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Effects of Massive Doses of P-Aminobenzoic Acid and Inositol on Reproduction in the Rat.

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A few years ago Martin¹ found that although rats grew adequately on purified rations containing 6 B complex factors (thiamine, riboflavin, pyridoxine, choline, nicotinic acid and calcium pantothenate), addition of inositol resulted in retardation of growth and a number of early deaths. Similar adverse effects were noted following the administration of *p*-aminobenzoic acid but not when *p*-aminobenzoic acid and inositol were fed concurrently. Subsequent studies with rats have not confirmed these results,² although Sure³ observed a toxic effect of inositol on lactation and Ershoff and McWilliams⁴ noted reduced fertility when inositol was fed along with purified rations containing both *p*-aminobenzoic acid and sulfaguanidine. In the present experiment rats were raised to maturity on purified rations containing massive doses of *p*-aminobenzoic acid or inositol and the adequacy of such

diets for reproduction was determined.

Procedure and Results. Forty-two female rats of the Long-Evans strain were selected at 23 days of age and an average weight of 41.8 g. They were kept in metal cages with raised screen bottoms to prevent access to feces and were fed *ad libitum* the 7 diets listed in Table I (6 animals per group). They were weighed weekly, and vaginal smears were taken daily from the 48th day. After the 60th day the animals were bred to males of proven fertility.

Growth. No significant difference in rate of growth or gross appearance was observed except perhaps in the rats fed diet C. After 60 days the animals on this diet averaged 173.8 g in weight; average weights for those on the other diets ranged from 184.2 g on diet G to 204.8 g on diet F.

Reproduction. No significant difference in reproductive performance was observed.

TABLE I.
Composition of Experimental Diets.

Dietary component	A	B	C	D	E	F	G
Casein*	30.0	30.0	30.0	30.0	30.0	30.0	30.0
Salt mixture†	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Sucrose	65.5	64.5	63.5	64.5	63.5	65.5	55.5
<i>p</i> -aminobenzoic acid		1.0	2.0		1.0		
Inositol				1.0	1.0		
Folic acid						0.0005	
Yeast‡							10.0

To each kg of diets A-F, were added 80 mg thiamine hydrochloride, 20 mg riboflavin, 20 mg pyridoxine hydrochloride, 100 mg calcium pantothenate, 100 mg nicotinic acid, 5 mg 2-methylnaphthaquinone and 1.2 g choline chloride. To each kg of diet G were added 5 mg 2-methylnaphthaquinone and 1.2 g choline chloride. In addition each rat on diets A-G received the following supplement 3 times weekly: 500 mg cottonseed oil (Wesson), 1.0 mg alpha-tocopherol, and a vitamin A-D concentrate containing 50 U.S.P. units of vitamin A and 50 U.S.P. units of vitamin D.||

* Vitamin Test Casein, General Biochemicals, Inc., Chagrin Falls, Ohio.

† Sure's Salt Mixture No. 1.⁵

‡ Brewers' type yeast No. 200, Anheuser-Busch, Inc., St. Louis, Mo.

|| Nopeo Fish Oil Concentrate, assaying 800,000 U.S.P. units of vitamin A and 80,000 U.S.P. units of vitamin D per gram.

¹ Martin, Gustav J., *Am. J. Physiol.*, 1942, **136**, 124.

² Ershoff, B. H., *Proc. Soc. Exp. Biol. and Med.*, 1944, **56**, 190.

³ Sure, Barnett, *J. Nutrition*, 1943, **26**, 275.

⁴ Ershoff, B. H., and McWilliams, H. B., *Proc. Soc. Exp. Biol. and Med.*, 1943, **54**, 227.

⁵ Sure, Barnett, *J. Nutrition*, 1941, **22**, 499.

All the rats cast litters, although in 3 instances the initial breeding proved unsuccessful. Number of young per litter varied from 2 to 13, with averages between 7.2 and 8.4 on the several diets. An average of 0.8 to 1.2 young per litter were born dead (omitting one litter on diet C which consisted of 9, all born dead). In all groups the young averaged 5 to 5½ g at birth and appeared grossly to be normal in all respects.

Lactation. At birth litters were reduced to 6 each. The young were nursed and weaned on all diets except E and F. On each of diets B, D and G, 3 mothers successfully nursed their young, which were weaned at 21 days of age at average weights of 36 to 41 g. Two litters on diet A were nursed, but only 5 of the 12 young survived until weaning (average weight at weaning, 22.8 g). The one litter weaned on diet C consisted of 3 survivors, average weight

24.6 g.

The findings indicate that the massive doses of inositol or *p*-aminobenzoic acid exerted no deleterious effects on growth or reproduction and that lactation may occur on diets containing 1% *p*-aminobenzoic acid or inositol. The cause of the poor lactation is unknown, but deficiency of folic acid was probably not a factor. To judge from the work of Maynard and Rasmussen,⁶ failure of lactation may have been due in part to insufficiency of dietary fat.

Summary. No adverse effects on growth or reproduction were noted in female rats fed purified rations containing 1% *p*-aminobenzoic acid or inositol. Lactation was inadequate both in control and experimental rations, although some young were weaned on each of the above diets.

⁶ Maynard, L. A., and Rasmussen, E., *J. Nutrition*, 1942, **23**, 385.

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Relief of Cardiac Pain by Local Block of Somatic Trigger Areas.

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Weiss and Davis¹ noted that referred pain from viscera could be abolished by procaine infiltration of tender areas in the somatic reference zone. Their observations became buried, however, in the controversy which developed over the mechanism of visceral pain reference and the role of afferent somatic impulses in this phenomenon. As a result, the therapeutic implications of their results have received little recognition. In agreement with their findings, our data indicate that under suitable conditions, cardiac pain may be abolished by local block of the noxious impulses which arise in trigger areas in the reference zone.

Procaine Infiltration. We became interested in this problem during studies on ex-

tracardiac sources of pain in the chest and arm, which in some respects simulates coronary artery pain.² By the technic of needling tender spots in the muscles in patients with various myalgic syndromes, we discovered the existence of a group of trigger areas, located chiefly along the sternal borders, mechanical stimulation of which uniformly induced a reference of pain perceived beneath the sternum and deep inside the chest; if located on the left side the referred pain was often described as "felt directly in the heart." Other trigger areas in the chest and shoulder regions induced a radiation of pain to the entire pectoral area, the interscapular region, neck and arm.

At that time we believed² that since local

¹ Weiss, S., and Davis, D., *Am. J. Med. Sci.*, 1928, **176**, 517.

² Travell, J., Rinzler, S., and Herman, M., *J. A. M. A.*, 1942, **120**, 417.