Serum somatomedin activity of rats was measured under several dietary conditions by $^{35}S$ incorporation into chick embryo pelvic rudiment. The mean (± SD) serum somatomedin activity (U/ml) was reduced following 3 days of fasting (0.41 ± 0.12) and increased to prefasting levels in animals fed a balanced diet (0.95 ± 0.11) for 2 days. The increase in mean somatomedin activity following 2 days of refeeding a high-protein diet (0.79 ± 0.09) was greater than that observed with a high-carbohydrate (0.56 ± 0.10) or a high-fat (0.60 ± 0.10) diet, but the level was not completely restored to normal. The data confirm the previous finding that fasting reduces serum somatomedin activity and suggest that the protein content of the diet plays a major role in the restoration of serum somatomedin activity following refeeding.

POOR NUTRITION is frequently associated with impaired growth despite normal or elevated blood levels of somatotropin. Somatotropin stimulates linear growth indirectly by the formation of secondary growth-promoting factors. Somatotropin-dependent serum factors that are identified by their ability to stimulate the in vitro incorporation of sulfate into chondroitin of cartilage are designated "somatomedins."

Serum somatomedin activity is decreased in children with protein–calorie malnutrition and increases toward normal following refeeding. Fasting in rats results in a decrease in serum somatomedin activity that is not secondary to somatotropin deficiency, since treatment with somatotropin does not prevent the fall in somatomedin activity that is associated with fasting. Refeeding a balanced diet also results in a return of somatomedin activity toward normal.

The present study was designed to examine the nutritional factors responsible for the increase of serum somatomedin activity after refeeding.

**MATERIALS AND METHODS**

Male Sprague-Dawley rats, 3-4 wk old and weighing 60-70 g were obtained from Holtzman Co., Madison, Wis. Semisynthetic diets were obtained from ICN Pharmaceutical (Cleveland, Ohio). Diet composition was as follows: a balanced control diet contained 25% casein, 59% carbohydrate, 10% vegetable oil; a high-protein diet contained 62% casein, 27% starch, 5% vegetable oil; a high-carbohydrate diet contained 8% casein, 83% carbohydrate, 3% vegetable oil; and a high-fat diet contained 15% casein, 37% carbohydrate, 42% vegetable oil. In each of the diets that was high in one nutrient, the ratio of the other dietary constituents was kept constant. All the diets contained 4% salt mixture, 2% α-cellulose, and fortified vitamins, and they all were in pellet form of similar bulk, except the high-fat diet, which was in liquid oil form.

After 2 wk ad libitum feeding of the balanced diet, the rats were kept fasting in separate cages for 3 days. Six animals were sacrificed after the 2-wk control period and after the 3-day fast. The remaining animals were divided into four dietary groups and were sacrificed after 48 hr. Serum was collected by cardiac puncture. Serum somatomedin activity was measured by the method of Hall using the serum stimulation of incorporation of $^{35}S$ into 12-day-old chick embryo rudiments.
Table 1. Effect of Fasting and Refeeding on Somatomedin Activity (Mean ± SD)

<table>
<thead>
<tr>
<th>Refeeding Diet</th>
<th>Balanced</th>
<th>Fasting</th>
<th>Balanced</th>
<th>High Protein</th>
<th>High CHO</th>
<th>High Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of animals</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Food consumption (g/day)</td>
<td>13.3 ± 0.8</td>
<td>0</td>
<td>13.6 ± 1.1</td>
<td>11.3 ± 0.9</td>
<td>11.6 ± 1.0</td>
<td>10.7 ± 1.5</td>
</tr>
<tr>
<td>Caloric intake (kcal/day)</td>
<td>67.7 ± 0.8</td>
<td>0</td>
<td>64.40 ± 5.13</td>
<td>45.7 ± 3.6</td>
<td>45.3 ± 3.9</td>
<td>62.70 ± 8.79</td>
</tr>
<tr>
<td>Somatomedin activity (U/ml)</td>
<td>1.05 ± 0.08</td>
<td>0.41* ± 0.12</td>
<td>0.951 ± 0.11</td>
<td>0.79†‡ ± 0.09</td>
<td>0.56* ± 0.10</td>
<td>0.60*§ ± 0.10</td>
</tr>
</tbody>
</table>

*Significantly different from balanced diet, p < 0.01.
†Significantly different from fasting, p < 0.01.
‡Significantly different from balance diet, p < 0.05.
§Significantly different from fasting, p < 0.05.

RESULTS AND DISCUSSION

Serum somatomedin activity under the various dietary conditions is presented in Table 1. Serum somatomedin activity was reduced by fasting and restored to control values by refeeding a balanced diet, which confirms previous reports concerning the effect of fasting on somatomedin activity.4 The sulfate incorporation of cartilage incubated in all dilutions of sera obtained from fasting animals was lower than that of cartilage incubated in the media alone. The presence of an inhibitor of somatomedin activity is a possible explanation for this finding, since previous studies have shown that a heat-labile inhibitor of somatomedin activity is apparent following fasting.3 Finding a negative slope of the dose–response lines would have provided convincing evidence for the presence of an inhibitor, but the slope of the dose–response lines remained positive or flat in our studies.

Refeeding a high-protein diet resulted in a greater increase in somatomedin activity than refeeding either a high-carbohydrate or a high-fat diet. However, the high-protein diet did not restore somatomedin activity completely to the level observed in the animals fed a balanced diet. One possible explanation for this finding is that the caloric intake was somewhat reduced in the animals fed the high-protein diet. It should be stressed, however, that the group of animals that consumed the high-fat diet (which was isocaloric with the balanced diet) demonstrated an increase in serum somatomedin activity that was not as great as the increase observed in the high-protein group.

Our findings concerning the relative importance of various dietary constituents in restoring serum somatomedin activity conflict with a recent report by Phillips and Belosky;6 these authors found that somatomedin activity is increased most by refeeding fat and least by refeeding protein when the calories consumed were identical. Their experiments differed from ours in the dietary composition, caloric consumption, number of days of refeeding, and method used to measure somatomedin activity (porcine cartilage as opposed to the chick embryo assay).
REFERENCES