line vitamin B_{12} is without lipotropic activity in rats fed a high-fat diet. They did, however, obtain a partial lipotropic effect of crystalline vitamin B_{12} when administered to rats receiving a low-fat-low-protein diet, although the effect was less than that obtained with methionine. A combination of methionine and vitamin B_{12} did not further prevent the fatty changes in the liver.

A sub-optimal amount of choline, equal to or greater than that present in liver extract and vitamin B_{12} concentrate, was also without lipotropic effect. Crystalline vitamin B_{12} in combination with choline did not exert any sparing effect on the choline as judged by the failure to prevent an increase in liver fat (Table III). Thus, although vitamin B_{12} has a choline sparing effect on the growth of chicks or in the prevention of hemorrhagic renal necrosis in rats(5,6,7), it is without sparing action in preventing hepatic injury in rats receiving a high-fat diet with casein as the source of protein. As the lipotropic activity of liver extract or vitamin B_{12} concentrate is not due to the factors discussed above, the effect of these materials must be due to other known or unknown agents which influence the synthesis or transport of methyl groups. The possible effects of combinations of crystalline vitamin B_{12} and sub-optimal amounts of folic acid, with or without choline, are being studied.

Summary. With the diet employed, one cc of crude liver extract administered subcutaneously 3 times a week represents the approximate minimal effective dose of this material for lipotropic activity. The same dose of liver extract administered orally also has lipotropic activity but slightly less than that obtained on subcutaneous administration. The lipotropic effect of crude liver extract or vitamin B_{12} concentrate is not due to the small amounts of choline, inositol and folic acid present in these materials. Crystalline vitamin B_{12} alone is without lipotropic effect. Small amounts of choline, alone or in combination with crystalline vitamin B_{12}, also failed to prevent fatty changes in the liver.

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Effect of B Complex Vitamins on Liver and Heart Glycogen Levels of Hyperthyroid Rats. (17998)

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The importance of some of the members of the B-complex vitamins in partially counteracting the growth-retarding effect of experimental hyperthyroidism in immature rats is generally recognized. When a high B-complex diet is further supplemented with dried liver or a water-insoluble residue of liver, animals grow at a nearly normal rate in spite of the hyperthyroid condition(1-5). Since hyperthyroidism usually leads to a marked reduction in the concentration of glycogen in the heart and liver, it was decided to determine whether these supplements which so favorably influence the growth rate of the immature animal, would also reduce the effect of hyperthyroidism on the liver and heart glycogen concentrations.

Method. Young albino rats averaging 55 g were put into individual cages and fed the various diets shown in Table I. Food intake was unrestricted but a daily record of food

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TABLE I.
Composition of the Various Diets.

	Diet 1	2	3	4
	g	g	g	g
Casein, vit. free	200	200	220	300
Sucrose	703	703	683	603
Crisco	50	50	50	50
Cellu flour	20	20	20	20
Salt mixture Wesson(6)	27	27	27	27
Choline chloride	1	1	1	1
Inositol	1	1	1	1
	mg	mg	mg	mg
Thiamine HCl	1	10	10	10
Riboflavin	2	20	20	20
Niacin	3.7	37	37	37
Ca pantothenate	3.7	37	37	37
Pyridoxine HCl	1.5	15	15	15
PABA	150	150	150	150
Biotin	—	—	2	2
Folic acid	—	—	2	2

Diet 5 was similar to Diet 4 except that it contained 100 g of liver meal instead of an equal quantity of casein.

One drop of reinforced oleum percomorphum (Mead Johnson) was given to each rat 5 days a week and one drop of wheat-germ oil twice a week. Each gram of the oleum percomorphum preparation contained 60,000 U.S.P. units of vit. A and 8,500 U.S.P. units of vit. D.

consumption was kept. At the end of the experimental period, which varied from 17 to 41 days, the animals, unstarved, were beheaded and allowed to bleed for about 15 seconds. The heart, after making incisions in it and squeezing out the blood, was put rapidly into a weighed test tube containing 30% potassium hydroxide. Two sections from the left lobe of the liver were treated similarly. Glycogen was then determined by the method of Goode *et al.*(7) with minor modifications. In using this method, we have found it advantageous to purify the glycogen by solution in water and reprecipitation with alcohol prior to acid hydrolysis. Studies on the rate of glycogenolysis in the livers of decapitated rats have shown that it is relatively slow. Heart glycogen disappears more rapidly, and for this reason the heart was removed first in order to get it into the potassium hydroxide as quickly as possible. Duplicate slices from the left lobe of the liver were analyzed in all cases. With few exceptions, the glycogen content of the 2 sections showed good agreement. The values given in Table II are the averages of the 2 determinations.

Results. It will be seen that the concentration of glycogen in both the heart and the liver of the hyperthyroid rat was low in practically all cases. Although the administration of diets high in the crystalline B-complex vitamins, especially when supplemented with defatted liver or the water-insoluble residue of liver, exerted a very favorable effect on the growth rate of the hyperthyroid animal, they did not influence demonstrably the effect of the hyperthyroid condition on the liver and heart glycogen concentrations. Some of the decrease in the concentration of glycogen in the heart may be secondary to the marked cardiac hypertrophy. The concentration of glycogen in the heart of the non-thyroid-fed control rats, in all experiments except No. 14, tended to be considerably lower than we usually find in our stock animals on Rockland rat pellets. No explanation for this difference is apparent at the present time. The addition of 30 μg of vitamin B_{12} per kilo of high-vitamin B-complex diet did not exert a demonstrable effect on the growth rate of the hyperthyroid animals. This finding is consistent with those reported previously by Ershoff(4,5). In other experiments we have found little stimulatory effect on growth from the administration of a 1:20 liver concentrate known to be active in the treatment of pernicious anemia. This also did not exert a favorable influence on the glycogen concentration of the liver and heart of the hyperthyroid animals.

Summary. Young hyperthyroid rats fed a diet high in crystalline B-complex vitamins grew fairly well but nevertheless showed a low concentration of glycogen in their livers and hearts. Additional supplementation with liver meal increased their growth rate to normal, but exerted no apparent favorable effect on the glycogen content of these organs. The decrease in cardiac glycogen concentration can be explained in part on the marked cardiac hypertrophy which is associated with experimental hyperthyroidism in the rat.

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TABLE II.
Effects of Dietary Supplements on Concentration of Glycogen in Liver and Heart of Hyperthyroid Rats

Exp. No.	No. of rats	Avg daily gain, g	Avg liver wt, g	Avg liver glycogen, %	Heart % body wt	Heart glycogen %	Heart glycogen Mg per 100 g body wt	Diet used
8	7	.16	3.9	.6 (.01-3.1)	.62	—	—	Diet 1 + .13% thyroid.
	6	.42	4.9	.4 (.01-0.8)	.64	—	—	As above + 2 mg biotin + 5 mg folic acid/kg.
	8	1.9	7.5	.5 (.01-0.6)	.63	—	—	Diet 2 + .13% thyroid.
	6	2.4	7.1	5.7 (4.1-8.4)	.34	—	—	Diet 1
14	7	1.7	6.6	.2 (.02-0.8)	.61	.11	.49	Diet 2 + .13% thyroid.
	8	1.7	6.5	.04 (.01-0.1)	.76	.08	.51	As above + 5 mg folic acid/kg.
	6	2.2	7.8	.04 (.01-0.1)	.64	.05	.40	As above + 5 mg folic acid + 2 mg biotin/kg.
	10	3.1	6.4	1.9 (.06-4.6)	.33	.46	1.56	Diet 2
34	6	2.9	9.5	1.9 (1.2-3.4)	.55	.06	.33	Diet 2 + 10% liver meal* + .25% thyroid.
	6	2.6	9.4	1.7 (.2-2.3)	.57	.12	.65	Diet 2 + 10% liver meal† + .25% thyroid.
	5	2.9	7.0	2.1 (.2-7.5)	.61	.06	.50	Diet 2 + .25% thyroid.
	10	3.0	5.0	7.0 (3.0-9.8)	.37	.24	.93	Diet 2.
40	5	3.2	10.0	.9 (.04-1.7)	.50	.16	.78	Diet 5 + .4% thyroid.
	4	2.3	7.8	.2 (.01-0.6)	.64	.11	.52	Diet 4 + .4% thyroid.
	5	3.2	8.3	5.5 (2.3-7.9)	.32	.26	.76	Diet 4.
39	8	2.8	5.2	.07 (.05-0.1)	.52	.11	.67	Diet 3 + 30 γ B_{12}/kg + .25% thyroid.
	4	2.9	5.9	.07 (.04-0.1)	.60	.11	.67	Diet 3 + .25% thyroid.

* Dried water insoluble residue from the manufacture of the anti-P.A. factor.
† Viobin, defatted liver.

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Progestational Activity of 1,2-*bis*-(p-Aminophenyl)-2-Methylpropanone-1 Dihydrochloride. (17999)

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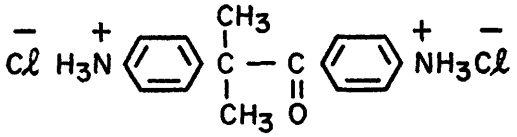
In the course of a comprehensive study of the relationship between chemical structure and biological activity in a series of substituted desoxybenzoins it was found that 1,2-bis-(p-aminophenyl)-2-methylpropanone-1 dihydrochloride exhibits progestational activity.



COMPOUND I.

The synthesis and properties of this compound have been previously described (Allen and Corwin) (1). We have employed a modification of the biological test for progesterone described by Clauberg(2). Juvenile female rabbits (New Zealand Whites) initially weighing between 600 and 800 g were utilized. Each test animal was pre-treated daily for 6

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2. Clauberg, C., *Zentralblatt f. Gynak*, 1930, v54, 2757