HYPERPIGMENTATION OF THE SKIN in Indian patients with megaloblastic anemia appears to have been first documented by Cook. Studies from this unit suggested that this was often associated with vitamin B₁₂ deficiency, although more recent studies following the introduction of folic acid assays, have shown that it can also occur in some cases of pure folic acid deficiency, and in mixed folic and vitamin B₁₂ deficiency. A similar hyperpigmentation has been reported in an African with vitamin B₁₂ deficiency anemia and in an American Negro with folic acid deficiency.

The pathogenesis of this hyperpigmentation is unknown, though its relationship to the deficiency state is clearly shown by the fact that it clears up with appropriate treatment.

Although not related to hypoadrenalism, the hyperpigmentation often resembles that seen in Addison’s Disease of the suprarenal. Since the latter is associated with raised melanocyte-stimulating hormone (MSH) levels in the blood, one possibility was that vitamin B₁₂ or folic acid deficiency in some way increased the levels of circulating MSH. This communication reports the results of MSH assays in such patients.

MATERIALS AND METHODS

The subjects were four patients with megaloblastic anemia and typical marked hyperpigmentation. In two patients the anemia was associated with tropical sprue; one adult had “dietary” B₁₂ and folic acid deficiency and one child had pure dietary vitamin B₁₂ deficiency. Two controls were also studied. Serum vitamin B₁₂ and folic acid concentrations were measured by microbiological assay using Euglena gracilis Z strains and Lactobacillus casei as the test organisms. Plasma cortisol levels at 8 a.m. were determined by a fluorimetric method. Plasma MSH levels were determined by radioimmunoassay. Heparinized plasma was obtained and immediately lyophilized. Samples were then stored at −20°C for not more than two weeks and sent by air to Nashville where the assays were performed “blind.”

RESULTS

The details of the subjects studied and the results of the assays are set out in the accompanying table. All four patients were treated—cases 1–3 with

First submitted July 15, 1969; accepted for publication August 12, 1969.
This work was supported in part by PL-480 grant 01 329 01.
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<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Hemoglobin Gm./100 ml.</th>
<th>Marrow</th>
<th>Serum Fe₂ pg./ml.</th>
<th>Serum Folate ng./ml.</th>
<th>Plasma Cortisol μg./100 ml</th>
<th>β-MSH Level pg./ml, Before Treatment</th>
<th>β-MSH Level pg./ml, After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>60</td>
<td>Tropical sprue</td>
<td>7.8</td>
<td>Megaloblastic</td>
<td>64</td>
<td>3.6</td>
<td>18</td>
<td>42</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>42</td>
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<td>10.0</td>
<td>Megaloblastic</td>
<td>80</td>
<td>2.6</td>
<td>10</td>
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</tr>
<tr>
<td>3</td>
<td>M</td>
<td>22</td>
<td>Dietary B₁₂ and folate deficiency</td>
<td>14.0</td>
<td>Megaloblastic</td>
<td>80</td>
<td>3.0</td>
<td>16</td>
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</tr>
<tr>
<td>4</td>
<td>M</td>
<td>10 mos.</td>
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<td>9.0</td>
<td>Megaloblastic</td>
<td>68</td>
<td>46.0</td>
<td>12</td>
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</tr>
<tr>
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<td>29</td>
<td></td>
<td>—</td>
<td>Normoblastic</td>
<td>220</td>
<td>8.2</td>
<td>9</td>
<td>70</td>
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<tr>
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<td>Normoblastic</td>
<td>180</td>
<td>9.0</td>
<td>14</td>
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</table>
vitamin B₁₂ and folic acid, and case 4 with vitamin B₁₂ alone, and in each case the hyperpigmentation disappeared.

**Discussion**

The results of the MSH assays in the two control subjects are within the normal range of the method (20–110 pg/ml), and suggest that the handling and transport of the sera did not affect the results of the assay. All four patients with hyperpigmentation also had normal β-MSH levels. In two patients levels were also measured after treatment, and these were also within the normal range. The hyperpigmentation in these patients cannot, therefore, be ascribed to an increased level of MSH in the plasma and some other explanation must be sought to explain this phenomenon.

**Conclusion**

Plasma β-MSH levels were normal in four subjects with hyperpigmentation associated with megaloblastic anaemia.

**References**


