND CHRONIC DIARRHEA**

If the diarrhea lasts more than 2 weeks, i.e., becomes protracted, nutritional management becomes a principal part of the therapy. Treatment is generally based on dietary manipulation, and it has been stated by several authors that it is essential to maintain nutrition by continuing adequate food intake even if this actually prolongs diarrhea.

Mann and co-workers (20) have recently studied the effect of diet on the utilization of carbohydrate, fat, and protein in infants with prolonged diarrhea. They sorted the 22 infants into three groups (Fig. 6) according to the dietary management: group I received full-cream milk; group II received soy milk;
group III received low-lactose milk. The average age of the babies was 3 to 5 months, and they were moderately malnourished at the time of the study, weighing 68 to 80% of their expected weight for age.

Metabolic balance studies were performed on day 8 and on days 9 to 11 of the hospitalization, i.e., approximately 12 to 14 days after the commencement of diarrhea (Fig. 7). The stool weight was the largest on the full-cream-milk diet in both periods of the study. Total stool reducing substances were the most pronounced on the low-lactose diet, and the stool lactate level was the highest. Apparently, nitrogen absorption tended to be best on the low-lactose-milk diet.

The nitrogen, i.e., protein intake was almost identical in the three groups of infants (Fig. 8). Both apparent nitrogen absorption and nitrogen retention were obviously influenced by the severity of the diarrhea. With decreasing stool weight,
both the apparent N absorption and N retention improved. The best N retention was observed with the low-lactose-milk diet.

An appreciable difference was observed between the apparent N absorption and the stable-isotope $^{15}$N-labeled yeast protein absorption (Fig. 9). On the full-cream-milk or soy-milk diet, the latter was almost twice as high as the apparent N absorption, indicating that a large portion of nitrogen loss was endogenous in origin.

Apparent fat absorption and fat retention were also influenced by the stool weight and were very poor on all three diets (Fig. 10). Some improvement in fat absorption could be observed on the low-lactose-milk diet.

From the measurements of carbohydrate, protein, and fat in the stool, one can calculate the energy losses in excreta and calculate the partition of gross

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**FIG. 7.** Median stool weight, total stool reducing substance (total sugar), stool lactate, and apparent nitrogen absorption on day 8 and days 9 to 11 inclusive of the diarrhea in three groups of infants whose dietary management thoroughly differed: full-cream milk ($\square$); soy milk ($\blacksquare$); low-lactose milk ($\blacklozenge$). (From Mann et al., ref. 20, with permission.)
DAY 9-11

STOOL WEIGHT

NITROGEN INTAKE

80-

20-

APPARENT N-ABSORP.

NITROGEN RETENTION

80%–

20%–

FIG. 8. Median stool weight, nitrogen intake, apparent nitrogen absorption, and nitrogen retention on days 9 to 11 inclusive in infants with prolonged diarrhea and fed on full-cream cow's milk (□), soy milk (□), or low-lactose milk (■). (From Mann et al., ref. 20, with permission.)

ON DAY 8

Apparent N-absorp.  N\textsuperscript{15}-yeast protein absorp.

ON DAY 9-11

Apparent N-absorption

FIG. 9. Relationship between apparent nitrogen absorption and \textsuperscript{15}N-yeast protein absorption in infants with diarrhea fed on full-cream cow's milk (□), soy milk (□), or low-lactose milk (■). (From Mann et al., ref. 20, with permission.)
DAY 9-11

STOOL WEIGHT

FAT INTAKE

APPARENT FAT ABSORP.

FAT RETENTION

FIG. 10. Median stool weight, fat intake, apparent fat absorption, and fat retention on days 9 to 11 inclusive of the diarrhea in infants fed on full-cream cow's milk (○), soy milk (□), and low-lactose milk (■). (From Mann et al., ref. 20, with permission.)

calorie intake (Fig. 11). In a healthy breast-fed infant at an age of 3 to 6 months, the fecal loss of energy amounts to about 11 kcal/kg per day. The resting metabolic rate, measured by indirect calorimetry, is about 55 kcal/kg per day; 15 kcal/kg per day is spent for muscular activity, and 11 kcal is for chemical thermogenesis, saving 19 kcal/kg per day energy retention for growth (4,9-12). Thus, ingestion of 110 kcal/kg per day can provide an adequate intake for growth. Infants with prolonged diarrhea lose a considerably greater amount of energy in excreta. Since their resting metabolic rate and the other components of energy metabolism are virtually unchanged, with a gross calorie intake of 110 kcal/kg per day, they are all in negative balance irrespective of diet. Growth is beyond question.

The results presented in Figs. 3 to 11 clearly demonstrate that the continuing wastage of essential nutrients in the presence of impaired absorption makes it unlikely that an adequate oral food intake can be achieved in the infant or child
with severe diarrhea. A solution to this problem would be either (a) to increase
the oral intake considerably above 160 kcal/kg per day or (b) to introduce total
intravenous nutrition early as the sole or supplemental therapy.

The addition of parenteral nutrition to oral feeding can terminate or reduce
the severity of the diarrhea. A comparison of the effects of milk feeding and
intravenous therapy on the volume and acidity of the stool in infant diarrhea
is demonstrated in Fig. 12. A sharp decrease in stool volume followed the
introduction of intravenous therapy in both patients. Stool lactate and organic
acid concentration are decreased as well (21).

The effect of somewhat longer-term parenteral nutrition on weight gain is
demonstrated in Table 1. Thirty-four malnourished infants with intractable
diarrhea were studied. Three modalities of parenteral nutrition—peripheral,
central, and supplemental—were also compared. The best weight gain (31 g/
day) was obtained when the i.v. alimentation was administered through a central
line with 116 kcal/kg per day and a protein intake of 3.4 g/kg per day (22).

Kelts and co-workers (23) demonstrated the beneficial effect of supplemental
parenteral nutrition on body weight and composition in children having chronic
diarrhea as a result of Crohn's disease (Fig. 13). Each dietary regimen was
maintained for several weeks and concluded with a metabolic balance study.

Following a customary diet consumed in period I, in period II each patient
FIG. 12. The effect of milk intake and intravenous therapy on stool volume, acidity, and concentration of lactate and organic acids in infants with acute and chronic diarrhea. Cases 1 to 6 are 1/2 to 4 months old, duration of diarrhea 1/2 to 2 days; CRM was a 4-month-old infant, duration of diarrhea 5 days; MAFV was a 6-month-old, and the diarrhea lasted for 6 days; APB was 1 1/2 months old and suffered from intermittent diarrhea since birth. (From Torres-Pinedo et al., ref. 21, with permission.)

received for 6 to 8 weeks combined parenteral and enteral intake at a gross energy level of 75 kcal/kg per day. In period III, the children resumed a customary diet similar to that ingested in period I.

As a result of supplemental parenteral alimentation, all patients experienced
TABLE 1. Duration of parenteral nutrition, nutrient intake, and weight gain in 34 malnourished infants with intractable diarrhea

<table>
<thead>
<tr>
<th>Type of parenteral nutrition (mean and range)</th>
<th>Peripheral, total (35 periods in 33 patients)</th>
<th>Central, total (11 periods in 11 patients)</th>
<th>Supplemental (32 periods in 29 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (days)</td>
<td>29 (5–50)</td>
<td>13 (4–20)</td>
<td>12 (1–26)</td>
</tr>
<tr>
<td>Energy intake (kcal/kg per day)</td>
<td>93 (67–121)</td>
<td>116 (93–137)</td>
<td>106 (77–190)</td>
</tr>
<tr>
<td>Protein intake (g/kg per day)</td>
<td>2.9 (1.5–3.9)</td>
<td>3.4 (2.0–4.0)</td>
<td>2.8 (1.4–4.0)</td>
</tr>
<tr>
<td>Weight gain (g/day)</td>
<td>0.9b</td>
<td>31</td>
<td>8</td>
</tr>
</tbody>
</table>

* Records of one child were incomplete and have not been included in the computation. This child received total parenteral nutrition (TPN) for 8 months and grew normally.

At the start of peripheral TPN, 16 of 33 patients were edematous; thus, the mean weight gain is spuriously low. If these subjects are excluded, the mean weight gain is 18.6 g/day (22).

significant weight gain (Fig. 14), averaging almost 5 kg from period I to period III, and maintained or gained weight in the year after therapy. The significant increase in total body potassium and creatinine excretion indicates increased

FIG. 13. Study protocol for children with chronic diarrhea and growth failure in Crohn's disease (n = 7). In period I, the patients received their customary diet [protein 16%, fat 29%, and carbohydrate 54%; daily caloric intake was 82% of the recommended daily allowance (RDA)]. During period II, the oral feeding was supplemented by parenteral nutrition (composition of this combined diet: protein 14%, fat 29%, and carbohydrate 58%; daily caloric intake 136% of the RDA). For period III, the children returned to their customary diet (protein 13%, fat 30%, and carbohydrate 56%; daily caloric intake 78% of the RDA). The letters in the bars refer to groups of laboratory investigations obtained during each period as follows: A, complete blood count, serum total protein, albumin, carotene, folic acid, and vitamin B₁₂ levels, ⁴₀K counting, basal metabolic rate, and creatinine excretion; B, tests of absorptive function; C, tests of endocrine function (23,24).
FIG. 14. Changes in body weight (left panel), total body potassium (middle panel), and creatinine excretion (right panel) induced by nutritional therapy (period II) in children with Crohn's disease. The daily caloric intake was well below the recommended daily allowance (RDA) in periods I and III (82 and 78% of RDA, respectively), whereas during the 6 to 8 weeks of period II, the energy intake was greatly increased to 136% of RDA by combined parenteral and oral intake (23,24).

lean body mass in addition to a gain of fat and water, as reflected in the increase of body weight.

In summary, one can conclude that (a) in the routine clinical management of infants and children with acute diarrhea, oral rehydration and maintenance therapy have definite beneficial effects; however, (b) nutritional adequacy with these therapies can probably be achieved only in well-nourished infants and children who have enough energy reserves to cover maintenance metabolism during the oral maintenance therapy; and (c) if oral feeding (with either customary or elemental diet) fails, supplemental parenteral nutrition offers a feasible means to deliver the needed increases in caloric and macronutrient supply.

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