Hedin and Rowland (1) showed in 1901 that the press-juice of muscle contains a proteolytic enzyme, relatively weak, which acts in neutral, acid, and alkaline media. The digestion of the proteins in the press-juice goes less well in acid than in alkaline reacting media. So far as we are aware no other work has been published on the autolysis of muscle tissue as related to its H ion concentration, and it is evident that no conclusions can be drawn from the behavior of press-juice as to whole muscle tissue. Muscles are well known to undergo atrophy and under the same conditions which cause atrophy of epithelial organs; namely, a diminished blood supply. It was considered worth while, therefore, to study in some detail the autolytic behavior of muscle tissue and the effect which reaction has upon it. A preliminary report was made on this work in 1918 (2), in which it was stated that muscle tissues, striated, smooth, and cardiac, were found to autolyze at increased speed and to a greater extent in a slightly acid medium than in the control or alkaline digests. Our subsequent work has abundantly confirmed this result as far as mammalian tissue is concerned, but has brought out some striking anomalies in the behavior of muscle tissue from some of the lower animals.

In Tables I to IV we have selected a few typical cases from the large number collected\(^1\) to illustrate the autolytic behavior of various types of muscles. The technique employed is the same as

\(^1\) We desire to express our indebtedness to Drs. Sneeberger and Hattleberg, and Miss Gormley who collected much data confirming the findings reported here.
that used in previous studies. Autolysis is measured by amino acid production in trichloroacetic acid filtrates from the precipitated samples of tissue.

**Warm Blooded, Striated Muscle.**

**TABLE I.**

**Dog Muscle.**

| No. | Condition | 0.2 N amino acids. | Digestion. |
|-----|-----------|--------------------|------------|
|     |           | cc. cc. cc. cc. cc. cc. per cent | cc. cc. cc. cc. cc. cc. per cent |
| 0   | 1         | 5                  | 10         | 40         |
| I   | Control   | 0.10 0.25 0.55 0.60 0.85 0.95 0.85 | 7.7         |
| II  | +25 cc. 0.2 N HCl | 0.10 0.40 0.85 0.90 1.25 1.40 1.30 | 9.4         |
| III | +50 “ 0.2 “ | 0.10 0.55 1.25 1.75 1.70 1.85 1.75 | 12.6        |
| IV  | +100 “ 0.2 “ | 0.10 0.10 0.35 0.30 0.40 0.45 0.35 | 2.5         |
| V   | +12.5 “ 0.2 “ | 0.10 0.25 0.35 0.45 0.45 0.45 0.35 | 2.5         |
| VI  | NaOH      | 0.10 0.25 0.35 0.30 0.40 0.45 0.35 | 2.5         |
|     | Control +25 cc. 0.2 N NaOH | 0.10 0.25 0.35 0.30 0.40 0.45 0.35 | 2.5         |

Total N in 5 cc. brei ...................... 11.05 cc. 0.2 N.

**TABLE II.**

**Beef Muscle.**

| No. | Condition | 0.2 N amino acids. | Digestion. |
|-----|-----------|--------------------|------------|
|     |           | cc. cc. cc. cc. cc. cc. per cent | cc. cc. cc. cc. cc. cc. per cent |
| 0   | 1         | 5                  | 10         | 40         |
| I   | Control   | 0.15 0.25 0.30 0.40 0.45 0.30 0.30 | 2.16        |
| II  | +5 cc. 0.2 N HCl | 0.15 0.25 0.35 0.55 0.60 0.45 0.32 | 2.49        |
| III | +10 “ 0.2 “ | 0.15 0.25 0.50 0.75 0.80 0.65 0.68 | 2.49        |
| IV  | +20 “ 0.2 “ | 0.15 0.30 0.55 0.90 1.10 0.95 0.85 | 2.65        |
| V   | +30 “ 0.2 “ | 0.15 0.30 0.55 1.15 1.30 1.15 0.82 | 2.65        |
| VI  | +50 “ 0.2 “ | 0.15 0.30 0.70 1.15 1.25 1.10 0.93 | 2.65        |
| VII | +100 “ 0.2 “ | 0.15 0.15 0.25 0.30 0.35 0.20 0.14 | 2.65        |
| VIII| +5 “ 0.2 “ NaOH | 0.15 0.15 0.30 0.40 0.45 0.30 0.21 | 2.65        |
| IX  | +20 “ 0.2 “ | 0.15 0.20 0.25 0.30 0.40 0.25 0.18 | 2.65        |
| X   | +30 “ 0.2 “ | 0.15 0.15 0.25 0.35 0.35 0.20 0.14 | 2.65        |

Total N in 5 cc. brei .................................. 11.10 cc. 0.2 N.
### TABLE III.

**Chicken Muscle.**

| No. | Condition                    | 0.2 N amino acids | Digestion |
|-----|------------------------------|-------------------|-----------|
|     |                              | Days              | per cent  |
|     |                             | cc.  | cc.  | cc.  | cc.  | 0 | 3 | 7 | 10 | 20 | 30 | 40 |
| I   | Control (red muscle)         | 0.25 | 0.35 | 0.60 | 0.65 | 0.40 | 5.62 |
| II  | +25 cc. 0.2 N HCl            | 0.25 | 0.30 | 0.85 | 0.95 | 0.70 | 8.22 |
| III | +50 " 0.2 " "               | 0.25 | 0.50 | 1.00 | 1.20 | 0.95 | 10.39 |
| IV  | +75 " 0.2 " "               | 0.25 | 0.55 | 0.95 | 0.95 | 0.70 | 8.22 |
| V   | +100 " 0.2 " "              | 0.25 | 0.45 | 0.45 | 0.45 | 0.20 | 3.89 |
| VI  | +12.5 " 0.2 " NaOH          | 0.25 | 0.20 | 0.20 | 0.30 | 0.05 | 2.60 |
| VII | +25 " 0.2 " "               | 0.25 | 0.20 | 0.25 | 0.50 | 0.25 | 4.32 |

Total N in 6.25 cc. brei. 12 cc. 0.2 N.

|   | Control (white muscle)       | 0.25 | 0.35 | 0.45 | 0.45 | 0.20 | 3.48 |
|   | +25 cc. 0.2 N HCl            | 0.25 | 0.50 | 0.85 | 0.70 | 0.45 | 5.41 |
| X  | +50 " 0.2 " "               | 0.25 | 0.50 | 1.00 | 0.85 | 0.60 | 6.57 |
| XI | +100 " 0.2 " "              | 0.25 | 0.35 | 0.50 | 0.40 | 0.15 | 3.09 |
| XII| +12.5 " 0.2 " NaOH          | 0.25 | 0.40 | 0.25 | 0.25 | 0.00 | 1.93 |
| XIII| +25 " 0.2 " "              | 0.25 | 0.40 | 0.45 | 0.25 | 0.00 | 1.93 |

Total N in 6.25 cc. brei. 13.5 cc. 0.2 N.

### TABLE IV.

**Rabbit Muscle.**

| No. | Condition                    | 0.2 N amino acids | Digestion |
|-----|------------------------------|-------------------|-----------|
|     |                             | Days              | per cent  |
|     |                             | cc.  | cc.  | cc.  | cc.  | 0 | 1 | 5 | 10 | 20 | 30 | 40 |
| I   | Control                      | 0.20 | 0.20 | 0.30 | 0.30 | 0.65 | 0.45 |
| II  | +25 cc. 0.2 N NaOH           | 0.20 | 0.20 | 0.25 | 0.25 | 0.30 | 0.35 |
| III | +10 " 0.2 " "               | 0.20 | 0.25 | 0.25 | 0.25 | 0.55 | 0.35 |
| IV  | +5 " 0.2 " "                | 0.20 | 0.25 | 0.25 | 0.25 | 0.45 | 0.25 |
| V   | +5 " 0.2 " HCl              | 0.20 | 0.30 | 0.40 | 0.55 | 1.00 | 0.80 |
| VI  | +10 " 0.2 " "               | 0.20 | 0.30 | 0.47 | 0.70 | 1.20 | 1.00 |
| VII | +25 " 0.2 " "               | 0.20 | 0.30 | 0.55 | 0.90 | 1.20 | 1.00 |
| VIII| +50 " 0.2 " "               | 0.20 | 0.37 | 0.55 | 0.75 | 1.00 | 0.80 |
| IX  | +100 " 0.2 " "              | 0.20 | 0.25 | 0.25 | 0.25 | 0.45 | 0.25 |
| X   | +150 " 0.2 " "              | 0.20 | 0.20 | 0.25 | 0.25 | 0.45 | 0.25 |
The data above show clearly that the usual mechanism determining autolysis in epithelial tissues is operative in striated muscle. The extent of digestion even under optimum conditions is, however, very much less. This may be explained in part as due to the relatively large mass of connective tissue present in striated muscle, which does not become substratum for the proteases present under the conditions of the experiment, nor under conditions met with in the body. We believe it is also indicative of structural proteins within the muscle fibers themselves which are not digested. This resistance of the muscle proteins to cleavage is a striking difference between it and epithelial tissues. To it we attribute the greater persistence of muscle cells undergoing atrophy as compared with many glandular atrophies. Another point of interest is the greater extent to which autolysis proceeds in the active pigmented muscle of fowl as compared with the less active unpigmented muscle tissue. There appears to be more potential substratum in the active tissue than in the inactive.

**Warm Blooded, Cardiac Muscle.**

**TABLE V.**

Pig Heart Muscle.

| No. | Condition. | 0.2 N amino acids. | Net gain. | Digestion. |
|-----|------------|-------------------|-----------|------------|
|     |            | Days.             | cc.       | cc.        | cc.        | cc.        | cc.        | cc.        | Digestion. |
| I   | Control    | 0.20 0.40 0.55 0.60 0.95 1.00 0.80 | 6.53      |
| II  | +5 cc.0.2 N HCl | 0.20 0.50 0.75 1.00 1.25 1.40 1.29 | 9.81      |
| III | +10 " 0.2 " " " | 0.20 0.50 0.75 1.00 1.25 1.55 1.35 11.02 |
| IV  | +25 " 0.2 " " " | 0.20 0.55 1.00 1.30 1.55 1.65 1.45 11.84 |
| V   | +50 " 0.2 " " " | 0.20 0.65 1.00 1.20 1.30 1.60 1.40 11.43 |
| VI  | +75 " 0.2 " " " | 0.20 0.35 0.35 0.40 0.40 0.20 0.20 6.63 |
| VII | +100 " 0.2 " " " | 0.20 0.20 0.25 0.25 0.30 0.35 0.15 1.22 |
| VIII| +12.5 " 0.2 " " " | 0.20 0.30 0.30 0.35 0.35 0.35 0.15 1.22 |
| IX  | Control +25 cc.0.2 N NaOH | 0.20 0.25 0.30 0.30 0.30 0.30 0.10 0.9 |
|     | Control +25 cc.0.2 N NaOH | 0.20 0.25 0.30 0.30 0.30 0.30 0.10 0.9 |
**K. K. Chen and H. C. Bradley**

**TABLE VI.**

*Beef Heart.*

| No. | Condition | 0.2 N amino acids. | Autolysis. |
|-----|-----------|-------------------|------------|
|     |           | Days.             | Net gain.  | per cent |
|     |           | cc. cc. cc. cc. cc. |            |          |
| I   | Control   | 0.15 0.30 0.35 0.40 0.55 | 0.60 | 0.60 | 0.45 | 4.0 |
| II  | +5 cc. 0.2 N HCl | 0.15 0.30 0.50 0.55 | 0.70 | 0.85 | 0.70 | 6.2 |
| III | +10 " 0.2 " " " | 0.15 0.35 0.75 0.75 | 0.90 | 1.05 | 0.90 | 8.0 |
| IV  | +25 " 0.2 " " " | 0.15 0.35 0.85 0.90 | 1.15 | 1.35 | 1.00 | 8.6 |
| V   | +50 " 0.2 " " " | 0.15 0.40 0.75 0.85 | 1.05 | 1.00 | 0.85 | 7.6 |
| VI  | +100 " 0.2 " " " | 0.15 0.15 0.20 0.20 | 0.25 | 0.25 | 0.10 | 0.9 |
| VII | +5 " 0.2 " NaOH | 0.15 0.25 0.30 0.35 | 0.40 | 0.25 | 4.9 |
| VII | +10 " 0.2 " " " | 0.15 0.20 0.25 0.30 | 0.35 | 0.35 | 0.20 | 1.8 |
| IX  | +20 " 0.2 " " " | 0.15 0.20 0.25 0.25 | 0.25 | 0.25 | 0.10 | 0.9 |
| X   | +30 " 0.2 " " " | 0.15 0.15 0.20 0.20 | 0.20 | 0.20 | 0.05 | 0.5 |

Total N in 6.25 cc. brei: 11.05 cc. 0.2 N.

**Warm Blooded, Smooth Muscle.**

Cardiac and smooth muscle are thus seen to behave like skeletal muscle. Acidity conditions autolysis while maintenance of neutrality or alkalinity inhibits digestion. Under optimum conditions autolysis is very small when compared with epithelial tissues.

**TABLE VII.**

*Pig Stomach.*

| No. | Condition | 0.2 N amino acids. | Autolysis. |
|-----|-----------|-------------------|------------|
|     |           | Days.             | Net gain.  | per cent |
|     |           | cc. cc. cc. cc. cc. |            |          |
| I   | Control   | 0.15 0.30 0.45 0.50 0.45 | 0.30 | 0.30 | 3.7 |
| II  | +5 cc. 0.2 N HCl | 0.15 0.30 0.55 0.60 0.60 | 0.45 | 0.45 | 4.9 |
| III | +25 " 0.2 " " " | 0.15 0.40 0.80 0.95 | 0.90 | 0.75 | 7.3 |
| IV  | +50 " 0.2 " " " | 0.15 0.45 0.80 1.00 | 1.00 | 0.90 | 8.6 |
| V   | +100 " 0.2 " " " | 0.15 0.20 0.30 0.50 | 0.25 | 0.10 | 2.0 |
| VI  | +20 " 0.2 " NaOH | 0.15 0.20 0.20 0.35 | 0.30 0.15 | 2.4 |
| VII | +30 " 0.2 " " " | 0.15 0.15 0.20 0.20 | 0.20 0.05 | 1.6 |
TABLE VIII.

**Beef Stomach.**

| No. | Condition | 0.2 N amino acids. | Net gain. |
|-----|-----------|--------------------|----------|
|     |           | Days              |          |
|     |           | cc.   | cc.   | cc.   | cc.   | Autolysis. | per cent |
| I   | Control   | 0.250 | 0.350 | 0.550 | 0.550 | 0.30      | 4.5      |
| II  | +25 cc. 0.2 N HCl | 0.250 | 0.300 | 0.500 | 0.550 | 0.30      | 4.5      |
| III | +50 cc. 0.2 N HCl | 0.250 | 0.300 | 0.600 | 0.700 | 0.45      | 8.8      |
| IV  | +100 cc. 0.2 N HCl | 0.250 | 0.250 | 0.250 | 0.250 | 0.00      |          |
| V   | +10 cc. 0.2 N NaOH | 0.250 | 0.350 | 0.350 | 0.350 | 0.10      | 2.9      |
| VI  | +25 cc. 0.2 N NaOH | 0.250 | 0.250 | 0.350 | 0.350 | 0.10      | 2.9      |

**pH Changes in Autolyzing Muscle.**

In Table IX are given the changes in H ion concentration which muscle tissue undergoes during autolysis. In addition to the control, various reactions have been experimentally induced which cover the usual range in digestion experiments. It will be seen that the drift resembles similar changes in autolyzing liver brei (3). The reactions tend to converge toward a mean value of about pH 7—.

TABLE IX.

**Rabbit Muscle.**

| No. | Condition | pH |
|-----|-----------|----|
|     |           | Days |
|     |           | 0   | 1   | 2   | 4   | 7   | 10  | 20  |
| I   | 50 cc. 0.2 N NaOH | 10.34 | 9.49 | 9.57 | 9.08 | 8.63 | 8.39 | 8.04 | 8.04 |
| II  | 25 cc. 0.2 N HCl | 8.60 | 7.61 | 7.55 | 7.30 | 7.19 | 7.37 | 7.05 | 7.09 |
| III | 10 cc. 0.2 N HCl | 6.87 | 6.62 | 6.53 | 6.53 | 6.49 | 6.53 | 6.49 | 6.51 |
| IV  | 5 cc. 0.2 N HCl | 6.40 | 6.28 | 6.26 | 6.25 | 6.25 | 6.25 | 6.25 | 6.23 |
| V   | Control.      | 5.73 | 5.55 | 5.37 | 5.91 | 5.92 | 5.95 | 5.96 | 5.91 |
| VI  | 5 cc. 0.2 N NaOH | 4.93 | 5.10 | 5.17 | 5.17 | 5.17 | 5.17 | 5.17 | 5.17 |
| VII | 10 cc. 0.2 N HCl | 4.35 | 4.57 | 4.59 | 4.59 | 4.59 | 4.59 | 4.59 | 4.59 |
| VIII| 25 cc. 0.2 N HCl | 4.02 | 4.15 | 4.31 | 4.42 | 4.50 | 4.68 | 4.77 | 4.79 |
| IX  | 50 cc. 0.2 N HCl | 2.13 | 3.49 | 3.41 | 3.53 | 3.53 | 3.53 | 3.53 | 3.53 |
| X   | 100 cc. 0.2 N HCl | 1.46 | 2.26 | 2.34 | 2.38 | 2.38 | 2.40 | 2.46 | 2.53 |
| XI  | 150 cc. 0.2 N HCl | 1.02 | 1.68 | 1.75 | 1.79 | 1.72 | 1.72 | 1.54 | 1.53 |
Smooth and cardiac muscle give essentially the same picture as striated muscle, though with less pronounced neutralization of the alkaline breis. In one case pig heart muscle developed the unusually high pH of 5.76 in 4 hours.

**Cold Blooded Muscles.**

While the warm blooded muscles have been characterized by a slow and small autolysis they have all behaved very much alike. In the group of cold blooded muscles examined, however, we have found some interesting variations. Frog striated muscle behaves very much like mammalian tissue. Muscles from the true fishes (teleosts) show marked difference between species, and differ markedly also from muscles of the sharks (elasmobranchs). The muscles from lower cold blooded forms are still more strikingly different from mammalian.

Carp muscle evidently contains considerable potential substratum, as shown by the digestion in the presence of added acid. It does not, however, develop sufficient acidity post mortem to convert any of the muscle proteins into the digestible acid-protein form. The question arises, therefore, as to whether the carp ever undergoes atrophies of its musculature during normal life, or to what extent it can mobilize its proteins in fasting through an acidotic process, general or local. In the case of the salmon it

**TABLE X. Frog Muscle.**

| No. | Condition | 0.2 N amino acids | Days | Autolysis |
|-----|-----------|------------------|------|-----------|
|     |           | cc.              | cc.  | cc.       | cc. | per cent |
| I   | Control   | 0.15             | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |
| II  | +10 cc. 0.2 N HCl | 0.15          | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |
| III | +25 " 0.2 " "   | 0.15          | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |
| IV  | +50 " 0.2 " "   | 0.15          | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |
| V   | +100 " 0.2 " "  | 0.15          | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |
| VI  | +25 " 0.2 " NaOH | 0.15          | 0.30 | 0.55      | 0.60| 0.70      | 0.55 | 7.2  |

Total N in 6.25 cc. brei..........................10.44 cc. 0.2 N.
### Table XI.

**Perch Muscle; Average of Three Experiments.**

| No. | Condition | Net gain in 10 days |
|-----|-----------|---------------------|
| I   | Control   | 0.15                |
| II  | +6.25 cc. 0.2 N HCl | 0.30                |
| III | +12.5 " 0.2 " "     | 0.55                |
| IV  | +25 " 0.2 " "       | 0.80                |
| V   | +50 " 0.2 " "       | 0.45                |
| VI  | +125 " 0.2 " "      | 0.10                |

### Table XII.

**Carp Muscle.**

| No. | Condition | 0.2 N amino acids | Net gain. | Autolysis. |
|-----|-----------|-------------------|-----------|------------|
|     |           | Days.              | cc. cc. cc. cc. cc. | per cent |
| I   | Control   | 0.30 0.35 0.35 0.30 0.30 0.30 0.00 | 2.5 | |
| II  | +10 cc. 0.2 N HCl | 0.30 0.35 0.55 0.80 0.95 1.20 0.90 10.16 | |
| III | +25 " 0.2 " "     | 0.30 0.45 0.90 0.90 1.35 1.50 1.20 12.70 | |
| IV  | +50 " 0.2 " "     | 0.30 0.50 0.70 1.10 1.35 1.55 1.25 13.12 | |
| V   | +100 " 0.2 " "    | 0.30 0.25 0.25 0.25 0.25 0.25 0.00 | |
| VI  | +10 " 0.2 "       | 0.30 0.30 0.30 0.30 0.25 0.20 0.00 | |

Total N in 6.25 cc. brei..........................11.8 cc. 0.2 N.

### Table XIII.

**Mackerel Muscle.**

| No. | Condition | 0.2 N amino acids | Net gain. |
|-----|-----------|-------------------|-----------|
|     |           | Days.              | cc. cc. cc. cc. cc. |
| I   | Control   | 0.20 0.75 0.85 1.60 1.78 1.95 1.75 | |
| II  | +10 cc. 0.2 N HCl | 0.20 0.95 1.52 1.50 2.95 3.47 3.27 | |
| III | +25 " 0.2 " "     | 0.20 0.95 1.51 1.40 2.50 2.95 2.75 | |
| IV  | +50 " 0.2 " "     | 0.20 1.02 1.30 1.90 2.57 2.90 2.70 | |
| V   | +10 " 0.2 " NaOH  | 0.20 0.35 0.33 0.40 0.62 0.83 0.63 | |
| VI  | +25 " 0.2 " "     | 0.20 0.31 0.32 0.50 0.53 0.70 0.50 | |
appears that during the long fast and migration, much of the muscle tissue itself is autolyzed and furnishes the necessary material for the maturing of the sperm and eggs. Whether the carp is able to call upon reserve protein from its muscle tissue would seem to depend largely on whether in fasting a considerable generalized acidosis develops. Postmortem acidity, if any develops, is insufficient to cause its muscle proteins to autolyze. We expect to obtain more data upon the behavior of carp muscle.

**TABLE XIV.**

*Menhaden Muscle.*

| No. | Condition | 0.2 N amino acids. | Net gain in 22 days. |
|-----|-----------|-------------------|---------------------|
|     |           | Days.             | cc. cc. cc. cc. cc. cc. |
| I   | Control   | 0.17 0.27 0.50 1.13 1.35 1.83 | 1.66 |
| II  | +10 cc 0.2 N HCl | 0.17 0.46 0.88 1.85 1.90 2.65 | 2.48 |
| III | +25 " 0.2 " | 0.17 0.50 0.86 1.45 1.60 2.20 | 2.03 |
| IV  | +10 " 0.2 " NaOH | 0.17 0.22 0.26 0.48 0.45 0.77 | 0.60 |
| V   | +25 " 0.2 " | 0.17 0.25 0.30 0.45 0.50 0.75 | 0.58 |

**TABLE XV.**

*Scup Muscle.*

| No. | Condition | 0.2 N amino acids. | Net gain in 21 days. |
|-----|-----------|-------------------|---------------------|
|     |           | Days.             | cc. cc. cc. cc. cc. cc. |
| I   | Control   | 0.10 0.10 0.10 0.17 0.24 0.35 | 0.25 |
| II  | +10 cc 0.2 N HCl | 0.10 0.20 0.40 0.68 0.94 1.20 | 1.10 |
| III | +25 " 0.2 " | 0.10 0.15 0.30 0.50 0.90 1.10 | 1.00 |
| IV  | +10 " 0.2 " NaOH | 0.10 0.08 0.09 0.10 0.20 0.25 | 0.15 |
| V   | +25 " 0.2 " | 0.10 0.09 0.09 0.09 0.10 0.27 | 0.17 |

In this series of salt water fish we find the most active fish, the mackerel, showing the largest autolysis in the control and in the acidified breis as well. While the data are perhaps too meager to draw any conclusions, it at least points in the same direction as the study of pigmented and non-pigmented fowl muscle; namely, that the more active the muscle the more potential substratum it contains and the more acid is produced post mortem also, converting some of the potential substratum into digestible form.
Shark muscle all runs strikingly below the autolytic figures from the bony fishes. The shark is rather sluggish and quickly tires when caught.

### TABLE XVI.
**Hammer Head Shark.**

| No. | Condition | 0.2 N amino acids | Net gain in 20 days |
|-----|-----------|-------------------|--------------------|
| I   | Control   | 0.35 cc. 0.30 cc. 0.50 cc. 0.61 cc. 0.70 cc. | 0.35 |
| II  | +10 cc. 0.2 N HCl | 0.35 cc. 0.43 cc. 0.45 cc. 0.57 cc. 0.74 cc. | 0.50 |
| III | +25 " 0.2 " " " | 0.35 cc. 0.40 cc. 0.47 cc. 0.58 cc. 0.75 cc. | 0.55 |
| IV  | +10 " 0.2 " NaOH... | 0.35 cc. 0.32 cc. 0.30 cc. 0.42 cc. 0.50 cc. | 0.10 |
| V   | +25 " 0.2 " " " | 0.35 cc. 0.32 cc. 0.38 cc. 0.43 cc. 0.45 cc. | 0.10 |

### TABLE XVII.
**Mackerel Shark Muscle.**

| No. | Condition | 0.2 N amino acids | Net gain in 14 days |
|-----|-----------|-------------------|--------------------|
| I   | Control   | 0.10 cc. 0.25 cc. 0.30 cc. 0.40 cc. | 0.30 |
| II  | +25 cc. 0.2 N HCl | 0.10 cc. 0.25 cc. 0.35 cc. | 0.40 |
| III | +25 " 0.2 " " " | 0.10 cc. 0.20 cc. 0.20 cc. | 0.10 |

### TABLE XVIII.
**Dog Fish Muscle.**

| No. | Condition | 0.2 N amino acids | Net gain |
|-----|-----------|-------------------|---------|
| I   | Control   | 0.25 cc. 0.30 cc. 0.40 cc. 0.60 cc. 0.65 cc. | 0.40 |
| II  | +12.5 cc. 0.2 N HCl | 0.25 cc. 0.50 cc. 0.75 cc. | 0.55 |
| III | +25 " 0.2 " " " | 0.25 cc. 0.30 cc. 0.45 cc. | 0.70 |
| IV  | +12.5 " 0.2 " " NaOH... | 0.25 cc. 0.30 cc. 0.35 cc. | 0.15 |

In Tables XIX and XX are the autolytic data on muscles of two mollusces. Sycotypus is a carnivorous gasteropod, slow of movement and evidently of low organization and metabolic
activity. The squid is the most active type of mollusc, a rapid swimmer, with well developed sense organs and nervous organization. It gives every evidence of a relatively high pitched metabolic rate.

In both forms muscle autolysis is very small, and but slightly increased by increased acidity. In these types we find no evidence of increased potential substratum in the more active muscle. It is

| TABLE XIX. |
|-------------|
| **Sycotypus Muscle.** |

| No. | Condition          | 0.2 N amino acids. | Net gain in 20 days. |
|-----|--------------------|--------------------|----------------------|
| I   | Control            | cc.                | cc.                  | cc.                  | cc.                  | 0.50     |
| II  | +40 cc. Na acetic acid | 0.55               | 0.65                 | 0.65                 | 1.05                 | 0.65     |

| TABLE XX. |
|-------------|
| **Squid Muscle.** |

| No. | Condition                  | 0.2 N amino acids. | Net gain. |
|-----|---------------------------|--------------------|----------------|
| I   | Control                   | cc.                | cc.           | cc.           | cc.           | 0.45     |
| II  | +12.5 cc. 0.2 N HCl       | 0.65               | 0.90           | 1.00          | 1.10          | 0.45     |
| III | +12.5 cc. 0.2 N NaOH      | 0.65               | 0.90           | 0.95          | 1.05          | 0.40     |
| IV  | +5 gm. CaCO₃              | 0.65               | 0.85           | 1.05          | 1.10          | 0.45     |

doubtful whether atrophic changes in the muscles of these forms ever go on in the same functional way in which they occur in the salmon or in the mammal for example. Muscle proteins themselves appear to be too resistant to digestion to provide a substantial reserve of protein material for use by the animal, either as fuel during fasting, or for developing ova or sperm. We expect to subject this to further experimentation with the living animals, however.
DISCUSSION.

In general, we find that warm blooded muscle tissue autolyses under much the same conditions as glandular tissue. It does not, however, digest to the same extent as glandular tissue. This difference is due, we believe, to the greater connective tissue content of muscle, and also to the presence within the muscle cells of structural proteins which are not affected by the cell proteases under any condition. Only a small fraction of the total muscle proteins are susceptible to atrophic hydrolysis. If the structural proteins digest it must be by an extremely slow process, or it may involve other enzymes than those found in muscle; for example, the enzymes of phagocytic cells. Muscle atrophy is always a slow process clinically, and corresponds thus with the reaction as found in vitro. Muscle tissue can evidently contribute through hydrolysis toward maintenance of the organism as a whole in prolonged fasting. But the slowness of the protein hydrolysis tends to conserve to the organism a structurally complete muscular machine.

In the muscles of the higher, warm blooded animals we find what seems to be a relation between activity, pigmentation, and autolysis. The more active muscles contain more protein susceptible of autolysis than the less active muscles. Thus the active leg muscles of the chicken, heavily pigmented with hemoglobin, yield more amino acids on autolysis than the inactive, unpigmented breast muscles. That the muscle protein fraction which is potential substratum is essential for contraction would seem to be indicated by the loss of contractile power in an atrophied muscle where the cells are still present and intact.

In some of the very active fishes muscle autolysis is more extensive than in the warm blooded animals, and much more so than in more sluggish fishes. Here again there appears to be a relation between the autolyzable protein fraction in muscle and the activity of the muscle. In fish like the mackerel a very considerable fraction of muscle protein could be mobilized for fuel or for growth of the sex structures. In the case of the salmon we know that extensive muscle atrophy takes place during the migration to the spawning beds (4). During this period no food is eaten, but the salmon swims great distances and at the same time matures.
K. K. Chen and H. C. Bradley

large quantities of ova or sperm. The proteins of the muscle tissue are very extensively mobilized during this period, and presumably by the autolytic mechanism. In the more sluggish types of fish examined it does not appear that extensive atrophies can take place. In the single specimen of carp examined there proved to be potential substratum present, but in death the muscle cells developed so little acid that the proteins were not converted into substratum. If this is representative of the year round condition of the carp, it seems clear that only a generalized acidosis could make available for other uses the proteins of the musculature.

In the frog leg muscles we have about the same degree of autolysis as in the more sluggish types of fish. Nevertheless, the involution of the tadpole's tail is a striking example of complete removal of a mass of muscle tissue—a very unusual atrophy. This, we believe, cannot be referred to the autolytic mechanism alone, but must be accompanied by phagocytic action as well.

In the muscle tissue of molluscs we find a small autolysis developing, with very little increase by the addition of acid. Such muscles would appear incapable of more than a very slight atrophy indeed. Activity appears to make no difference in the degree of autolysis.

In the disuse atrophies of mammalian striated muscle we have loss of protein mass accompanied with very considerable loss of contractile power. With returning use, such muscles regularly hypertrophy again and the contractile strength is regained. This protein fraction, having a definite relation with contractile power, is, we believe, mobilized rather slowly as compared with gland proteins, but is, nevertheless, subject to similar fluctuations up and down. If acidity develops, this fraction is susceptible to autolysis and diminution. In severe and prolonged exercise accompanied with excessive fatigue, it is possible that a small amount of this contractile fraction is lost, so that the period for complete recovery may conceivably be conditioned by the time required to resynthesize it. We are subjecting this theory to more crucial tests by experimental atrophies of muscle in the living animal.

SUMMARY.

1. Warm blooded, striated, cardiac, and non-striated muscles are found to autolyze at increased speed and, to a greater extent,
in the presence of acids. The optimum concentration is usually between 0.04 and 0.02 N, or at a pH of about 4.5 to 5.0.

2. Under optimum conditions in vitro less than 15 per cent of muscle proteins digest to amino acids.

3. In vivo, atrophies of muscle tissue follow conditions which lead to acidosis of the muscle cells. Diminished blood supply from whatever cause produces such atrophic changes. Under ordinary conditions the atrophic changes are limited in extent and do not lead to death and removal of entire cells. Such limited atrophies may, however, result in almost complete loss of contractile power.

4. That fraction of muscle tissue which is found to be susceptible of autolysis appears to be particularly associated with the contractile function of the tissue. An atrophy of a few per cent of the total muscle protein mass, is accompanied by a disproportionately large loss of strength.

5. It is suggested that in prolonged excessive exercise and fatigue, sufficient acidity may develop in a muscle so that some of the contractile protein fraction is lost by autolysis. This may be a factor in determining the length of time required for complete recovery of strength from such excessive fatigue.

6. The intracellular proteases of muscle do not appear capable of completely digesting muscle tissue. Where muscle cells die it is believed phagocytic intervention is probably necessary for their complete removal.

7. In the types of fish muscle examined, the extent of autolysis or atrophy appears to be determined by the activity of the muscles. The more active, the greater the possible mobilization by autolysis of muscle proteins.

8. In the molluscs examined autolysis is slight, and practically unaffected by reaction. Activity does not alter the degree of autolysis.

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STUDIES OF AUTOLYSIS: X. THE AUTOLYSIS OF MUSCLE
K. K. Chen and H. C. Bradley

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