Endocrine and Amino Acid Changes in Protein Energy Malnutrition (PEM)

Both qualitative and quantitative changes in circulating amino-acid levels have been reported in PEM. Factors determining the concentration and pattern of serum amino acids include:

1. the amount and composition of dietary protein;
2. muscle protein metabolism;
3. the labile protein reserve in the liver and other tissues.

Both in muscle and liver, protein metabolism is influenced by multiple hormones including growth hormone (GH), insulin, somatomedin-C (Sm-C), and cortisol.

To investigate the relationship between serum amino acids and endocrine changes during severe malnutrition we have measured the fasting concentrations of circulating free amino acids, albumin, cortisol, insulin, GH, and Sm-C in 40 children with PEM: 10 with kwashiorkor, 10 with marasmic kwashiorkor, 10 with marasmus, and 10 underweight for their age. Eight age-matched well nourished children served as controls. All the anthropometric measurements and lab tests were repeated after 3 weeks of nutritional rehabilitation using diets containing 2-3 g protein/kg/day and 150 kcal/kg/day.

Levels of some essential amino acids (leucine, isoleucine, lysine, histidine, and tyrosine) were significantly reduced in the kwashiorkor and marasmic kwashiorkor groups whereas the non-essential amino acid concentrations were either unaltered (alanine and glutamine) or increased (glycine, serine, and glutamic acid; Table 1). Consequently, the non-essential/essential (N/E) ratio was significantly high in patients with kwashiorkor (4.1 ± 1.6) and marasmic kwashiorkor (4.6 ± 1.5). This ratio was not markedly affected in marasmic (2.2 ± 1.0) or underweight children (1.9 ± 0.4). Serum albumin and basal insulin levels were significantly decreased in both oedematous groups of PEM. High serum GH and cortisol levels, and low Sm-C concentrations have been found in all groups with severe PEM. All these amino acid and hormonal changes came back to normal after 3 weeks of nutritional rehabilitation (Table 2).

Many factors share in the production of low circulating levels of essential amino acids in patients with kwashiorkor and marasmic kwashiorkor.

1. The quantitative and qualitative deficiencies of these amino acids in their diet. In our study the diets consumed by children with nutritional oedema were predominantly carbohydrate with insufficient protein content of incomplete quality. Their food consisted of sugars, rice (deficient in lysine, isoleucine, threonine, and methionine with protein/carbohydrate (P/C) ratio of 7:78, maize starch (deficient in lysine and tryptophan with P/C ratio of 10:67, and sweet potatoes (deficient in tyrosine and cysteine with P/C ratio of 2:26).

2. The high serum cortisol concentrations and the markedly protein-deficient diets of these patients can induce the activity of branched chain amino acid transaminases in muscle.

3. During starvation the supply of the branched chain amino acids through muscle protein catabolism is usually low despite high circulating cortisol levels.

The rate of synthesis of plasma albumin by the liver depends on the concentrations of amino acids, especially the branched chain amino acids. These low levels of amino acids explain the hypoalbuminaemia and oedema in patients with kwashiorkor and marasmic kwashiorkor. In addition, the positive correlation between insulin and albumin concentrations in these children (r = 0.52, P < 0.001) may reflect an important relationship between these parameters.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Leuc. ± SD</th>
<th>Isoleu ± SD</th>
<th>Lys ± SD</th>
<th>His ± SD</th>
<th>Tyr ± SD</th>
<th>Alan ± SD</th>
<th>Glut. ± SD</th>
<th>Glyc ± SD</th>
<th>Ser ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kwash</td>
<td>82 ± 25</td>
<td>31 ± 11</td>
<td>34 ± 33</td>
<td>72 ± 45</td>
<td>22 ± 9</td>
<td>262 ± 136</td>
<td>368 ± 176</td>
<td>341 ± 128</td>
<td>204 ± 89</td>
</tr>
<tr>
<td>M-K</td>
<td>59 ± 16</td>
<td>33 ± 10</td>
<td>61 ± 15</td>
<td>80 ± 31</td>
<td>24 ± 15</td>
<td>458 ± 173</td>
<td>296 ± 220</td>
<td>341 ± 116</td>
<td>252 ± 112</td>
</tr>
<tr>
<td>Maras.</td>
<td>88 ± 67</td>
<td>58 ± 36</td>
<td>161 ± 71</td>
<td>111 ± 51</td>
<td>46 ± 32</td>
<td>303 ± 117</td>
<td>268 ± 148</td>
<td>248 ± 77</td>
<td>163 ± 65</td>
</tr>
<tr>
<td>Underwt.</td>
<td>109 ± 42</td>
<td>60 ± 28</td>
<td>142 ± 52</td>
<td>85 ± 26</td>
<td>63 ± 21</td>
<td>262 ± 77</td>
<td>210 ± 93</td>
<td>227 ± 69</td>
<td>158 ± 77</td>
</tr>
<tr>
<td>Controls</td>
<td>132 ± 41</td>
<td>66 ± 23</td>
<td>159 ± 50</td>
<td>105 ± 39</td>
<td>67 ± 23</td>
<td>319 ± 52</td>
<td>231 ± 86</td>
<td>219 ± 68</td>
<td>160 ± 52</td>
</tr>
</tbody>
</table>

* Normal v. children with PEM \(P<0.01\).

Kwash = kwashiorkor, M-K = marasmic kwashiorkor; Maras = marasmus.
Table 2

<table>
<thead>
<tr>
<th>Condition</th>
<th>IGF-I (U/ml)</th>
<th>GH (ng/ml)</th>
<th>Insulin (U/ml)</th>
<th>Cortisol (g/ml)</th>
<th>Albumin (gm/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kwashiorkor (b)</td>
<td>0.072±0.038**</td>
<td>19.4±7.9**</td>
<td>6.3±4.7**</td>
<td>29.9±16.3**</td>
<td>2.4±0.6**</td>
</tr>
<tr>
<td>Kwashiorkor (a)</td>
<td>0.212±0.154*</td>
<td>8.1±3.7*</td>
<td>10.3±12.2*</td>
<td>14.8±3.7*</td>
<td>3.7±0.8*</td>
</tr>
<tr>
<td>Marasmic kwashiorkor (b)</td>
<td>0.046±0.025**</td>
<td>31.6±17.6**</td>
<td>6.2±4.4**</td>
<td>38.6±27.1**</td>
<td>2.4±1.0**</td>
</tr>
<tr>
<td>Marasmic kwashiorkor (a)</td>
<td>0.153±0.126*</td>
<td>6.5±3.0*</td>
<td>18.9±15.4*</td>
<td>13.9±5.6*</td>
<td>3.7±0.8*</td>
</tr>
<tr>
<td>Marasmus (b)</td>
<td>0.121±0.12**</td>
<td>18.4±16.4**</td>
<td>11.8±11.7**</td>
<td>18.5±9.1**</td>
<td>3.8±1.7**</td>
</tr>
<tr>
<td>Marasmus (a)</td>
<td>0.252±0.162*</td>
<td>6.0±5.1*</td>
<td>17.4±14.1*</td>
<td>14.2±4.6*</td>
<td>3.8±0.6*</td>
</tr>
<tr>
<td>Underweight</td>
<td>0.187±0.29</td>
<td>6.5±5.1</td>
<td>16.2±13.0</td>
<td>11.4±4.9</td>
<td>3.8±1.3</td>
</tr>
<tr>
<td>Control</td>
<td>0.197±0.102</td>
<td>5.9±2.3</td>
<td>13.2±10.2</td>
<td>11.1±7.0</td>
<td>3.2±0.5</td>
</tr>
</tbody>
</table>

Before treatment v. after treatment, * P<0.05; normal v. children with PEM, ** P<0.05.

Role played by insulin to support hepatic protein synthesis.

In marasmic infants, despite the low total dietary energy supply, the P/C ratio was virtually normal (diluted milk formula with P/C ratio of 1:3 or insufficient breast milk with P/C ratio of 1:7). Both milks have excellent amino acid scores. This exogenous source can preserve the serum amino acid pattern along with the proper catabolism of muscle protein (endogenous source). The resulting normal amino acid concentrations support the hepatic synthesis of albumin and prevent the development of oedema.

Suskind et al.\(^3\) suggest a relation between depression of one or more circulating amino acid(s) concentration and elevation of GH levels. In our study serum GH levels correlated significantly with circulating tyrosine \(r=0.57, P<0.001\). In addition, decrements in GH levels with treatment correlated significantly with increment of tyrosine concentrations \(r=0.45, P<0.05\). These data suggest that low serum tyrosine level might be the prime candidate leading to GH stimulation during PEM, via influencing brain neurotransmitter levels.\(^4\)

In summary, various alterations in hormonal levels try to defend the body against malnutrition. The elevated GH levels stimulate lipolysis, whereas low somatomedin-C concentrations and decreased insulin secretion inhibit lipogenesis. Both processes assure fuel supply (fatty acids) to the peripheral tissues through effective breakdown of adipose tissue. Moreover, the increased muscle protein catabolism mediated by elevated basal cortisol levels and depressed anabolic activity due to selective decrease in somatomedin-C production assure an adequate supply of amino acids to the liver. This metabolic intermediate allows gluconeogenesis and protein synthesis to proceed and guards against the development of hypoalbuminaemia in marasmic children. Failure of this dietary-hormonal adaptation leads to disturbed amino acid pattern, hypoalbuminaemia, and consequently oedema in children with kwashiorkor and marasmic kwashiorkor.

Ashraf T. Soliman, MD, Abd El Hadi I Hassan, MD and Alan D. Rogol, MD, PhD
Department of Pediatrics, Universities of Alexandria and Virginia Schools of Medicine

References

Sir,

Simple Indicator for Screening of Low Birth Weight (LBW) Infants in the Community

Low birth weight (LBW) is highly predictive of perinatal and neonatal mortality.\(^1,2\) In India, LBW accounts for 50 per cent or perinatal deaths and identifying this group of infants for minimal perinatal care can be of great value in reducing mortality.\(^2,3\) Eighty per cent of deliveries occur at home in rural India. Though birth weight is the most accurate index of fetal well being, use of sensitive balances poses a problem in rural areas with poor transportation facilities and operational difficulties. Therefore, a simple, inexpensive, but accurate tool with good replicability is needed for the grass root level workers.

Birth weights of 256 infants born in maternity hospital were recorded with a lever baby balance (accuracy of ±5 g) within 24 hours of birth. Crown-heel length (CHL), crown-rump length (CRL), head circumference (HC), chest circumference (CHC), arm circumference (AC), and calf circumference (CC) were measured by standard techniques. The validity of CC in identifying malnourished preschool children has been established earlier.\(^4\) The data was analysed in relation to birth weight. The results indicate that all the anthropometric measurements showed significant correlation with birth weight, highest with CC followed by AC (Table 1).

The multiple linear regression model of birth weight was found to be best with CC, AC, and CHL in that order with coefficient of determination \(R^2\) being 76 per cent for CC. Addition of other measurements did not improve the values of \(R^2\). Estimated value of CC for birth weight of 2.5 kg was 10 cm. Similar figures were derived for arm circumference and crown-heel length with 95 per cent confidence limits. Classifying the newborn with critical values of birth weight, CC, AC, and CHL for comparing sensitivity and specificity indicated that sensitivity was highest with calf circumference (96 per cent) with under estimation of LBW being 4 per cent followed by AC (83 per cent) and CHL (73 per cent) in which under estimation of LBW was 17 and 28 per cent, respectively. Specificity was more or less similar (80–82 per cent) with all the measurements. A high degree of sensitivity and simplicity of the technique, thus makes CC a good screening procedure to identify LBW infants. Village health workers can be trained to identify the risk infants for referral to nearest hospital or health centre using this approach.

L. RAMAN, J. NEELA, N. BALAKRISHAN, \(\text{and}\) K. VISWESWARA RAO
National Institute of Nutrition, Indian Council of Medical Research, Jamai Osmania, P.O. Hyderabad 500007

References

Sir,

Simultaneous Outbreak of Varicella and Measles in a Nigerian Secondary School

Varicella and Measles are diseases of children and are most common in closed communities like schools and family circles. An outbreak of varicella and measles was reported in a girls' secondary school (population: 750 students) in Ondo state of Nigeria on the 7 May 1990, a week after resumption of school after the Easter holidays. The physical structure of the school consists of 23 rooms used as hostels with 32 students per room.