IN recent years interest has increased in the dietary administration of creatine or creatine precursors to experimental animals to study their effects upon growth and creatine content of muscle and upon bodyweight gain. Fisher et al. (1956a,b) have shown that the muscle creatine level of 1-day old chicks, on a 25% casein purified diet, increases linearly over a 4-week period. They have shown that with such diets arginine is the most limiting amino acid and that by supplying both arginine and glycine to the 25% casein purified diet, growth equal to that of chicks on practical diets is obtainable. Monson et al. (1955), Wietlake et al. (1954) and Edwards et al. (1958) obtained similar results. Poutsiaka (1956) and Baron (1958) increased muscle creatine and growth rate of rats when their 12% casein purified diet was supplemented with glycocyamine and methionine.

Baker et al. (1961) have recently reported failure to increase growth or muscle creatine by parenteral administration of creatine or creatine precursors to the suckling pig. The present study was conducted to determine if the addition of creatine or creatine precursors to a purified diet containing 30% casein for the baby pig will improve his rate of growth and feed economy and increase the size and creatine content of muscle.

Experimental

Two trials were conducted utilizing 24 baby pigs. Pigs were taken from the sow at 3 or 4 days of age and housed individually in wire-bottomed steel cages. The diet was fed as a homogenized synthetic milk similar to that utilized by Miller et al. (1954). After a 4-day adjustment period the pigs were allotted to groups and started on trial. The control lot received the complete synthetic milk diet, the creatine-fed lot received the same diet supplemented with 0.2% creatine monohydrate, and a third lot received the control diet supplemented with 0.28% L-arginine hydrochloride plus 0.1% glycine. The length of the experimental feeding period was 32 and 42 days in trials 1 and 2, respectively.

Pig weights were taken every 4 days. Twenty-four hour urine samples were collected weekly from all pigs. Creatine and creatinine determinations were made on the urine samples using the procedure of Clark and Thompson (1949). Two pigs from each regime were sacrificed at the conclusion of the trials to make gross pathological inspection and to obtain certain organ and muscle weights. The creatine content of the right superficial digital flexor and gastrocnemius muscles was determined by the method of Poutsiaka (1956). All data were analyzed using the multiple range test of Duncan (1955).

Results and Discussion

In both trials the pigs were about 1 week old when experimental feeding was commenced. The rate of food consumption was very satisfactory throughout the feeding periods. A comparison of growth and the efficiency of food utilization of pigs on the three dietary regimes is presented in table 1. In the first trial the creatine-fed pigs gained 14% faster on 8% less feed than the control group but these differences were not statistically significant (P>.05). The performance of pigs receiving added arginine and glycine was similar to that of the control pigs.

Since it has been shown that the younger chick (Fisher et al., 1956a,b) and pig (Baker et al., 1961) have lower muscle creatine levels than other animals, it was considered advisable in the present study to utilize smaller pigs in the second trial believing that the physiologically younger animals would receive a greater benefit from dietary creatine or creatine precursors. Such was not the case. As
TABLE 1. GROWTH AND FOOD UTILIZATION OF BABY PIGS RECEIVING SYNTHETIC MILK DIETS SUPPLEMENTED WITH CREATINE OR CREATINE PRECURSORS

<table>
<thead>
<tr>
<th>Item</th>
<th>Control</th>
<th>Creatine</th>
<th>Arginine + glycine</th>
<th>Control</th>
<th>Creatine</th>
<th>Arginine + glycine</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pigs</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Days on experiment</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>42</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Av. initial wt., lb.</td>
<td>5.0 ±0.5</td>
<td>5.0 ±0.2</td>
<td>5.0 ±0.2</td>
<td>3.5 ±0.1</td>
<td>3.5 ±0.1</td>
<td>3.5 ±0.1</td>
</tr>
<tr>
<td>Av. daily gain, lb.</td>
<td>0.50±0.06</td>
<td>0.57±0.02</td>
<td>0.51±0.02</td>
<td>0.43±0.01</td>
<td>0.43±0.01</td>
<td>0.43±0.02</td>
</tr>
<tr>
<td>Av. daily solids consumed, lb.</td>
<td>0.59±0.05</td>
<td>0.62±0.05</td>
<td>0.57±0.02</td>
<td>0.57±0.01</td>
<td>0.57±0.01</td>
<td>0.57±0.01</td>
</tr>
<tr>
<td>Solids/gain</td>
<td>1.20±0.06</td>
<td>1.10±0.01</td>
<td>1.12±0.05</td>
<td>1.31±0.03</td>
<td>1.31±0.01</td>
<td>1.31±0.06</td>
</tr>
</tbody>
</table>

* 0.2% creatine monohydrate added to control diet.
* 0.28% L-arginine hydrochloride and 0.1% glycine added to diet.

Twenty-four hour urine collections were made weekly on each pig in both trials. Data from both trials were combined and are summarized in table 2. Daily urine volume as well as urinary creatine and creatinine excretion were highly variable. Urinary excretion of creatine was significantly greater by those pigs receiving creatine in the diet. Urinary creatinine excretion by these pigs was also somewhat greater. There was no increase in urinary excretion of creatine or creatinine by pigs receiving additional arginine and glycine in the diet indicating little or no creatine biosynthesis from the added precursors.

Examination of the pigs which were sacrificed at the end of the two trials did not reveal any abnormal findings. Relative organ weights were similar for pigs from each regimen. At no time during the course of the trials was there any indication of toxicity, reduced appetite or impaired growth from the inclusion of creatine in the diet.

Results obtained in this study indicate that creatine supplemented to a 30% casein diet is largely excreted by the baby pig and does not increase muscle creatine content or growth. Failure of dietary creatine to increase muscle creatine can be well explained by the recent work of Walker (1960, 1961), Fitch et al. (1960) and Coleman (1961) showing a marked repression of mouse kidney transamidinase or chick and duck liver transamidinase activity when either creatine or guanidinoacetate is included in the diet. As a consequence, creatine biosynthesis is depressed when an exogenous source of creatine is available. Van Pilsum (1961) has expressed the belief that creatine competes with glycine for attachment on the site of transamidinase synthesis. Walker (1960, 1961) and Fitch et al. (1960) have explained the reduction of transamidinase activity as resulting from a feedback mechanism since there is no
TABLE 3. MUSCLE SIZE AND CREATINE CONTENT

<table>
<thead>
<tr>
<th>Item</th>
<th>Control</th>
<th>Creatine</th>
<th>Arginine + glycine</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pigs</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Body-weight (kg.)</td>
<td>10.1 ± 1.9</td>
<td>10.7 ± 1.0</td>
<td>10.1 ± 0.8</td>
</tr>
<tr>
<td>Muscle weight (gm.)</td>
<td>48.2 ± 5.0</td>
<td>56.1 ± 1.3</td>
<td>46.3 ± 3.8</td>
</tr>
<tr>
<td>Muscle creatine b</td>
<td>3.02± 0.24</td>
<td>3.11±0.10</td>
<td>2.90±0.12</td>
</tr>
<tr>
<td>Total muscle creatine (mg.)</td>
<td>146.7±26.8</td>
<td>174.7±9.2</td>
<td>135.0±16.3</td>
</tr>
</tbody>
</table>

a Right superficial digital flexor and gastrocnemius muscles, fresh tissue weight.  
b Milligrams per gram of fresh tissue.

enzyme activity reduction when creatinine replaces creatine in the diet. The addition of the amino acid precursors of guanidoacetate, arginine and glycine, to a diet already adequate in the amino acids as in the present study does not appear to influence the rate of creatine biosynthesis. Baker et al. (1961) have obtained similar results when creatine precursors were administered intraperitoneally to pigs nursing their dams. The two studies indicate that in the baby pig creatine biosynthesis is largely unaffected by supplemental creatine precursors whether supplied parenterally or in the diet.

Summary

Twenty-four baby pigs receiving a synthetic milk diet containing 30% casein were utilized to determine if the inclusion of 0.2% creatine monohydrate or an equimolar amount of the creatine precursors, arginine and glycine, would improve growth rate, muscle size and creatine content. Neither of these regimens was effective in improving any of these criteria. Dietary creatine which was absorbed appeared to be largely excreted as urinary creatine or creatinine. The supplemental creatine precursors, arginine and glycine, apparently were not utilized in creatine biosynthesis.

Literature Cited