Effects of Hypophysectomy, Growth Hormone, and Thyroxine on Protein Turnover in Heart*

(Received for publication, October 10, 1974)

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SUMMARY

Cardiac atrophy following hypophysectomy was accompanied by decreased heart content of RNA and polysomes and increased levels of ribosomal subunits, suggesting that protein synthesis was restricted by a reduced supply of ribosomes and an imbalance between rates of peptide-chain initiation and elongation. During perfusion in vitro, provision of palmitate restored the normal balance between rates of initiation and elongation but protein synthesis was lower in hearts of hypophysectomized than normal rats, reflecting the lower RNA content of hearts from hormone-deficient animals. After the period of atrophy had passed, or after treatment with growth hormone and thyroxine, heart RNA content and rates of protein synthesis were equal to or greater than those found in normal hearts. When plasma levels of amino acids, glucose, fatty acids, and insulin, and rates of beating and ventricular pressure development observed in normal and hypophysectomized rats were simulated during in vitro perfusion, hearts from hormone-deficient rats had reduced rates of protein synthesis but unaltered rates of degradation. Cathepsin D activity in heart homogenates (+ Triton X-100) was elevated during cardiac atrophy when expressed per g of tissue but not when expressed per heart.

Ribosome-catalyzed reactions appear to limit the synthesis of myocardial proteins (6-9). Insulin (9), availability of amino acids (10), supply of non-carbohydrate substrates (11), and an increase in heart work (12) stimulated peptide-chain initiation in isolated hearts. After hypophysectomy, plasma levels of insulin, thyroxine, growth hormone, glucose, and fatty acids were reduced and the rate of ventricular pressure development was lower (13, 14). When growth hormone was added to the perfusate of isolated hearts of hypophysectomized rats, an increase in incorporation of labeled amino acids into protein occurred (15).

Protein degradation in heart muscle also appears to be under hormonal control (16). In isolated hearts, insulin inhibited degradation and increased latency of lysosomal enzymes. These changes were consistent with a model of degradation (17, 18) that involves nondifferentiated engulfment and release of cellular constituents by lysosomes. Proteins may be inactivated and denatured within the organelle. Recently, Wildenthal and Mueller (19) reported that regression of cardiac hypertrophy following cessation of thyroxine administration to thyrotoxic rats was accompanied by a 40% increase in the activity of cathepsin D. In other studies, activities of acid hydrolases increased during the period of atrophy following muscular denervation (20).

The present experiments were designed to assess the contribution of changes in the rates of protein synthesis and degradation to atrophy of the heart in hypophysectomized animals.

EXPERIMENTAL PROCEDURE

Heart Perfusion—Female Sprague-Dawley rats (150 to 300 g), normal and hypophysectomized, were obtained from the Charles River Breeding Laboratory. Rats were killed 5 to 35 days after hypophysectomy. Normal rats of the same age served as controls. Fed, heparin-treated (sodium heparin, 2.5 mg, intraperitoneally) rats were anesthetized with sodium pentobarbital (12.5 mg, intraperitoneally). Hearts were rapidly excised, dropped into a beaker of 0.15 m NaCl (2°), and perfused by a modified Langendorf technique (21). A preliminary perfusion was carried out for 10 min using Krebs-Henseleit bicarbonate buffer, gassed with 96% O2-5% CO2 and containing glucose (15 mM) and amino acids at the level to be present during the subsequent period of recirculation. This buffer passed through the heart a single time and was discarded. Recirculation of a measured volume of buffer containing [14C]phenylalanine, other nonradioactive amino acids at 1 or 5 times normal plasma levels, and glucose or albumin-bound (4%) palmitate (11) followed the preliminary perfusion. These amino acid levels were reported earlier (10). The first 10 ml of radioactive buffer were washed through the heart and discarded to reduce dilution of phenylalanine specific activity. Recirculation

Hypophysectomy results in atrophy of the heart as compared to normal rats of the same body weight (1, 2). During atrophy of skeletal muscle, protein synthesis was inhibited while degradation was accelerated, suggesting coordinated control of these pathways (3). On the other hand, Millward (4) reported that growth hormone and thyroxine stimulated growth of the heart (1, 2). Stimulation of growth of skeletal muscle by growth hormone was reported to (5).

* This research was supported by Grant HL 11534 from the National Heart and Lung Institute.

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was continued for 1 hour with the aortic pressure maintained at 60 mm Hg, except as indicated.

Hormones—Bovine growth hormone (NIH-GH-B15), t-thyroxine (Sigma No. T-2501), and crystallized beef insulin (Lilly PJ-4600) were used for hormone treatment. Growth hormone and thyroxine were dissolved in slightly alkaline 0.15 m NaCl and diluted to 0.5 mg/ml and 25 μg/ml, respectively. Growth hormone was given intramuscularly, 100 μg daily, and thyroxine was given subcutaneously, 5 μg daily, for 7 days beginning 8 days after operation. The final injection of the hormone was given 3 hours prior to the experiments. Insulin was added to the perfusion medium at a concentration of 25 milliunits/ml, except as noted.

Estimates of Rates of Protein Turnover, Amino Acid Content, and Specific Activity—Hearts or perfusates were prepared for analysis of amino acid content and specific activity, as described previously (10). Incorporation of [14C]phenylalanine into whole heart protein was estimated using a gas flow planchet counter (10). When perfusate phenylalanine levels were 0.4 mM or greater, specific activities of perfusate and intracellular phenylalanine were equal, and rates of protein synthesis were calculated using perfusate specific activities (22). Amino acid levels were estimated by ion exchange chromatography, using a Beckman amino acid analyzer (10). Protein degradation was calculated from estimates of the rate of dilution of the specific activity of the free phenylalanine pool (16).

Analysis of RNA, Polysomes, Ribosomal Subunits, and Lysosomal Enzymes—For determination of tissue RNA, frozen heart powder was mixed with 0.6 N perchloric acid, and the precipitate was washed twice with the same solution by resuspension and centrifugation. RNA was estimated by alkaline hydrolysis (23). Protein degradation was calculated from estimates of the rate of dilution of the specific activity of the free phenylalanine pool (16).

Results

Measurements of Parameters Related to Protein Turnover in Hypophysectomized Rats—Within the first week after hypophysectomy, heart weight fell by 25%; after 2 weeks, heart size stabilized at 65% of the preoperative value (1, 2, 27). Treatment of hypophysectomized rats with growth hormone, thyroxine, and a combination of growth hormone and thyroxine increased heart weight by 15, 29, and 45%, respectively (27). Treatment of normal animals with a combination of these hormones had no effect on heart weight.

Since protein synthesis in heart muscle is stimulated by increasing levels of insulin and fatty acids (9, 11), these levels were measured in the serum of hypophysectomized rats. Serum levels of free fatty acid were 0.517 ± 0.017 mM (11 observations), 0.327 ± 0.012 mM, and 0.439 ± 0.009 mM (13 observations) 5, 15, or 35 days following hypophysectomy, respectively. These levels in unoperated paired controls averaged 0.562 ± 0.014 (23 observations) and did not change significantly during this time period. Insulin levels were 21 ± 3.3 microunits/ml (4 observations) and 18 ± 3 microunits/ml (4 observations) at 15 and 35 days after operation, as compared to 44 ± 2.3 microunits/ml (4 observations) in unoperated controls.

Levels of ribosomal subunits and polysomes reflect relative rates of peptide-chain initiation and elongation (9). Hearts of rats that were hypophysectomized 5 to 15 days before death contained increased levels of ribosomal subunits and reduced levels of polysomes (Table I). These findings were consistent with a relatively greater restraint on initiation than elongation of chains during the period of atrophy. Thirty days after hypophysectomy, when a smaller but stable heart size was achieved, subunit and polysome levels were not significantly different from normal. Treatment of hypophysectomized rats with growth hormone and thyroxine reduced levels of ribosomal subunits and increased levels of polysomes, suggesting that the hormones were able to restore the normal relationship between rates of initiation and elongation of chains.

Table I

<table>
<thead>
<tr>
<th>Animal</th>
<th>Days post-operative</th>
<th>RNA content (mg RNA/mg heart)</th>
<th>RNA content, sucrose gradient peaks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>mg RNA/mg heart</td>
<td>mg RNA/l mg RNA in heart homogenate</td>
</tr>
<tr>
<td>Series I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
<td>2.88 ± 0.05 (22)</td>
<td>0.188 ± 0.012</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>15</td>
<td>2.54 ± 0.05 (14)</td>
<td>0.196 ± 0.019</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>2.65 ± 0.04 (17)</td>
<td>0.133 ± 0.023</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.08 ± 0.12 (6)</td>
<td>0.154 ± 0.006</td>
</tr>
<tr>
<td>Series II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>15</td>
<td>2.86 ± 0.04 (9)</td>
<td>0.226 ± 0.014</td>
</tr>
<tr>
<td>+GH,T&lt;sub&gt;4&lt;/sub&gt;</td>
<td></td>
<td>3.15 ± 0.08 (6)</td>
<td>0.171 ± 0.019</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>15</td>
<td>2.67 ± 0.05 (12)</td>
<td>0.171 ± 0.019</td>
</tr>
<tr>
<td>+GH</td>
<td>15</td>
<td>2.84 ± 0.05 (6)</td>
<td>0.226 ± 0.014</td>
</tr>
<tr>
<td>+T&lt;sub&gt;4&lt;/sub&gt;</td>
<td>15</td>
<td>3.18 ± 0.08 (6)</td>
<td>0.171 ± 0.019</td>
</tr>
<tr>
<td>+GH,T&lt;sub&gt;4&lt;/sub&gt;</td>
<td>15</td>
<td>3.30 ± 0.08 (12)</td>
<td>0.235 ± 0.023</td>
</tr>
</tbody>
</table>

- p < 0.05 versus normal.
- p < 0.02 versus normal.
- p < 0.05 versus hypophysectomized.
- p < 0.025 versus hypophysectomized, paired analysis.
and albumin-bound palmitate to give maximal rates of synthesis
buffer containing 5 times normal plasma levels of amino acids
those found in unperfused normal hearts. However, levels of
amino acid, the level in these hearts was equal to or greater than
intracellular levels of free amino acids (27). In the case of each
hearts of hypophysectomized rats was not associated with low
specific activity of 595,000 dpm/rmol. When hearts were perfused
under these conditions, the lower rate of protein synthesis in
palmitate and 5 times normal plasma levels of amino acids (27).

Measurement of Protein Synthesis—Earlier studies (27) showed
that the rate of phenylalanine incorporation into protein was the
same in hearts of normal and hypophysectomized rats during
perfusion for 1 hour with buffer containing 0.08 mM phenylala-
nine and 15 mM glucose. Under these conditions, levels of poly-
somes fell and ribosomal subunits increased, indicating that a
block in peptide-chain initiation was present in both groups of
hearts. In the present experiments, hearts were perfused (a) with
buffer containing 5 times normal plasma levels of amino acids and
albumin-bound palmitate to give maximal rates of synthesis (11); (b) with buffer containing levels of amino acids, fatty
acids, glucose, and insulin that approximated those found in the
serum of normal and hormone-deficient animals. In the latter
groups, rates of ventricular pressure development and heart rate
also were adjusted to more closely simulate normal and hypoph-
ysectomized conditions.

When hearts from normal rats were perfused with buffer con-
taining palmitate and 5 times normal plasma levels of amino acids
(Table II), RNA content of sucrose gradient peaks representing
the large and small ribosomal subunits were 0.215 ± 0.015 and
0.101 ± 0.020 mg of RNA/3 mg of RNA in the heart homoge-
neate, respectively (3 observations). Hearts of hypophysec-
tomized rats, perfused under these conditions, contained 0.181 ±
0.030 and 0.079 ± 0.020 mg of RNA in these gradient fractions
(3 observations). None of these values were significantly different
from those found in normal unperturbed hearts. Rates of protein
synthesis were lower in hearts of hypophysectomized rats (5 to
15 days after operation) than in hearts of normal rats (Table II,
Series I). After a longer period (24 to 30 days), protein syn-
thetoe occurred at the same rate in both groups of hearts.

The reduced rate of protein synthesis in hearts from hypophy-
sectomized rats (5 to 15 days after operation) could have been
due to a delay in reaggregation of ribosomes at the beginning of
the perfusion period. A delay of 30 min occurred before pal-
mitate fully reaggregated ribosomal subunits in perfused hearts
of normal rats (11). When hearts were perfused for 2 hours in
the presence of palmitate and 5 times normal plasma levels of
amino acids, rates of protein synthesis during the second hour
were lower in hearts from hypophysectomized rats (Table II,
Series II) even though the ribosomes were reaggregated.

Reaggregation of ribosomal subunits in hearts of hypophysec-
tomized rats did not appear to depend on synthesis of mRNA
(Fig. 1). After 1 hour of perfusion with buffer containing actino-
mycin D, levels of ribosomal subunits were lower than in unper-
fused hearts of hypophysectomized rats, but similar to levels
found in normal hearts.

Treatment of hypophysectomized rats with growth hormone or
thyroxine (or both) increased the rate of protein synthesis (Table II,
Series I). Administration of a combination of growth hormone and thyroxine was more effective than growth hormone
hearts were simulated by electrical pacing to values similar to those found in normal and hypophysectomized animals. Electrocardiographic measurements in anesthetized animals indicated that the heart rate (beats per min) was 348 ± 18 (12 observations) and 252 ± 13 (11 observations) in normal and hypophysectomized rats, respectively. When these hearts were perfused in vitro, without pacing, the rate of normal hearts was 210 ± 5 beats per min (12 observations) and the rate of hearts of hypophysectomized rats was 150 ± 5 (15 observations). Variations in peak systolic pressure development were simulated by adjusting the aortic perfusion pressure by altering the speed of the peristaltic pump. In the Lan-

d Emergency preparation, intraventricular pressure rose to values slightly above the perfusion pressure with each beat (21). Simu-
lated conditions were as follows. Normal: 0.7 mm glucose, 0.5 mm palmitate, 40 micromons/ml insulin, 120 mm Hg perfusion pres-
sure, 300 beats per min; Hypophysectomized: 4.3 mm glucose, 0.3 mm palmitate, 15 micromons/ml of insulin, 100 mm Hg perfusion pressure, 270 beats per min. Tissue levels of ATP were not affected by the condition of perfusion and averaged 161 ± 0.9 (11 observations) and 15.9 ± 0.5 μmol/g (11 observations) after 30 or 60 min, respectively. Cretanine phosphate levels were 11.0 ± 0.9 (11 observ-
ations) and 14.9 ± 0.6 (11 observations) under the same condi-
tions. Values are means ± standard error of the number of obser-
vations in parentheses.

<table>
<thead>
<tr>
<th>Condition of animal</th>
<th>Condition of perfusion</th>
<th>Protein synthesis</th>
<th>RNA content, sucrose gradient peaks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>μmol/phenylalanine incorporated/g protein</td>
<td>mg RNA/3 mg in heart homogenate</td>
</tr>
<tr>
<td>Normal</td>
<td>Unperfused</td>
<td>1.14 ± 0.08 (12)</td>
<td>0.210 ± 0.017</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>Unperfused</td>
<td>0.92 ± 0.03 (9)</td>
<td>0.203 ± 0.012</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>0.123 ± 0.016 (12)</td>
<td>0.171 ± 0.017</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>Hypophysectomized</td>
<td>0.139 ± 0.011 (6)</td>
<td>0.139 ± 0.011 (6)</td>
</tr>
</tbody>
</table>

a p < 0.05 versus normal, unperfused, by paired analysis.
b p < 0.05 versus hypophysectomized, unperfused.
c p < 0.05 versus simulated normal conditions.

Measurements of Protein Degradation and Lysosomal Enzyme Activities—In the first series of experiments (Table IV), net release of phenylalanine and protein degradation were measured in hearts perfused with buffer containing glucose and amino acids. Net release, reflecting the balance between rates of protein synthesis and degradation, occurred in both groups of hearts, but was lower in hearts from hypophysectomized animals (5 to 35 days, postoperative). Protein degradation was somewhat lower 10 days after hypophysectomy. In Series II, net release of phenylalanine was not detected in hearts of normal or hypophysecto-
mized animals perfused in the presence of insulin. The hormone reduced protein degradation about 50%. Rates of degradation in hearts of hypophysectomized rats were the same as in normal hearts.

When normal and hypophysectomized conditions were simu-
lated in vitro as had been done with protein synthesis, neither net release of phenylalanine nor the rate of protein degradation were significantly different (Series III). However, the difference be-
tween these rates, which gave an approximation of the rate of protein synthesis, was greater under normal conditions (0.12 ± 0.01 μmol of phenylalanine/g-hour) than under hypophysecto-
mized conditions (0.08 ± 0.01). A more direct assessment of degradation rates was obtained by measuring net release of phenylalanine in the presence of cycloheximide. Release was unaffected by perfusion of hearts under simulated normal or hypophysectomized conditions or by the period after hypophy-
sectomy (Series IV).

During the period of rapid atrophy following hypophysectomy (5 to 8 days, postoperative), total activity of cathepsin D in-
creased while the fraction assayable in the absence of Triton was the same as in normal hearts (Table V). The fraction of cathepsin D activity recovered in the 104 x g pellet was increased somewhat 5 days after hypophysectomy. On the other hand, total activity of β-acetylglucosaminidase was lower in hearts of hypophysectomized rats (5 days postoperative) but a higher fraction of total activity was recovered in the 104 x g pellet. The fraction of activity assayable in the absence of Triton was the same as in normal hearts after 5 days but increased somewhat 8 and 14 days postoperatively. These changes in the total ac-
tivities of cathepsin D and β-acetylglucosaminidase were similar to those reported by Wildenthal and Mueller (19).

DISCUSSION

Plasma levels of insulin, fatty acids, and amino acids, and tissue levels of high energy phosphates in normal animals are sufficient to accelerate peptide-chain initiation in heart muscle and to shift the restraint on protein synthesis to reactions involved in elonga-
tion and termination of chains (9, 11). These findings suggested that protein synthesis was limited by the quantity of ribosomes available to take part in formation of peptide bonds.

During cardiac atrophy in hypophysectomized rats, two changes may have contributed to a decreased rate of protein synthesis. The first is a reduction in the total RNA per g of heart, reflecting a reduction in the number of ribosomes, and the second is an imbalance between rates of initiation and elongation of chains. In the latter case, a reduction in polysomes and an in-
crease in ribosomal subunits is consistent with inhibition of chain initiation; alternatively, these changes could result from accelerated rates of chain elongation and termination. This possibility
Lysosomal enzyme activities were estimated in unperfused hearts from normal or hypophysectomized rats 5 to 14 days after operation. Values are the mean ± standard error of the number of observations indicated in parenthesis.

### Table IV

**Effect of hypophysectomy and hormone treatment on protein degradation**

<table>
<thead>
<tr>
<th>Animal</th>
<th>Days postoperative</th>
<th>Phenylalanine release</th>
<th>Net release</th>
<th>Protein degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>(9) 0.12 ± 0.01</td>
<td>0.21 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>(6) 0.05 ± 0.01a</td>
<td>0.19 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>(8) ND</td>
<td>0.10 ± 0.01a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>(5) ND</td>
<td>0.12 ± 0.01a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>(12) 0.07 ± 0.01</td>
<td>0.19 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>(12) 0.09 ± 0.01</td>
<td>0.17 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>(15) 0.32 ± 0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>(5) 0.29 ± 0.02a</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- *p < 0.005 versus normal
- a p < 0.01 versus no insulin, Series I.

### Table V

**Effect of hypophysectomy on activity of lysosomal enzymes**

Lysosomal enzyme activities were estimated in unperfused hearts from normal or hypophysectomized rats 5 to 14 days after operation. Values are the mean ± standard error of the number of observations indicated in parenthesis.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Days postoperative</th>
<th>Whole homogenate</th>
<th>10^4 X g pellet</th>
<th>10^4 X g pellet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+Triton, activity</td>
<td>−Triton</td>
<td>Activity</td>
</tr>
<tr>
<td>Cathepsin D activity (2 X 10^4-cpm/g. 30 min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>(16)</td>
<td>117 ± 5</td>
<td>18 ± 1</td>
<td>15.4 ± 0.9</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>5 (4)</td>
<td>138 ± 2^a</td>
<td>21 ± 1^b</td>
<td>15.3 ± 0.5</td>
</tr>
<tr>
<td>8 (4)</td>
<td>139 ± 2^a</td>
<td>24 ± 1^a</td>
<td>17.6 ± 0.7</td>
<td>87 ± 4^a</td>
</tr>
<tr>
<td>14 (8)</td>
<td>119 ± 9</td>
<td>22 ± 1^b</td>
<td>16.4 ± 1.0</td>
<td>71 ± 5</td>
</tr>
</tbody>
</table>

- *p < 0.01 versus normal.
- a p < 0.05 versus normal.
leave 1.0% per day to be accounted for either by a restraint on peptide-chain initiation or an accelerated rate of degradation.

Measurements of protein degradation during in vitro perfusion of normal and hypophysectomized rats were undertaken in an attempt to determine whether the rate was modified in hormone-deficient hearts. Perfusion with buffer containing amino acids and glucose resulted in phenylalanine release, but the rate was lower in hormone-deficient hearts. Degradation was either unchanged or reduced in hearts of hypophysectomized as compared to normal rats. When insulin was added to the perfusate, net release of phenylalanine was zero in both groups of hearts and degradation was reduced by 40 to 50%. When normal and hypophysectomized conditions were simulated in vitro, net release and protein degradation were the same under both conditions of perfusion. Measurement of degradation by this method underestimated the rate by 35% due to re-reincorporation of non-radioactive phenylalanine prior to mixing with the total pool of [14C]phenylalanine (16). When protein degradation was measured in hearts in which protein synthesis was inhibited with cycloheximide, the rates were the same under simulated normal and hypophysectomized conditions. These rates also were underestimated about 20% due to inhibition of proteolysis by the drug (16, 30, 31). In order to obtain an additional assessment of the rate of degradation, phenylalanine release (Table IV) and protein synthesis (Table III) were summed. Under simulated normal and hypophysectomized conditions, rates of proteolysis were 0.26 and 0.24 μmol of phenylalanine/g of heart-hour, respectively. These measurements, under a variety of in vitro conditions, indicated that protein degradation was not increased in hearts of hypophysectomized rats undergoing atrophy. However, rates of degradation measured in vitro may not faithfully reflect the in vivo rate, as indicated by net release of phenylalanine under simulated normal conditions.

A model of protein degradation (17, 18) involving lysosomes was suggested to account for protein degradation in heart muscle (16). Enzymatic inactivation and denaturation within the organelles would depend upon the susceptibility of individual proteins to proteolysis. During atrophy of hearts of hypophysectomized rats, the total activity of cathepsin D, as assayed in the whole homogenate in the presence of Triton, increased about 19%. The percentage of total activity assayable without Triton increased about 34%, due to reincorporation of non-radioactive phenylalanine prior to mixing with the total pool. The total activity of cathepsin D did not reflect the rate of degradation, these results could reflect heterogeneity of lysosomes within the myocardium (32-34).

REFERENCES

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A C Hjalmarson, D E Rannels, R Kao and H E Morgan


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