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

(Received for publication, October 10, 1974)

ÅKE C. HJALMARSON,‡ D. EUGENE RANNELS, RACE KAO, AND HOWARD E. MOHRAN
From the Department of Physiology, College of Medicine, The Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pennsylvania 17033

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.

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 of skeletal muscle in fasted-refed rats was accompanied by faster rates of both protein synthesis and degradation. Treatment of hypophysectomized rats with either growth hormone or thyroxine stimulated growth of the heart (1, 2). Stimulation of growth of skeletal muscle by growth hormone was reported to normal rats of the same body weight (1, 2). During atrophy of the heart in hypophysectomized animals, 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 thyrotropic 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% O2-4% 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...
RESULTS

Measurements of Parameters Related to Protein Turnover in Hypophysectomized Rate—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 the 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.

Effect of hypophysectomy and hormone treatment in vivo on heart RNA content and ribosomal aggregation

Sucrose gradient fractions were collected as described earlier (9). Growth hormone (GH), thyroxine (T₄), or both hormones (GH, T₄) were injected for 7 days prior to death, as indicated. In experimental series II, “untreated” rats received daily injections of saline. Values represent the mean ± standard error of the number of observations indicated in parentheses. Statistical analysis was performed comparing values within the same experimental series.

| Animal              | Days post-              | RNA content mg/g heart | RNA content mg RNA/3 mg RNA in heart homogenate |
|---------------------|-------------------------|------------------------|-----------------------------------------------|
|                     | operative               |                        | Polysomes                                      | Large subunit                                      | Small subunit                                      |
|                     |                         |                        | mg RNA/3 mg RNA                               | mg RNA/3 mg RNA                                   | mg RNA/3 mg RNA                                    |
| Series I             |                         |                        |                                               |                                               |                                               |
| Normal              |                         | 2.88 ± 0.05 (22)       | 0.188 ± 0.021                                 | 0.173 ± 0.010                                     | 0.094 ± 0.009                                     |
|                     |                         |                        |                                               |                                               |                                               |
| Hypophysectomized   |                         | 5                      | 0.169 ± 0.019                                 | 0.228 ± 0.004*                                    | 0.119 ± 0.008                                     |
|                     |                         | 15                     | 0.133 ± 0.023*                               | 0.258 ± 0.022*                                    | 0.162 ± 0.015                                     |
|                     |                         | 30                     | 0.154 ± 0.000*                               | 0.104 ± 0.021                                     | 0.118 ± 0.015                                     |
| Series II            |                         |                        |                                               |                                               |                                               |
| Normal              | +GH, T₄                 | 2.86 ± 0.04 (9)        | 0.226 ± 0.014*                               | 0.210 ± 0.017*                                   | 0.123 ± 0.016                                     |
|                     |                         | 3.15 ± 0.08 (6)*       |                                               |                                               |                                               |
| Hypophysectomized   | +GH                     | 2.67 ± 0.05 (12)       | 0.171 ± 0.019                                | 0.280 ± 0.020*                                   | 0.171 ± 0.017*                                    |
|                     | +T₄                     | 2.84 ± 0.05 (8)*       |                                               |                                               |                                               |
|                     | +GH, T₄                 | 3.18 ± 0.08 (6)*       |                                               |                                               |                                               |
|                     |                         | 3.30 ± 0.08 (12)       | 0.235 ± 0.023*                               | 0.220 ± 0.016*                                   | 0.130 ± 0.010*                                    |

a p < 0.05 versus normal.

b p < 0.02 versus normal.

c p < 0.05 versus hypophysectomized.

d p < 0.025 versus hypophysectomized, paired analysis.
elgation of peptide chains. In other experiments, treatment of normal rats with growth hormone and thyroxine had no effect on levels of polysomes and subunits.

During the rapid phase of cardiac atrophy (5 days, postoperative) RNA levels were reduced by 12% (Table I). When a stable heart size was achieved, RNA levels in hearts of hormone-deficient rats returned to normal. Injections of growth hormone increased RNA to normal levels. Thyroxine, or a combination of both hormones, increased RNA content in hearts of hypophysectomized rats by approximately 20%. Injection of both hormones raised RNA content of normal hearts by 10%.

**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 phenylalanine and 15 mM glucose. Under these conditions, levels of polysomes 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 (1.5 mM)-albumin (4 mg/ml, 5 times normal plasma levels of amino acids, containing palmitate and 5 times normal plasma levels of amino acids (27). Under these conditions, levels of polysomes 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 (1.5 mM)-albumin (4 mg/ml, 5 times normal plasma levels of amino acids, containing palmitate and 5 times normal plasma 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 hypophysectomized conditions.

When hearts from normal rats were perfused with buffer containing 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 homogenate, respectively (3 observations). Hearts of hypophysectomized 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 unperfused 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 synthesis occurred at the same rate in both groups of hearts.

The reduced rate of protein synthesis in hearts from hypophysectomized 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 palmitate 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 hypophysectomized rats did not appear to depend on synthesis of mRNA (Fig. 1). After 1 hour of perfusion with buffer containing actinomycin D, levels of ribosomal subunits were lower than in unperfused hearts of hypophysectomized rats, but similar to levels found in normal hearts.

**Table II**

| Animal            | Days post-operative | Protein synthesis (µmol phenylalanine/g protein) |
|-------------------|---------------------|-----------------------------------------------|
| **Series I**      |                     |                                               |
| Normal            |                      | 1.41 ± 0.03 (51)                              |
| +GH, T<sub>1</sub> | 5                   | 1.47 ± 0.03 (6)                               |
| Hypophysectomized |                      | 1.18 ± 0.04 (3)<sup>a</sup>                   |
| +GH               | 15                  | 1.23 ± 0.03 (43)<sup>a</sup>                  |
| +T<sub>1</sub>     | 15                  | 1.66 ± 0.07 (3)<sup>a,b</sup>                 |
| +GH, T<sub>1</sub> | 15                  | 1.78 ± 0.05 (3)<sup>a,b</sup>                 |
| **Series II**     |                     |                                               |
| Normal            | 15                  | 1.92 ± 0.04 (12)<sup>a,b</sup>                |
| Hypophysectomized | 15                  | 1.39 ± 0.06 (13)                              |

<sup>a</sup> p < 0.01 versus appropriate normal.

<sup>b</sup> p < 0.02 versus hypophysectomized, untreated, 5 to 24 days.
Hearts were perfused for 1 hour with buffer containing normal plasma levels of amino acids and 0.80 mM phenylalanine. Hypophysectomized rats were used 12 days after operation. In vivo heart rates 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-}

### TABLE III
Simulation of normal and hypophysectomized states during perfusion in vitro

| Condition of animal | Condition of perfusion | Protein synthesis | RNA content, sucrose gradient peaks |
|---------------------|------------------------|-------------------|------------------------------------|
|                     |                        | µmol/phenylalanine incorporated/g protein | mg RNA/3 mg in heart homogenate |
| Normal              | Unperfused             | 0.210 ± 0.017     | 0.123 ± 0.016 (12) |
| Hypophysectomized   | Unperfused             | 0.280 ± 0.020b    | 0.171 ± 0.017 (12)a |
| Normal              | Normal                 | 1.14 ± 0.08 (12)  | 0.173 ± 0.011 |
| Hypophysectomized   | Hypophysectomized      | 0.92 ± 0.03 (9)   | 0.203 ± 0.012b |

* 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.

alone in the dosage used. In other experiments, treatment of normal rats with growth hormone and thyroxine had no effect on protein synthesis.

When perfusion pressure, heart rate, and perfusate content of glucose, insulin, and fatty acids were adjusted to simulate conditions in normal and hypophysectomized rats (Table III), levels of ribosomal subunits were equal to or below those found in unperfused hearts of normal rats. The rate of protein synthesis was 19% lower in hearts of hypophysectomized rats when perfused under conditions simulating those in hormone-deficient as compared to normal rats.

**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 hypophysectomized 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 simulated 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 between 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 hypophysectomized 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 hypophysectomy (Series IV).

During the period of rapid atrophy following hypophysectomy (5 to 8 days, postoperative), total activity of cathepsin D increased 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 × 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 × 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 activities 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 elongation 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 increase 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...
P-Acetylglucosaminidase activity

Series II

rentheses. ND, none detected.

from normal or hypophysectomized animals were perfused under conditions simulating the normal or hypophysectomized state, respectively, as described in Table III. In Series IV, cycloheximide was included in the perfusate (2 × 10⁻⁶ M). Values represent the mean ± standard error of the number of observations in parentheses. ND, none detected.

Hearts in Series I were perfused for 1 hour with buffers containing normal plasma levels of amino acids, 0.01 mM phenylalanine, and 16 mM glucose. In experimental Series II, insulin (25 milliunits/ml) were added to this buffer. In Series III and IV, hearts from normal or hypophysectomized animals were perfused under conditions simulating the normal or hypophysectomized state, respectively, as described in Table III. In Series IV, cycloheximide was included in the perfusate (2 × 10⁻⁶ M). Values represent the mean ± standard error of the number of observations in parentheses. ND, none detected.

TABLE IV

Effect of hypophysectomy and hormone treatment on protein degradation

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.

| Animal | Days post-operative | Phenylalanine release | Protein degradation |
|--------|---------------------|-----------------------|---------------------|
|        |                     | Net release | Protein degradation |
|        |                     | (μmol released/g-hour) | (μmol released/g-hour) |
| Series I | Normal | 5 | (9) 0.12 ± 0.01 | 0.21 ± 0.01 |
|         | Hypophysectomized | 15 | (6) 0.05 ± 0.01* | 0.19 ± 0.01 |
|         |         | 35 | (6) 0.05 ± 0.02* | 0.14 ± 0.02* |
| Series II | Normal | 5 | (8) ND | 0.10 ± 0.01* |
|         | Hypophysectomized | 15 | (5) ND | 0.12 ± 0.01* |
|         |         | 35 | (4) ND | 0.11 ± 0.01* |
| Series III | Normal | 5 | (12) 0.07 ± 0.01 | 0.19 ± 0.01 |
|         | Hypophysectomized | 15 | (12) 0.09 ± 0.01 | 0.17 ± 0.01 |
| Series IV | Normal | 5 | (15) 0.32 ± 0.01 | 0.19 ± 0.01 |
|         | Hypophysectomized | 12 | (11) 0.32 ± 0.02 | 0.17 ± 0.01 |

a p < 0.001 versus normal
b p < 0.01 versus no insulin, Series I.

cardiac atrophy. When plasma levels of insulin, glucose, fatty acids, and amino acids, and the mechanical performance of hearts of hypophysectomized rats were simulated in vitro, levels of ribosomal subunits fell. Thus, the imbalance between rates of initiation and elongation that was found in vivo could not be reproduced in vitro. Factors accounting for this imbalance in vivo are unknown.

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.

| Animal | Days post-operative | Whole homogenate | 10⁴ × g pellet |
|--------|---------------------|-----------------|----------------|
|        |                     | + Triton, activity | − Triton | | | | − Triton |%
|        |                     | Activity | % of Total | Activity | % of Total | Activity | % of Total |
| Cathepsin D activity (2 × 10⁻⁴-cpm/g 30 min) | | | | | | | |
| Normal | (16) | 117 ± 5 | 18 ± 1 | 15.4 ± 0.9 | 65 ± 2 | 55.6 ± 1.9 | |
| Hypophysectomized | 5 (4) | 138 ± 2* | 21 ± 1* | 15.3 ± 0.5 | 93 ± 1* | 67.4 ± 0.5* | |
| 8 (4) | 149 ± 2* | 24 ± 1* | 17.6 ± 0.7 | 87 ± 4* | 62.7 ± 4.0 | |
| 14 (8) | 119 ± 9 | 22 ± 1* | 16.4 ± 1.0 | 71 ± 5 | 51.8 ± 2.2 | |
| 8-Acetylglucosaminidase activity (μmol/g 30 min) | | | | | | | |
| Normal | (16) | 16.8 ± 0.3 | 4.2 ± 0.1 | 25.3 ± 0.5 | 6.3 ± 0.3 | 37.4 ± 1.2 | |
| Hypophysectomized | 5 (4) | 19.9 ± 0.2* | 4.5 ± 0.3 | 28.5 ± 2.0 | 7.4 ± 0.1* | 40.3 ± 1.0* | |
| 8 (4) | 16.4 ± 0.2 | 4.9 ± 0.1* | 30.0 ± 0.9* | 6.7 ± 0.3 | 41.1 ± 2.2 | |
| 14 (8) | 15.6 ± 0.6 | 4.9 ± 0.1* | 31.6 ± 1.4* | 5.9 ± 0.4 | 37.7 ± 1.3 | |

a p < 0.01 versus normal.
b 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 vivo, 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 reincorporation of nonradioactive phenylalanine prior to mixing with the total pool of [3H]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 vivo may not faithfully reflect the in vitro 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 was unchanged while that sedimentable at 104 x g was higher. The percentage of total activity assayable without Triton increased 5 days after hypophysectomy (normal, 8.6 ± 0.03; hypophysectomized, 7.4 ± 0.07 μmol/heart-30 min). These data indicated that the higher total activity of cathepsin D need not be attributed to increased synthesis of the enzyme but could have resulted from slower degradation of cathepsin D than of whole heart protein. On the other hand, β-acetylglucoaminidase activity decreased in proportion to heart size. As an alternative to differing rates of enzyme degradation, these results could reflect heterogeneity of lysosomes within the myocardium (32-34).

REFERENCES

1. WHITON, W. Y., GRIM, A. F., AND KING, T. M. (1962) Circ. Res. 10, 553-558
2. BEZNIJ, M. (1964) Circ. Res. 15, 141-150
3. GOLDBERG, A. G. (1969) J. Biol. Chem. 244, 3223-3229
4. MILLWARD, D. J. (1974) in Symposium on the Interrelationship of Alcohol and Malnutrition on Protein Synthesis, Pergamon Press, New York, in press
5. GOLDBERG, A. G. (1969) J. Biol. Chem. 244, 3217-3222
6. EARL, D. C. N., AND LONNER, A. (1966) Arch. Biochem. Bio-
phys. 115, 445-449
7. SCHREIBER, S. S., ORTIZ, M., EVANS, C., SILVER, E., AND
ROTHSCHILD, M. A. (1966) Am. J. Physiol. 215, 1250-1259
8. WOOL, I. G., STERNAIT, W., SUREHARA, K., LOW, R. B.,
BAILEY, P., AND OYER, D. (1968) Recent Prog. Horm. Res. 24, 139-208
9. MORGAN, H. E., JEFFERSON, L. S., WOLPERT, E. B., AND RAN-
NELS, D. E. (1971) J. Biol. Chem. 246, 2153-2170
10. MORGAN, H. E., EARL, D. C. N., BROOKS, A., WOLPERT, E. B.,
GOD, K. E., AND JEFFERSON, L. S. (1971) J. Biol. Chem. 246, 2152-2162
11. RANDELL, D. E., HAMILTON, A. E., AND MORGAN, H. E. (1974) Am. J. Physiol. 226, 528-539
12. HAMILTON, A. E., AND ISAKSSON, O. (1972) Acta Physiol. Scand. 86, 342-352
13. DAUGBAY, W. H. (1968) in Textbook of Endocrinology (Wil-
liams, R. H., ed) pp. 37-84, Saunders, Philadelphia
14. ROMO, M. J., HAMILTON, A. E., MORGAN, H. E., BAR-
rett, M. J., AND GODTSTEIN, R. A. (1972) Circ. Res. 31, 497-499
15. AHEREK, K., HAMILTON, A. E., AND ISAKSSON, O. (1969) Acta Physiol. Scand. 76, 23A-24A
16. RANDELL, D. E., KAO, R., AND MORGAN, H. E. (1975) J. Biol.
Chem. 250, 1694-1701
17. SEGAL, H. L., MATSUBARA, T., HAIDER, M., AND ABRAHAM,
G. J. (1969) Biochem. Biophys. Res. Commun. 36, 764-770
18. HAMPER, M., AND SEGAL, H. L. (1972) Arch. Biochem. Bio-
phys. 148, 298-327
19. WINDTHERAL, K., AND MUELLER, E. A. (1974) Nature 249, 478-
479
20. WEINSTOCK, I. M., AND DODD, A. A. (1969) in Lysosomes in
Biologically and Pathology (DINGLE, J. T., AND FELL, H. B.,
ed) Vol. 1, pp. 450-460, American Elsevier, New York
21. NEILL, J. R., LEBERBAMISER, N. H., BATTERSBY, E. J.,
AND MORGAN, H. E. (1967) Am. J. Physiol. 221, 804-814
22. RANDELL, D. E., AND MORGAN, H. E. (1973) Fed. Proc. 32,
532
23. FLECK, A., AND MUNRO, H. N. (1962) Biochim. Biophys. Acta
51, 572-583
24. BARBET, J. (1972) in Lysosomes (DINGLE, J. T., ed) pp.
40-163, Elsevier, New York
25. NOBLE, R. P. (1966) J. Lipid Res. 7, 745-749
26. HALE, C. N., AND RANDLE, P. J. (1973) Biochem. J. 88, 137-
146
27. MORGAN, H. E., HAMILTON, A. E., AND RANDELL, D. E.
(1973) in Recent Advances in Studies on Cardiac Structure and
Metabolism, Vol. 3, Myocardial Metabolism (DHALIA, N. S., ed) pp.
501-573, University Park Press, Baltimore
28. EARL, D. C. N., AND KORNER, A. (1966) Arch. Biochem. Bio-
phys. 115, 445-449
29. FAB, M., AND GARibern, P. J. (1974) J. Biol. Chem. 249,450-451
30. HEBERK, A., AND TOMKIN, G. M. (1971) J. Biol. Chem. 246,
710-714
31. BALLARD, F. A., AND HOPGOOD, M. F. (1973) Biochem. J. 136,
259-264
32. CONNICO, P. G., AND BIRD, J. W. C. (1970) J. Cell Biol. 45,
321-333
33. ERLON, D. W., WATI, M., AND WIBULC, W. (1972) Biochem-
istry 11, 472-476
34. TOPPING, T. M., AND TRAVIS, D. F. (1974) J. Ultrastruct. Res. 40, 1-22
Effects of hypophysectomy, growth hormone, and thyroxine on protein turnover in heart.
A C Hjalmarson, D E Rannels, R Kao and H E Morgan

J. Biol. Chem. 1975, 250:4556-4561.

Access the most updated version of this article at http://www.jbc.org/content/250/12/4556

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 0 references, 0 of which can be accessed free at http://www.jbc.org/content/250/12/4556.full.html#ref-list-1