ABSTRACT
Ornithine decarboxylase, a possible rate-limiting enzyme in the synthesis of polyamines, was assayed in hearts of normal rats, sham-operated rats, and rats subjected to aortic constriction. In the hearts of rats with constricted aortas, significantly increased enzyme activity compared with that in the hearts of sham-operated rats was observed 2, 4, 6, and 8 hours and 3, 5, and 10 days after operation, and two peaks in activity occurred—one at 4 hours and the other at 5–10 days. Increased ornithine decarboxylase activity was one of the earliest changes associated with cardiac hypertrophy. The changes in enzyme activity correlated well with the subsequent hypertrophy in the hearts of rats with aortic constriction and with the regression in the hearts of sham-operated rats, suggesting a role for polyamines in the regulation of cardiac growth. The early increase in ornithine decarboxylase activity in hearts of rats with aortic constriction was inhibited by actinomycin D, 8-azaguanine, and cycloheximide, indicating that RNA and protein synthesis are involved in the process. Actinomycin D given 30 minutes after operation or even at the time of aortic constriction failed to inhibit the increase in the enzyme activity, suggesting that the transcription required for the increase occurs early after operation. Cycloheximide given 1 hour before the rats were killed markedly decreased the enzyme activity, and the estimated half-life of cardiac ornithine decarboxylase was comparable to that of the reported short-lived liver ornithine decarboxylase. The study suggests that the synthesis of ornithine decarboxylase is influenced at the stage of transcription by mechanical stress on the myocardium and that polyamines might have a regulatory role in cardiac hypertrophy and regression.

KEY WORDS cardiac regression aortic constriction polyamines actinomycin D 8-azaguanine cycloheximide

The specific biochemical mechanism initiating cardiac hypertrophy is still not clear, but studies have concentrated on the increased nucleic acid and protein synthesis that is generally accepted as having a central role in the growth of any tissue. The polyamines, spermine and spermidine, and their precursor, the diamine, putrescine, are widely distributed among mammalian tissues (1). Studies on the relation of polyamines to growth in microorganisms and in animal tissues have suggested that spermine or spermidine or both might regulate the biosynthesis of nucleic acids and proteins. Direct addition of polyamines stimulates RNA polymerase activity (2–6) and DNA polymerase activity (7). Polyamines also form stabilizing complexes with DNA (8, 9), RNA (10), and ribosomes (11–14) and can stimulate protein synthesis in some cell-free ribosome systems (15–17). Correlations between polyamine concentrations and increases in protein and polynucleotide production have been observed during growth of bacteria (18, 19), chick embryos (20–22), and sea urchin eggs.
chloride (specific activity 26.4 mc/mmole), [U-14C]ornithine (specific activity 203 mc/mmole), [1,4-14C]putrescine dihydrochloride (specific activity 7.41 mc/mmole), L-ornithine monohydrochloride, putrescine dihydrochloride, pyridoxal-5-phosphate, dithiothreitol, 8-azaguanine, hydroxide of Hyamine 10x, actinomycin D, and NSD-1055 (4-bromo-3-hydroxybenzoxazolamine dihydrogen phosphate) were used.

Radioactive ornithine was dissolved in 0.1N HCl, evaporated to dryness in a rotary desiccator at 50°C, redissolved in 0.01N HCl, and frozen until it was used (36). In other experiments, it was dissolved in 0.5N H3PO4. Its volatile radioactivity was removed under vacuum in a desiccator with NaOH pellets for a few hours, and then its pH and ionic strength were adjusted for use. Actinomycin D was dissolved in 0.9% saline (800 µg/ml or 320 µg/ml), and 0.5 ml was injected intravenously. Cycloheximide was dissolved in saline (5 mg/ml or 400 µg/ml), and 1 ml or 0.5 ml was injected intraperitoneally. 8-Azaguanine was dissolved as described by Kwan and Webb (37) to give a final concentration of 8 mg/ml and a pH of 8.2; a total dose of 40 mg was injected intraperitoneally.

Assays.—For estimation of ornithine decarboxylase activity, the method of Russell and Snyder (31) was used with slight modification. At appropriate times, the rats were decapitated, and their hearts were removed and kept in chilled containers. After the atri and great vessels were removed, the hearts were blotted and weighed on a Mettler balance. The tissues were then homogenized in 50 mM sodium-potassium phosphate buffer, pH 6.8, containing, in some experiments, 0.5 mM dithiothreitol (5 ml buffer/g wet weight tissue), in a Thomas 4288 tissue homogenizer with a motor-driven pestle. The homogenate was centrifuged at 14,000 g at 4°C for 30 minutes, and samples of the supernatant fluid were taken for assay of ornithine decarboxylase activity.

In most experiments, incubations were carried out in a 25-ml flask equipped with a rubber stopper supporting a polyethylene center well which contained 0.3 ml of 1N Hyamine. Standard incubation mixtures consisted of 0.2 µmoles of pyridoxal-5-phosphate, 0.5 ml of enzyme preparation, 0.2 µmoles of L-ornithine including 0.5 µc of [1-14C]dl-ornithine, 0.5 µmoles of dithiothreitol, and 50 mM sodium-potassium phosphate buffer (pH 6.8) to make a final volume of 2 ml. Substrate was placed in the flask initially. All components of the system except the substrate were preincubated for 10 minutes at 37°C in separate test tubes and injected through the rubber stopper into the flask. The incubation was continued for 30 minutes at 37°C. The reaction was stopped by injecting 1 ml of 2N citric acid

1Actinomycin D was a gift from Merck Sharp & Dohme Laboratories.
2NSD-1055 was the generous gift of Dr. Diane H. Russell.

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into the reaction mixture through the rubber stopper. The mixture was agitated for another 30 minutes at 25°C to allow complete absorption of the evolved $^{14}$CO$_2$ by the Hyamine. The Hyamine was transferred and counted in 15 ml of scintillation fluid containing 0.5 g 2,5-diphenyl-oxazole/100 ml and 0.04 g 1,4-di-2-(5-phenyl-oxazolyl)benzene/100 ml in toluene in a Packard Tri-Carb liquid scintillation counter. The values were corrected for a blank processed like the others but with homogenizing solution instead of tissue extract. In a few experiments, NSD-1055 added to the routine assay mixture was used as a blank. The activity of ornithine decarboxylase was expressed as nmoles of released CO$_2$ per milliliter of tissue extract per 30 minutes unless indicated otherwise. Initial experiments were carried out with 5 $\mu$M l-ornithine, 0.05 mM pyridoxal-5-phosphate, and without the addition of dithiothreitol to the incubation and the homogenization mediums. In these experiments, a 15-ml vaccine bottle and a small glass vial were used for incubation rather than the 25-ml flask and the polyethylene center well described above. In this case, Hyamine was transferred to counting vials with repeated washes of the small glass vial. The activity, either in the presence or the absence of dithiothreitol, increased linearly with the amount of enzyme extract up to 0.8 ml and with the duration of incubation up to 45 minutes. The activity from two different enzyme extracts was additive.

For measurement of the stoichiometry between the release of $^{14}$CO$_2$ and the formation of [U-$^{14}$C]putrescine, incubations were carried out as described above with [U-$^{14}$C]d/-ornithine instead of [U-$^{14}$C]l-ornithine. Substrate concentration was varied by the addition of cold l-ornithine. The reaction was halted by the injection of 1 ml of 1 M putrescine and 30 mM ornithine in 20% trichloroacetic acid. Extractions of putrescine with butanol and electrophoresis were performed as described by Pegg and Williams-Ashman.

### Results

**Time Course after Aortic Constriction.**—Ornithine decarboxylase activity in rat hearts after aortic constriction and sham-operation was studied at 2, 4, 6, 8, and 18 hours and 2, 3, 5, 10, and 21 days postoperatively, using an initially low substrate concentration (5 $\mu$M l-ornithine) without the addition of dithiothreitol (Table 1); chloral hydrate was used for anesthesia. Hearts of unoperated, unanesthetized rats were the source of the 0-hour value. At 4 hours postoperatively, the enzyme activity in hearts of rats with constricted aortas was increased nearly twofold compared with that in hearts of control rats (0-hour value) and about threefold compared with that in hearts of sham-operated rats. Thereafter, the enzyme activity in hearts of rats with constricted aortas declined; by 18 hours postoperatively, the enzyme activity in hearts of rats with constricted aortas declined below that of unoperated control rats.

### Table 1

<table>
<thead>
<tr>
<th>Time after operation</th>
<th>Sham operation</th>
<th>Aortic constriction</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 hour</td>
<td>92 ± 11 (10)</td>
<td>131 ± 30 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>2 hours</td>
<td>109 ± 6 (8)</td>
<td>177 ± 38 (14)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>4 hours</td>
<td>50 ± 15 (13)</td>
<td>108 ± 20 (10)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6 hours</td>
<td>15 ± 5 (7)</td>
<td>85 ± 24 (4)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>8 hours</td>
<td>10 ± 1 (4)</td>
<td>37 ± 3 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>18 hours</td>
<td>26 ± 5 (11)</td>
<td>102 ± 23 (9)</td>
<td></td>
</tr>
<tr>
<td>2 days</td>
<td>85 ± 19 (7)</td>
<td>114 ± 14 (9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>3 days</td>
<td>81 ± 6 (9)</td>
<td>219 ± 23 (4)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>5 days</td>
<td>122 ± 14 (4)</td>
<td>225 ± 26 (9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>10 days</td>
<td>131 ± 12 (10)</td>
<td>129 ± 28 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>21 days</td>
<td>113 ± 27 (8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All values are means ± S.E. Numbers in parentheses indicate the numbers of sets of rats used for each assay; 2-4 hearts were pooled for each set. Assays were performed at low substrate concentration (5 $\mu$M l-ornithine) without addition of dithiothreitol. Chloral hydrate was used for anesthesia. $P$ values indicate the significance of the difference between the activities in rat heart after sham-operation and after aortic constriction at each time.

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in control rat hearts. The enzyme activity in hearts of sham-operated rats fell postoperatively for 8 hours with a half-life of 1.7 hours. The enzyme activity in rats with aortic constriction and in those with sham operations rebounded after 2 days, but the activity in the hearts of rats with aortic constriction exceeded that in the hearts of sham-operated rats from 3 to 10 days postoperatively.

The study of the time course of the ornithine decarboxylase activity after aortic constriction was repeated using ether anesthesia and an assay performed at a higher l-ornithine concentration (0.1 mM). Again, the same changes were observed. A significant increase in the enzyme activity in the hearts of rats with constricted aortas compared with that in the hearts of sham-operated rats was observed as early as 2 hours postoperatively; enzyme activity was 0.86 ± 0.12 nmoles of CO₂ for six sham-operated rats and 1.51 ± 0.24 nmoles of CO₂ for six rats with constricted aortas (P<0.05). At 4 hours, the values were 0.88 ± 0.20 nmoles of CO₂ for five sham-operated rats and 2.68 ± 0.57 nmoles of CO₂ for four rats with constricted aortas (P<0.02).

In view of a report that chloral hydrate inhibited protein synthesis in a protozoan (38), the effect of chloral hydrate on the cardiac ornithine decarboxylase activity was studied at 6 and 22 hours after administration of the anesthetic. Although no effect was observed at 6 hours, a significant depression of the enzyme activity was seen at 22 hours (Fig. 1). Ether anesthesia did not cause significant changes in the enzyme activity.

Figure 2 shows the heart weights after sham operation and after aortic constriction. In hearts of sham-operated rats, as well as in those of rats with constricted aortas, the
average loss in body weight 1 day after operation was about 6%. Within the first several days after the operation, heart weights in sham-operated rats declined by about 5%, and they took 3-5 days to return to their preoperative level. The decrease in heart weight was not attributable to loss of water in the heart. In rats with constricted aortas, the regression in heart weight did not occur. The fastest growth rate of the heart was achieved between 5 and 10 days postoperatively.

The rise and fall in ornithine decarboxylase activity seemed to correlate with the growth and the regression of the hearts. In sham-operated rats, the decline in the enzyme activity 4-18 hours postoperatively preceded the regression of the heart observed during the first 3 days, and the subsequent rise in the enzyme activity after 2 days fit very well with the return of developmental growth during days 3-21. In rats with aortic constriction, the increased work load on the heart caused it to stay constant or grow in spite of the general regression of tissues due to the operation. Except during the fall in the enzyme activity at 18 hours, which may reflect the effect of the general regression, ornithine decarboxylase activity was elevated above the level in the sham-operated rats. The high activity observed at 5 and 10 days may be related to the fast rate of growth of the heart in rats with aortic constriction at that time.

Some Properties of Cardiac Ornithine Decarboxylase.—Extracts from hearts of rats with aortic constriction for a period of 5-10 days were used for studies of the enzyme. Blanks were processed at every point of each experiment. Figure 3 shows that the apparent Km for L-ornithine as a substrate was about 0.03 mM without dithiothreitol. A slightly higher Km for L-ornithine as a substrate was reported with the three-hundredfold purified rat prostate ornithine decarboxylase (0.1 mM) (36), with the crude extract of rat prostate (0.2 mM) (30), and with the crude extract of regenerating liver (0.2 mM) (30). The release of CO₂ from L-ornithine by cardiac extracts was completely stoichiometric with the formation of putrescine (Fig. 3). The stoichiometry between evolution of CO₂ and production of putrescine from ornithine has been established in crude, ultracentrifuged, soluble fractions of homogenates of rat liver (39), rat prostate (30), and mouse skin (40). Cold L-ornithine added to the incubation medium was as effective as twice the amount of dL-ornithine in reducing the counts in Hyamine, indicating that cardiac ornithine decarboxylase is active only on L-ornithine. Maximal rate of ornithine decarboxylation occurred at pH 6.6-6.8 in the absence of dithiothreitol.

During the course of the study, a stimulatory effect of dithiothreitol on the ornithine decarboxylase activity was reported (41). The optimum dithiothreitol concentration in our incubation medium was 0.1-0.5 mM; this concentration caused an increase in the enzyme activity of about threefold (Fig. 4). At 5 mM, dithiothreitol was less stimulatory, and, in several other experiments, it was either nonstimulatory or inhibitory. The blank value, which is partially due to the nonenzymatic decarboxylation of ornithine by pyridoxal-5-phosphate, was lowest at 0.1-0.5 mM dithiothreitol. Therefore, 0.5 mM dithiothreitol was added routinely to the homogenizing medium, and the dithiothreitol concentration in the final incubation medium was adjusted to 0.25...
In contrast to our results, three-hundred-fold purified rat prostate ornithine decarboxylase is reported to have a lower Vmax at 0.5 mM dithiothreitol than it does at 5 mM (36). The possibility that isoenzymes of l-ornithine decarboxylase are present in mammalian cells requires further investigation.

In other studies of the characteristics of the enzyme, it was found that even the crude extracts used in these studies showed a nearly absolute requirement for pyridoxal-5-phosphate, with a saturation level at 0.05 mM and that the maximal rate of ornithine decarboxylation occurred at pH 6.7 in the presence of dithiothreitol, the same pH as without dithiothreitol.

The apparent Km for l-ornithine was slightly higher (0.06 mM) in the presence of dithiothreitol than it was in the absence of the drug (Fig. 5). Putrescine showed a competitive inhibition with an apparent Ki of 0.4 mM, which is slightly lower than the previously reported value (1 mM) (30, 36). Glycylglycine buffer at pH 7.2 (100 mM) was not superior to phosphate buffer either with or without dithiothreitol. Above 100 mM sodium-potassium phosphate, the enzyme activity was depressed, falling to about one-third of the value at 250 mM.

Effects of Actinomycin D, 8-Azaguanine, and Cycloheximide on Cardiac Ornithine Decarboxylase.—To elucidate the mechanism that controlled the activity of ornithine decarboxylase during the early stages of cardiac hypertrophy, the effects of actinomycin D, 8-azaguanine, and cycloheximide on the enzyme activity 4 hours after aortic constriction were studied. Only ether anesthesia was used. Actinomycin D, 160 μg or 400 μg, injected 40 minutes prior to operation completely abolished the response of the enzyme activity in the hearts of rats with aortic constriction 4 hours after the operation (Table 2). Actinomycin D injected 1–1.5 minutes before completion of the operation failed to inhibit the response completely. When 160 μg of actinomycin D was given 30 minutes after aortic constriction, virtually no effect was observed. The exact time required
for actinomycin D to diffuse into the cardiac cell nuclei and inhibit transcription is not known; however, the transcription required for the increased synthesis of ornithine decarboxylase appears to occur quite early after the aortic constriction. Even the dose of 400 μg, an amount which would eventually be lethal for this size of rat, given at the time of operation did not completely inhibit the increase in the enzyme activity. In one group of hearts from rats treated with actinomycin D and subjected to sham operations, a slight rise in the enzyme activity was observed, but the rise was not significant. In a group of normal rats, actinomycin D administration did not cause an increase in the enzyme activity 4 hours later.

In regenerating liver, actinomycin D is effective in preventing the increase in ornithine decarboxylase activity when it is administered intraperitoneally at the time of partial hepatectomy, and the sensitivity to actinomycin D lasts about 3 hours following the operation (42). Actinomycin D administered intraperitoneally has less effect than does the same amount of the drug administered intravenously on RNA labeling in the rat heart (43). Since actinomycin D was administered intravenously on RNA labeling in the rat heart (43), the earlier time required for effect in the heart as compared with that in the liver might reflect either a difference in the diffusion rate of the drug into the nuclei or a difference in the nature of the stimuli. The process of the enzyme induction in hearts of rats with constricted aortas seemed to be specifically susceptible to actinomycin D, since in hearts of sham-operated rats, the enzyme activity in hearts of sham-operated rats was the same in hearts of rats with aortic constriction (45). The enzyme activity in hearts of rats with aortic constriction was not attributable to a difference in uptake of actinomycin D by each heart, since uptake is not attributable to a difference in the same level as it did in a control heart. This finding is not attributable to actinomycin D, since in hearts of sham-operated rats, the enzyme synthesis appeared to proceed at the same level as it did in a control heart. This finding is not attributable to actinomycin D, since in hearts of sham-operated rats, the enzyme synthesis appeared to proceed at the same level as it did in a control heart.

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**Table 2**

**Effect of Actinomycin D on Cardiac Ornithine Decarboxylase Activity (nmol CO₂/mg 30 min⁻¹)**

<table>
<thead>
<tr>
<th></th>
<th>Saline control (μg)</th>
<th>Actinomycin D (μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(400, 60 min)</td>
<td>(100, 1.5 min)</td>
</tr>
<tr>
<td></td>
<td>(100, 1.5 min)</td>
<td>(100, 1.5 min)</td>
</tr>
<tr>
<td></td>
<td>(100, 30 min)</td>
<td></td>
</tr>
<tr>
<td>Sham operation</td>
<td>1.16 ± 0.23 (4)</td>
<td>1.26 ± 0.04 (2)</td>
</tr>
<tr>
<td></td>
<td>1.64 ± 0.29 (8)</td>
<td>0.88 ± 0.19 (9)*</td>
</tr>
<tr>
<td></td>
<td>0.98 ± 0.12 (4)</td>
<td>0.88 ± 0.19 (5)*</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Actinomycin D, 180 or 400 μg dissolved in saline was given intravenously 40 minutes before the operation (−40 min), 1.5 minutes before the end of the operation (+1.5 min), or 30 minutes after the operation (+30 min). Controls received saline only. All rats were killed 4 hours after operation. All values are averages ± se, and number of rats tested is shown in parentheses. Control values were essentially the same regardless of time of saline injection; therefore, they were pooled together. P values indicate the significance of the difference between hearts from rats with sham operations and those with aortic constriction in each category. NS = not significant.

*P < 0.05 compared with the controls having aortic constriction. No other values were significantly different from the appropriate control.
Effect of 8-azaguanine on cardiac ornithine decarboxylase activity. 8-Azaguanine, 40 mg, dissolved in saline at pH 8.5 as described in the text was injected intraperitoneally 30 minutes prior to operation. Control rats received solvent only. All rats were killed 4 hours after operation. Means ± SE from 4-7 hearts are shown.

Constricted aortas by the administration of 8-azaguanine or cycloheximide (Fig. 6 and Table 3).

The purine analogue, 8-azaguanine, inhibits protein synthesis apparently through the formation of fraudulent or defective mRNA (37). 8-Azaguanine administered 30 minutes prior to the operation depressed the enzyme activity in hearts of rats with aortic constriction as well as in hearts of sham-operated rats (Fig. 6).

Cycloheximide, which inhibits protein synthesis at the level of peptide chain formation (44), was potent in decreasing the enzyme activity in hearts of rats subjected to sham operation or to aortic constriction, even when it was administered as late as 1 hour prior to death (Table 3). The half-life of ornithine decarboxylase in the heart, when the 3-hour values were estimated by interpolation, was 26 minutes for sham-operated rats and 33 minutes for rats with constricted aortas following administration of cycloheximide. Shorter, yet comparable, half-life periods of the enzyme have been reported for rat liver following administration of cycloheximide (10-15 minutes) and of puromycin (12 minutes) and during the decline of enzyme activity after stimulation by growth hormone (24 minutes) (42, 45).

Discussion

One of the most striking findings emerging from this study is the quick, sensitive response of ornithine decarboxylase that precedes cardiac hypertrophy or regression observed days later. In this experimental model of rat cardiac hypertrophy produced by constriction of the aorta, the earliest demonstrable changes in nucleic acid and protein metabolism are (1) an increase in labeling of RNA by $^{32}$P at 4 hours after operation (35, 46), (2) an increase in labeling of total protein at 6 hours (43), and (3) an increase in RNA synthesis at 4-8 hours when corrected for precursor labeling (35). RNA polymerase activity in vitro was not stimulated until 12 hours in one study (47), but recently a biphasic response similar to that of ornithine decarboxylase was reported with peaks at 4 hours and at 3-4 days (48). The early changes in synthesis of polyamines suggest an important role for these

| TABLE 3 |
| Effect of Cycloheximide on Cardiac Ornithine Decarboxylase Activity (nmoles CO$_2$/ml 90 min$^{-1}$) |
|----------|----------|----------|
|          | Control  | Cycloheximide |
| Sham operation | 0.90 ± 0.21 (4) | 0.18 ± 0.06 (6) |
| Aortic constriction | 2.31 ± 0.46 (6) | 0.62 ± 0.10 (5) |
|              |          | 0.08 ± 0.07 (4)* |

Cycloheximide, 200 µg, was given intraperitoneally 3 hours after operation. Control rats received 0.5 ml of saline. All rats were killed 4 hours after operation, and the enzyme was measured. Averages ± SE are shown. The number of rats is given in parentheses.

This group received 5 mg of cycloheximide at the time of operation.
substances in the growing heart. In the rabbit, both ornithine decarboxylase and S-adenosylmethionine decarboxylase, which catalyzes the formation of spermidine from putrescine and S-adenosylmethionine, were recently found to be increased in the right ventricle 4 hours after pulmonary constriction (29). An increase in spermine concentration in the rabbit heart after aortic constriction has been reported to occur as early as 2 hours after operation (28).

It has been a generally accepted practice to use sham-operated animals as a control for animals with aortic or pulmonary constriction. The metabolic changes in sham-operated animals should be considered, because changes in animals with aortic or pulmonary constriction are superimposed on these alterations. In view of the usual relationship between body weights and heart weights in growing rats (49), some regression of the heart might be expected with loss of body weight provided an alteration in fluid balance is excluded. In our study, the reduction in the ornithine decarboxylase activity in hearts of sham-operated rats at 6 hours after the operation may be as meaningful as the increase in the enzyme activity as early as 2 hours after aortic constriction in indicating a regulatory role for the enzyme in the growth of the heart.

Chloral hydrate is known to be a depressant of cardiac contractility, as are many other anesthetics. It is not certain whether chloral hydrate depresses the ornithine decarboxylase activity in the heart at 22 hours after administration by direct inhibition of protein synthesis or by some less direct mechanism. Inhibition of protein synthesis in protozoa is immediate and requires a high concentration of chloral hydrate (38).

The stimulation of ornithine decarboxylase in cardiac hypertrophy is not as spectacular as is that seen in the regenerating liver (31, 32) or in response to growth hormone administration in liver (45) or kidney (50). The relatively high base-line activity of the enzyme in the heart may account for the apparently modest increase in the enzyme activity in cardiac hypertrophy. The Vmax of the stimulated ornithine decarboxylase was only slightly higher in the kidney stimulated with growth hormone than it was in the hypertrophying heart (50).

Growth hormone also stimulates the ornithine decarboxylase activity in the hypophysectomized rat heart 4 hours after administration (50). The increase is, interestingly, about twofold, similar to the increase in cardiac hypertrophy. Although an increased growth hormone secretion may not account for the early rise in the hearts of rats with aortic constriction, an interaction between growth hormone and direct stress by aortic constriction might be involved in the effect on cardiac ornithine decarboxylase.

If the polyamines play an important role in cardiac hypertrophy, the regulation of ornithine decarboxylase activity is of the utmost interest. Our study indicates that RNA and protein synthesis are involved in the response to aortic constriction that results in a rapid, though modest, increase in the activity of ornithine decarboxylase.

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Ornithine Decarboxylase in Cardiac Hypertrophy in the Rat
S. MATSUSHITA, R. K. SOGANI and M. S. RABEN

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