Catch-Up Growth in Malnourished Children

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Body weight and height (length) are important anthropometric indices of the nutritional status of children. From the fact that nearly 100 million children under 5 years of age throughout the world suffer from varying degrees of protein-energy malnutrition (PEM) (1), it may be justifiably assumed that the single most important cause of growth retardation in childhood is PEM.

In malnutrition, nutrient availability is decreased either because of inadequate food intake or because of impaired nutrient absorption or both. Malnutrition itself may decrease the absorptive capacity of the intestinal mucosa. Furthermore, PEM decreases the host's resistance to infection and leads to frequent infectious episodes including recurrent diarrhea, which may cause malabsorption and/or increased nutrient requirements (2). Malabsorption may also be caused by such chronic diseases as cystic fibrosis, inflammatory bowel disease, and chronic renal disease. Thus, growth retardation in childhood may be the result of primary malnutrition or secondary to a chronic disease process.

In this chapter, we discuss the nutritional support of the growth-retarded child and the general pattern of catch-up growth, a term commonly used to denote recovery from malnutrition. Although energy, protein, vitamins, and minerals are all essential for supporting growth and maintenance of body tissues, the following discussion focuses on energy and protein, which are fundamentally involved in cellular metabolism and growth. In practice, nutritional rehabilitation is often accompanied by antibiotic therapy for the treatment and prevention of infection in the malnourished children (2).

NUTRITIONAL SUPPORT OF THE MALNOURISHED CHILD

In severe PEM, dietary treatment is tailored to the needs of the child in three distinct phases of recovery: a stabilization (initial rehydration) phase, a rapid in-hospital catch-up growth phase, and a follow-up growth phase.

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Stabilization

In this early critical phase, which may last through the first few days of hospitalization, treatment is aimed at replacing fluid and electrolyte deficits while providing sufficient calories and protein to meet daily maintenance requirements. For children with a history of severe diarrhea and intravascular dehydration, initial rehydration may be achieved intravenously with Ringer's lactate and half-normal saline containing appropriate quantities of $K^+$ and $Mg^{2+}$. This may be followed by maintenance i.v. therapy using $\frac{1}{4}N$ saline until oral therapy is initiated (3).

Following initial intravenous rehydration, various oral formulas have been used. In Jamaica, a liquid regimen consisting of full-cream milk powder (27 g/liter), peanut oil (20 g/liter) and sugar (100 g/liter), with added supplements of potassium (4-5 mEq/kg per day), magnesium (2-3 mEq/kg per day), folic acid (100 μg/day), and iron (150 mg/day elemental iron in divided doses) has been used. This formula provides approximately 70 kcal and 0.44 g of protein per 100 ml. A daily volume of 136 ml/kg, equivalent to 95 kcal/kg and 0.6 g protein/kg, is divided equally into 8, 12, or 24 feedings per day (4).

Malnourished northern Thai children have been treated similarly with liquid formulas providing 1 g protein/kg per day and increasing calories from 25 to 100 kcal/kg per day during this early critical phase (5). In Guatemala, formulas starting with 0.8 to 1.0 g protein/kg per day and 80 to 100 kcal/kg per day on the first day and increasing to 3.5 to 4.5 g protein/kg per day and 150 to 160 kcal/kg per day on the seventh day have been used (6).

Rapid Catch-up Growth

At the time of hospitalization, the child may be anorectic. However, following rehydration and control of infection, the child will begin to increase his dietary intake spontaneously. During the rapid catch-up growth phase, the aim of dietary therapy is to achieve, with safety, the greatest rate of weight gain within the shortest period of time. Both ad libitum feeding and force feeding have been practiced during this phase.

Prediction of the child's rate of weight gain and the time required for recovery of a weight deficit may be made from the weight-for-height deficit and the caloric intake, providing adequate protein intake is achieved (Table 1). As the child reaches his expected weight for height, his appetite spontaneously decreases, and the rate of weight gain falls to that normal for his height. The control of appetite appears to be in relation to the weight deficit. In treating children with PEM, the calorie and protein content have been adjusted to varying levels, usually to provide 150 to 200 kcal/kg per day and 3 to 6 g of protein/kg per day (3-10).

In a study done in Thailand (5) designed to determine the effect of protein and calories on recovery, four formula diets containing: (I) 1 g of protein, 100
CATCH-UP GROWTH

TABLE 1. Predicted catch-up growth at different energy intakes

<table>
<thead>
<tr>
<th>Total intake (kcal/day)</th>
<th>Excess (kcal/day)</th>
<th>Weight gain (g/day)</th>
<th>Days to gain 3,000 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>700</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>760</td>
<td>60</td>
<td>10</td>
<td>300</td>
</tr>
<tr>
<td>820</td>
<td>120</td>
<td>20</td>
<td>150</td>
</tr>
<tr>
<td>940</td>
<td>240</td>
<td>40</td>
<td>75</td>
</tr>
<tr>
<td>1180</td>
<td>480</td>
<td>80</td>
<td>38</td>
</tr>
<tr>
<td>1660</td>
<td>960</td>
<td>160</td>
<td>19</td>
</tr>
</tbody>
</table>

*Example: weight of child at admission, 7 kg; expected weight for height, 10 kg; weight-for-height deficit, 3 kg. Assumption: maintenance energy requirement is 100 kcal/kg per day, and excess energy necessary for each gram of weight gain is 6 kcal.

Adapted from Kerr et al. (8), with permission.

kcal/kg; (II) 4 g of protein, 100 kcal/kg; (III) 1 g of protein, 175 kcal/kg; and (IV) 4 g of protein, 175 kcal/kg were employed. Forty-nine children classified as “marasmic” (N = 20), “marasmic-kwashiorkor” (N = 16) and “kwashiorkor” (N = 13) were studied. After a stabilization period of 1 week (during which all subjects were fed 1 g protein/kg per day and increasing energy from 25 to 100 kcal/kg per day), all children were randomly assigned to the four dietary groups and fed formula diets I to IV for an experimental period of 3 weeks. Following this, all children were fed diet IV (the adequate diet) (Table 2) for an additional 6-week period, which was followed by an additional 2 weeks of ad libitum feeding of milk formula plus solid foods.

During the experimental period, the children in groups I and II failed to gain weight (Fig. 1). During the subsequent 6-week period, all groups gained weight. On diet IV, all groups gained weight constantly throughout the 9-week period. It appeared that restriction of calories during the initiation of cure in marasmic children or the restriction of protein in children with kwashiorkor reduced the rate of weight gain. Both calories and protein were required for initiation of cure and optimal weight gain, with 4 g of protein and 175 kcal per kg body weight being sufficient to stimulate maximal recovery. The weight increments of all groups tended to plateau during the final 2 weeks of ad libitum feeding.

In the same study, serum albumin as an index of visceral protein synthesis was also measured during treatment (Figs. 2, 3) (23). As expected, the marasmic children had greater serum albumin levels on admission than did children with kwashiorkor. Patients fed 4 g protein/kg per day regardless of caloric intake normalized their serum albumin concentrations, with greater protein intakes having no effect on the rate of albumin regeneration. Diets containing 4 protein/kg per day and 100 kcal/kg per day were sufficient to regenerate serum albumin but did not stimulate weight gain.

When the children with PEM were offered ad libitum solid food, their energy intake increased to 160 to 180 kcal/kg per day by the second week of hospitalization. Intake was maintained at that level for the first 3 to 4 weeks of hospitalization, after which it gradually decreased to 140 to 150 kcal/kg per
TABLE 2. Vitamin and mineral supplementation of the milk-based formula supplemented with dextrose and corn oil (diet IV)*

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Unit</th>
<th>Daily initial therapy i.m. or i.v. for 3 days beginning on day 2</th>
<th>Daily maintenance therapy from the fifth day until the end of week 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamin</td>
<td>mg</td>
<td>5.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>mg</td>
<td>5.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>mg</td>
<td>2.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Nicotinamide</td>
<td>mg</td>
<td>37.5</td>
<td>11.0</td>
</tr>
<tr>
<td>Pantothenate</td>
<td>mg</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>mg</td>
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<td>30.0</td>
</tr>
<tr>
<td>Folic acid</td>
<td>mg</td>
<td>1.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>μg</td>
<td>7.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>I. U. b</td>
<td>5,000</td>
<td>2,500</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>I. U. b</td>
<td>400</td>
<td>400</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>I. U.</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>μg</td>
<td>300</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Dose (mEq/kg per day)</th>
<th>Mineral</th>
<th>Dose (mEq/kg per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>2.7</td>
<td>I</td>
<td>0.00008</td>
</tr>
<tr>
<td>K</td>
<td>5.0</td>
<td>F</td>
<td>0.006</td>
</tr>
<tr>
<td>Ca</td>
<td>7.3</td>
<td>Al</td>
<td>0.070</td>
</tr>
<tr>
<td>Mg</td>
<td>1.4</td>
<td>Mo</td>
<td>0.001</td>
</tr>
<tr>
<td>Zn</td>
<td>0.014</td>
<td>Cr</td>
<td>0.366</td>
</tr>
<tr>
<td>Mn</td>
<td>0.018</td>
<td>Se</td>
<td>0.003</td>
</tr>
<tr>
<td>Cu</td>
<td>0.0028</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adapted from Suskind (3). Per kilogram body weight per day, this diet supplies 175 kcal, 4 g protein, 9.5 g fat, and 18.3 g carbohydrate.

Therapeutic doses of the fat-soluble vitamins are given as indicated to combat overt deficiency disease.

day. By discharge at 12 weeks, when the children had attained optimum weight for height, their energy intake had fallen to 100 to 120 kcal/kg per day (3).

Following an early report of the existence of a linear relationship between caloric intake and rate of weight gain during recovery from malnutrition (11), physicians initiated the use of ad libitum feeding of an energy-dense formula in Jamaica. This formula, which provided 135 kcal and 3.1 g protein per 100 ml formula, was supplemented with potassium, magnesium, iron, folic acid, and vitamin C (8). When feedings were given every 3 or 4 hr, intakes often exceeded 200 kcal/kg per day. Catch-up growth rates as high as 20 times the normal growth rate have been obtained with these high-energy dietary regimens. Greater rates of weight gain were associated with higher caloric intakes (Fig. 4). Before discharge from the hospital, the children are introduced to a mixed semisolid diet similar to that which they will receive at home (4).

Iron intake is of special importance in the treatment of the malnourished child. While the malnourished child is being treated for bacterial infection, one may consider the use of intramuscular iron or high doses of oral iron in the
FIG. 1. Effect of varying levels of protein and calories on weight gain of children with PEM. Diet I, 1 g protein, 100 kcal; diet II, 4 g protein, 100 kcal; diet III, 1 g protein, 175 kcal; diet IV, 4 g protein, 175 kcal. (○) K, children with kwashiorkor; (■) MK, marasmic kwashiorkor; (▲) M, marasmus. (Adapted from Olson, ref. 5, with permission.)

FIG. 2. Changes in serum albumin during treatment of marasmus. Numbers above the bars indicate the day after the experimental period began. (Adapted from Thanangkul et al., ref. 23, with permission.)
FIG. 3. Changes in serum albumin during treatment of kwashiorkor. Numbers above the bars indicate the day after the experimental period began. (Adapted from Thanangkul et al., ref. 23, with permission.)

FIG. 4. The relationship between caloric intake and rate of weight gain in children recovering from malnutrition. The darker regression line fits the equation: \( y = -14.5 + 0.145x \) (\( r = 0.82, p < 0.01 \)). The lighter regression line fits the equation \( x = 121.0 + 4.6y \) (\( r = 0.82, p < 0.01 \)). (Adapted from Kerr et al., ref. 8, with permission.)
range of 100 to 200 mg of elemental iron per day (3). However, for those who do not require antibiotics during the early phase of recovery from PEM, one must be aware of the potential problems of overwhelming sepsis associated with the use of iron in the malnourished child.

There is a paucity of information about the composition of weight gain during catch-up growth and the relationship, if any, between the rate of weight gain and the composition of the tissue gained. In PEM, there are deficits of both total body fat and muscle mass. There may also be dehydration or edema. Body composition studies of children who died of malnutrition indicate that 50% of the weight deficit in wasted malnourished children may represent lack of fat (11). During recovery from malnutrition, the lost body fat is regained, as indicated by changes in skinfold thickness (8). Weight gain during recovery is accompanied by restoration of the body protein deficit as well, as indicated by total body potassium measurements in the recovered child (7,12). Although changes in body composition during catch-up growth are not fully understood, it appears that a dietary regimen high in calories and fat does not lead to the development of obesity or abnormal serum lipid patterns in children who are followed through school age (8). In children with kwashiorkor, there may be a loss of body weight associated with loss of body water during the first few days of treatment.

Height deficits cannot be made up during a short hospital stay. At the time of discharge from the hospital, the child who has recovered from PEM should be at his expected weight for height. However, the child is still underweight for age because nearly all severely malnourished children have some height deficit (greater in marasmus than in kwashiorkor) (13).

LONG-TERM FOLLOW-UP

There are several follow-up studies of expatients (“index” children) comparing them with “control” children who had not been admitted to the hospital for severe PEM but who had been matched with regard to such variables as age, sex, and socioeconomic status (14–19). In general, these studies, with the exception of two (16,17), demonstrated that previously malnourished children were significantly smaller than their age-matched controls. Such findings are difficult to interpret because it is difficult to assume that the index and control children differed only with regard to the occurrence of an episode of malnutrition and not in other factors that may affect growth.

Other studies have used siblings as comparisons (20–22). These studies have demonstrated that the growth rate of index children was equal to or better than that of the control children.

Data on weight for age, height for age, and weight for height for 124 Northern Thai children at the time of admission, discharge, and follow-up for a period of 3 years are presented in Fig. 5 (24). On admission, the children with marasmus (M), marasmic kwashiorkor (MK), and kwashiorkor (K) had weights for age of 48.3 ± 1.1%, 49.2 ± 1.4%, and 59.8 ± 1.7%, respectively. On discharge, weight
for age had increased significantly in the marasmic children to 65.9 ± 1.2% ($p < 0.001$), in the marasmic-kwashiorkor children to 69.5 ± 1.4% ($p < 0.001$), and in those with kwashiorkor to 78.2 ± 1.5% ($p < 0.001$). Follow-up evaluation revealed significant increments in weight for age from discharge to follow-up in the marasmus ($p < 0.05$) and marasmic kwashiorkor ($p < 0.05$) groups. The children with kwashiorkor who had the greatest weight for age on discharge did not demonstrate a significant increase in weight for age from discharge to follow-up.

There was no significant increase in height for age in any of the groups from admission to discharge (Fig. 5). The marasmic children, however, evidenced a significant increment in height for age from discharge to follow-up ($p < 0.01$). Although weight for height also increased significantly in all three groups from admission to discharge ($p < 0.001$), only the marasmic-kwashiorkor group showed a significant weight-for-height increase from discharge to follow-up ($p < 0.05$) (Fig. 5).

Following discharge from the hospital, children in all three groups had weight gains ranging from 90 to 100% of those expected of children following the 50th percentile of the Harvard Standard (Fig. 6). Height gains ranged from 100 to 130% of children following the 50th percentile of the Harvard Standard (Fig. 6). Although there was no significant difference in the percent of weight gain among the three clinical groups, the children with marasmus had a height velocity that was significantly greater ($p < 0.01$) than the children with marasmic

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**FIG. 5.** Weight-for-age, height-for-age, and weight-for-height curves of 124 northern Thai children at admission to hospital, discharge, and follow-up. *50th percentile of Harvard Standard. (Adapted from Suskind et al., ref. 24, with permission.)*
kwashiorkor. The data from all three groups were combined, and the weight and height gains calculated as a percentage of the expected gains of children following the 50th percentile of the Harvard Standard. During the first 24 months following discharge, weight gain was greater than 100% of standard (Fig. 7).
During the third year, weight gain decreased to less than 90% of standard. During the first, second, and third years following discharge, height gain continued at the rate of 173, 105, and 97% of the Harvard Standard (Fig. 8).

This study reveals some interesting patterns in previously malnourished children's catch-up growth (Fig. 5). On admission, children with marasmus and marasmic kwashiorkor had a significantly lower weight for age than the children with kwashiorkor. Patients with marasmus also had a lower height for age than either of the other two groups of children. While in the hospital, all three groups demonstrated significant increases in weight for age but no change in height for age. On follow-up, the groups with the greatest previous deficits showed the most significant increments; i.e., both the marasmus and marasmic-kwashiorkor groups had significant increases in weight for age, and the children with marasmus had significant increases in height for age. Children with kwashiorkor had a nonsignificant increase in mean weight for age and height for age from discharge to follow-up.

This study demonstrates that the most significant catch-up growth occurred during the first 2 years following discharge. A height velocity of 173% of the Harvard Standard was achieved during the first year following discharge (Fig. 8).

**FIG. 8.** Height velocity 1–11 months, 12–23 months, and 24–35 months after discharge from hospital. *50th percentile of Harvard Standard. (Adapted from Suskind et al., ref. 24, with permission.)**
In addition to significant gains during the first two years, children continued to grow at a linear rate that approximated that of a child following the 50th percentile of the Harvard Standard. One possible explanation for the significant weight and height increments observed during the first 2 years following discharge might be the parents' renewed interest in the formerly malnourished child, who was able to demand more attention and more food.

This study also demonstrates no significant difference in growth between the malnourished child on follow-up and his siblings. Of interest, however, was the rather surprising observation that significant differences occurred (in weight for age, height for age, and weight for height) between the siblings of those children with marasmus or marasmic kwashiorkor and the siblings of those with kwashiorkor (Fig. 9). In addition, the growth patterns of the siblings of marasmic patients did not vary greatly from those of marasmic-kwashiorkor patients. These observations suggest that children with marasmus and marasmic kwashiorkor may develop from a population of children with different nutritional and medical histories than those with kwashiorkor.

The follow-up studies described above demonstrate that children who are fully recovered from severe PEM in a hospital setting and returned to the same hostile environment are able to continue to show catch-up growth in spite of the fact that they returned to the same environment in which they had previously become malnourished.

ACKNOWLEDGMENT

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REFERENCES