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Studies on thyroid func-tion Ⅱ. Effect of thyroidectomy and thyroid extract on the urinary amino acids of animals

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Studies on thyroid func-tion Ⅱ. Effect of thyroidectomy and thyroid extract on the urinary amino acids of animals*

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Abstract

1. α-Aminoadipic acid and lysine are increased in the urine of thyroidectomized dog. 2. Pipecolic acid is increased in the urine of rat treated with thyroid extract. 3. Relation between thyroid function and lysine metabolism is discued.

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STUDIES ON THYROID FUNCTION*
II. EFFECT OF THYROIDECTOMY AND THYROID EXTRACT ON THE URINARY AMINO ACIDS OF ANIMALS

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In the previous papers[1,2,3,4], it has been reported that β-alanine, sarcosine, lysine and its metabolic intermediates are increased in the urine of both hyper- and hypothyroid patients, and the administration of thyroid extracts to the rabbits has led to the similar changes in the amino acid pattern of the urine and the muscle nitrogen pool. In this communication, further studies on the relation between lysine metabolism and thyroid function were carried out by using thyroidectomized and thyroxine treated animals.

METHODS

Thyroidectomy was carried out by the procedure stated in BOMSKOV's handbook[5]. For the induction of hyperthyroid state, 0.25 ml per day of "Thyradin" (Teikoku Zoki CO., Ltd.) was injected intraperitoneally into rats for seven days. One ml of Thyradin corresponds to 0.2 gm of fresh thyroid. Urine was collected under toluene and desalted by the method of CARSTEN[6]. Ion exchangers used were "Daiaion" SK-1 and SA-100 (Mitsubishi Kasei CO., Ltd.). The dipole ion fraction thus obtained was chromatographed in two ways on paper (Toyoroshi No. 50). Solvents used throughout this series of study were n-butanol-acetic acid-water (5 : 1.2 : 5 V/V) and phenol-water (4 : 1 ; 0.3% NH_3 in the chamber). 0.1% ninhydrin in water-saturated n-butanol was used for color development.

Since most of the amino acids ever appeared on paper have already been identified in the previous reports[1–4], further identification was unnecessary except one amino acid in this experiment.

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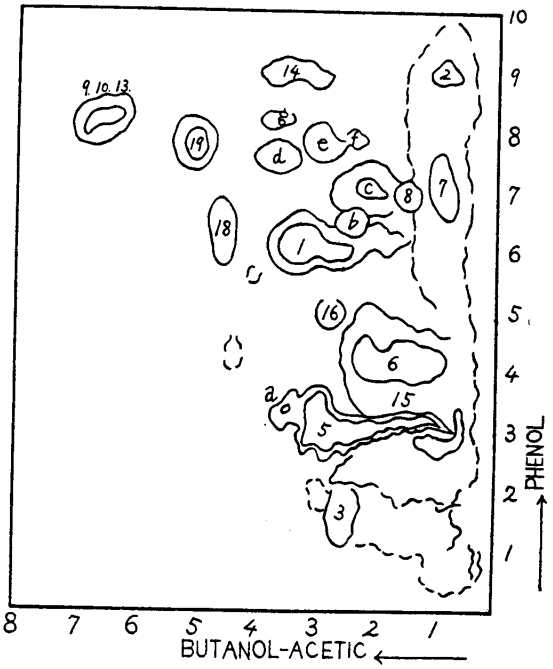
RESULTS

(I) *Effect of thyroidectomy on the urinary amino acid pattern of a young dog* :

Fig. 1 shows the paper chromatogram of urinary amino acids of a normal puppy weighing 3.1 kg. The little dog was fed on cow milk. γ-Aminobutyric acid (spot e) was the first amino acid met in the animal urine ever studied in this laboratory. Spot c appeared between β-alanine



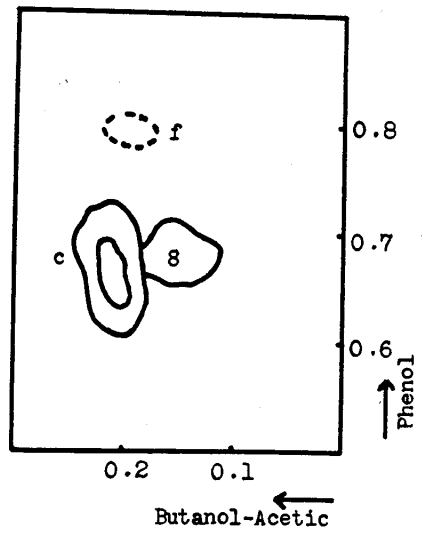
1. Alanine
2. Arginine
3. Aspartic acid
5. Glutamic acid
6. Glycine
7. Histidine
8. Hydroxyproline
9. Isoleucine
10. Leucine
13. Phenylalanine
14. Proline
15. Serine
16. Threonine
18. Tyrosine
19. Valine

a. α-Aminoadipic acid
b. β-Alanine
c. Unknown
d. β-Aminoisobutyric acid
e. γ-Aminobutyric acid
f. Sarcosine
g. δ-Aminovaleric acid

Fig. 1. Urinary Amino Acids of Normal Puppy Fed Cow Milk

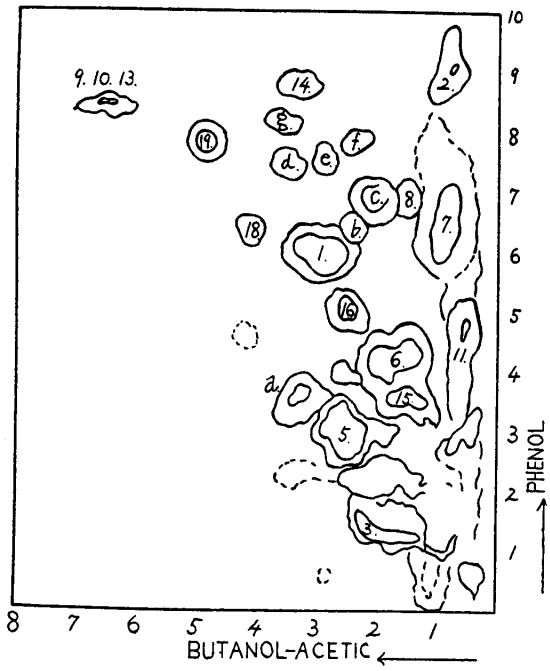
and hydroxyproline was the only amino acid yet unidentified. The relative situation between hydroxyproline and spot c on paper is similar to that of proline and pipecolic acid. So spot c was considered to be hydroxypipecolic acid, and expectedly it resisted the nitrite treatment as shown in Fig. 2. This spot c, however has no relation with the thyroid function, so further identification was not carried out with the known sample.

Fig. 3 shows the urinary amino acid pattern of the dog forty days after thyroidectomy. Compared with Fig. 1, the remarkable changes of the chromatogram are the increase of α-aminoadipic acid (spot a) and the



8. Hydroxyproline
c. Unknown
f. Sarcosine

Fig. 2. Urinary Amino Acids of Normal Dog After Nitrite Treatment



1. Alanine
2. Arginine
3. Aspartic acid
5. Glutamic acid
6. Glycine
7. Histidine
8. Hydroxyproline
9. Isoleucine
10. Leucine
11. Lysine
13. Phenylalanine
14. Proline
I5. Serine
16. Threonine
18. Tyrosine
19. Valine
a. α-Aminoadipic acid
b. β-Alanine
c. Unknown
d. β-Aminoisobutyric acid
e. γ-Aminobutyric acid
f. Sarcosine
g. δ-Aminovaleric acid

Fig. 3. Urinary Amino Acids of Thyoidectomized Dog

appearance of lysine (spot 11), thus indicating the intimate relation between thyroid function and lysine metabolism.

(II) *Effect of administration of thyroid extract on the urinary amino acid pattern of rats* :

Fig. 4 shows the paper chromatogram of urinary amino acids of a normal rat, and Fig. 5 shows that of the same rat after Thyradin treatment. A large spot of pipecolic acid has appeared after Thyradin treat ment. Although pipecolic acid is often contained in the normal rat urine, it appeared only after Thyradin treatment in this case.

DISCUSSION

It is well known that pipecolic acid and α-aminoadipic acid are the metabolites of lysine in the animal body[7].

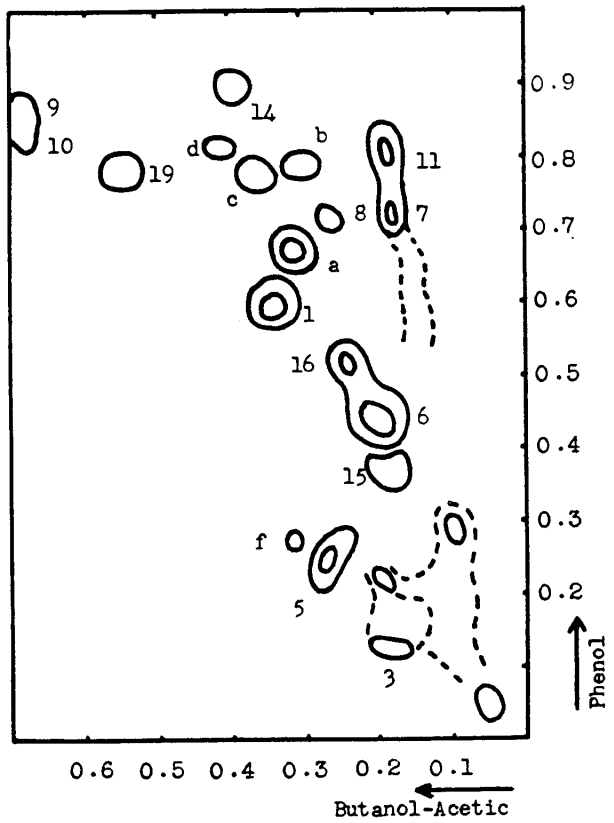


Fig. 4. Urinary Amino Acids of Normal Rat

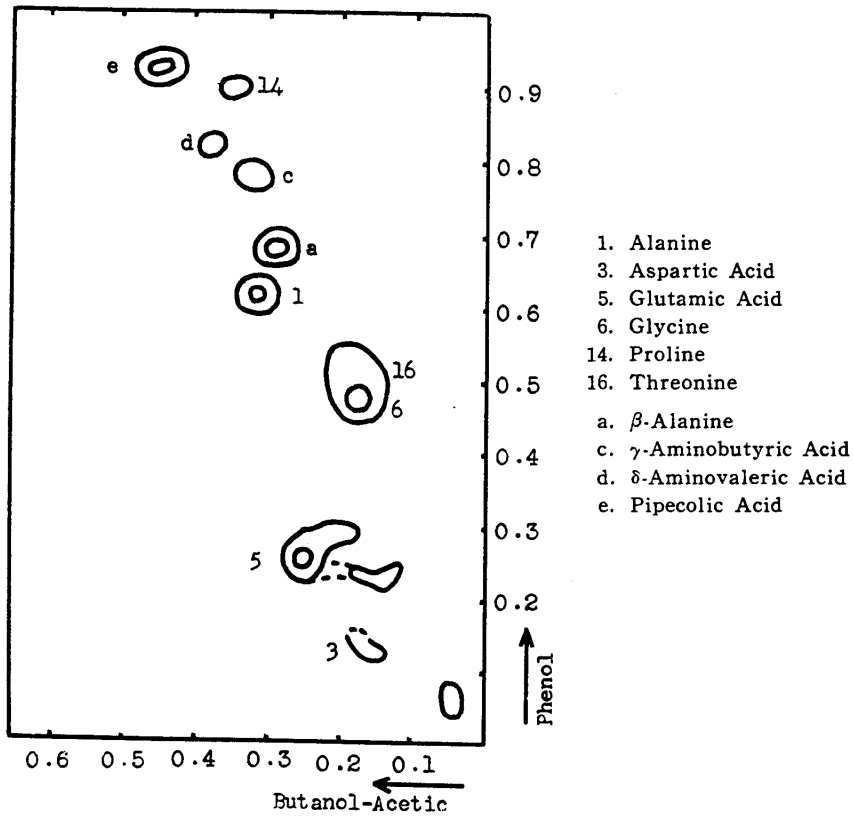


Fig. 5. Urinary Amino Acids of Thyradin Treated Rat

The present experiment and others[1,-4] showed that lysine and its metabolic intermediates were increased in the urine of hyper- and hypothyroid animals.

These facts may suggest that thyroxine is a control agent for the utilization of lysine in the animal body.

This assumption is in accord with the findings in that the cytochrome c contents of thyroidectomized rats is less than one half of the normal[8], and the lysine content of this important electron carrier is surprisingly high[9].

Although spot c (Figs. 1—3) is assumed to be hydroxypipecolic acid which is derived from hydroxylysine, it is not clear whether its origin comes from cow milk or from tissue constituent. This is the first report, and at any rat, it indicates the occurrence of hydroxypipecolic acid in the animal urine.

SUMMARY

1. α-Aminoadipic acid and lysine are increased in the urine of thyroidectomized dog.
2. Pipecolic acid is increased in the urine of rat treated with thyroid extract.
3. Relation between thyroid function and lysine metabolism is discussed.

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