THE B VITAMINS AND FAT METABOLISM

IV. THE SYNTHESIS OF FAT FROM PROTEIN

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(Received for publication, December 13, 1940)

It has been shown by us (1, 2) that in rats and in pigeons thiamine is required for the synthesis of fat from carbohydrate. Longenecker (3) has reported the synthesis of fat from protein in rats fed a diet containing casein, salts, and yeast. Hoagland and Snider (4) have confirmed Longenecker's results. In both cases yeast was supplied in the diet and it seemed desirable to determine whether thiamine or some other factor in the yeast was responsible for the synthesis of fat from protein.

Methods

White rats of the Wistar strain, reared in the Connaught Laboratories' colony, were employed. The general care of the animals has been reported previously (5). They were depleted of their body stores of the B vitamins and the body fat was reduced to a low level by placing them for 3 weeks on Basal Diet 1 (5). The rats were then fed Basal Diet 3, with the following composition in per cent by weight: casein (Labco) 96, salts mixture (Steenbock-Nelson Salts 40 (6)) 4, cod liver oil concentrate 0.015. During the period of protein feeding, vitamin and choline supplements were administered, by subcutaneous injection, in the following amounts per rat per day, unless otherwise indicated: thiamine hydrochloride (Merck) 20 γ, riboflavin (Hoffmann-La Roche) 20 γ, pyridoxine 40 γ, calcium pantothenate 100 γ, nicotinic acid (Eastman Kodak) 0.1 mg., choline hydrochloride (British Drug Houses) calculated as choline base 10 mg. We are indebted to Merck and Company, Inc., for gifts of pyridoxine and calcium pantothenate.
The rats were killed by stunning, the livers removed, and the total crude fatty acids in the livers and bodies were determined by methods previously published (1, 7).

EXPERIMENTAL

A number of experiments have been carried out. Since the results have been in good agreement, two typical experiments will be described.

Fig. 1. The effect of the B vitamins upon the body weight of rats fed a high protein diet. Supplements: Curve I, thiamine; Curve II, thiamine, riboflavin; Curve III, thiamine, riboflavin, calcium pantothenate; Curve IV, thiamine, riboflavin, calcium pantothenate, nicotinic acid; Curve V, thiamine, riboflavin, calcium pantothenate, nicotinic acid, choline; Curve VI, pyridoxine; Curve VII, pyridoxine, thiamine; Curve VIII, pyridoxine, thiamine, riboflavin; Curve IX, pyridoxine, thiamine, riboflavin, calcium pantothenate; Curve X, pyridoxine, thiamine, riboflavin, calcium pantothenate, nicotinic acid; Curve XI, pyridoxine, thiamine, riboflavin, calcium pantothenate, nicotinic acid, choline.

Series I—The effect of thiamine administered alone, and in various combinations with the other known factors of the vitamin B complex, was investigated. The body weight changes are shown in Fig. 1. The total crude fatty acids in the livers and bodies are given in Table I. All results are averages for nine rats.

Series II—Two groups, each of fifteen rats, received Basal Diet 3, thiamine, riboflavin, nicotinic acid, calcium pantothenate, and choline during the entire experiment. Group B was given, in addition, 20 γ of pyridoxine per rat per day. After 5 weeks
ten rats in each group were killed. At this time the average weight of the rats receiving pyridoxine was 30 gm. greater than that of the deficient animals in Group A.

The remaining five rats in Group B were continued on the same régime for 3 weeks longer. During this period the residual five rats in Group A were given 40 γ of pyridoxine daily. This caused a marked increase in body weight, so that at the end of the experiment the average weight of the rats in Group A was only 3 gm. less than that of the rats in Group B. The total crude fatty acids of the livers and bodies are given in Table I.

### TABLE I

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<th>Group</th>
<th>Supplements</th>
<th>Total crude fatty acids</th>
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* After 5 weeks.
† After 8 weeks.
‡ Pyridoxine was supplied during the last 3 weeks of the experiment.

### DISCUSSION

In the absence of pyridoxine there was a steady loss of weight in rats fed a diet high in protein but devoid of fat and carbohydrate, regardless of the administration of any of the other known
B vitamins. Pyridoxine administered with thiamine prevented weight loss. The further addition of pantothenic acid and riboflavin resulted in a gain in weight which was not augmented by nicotinic acid or choline. The necessity of pyridoxine for any gain in weight of rats fed a protein diet is in marked contrast to its slight activity when the diet is high in carbohydrate (5).

We have previously reported that pyridoxine would not prevent the deposition of fat in the liver which resulted when thiamine was administered to rats receiving a high carbohydrate diet (5). In the present experiments, in which the rats received a protein diet free of carbohydrate, a lower value for liver fat was obtained in all cases when pyridoxine was given. Under these conditions pyridoxine has the lipotropic effect which was reported by Haliday (8).

The administration of thiamine alone or in various combinations with riboflavin, pantothenic acid, nicotinic acid, and choline in all cases resulted in a lower value for body fat than that of the control group. The control rats were killed at the end of the deficiency period; therefore they had received neither the protein diet nor any of the B vitamin supplements. Choline was included in these tests in order that the body could handle fat normally and to prevent the possibility that fat synthesis might be impeded by accumulation of fat in the liver. Administration of all these known substances failed to give fat synthesis from protein.

A supply of pyridoxine alone resulted in the greatest loss of body fat, but if thiamine was also given the same amount of body fat was secured as in the control. This would indicate either that no fat had been burned by the animal during the 2 week period or that fat was being slowly synthesized from protein and was being used up in metabolic processes.

Pyridoxine, thiamine, riboflavin, and pantothenic acid administered together resulted in the greatest value for body fat, about double the value of the control. Approximately 30 per cent of the increase in body weight can be accounted for by increase in fat content. This clearly indicates fat synthesis which was not possible when these vitamins were given in the absence of pyridoxine. The further addition of nicotinic acid and choline did not increase the body fat.

Rats fed the protein diet and receiving supplements of thiamine,
riboflavin, pantothenic acid, nicotinic acid, choline, and pyridoxine gained weight and after 5 weeks the level of body fat was double that of a group receiving the same treatment except for the omission of pyridoxine. When these deficient animals were given pyridoxine, there was a fairly rapid increase in body weight and the amount of body fat was tripled in 3 weeks. This confirms the fact that pyridoxine is required for the synthesis of fat when the diet contains only protein.

No information is available to indicate the nature of the mechanism by which pyridoxine brings about fat synthesis from protein. As a hypothesis it is suggested that pyridoxine is necessary for such stages of protein metabolism as may be essential for the formation of carbohydrate. The previously demonstrated action of thiamine in promoting fat synthesis from carbohydrate would explain why pyridoxine alone has been found to have no effect in these experiments.

SUMMARY

While the administration of thiamine alone will cause the synthesis of fat from carbohydrate, it will not do so from protein. In the latter case pyridoxine is essential. This vitamin, in combination with thiamine, prevents a reduction in body fat of rats maintained on a protein diet. The synthesis of fat from protein is clearly evident when pyridoxine, thiamine, riboflavin, and pantothenic acid are supplied. Various combinations of the isolated members of the vitamin B complex do not cause the synthesis of fat from protein unless pyridoxine is present. It is suggested that pyridoxine is essential for the metabolism of protein.

This investigation was greatly assisted by a grant from the Division of Natural Sciences of the Rockefeller Foundation.

BIBLIOGRAPHY

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