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Dextrose Administration and Vitamins B.*

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Several components of the vitamin B complex appear to be necessary parts of enzyme-coenzyme systems of tissue oxidation. In the oxidation or dismutation of pyruvic acid by animal tissue, thiamine, riboflavin and nicotinic acid appear to be necessary.[1] Abderhalden and Wertheimer[2] found that pigeons in B_1 avitaminosis had glycogen accumulation in the liver and heart which increased as the vitamin deficiency progressed and which decreased when thiamine was given. Westenbrink[3] concluded that carbohydrate in the diet hastens the appearance of symptoms of thiamine deficiency in pigeons and that fat in the diet delays symptoms. He expressed the opinion that the symptoms were largely due to the accumulation of toxic products of improper carbohydrate metabolism. Platt and Lu[4] found that the pyruvic acid content of blood, urine and spinal fluid was increased in thiamine deficiency.

Helmholz and Bollman[5] found that intravenous injection of large amounts of dextrose in rabbits was more toxic and produced less diuresis than equivalent amounts of sucrose. The obvious conclusion was drawn that the toxic effects of excessive dextrose were associated with the metabolism of this substance, since sucrose is excreted unchanged. It may be possible that some of the toxic effects of excessive dextrose under these conditions are due to the rapid depletion of some of the enzyme-vitamin system involved in the oxidation of dextrose and its intermediary products. Several experiments in which large amounts of dextrose were administered intravenously to rabbits failed to show any advantage in the simultaneous administration of large amounts of thiamine, riboflavin, nicotinamide, pyridoxine and pantothenic acid. These animals had not been depleted

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1 Lipton, M. A., and Elvehjem, C. A., *Cold Spring Harbor Symp. Quart. Biol.*, 1939, **7**, 184; Lipmann, F., *ibid.*, 1939, **7**, 248.

2 Abderhalden, Emil, and Wertheimer, Ernst, *Arch. f. d. ges. Physiol.*, 1932, **230**, 601.

3 Westenbrink, H. J. K., *Arch. néerl. de physiol.*, 1935, **20**, 481.

4 Platt, B. S., and Lu, G. D., *Quart. J. Med.*, 1936, **5**, 355.

5 Helmholz, H. F., and Bollman, J. L., *J. Lab. and Clin. Med.*, 1940, **25**, 1180.

previously of vitamins and no deficiency was present at the beginning of the injection of dextrose.

Another attempt was made to indicate some difference in the utilization of large amounts of dextrose by vitamin B-deficient rats. Young rats were fed a vitamin B-deficient diet for 3 weeks and then given large amounts of dextrose as frequently as possible by stomach tube. Some rats received in addition large amounts of the B vitamins. Both groups of rats survived only 2 or 3 days under this regimen and no advantage was clear in either group.

A third group of experiments definitely indicated that vitamin deficient rats are better able to metabolize dextrose and survive protein deficiency when thiamine is added than when it is not. Rats previously deprived of vitamin B survived on a diet of dextrose from 2 to 4 times longer when thiamine was given than when it was not. Other components of the vitamin B complex, riboflavin, pyridoxine, pantothenic acid and choline appeared to be ineffective. Nicotinamide appeared to have some slight effect.

Experimental Procedure. Young rats of the Wistar strain which had been receiving a diet of Purina fox chow were placed on the following diet: casein, 10; sucrose, 80; butter, 4; salt mixture, Steenbock's No. 40, 4; powdered agar, 2 and cod liver oil concentrate, 0.015. The rats gained weight for several days but soon began to lose weight so that after 2 weeks they weighed the same or less than their original weight. Each rat was kept in an individual cage and any that did not continue to eat some of the diet each day were not used. Rats of 65 to 90 g body weight were used, and 12 were selected for each group. At least 10 of these continued throughout the experiment. Each group was selected so that the range of weight variation was small in each group. Such selection was necessary because the larger animals lost less weight and survived the diet better than the smaller ones. The experiments reported in this series were done after the rats had been on the vitamin B-free diet for 14 to 21 days. Dextrose was then substituted for the vitamin B-free diet and in addition each animal received by stomach tube 4 cc of 25% solution of dextrose twice daily.

The vitamins administered were injected subcutaneously in aqueous solution (0.1 cc) once daily during the time the animals received only glucose. Thiamine hydrochloride, pyridoxine hydrochloride and pantothenic acid were each given in amounts of 0.1 mg daily; riboflavin, 0.03 mg; nicotinamide, 1.0 mg, and choline chloride, 5.0 mg.

Results. With the vitamin B-free diet employed, young rats

(65 to 90 g) were found to survive for 23 to 45 days. Lack of appetite and undernutrition may be a great factor in the survival of the vitamin deficient animals. After 3 weeks of vitamin depletion these rats, continued on the vitamin-free diet, were restored by the subcutaneous injection, 3 times each week, of thiamine, riboflavin, nicotinamide, pyridoxine hydrochloride and pantothenic acid in the amounts given previously. These animals rapidly gained weight and appeared in good condition for 3 months, when the experiment was terminated.

After 14 days or more of vitamin depletion the rats survived fasting only 2 or 3 days. Substitution of dextrose for the diet and administration of dextrose by stomach tube enabled the rats to live considerably longer than the fasted rats (Table I). The length of life of the dextrose-fed rats was somewhat shorter than that of animals continued on the vitamin-free diet.

Table II lists the groups of rats which received dextrose and subcutaneous injections of vitamins. The average length of life for

TABLE I.
Rats Receiving Dextrose without Supplements.

Days receiving vit. B free diet	Avg wt, g	Lived,* days
14	66	7 (5-9)
16	69	11 (9-14)
18	71	16 (12-20)
21	74	11 (7-14)

*First figure is average survival; figures in parentheses indicate the shortest and the longest survival.

TABLE II.
Rats Receiving Dextrose and Vitamins.

Days receiving vit. B free diet	Avg wt, g	Lived,* days	Comparison†	Vitamins injected
14	67	26 (13-39)	372	Thiamine, riboflavin, nicotinamide, pyridoxine, pantothenic acid
16	67	27 (24-33)	245	
16	73	26 (18-32)	236	Thiamine, riboflavin, nicotinamide, pyridoxine, pantothenic acid, choline
18	74	32 (21-41)	200	Thiamine
21	74	41 (28-65)	372	Thiamine
18	77	25 (18-35)	156	Nicotinamide
18	69	17 (14-22)	106	Riboflavin
16	65	8 (5-13)	73	Choline
16	68	10 (7-14)	91	Pyridoxine
16	70	12 (8-15)	109	Pantothenic acid

*First figure is average survival; figures in parentheses indicate the shortest and the longest survival.

†Life compared with that of rats without supplement, per cent.

each group is given and the figures in parenthesis indicate the shortest and the longest survival. The length of life is compared with that of the rats receiving dextrose without vitamins. This comparison is made with the comparable control group of rats receiving only dextrose because of the variation in the different groups of control animals. It is obvious that the injection of the mixed vitamins definitely prolonged the life of the dextrose-fed rats. Thiamine alone had a similar effect, but riboflavin, choline, pyridoxine and pantothenic acid were without effect. Some prolongation of life was present in the rats receiving nicotinamide.

Rats not previously fed a vitamin deficient diet survived 25 days when receiving only dextrose in the diet and by stomach tube. The subcutaneous injection of thiamine did not significantly prolong the life of a similar group of animals receiving only dextrose (Table III).

Comment. In these experiments the survival of vitamin B-deficient rats receiving dextrose was slightly shorter than that of similar animals continued on the vitamin-free diet containing protein. The difference in survival time could be lengthened somewhat by administration of the vitamin B-free diet by stomach tube. Any shortening of the time of survival due to dextrose feeding seems to be referable to protein deficiency rather than to the thiamine deficiency. The slight difference in the survival time of the rats, not previously depleted of vitamins, which received dextrose alone and those which received dextrose and thiamine, also indicates that the protein deficiency is the major factor. Since the rats were receiving a diet rich in carbohydrate prior to the substitution of dextrose alone, one should not expect the relatively small increase of carbohydrate consumption to influence materially the time of onset of symptoms of thiamine deficiency.

The rats which received thiamine and dextrose after previous depletion of vitamin B survived definitely longer than similar animals not receiving thiamine. Also it should be noted that the vitamin B-depleted rats receiving dextrose alone did not survive as long as rats not previously depleted and receiving dextrose only. Thiamine enables rats to survive longer on a diet of dextrose (and also devoid

TABLE III.
Rats without Previous Vitamin Depletion Receiving Dextrose.

Avg wt, g	Lived,* days	Wt loss, g	Additional treatment
77	25 (19-29)	30	None
82	27 (20-39)	35	0.1 mg thiamine daily

*First figure is average survival; figures in parentheses indicate the shortest and the longest survival.

of protein and fat) than rats that do not receive thiamine. Unfortunately I have no direct data concerning any possible protein sparing action of thiamine in addition to that of the dextrose given. The loss of weight of both groups of animals was very similar, being rapid at first and slowing as time continued. At the time of death of the dextrose-fed rats the weight of those receiving thiamine was similar. With the further survival of the thiamine-treated rats loss of weight continued so that they weighed less than the dextrose rats at the time of death. The amount of dextrose consumed each day was similar in both groups of animals.

Summary. Young rats weighing 65 to 90 g were maintained for 14 to 21 days on a vitamin B-free diet (casein 10, sucrose 80, butter 4, salts, agar and vitamins A and D). At this time these animals survived fasting but 2 or 3 days. Substitution of a diet of dextrose, supplemented by dextrose solution by stomach tube, permitted survival of from 7 to 16 days.

Vitamin-depleted rats receiving dextrose and thiamine survived 2 to 4 times as long as those receiving only dextrose. Nicotinamide appeared to have some effect, but riboflavin, pyridoxine hydrochloride, pantothenic acid and choline had no appreciable effect in prolonging the life of the dextrose-fed rats. All of the foregoing vitamins given together had no further beneficial effect than when thiamine alone was given.

When dextrose was substituted immediately following an adequate vitamin-containing diet, rats survived 19 to 29 days. The injection of thiamine hydrochloride or the vitamin mixture did not appreciably alter the survival time of these animals.

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A Difference in Metabolic Requirements of Meningococcus and Gonococcus.*

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Gordon and McLeod[1] found that the gonococcus does not grow on a medium based on tryptic digest of casein and gave this point con-

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1 Gordon, J., and McLeod, J. W., *J. Path. and Bact.*, 1926, **29**, 13.