section shows the growth of our males on a suboptimal level of crude casein compared with optimal growth. The typical form of protein (amino acid) deficiency curve, *i.e.*, immediate reduction in growth rate with smooth return towards normal, is common to both top and bottom sections, but the difference in starting age and the difference in the exact protein levels makes the extent of deviation of the experimental growth from the control not strictly comparable.

heated egg albumen. The B factors were derived from rice bran extract and the egg albumen. Their male growth gives an excellent fit to the same line as shown for McIntire's data with 18% casein plus liver extract. Since rice bran extract does not contain the factor in question, egg albumen must either contain more of it than casein, or casein has a less favorable amino acid composition than egg albumen. Both feeding trials and amino acid composition (especially as regards the sulfur amino acids) point to a superiority of egg albumen over casein.

We have thus outlined an experimental basis for judging protein requirement for optimal growth in male and female rats. Experiments now in progress reveal that for 4 weeks there is no significant difference between two groups of male rats on diets with 30% Labco casein (otherwise identical with that of McIntire *et al.*), one with and the other without a supplement of 2% of liver extract. Judging both by our experience and McIntire's results, any existing difference should have reached its maximum by this time. The results will be published in detail when comparable experiments dealing with amino acid supplements to 18% casein have been completed.

Summary. It has been reported by McIntire *et al.* that a diet containing 18% purified casein and 6 pure B factors does not support optimal growth in male rats, and that the missing factor is present in liver extract. Evidence is presented to show that the factor, whatever it is, may not easily be found in the usual concentrated sources of B complex, but rather that it is associated, whether as an impurity or an essential amino acid, with protein of good quality.

14491

Effect of Massive Doses of Thiamine on Fertility and Lactation in the Albino Mouse.*

LEOPOLD R. CERECEDO AND LEONARD J. VINSON.

From the Department of Chemistry, Fordham University, New York City.

The experiments of Perla[1] showed that feeding rats with large amounts of thiamine resulted after one generation in interference with lactation, loss of maternal instinct, cannibalism, and progressive loss of fertility. Continuing this study, Perla and Sandberg[2] found that these symptoms were prevented by giving manganese chloride daily to the animals. If the diet was supplemented with manganese chloride alone, interference with lactation resulted, particularly marked after one generation. The observations of Perla were confirmed by Sure.[3] In contrast to the findings of Perla, and of Sure, Williams and Spies[4] reported normal reproduction in rats kept on stock diets supplemented with large amounts of thiamine through 3 generations. The

* This investigation has been supported in part by a grant from the John and Mary R. Markle Foundation.

1 Perla, D., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 169.

2 Perla, D., and Sandberg, M., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 522.

3 Sure, B., *J. Nutrition*, 1939, **18**, 187.

4 Williams, R. R., and Spies, T. D., *Vitamin B_1 and Its Use in Medicine*, Macmillan Co., New York, 1938, p. 286.

TABLE I.
Data on Reproduction and Lactation in Albino Mice Kept on a Basal Diet of Purina Dog Chow Supplemented with (a) Thiamine, (b) Thiamine + $MnCl_2$, and (c) $MnCl_2$.

Generation	Supplement	No. of mice	No. of litters born	No. of litters weaned
Parent	None	10	10	8
	Thiamine	10	7	7
	" + $MnCl_2$	5	5	4
	$MnCl_2$	5	5	5
F_1	Thiamine, 1st mating	5	5	0
	" 2nd "	5	3	3
	" + $MnCl_2$	5	4	4
	$MnCl_2$	5	4	4
F_2	Thiamine	5	5	4
	" + $MnCl_2$	5	3	3
	$MnCl_2$	5	4	4

present report presents data on the effects of massive doses of thiamine in the mouse. The action of manganese was also studied.

The basal diet consisted of finely ground Purina dog chow. Albino mice of our own strain were divided into 3 groups and fed the following rations: Group 1, basal diet plus 250 mg thiamine per kilo of diet; Group 2, basal diet plus 250 mg thiamine and 1 mg $MnCl_2$ per kilo; Group 3, basal diet plus 1 mg $MnCl_2$ per kilo. The mice were placed on the diets when 21 days old, at which time they weighed 8 to 10 g. The effects of the 3 diets were studied throughout 3 generations.

The growth rate in the 3 groups was practically the same and was similar to that obtained on Purina dog chow alone. In the rat, according to Sure,[3] a supplement of a large amount of thiamine has a stimulating effect on growth. The daily average intake of thiamine for the mice in Groups 1 and 2 during growth was 625-750 μg since the daily food intake amounted to 2.5-3.0 g.

As shown in Table I, reproduction and lactation did not appear abnormal throughout the 3 generations in any of the 3 groups. Second generation mice on the thiamine-supplemented diet destroyed their young upon being mated the first time. However, a subsequent mating saw them successfully wean their young. During reproduction and especially during lactation the intake of thiamine was greatly increased due to the increased food intake. During lactation the mothers consumed as much as 8 g of diet daily. Such an amount of diet would contain 2000 μg of thiamine. The amount of $MnCl_2$ ingested daily during growth was approximately 3 mg, and about 8 mg during lactation.

Summary. The effect of massive doses of thiamine on reproduction and lactation in the albino mouse has been studied. No harmful action was observed.