

3. In general, diethyldithiocarbamate produces stimulation in low doses and in high doses an initial inhibition followed by a marked stimulation in the oxygen intake of embryonic cells.

4. Partial recovery from high initial doses of the reagent occurs.

5. Copper salts are markedly antagonized when in the presence of the carbamate.

16749

Alkaline Phosphatase of the Serum in Experimental Lathyrism of the White Rat.

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Lathyrism, a condition associated with the consumption of considerable amounts of legumes of the genus *Lathyrus*, notably *Lathyrus sativus*, *clymenum*, and *cicera*, is a disease of frequent occurrence in man in certain regions of India, North Africa and Spain.¹⁻³ It has also been observed in domestic animals although marked species variation in susceptibility to the intoxicant has been noted. The causal agent, a toxic component of the seed, has not been isolated, nor is the mechanism of the production of the disease known. The intoxicant appears to act as a neurotoxin.⁴

Recently Rudra and Bhattacharya⁵ have reported a marked increase in serum alkaline phosphatase content in human lathyrism. Ten male patients, ranging in age from 16 to 45 years were studied. Neither the duration nor the intensity of the disease was stated, although it was observed that "usually the serum-phosphatase level is a measure of the

severity of the disease." In the group, the enzyme content of the serum ranged from 18.7 to 56.5 units (Bodansky), with an average of 38.7. In a group of 12 healthy males of the same age range, the phosphatase content varied from 0.8 to 5.7 units. The minimal value of the lathyrism group was 228% higher than the maximal value of the normal group.

Experimental lathyrism has been produced in young rats fed diets which contained considerable amounts of the seed of the flowering sweet pea (*Lathyrus odoratus*)^{6,7} and other species of *Lathyrus*. In view of the marked increases in alkaline phosphatase of the serum reported in human lathyrism, we have studied the enzyme content of the serum in experimental lathyrism of the white rat.

In preliminary experiments with young (50 g) rats, difficulty was experienced in obtaining amounts of serum sufficient for serial determinations during the course of the experiments. Subsequently we have employed somewhat older animals in which it was possible to secure repeated samples of blood for analysis as the symptoms of lathyrism developed. With older animals, however, the onset of lathyrism is greatly delayed and the

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TABLE I.
Alkaline Phosphatase of Serum of Rats Fed Sweet Pea and Edible White Pea Diets.

Period on diet, days*	Diet Rat No.	Phosphatase units (King-Armstrong)									
		Sweet pea					White pea				
		1	3	5	9	11	2	4	6	10	12
0		85	89	83	67	59	142	82	101	70	62
8-17		76	64	112	70	76	92	90	103	68	75
29-33		80	67	115	70	66	80	129	136	81	109
63		94	73	54	47	99	118	145	67	46	92

* The period at which samples of blood were collected varied somewhat within the ranges indicated for different rats. Rats 1 and 2, 3 and 4, etc., were paired in the feeding experiments.

changes in the bones^{6,7} are less marked.

Ten adult male rats (200 g) were fed the diet described previously⁷ (50% of ground sweet pea seed) for periods of 10 weeks. An equal number of controls, in paired feeding experiments, received the edible white pea of commerce (*Pisum sativum*, var. *arvense*). All animals which received the sweet pea diet developed lameness, spinal curvature, and, in a few cases, marked paralysis during the experimental period. Blood was obtained by clipping the end of the tail after the animal had been placed in a warm chamber at 56° for 5 min. After clotting, the serum was obtained by centrifugation; the centrifugate was decanted and the serum was centrifuged a second time. The upper portion of the second centrifugate was removed by a pipette and used for the phosphatase determination. Since the phosphatase content of white and red cells is much greater than that of the serum, it was necessary to remove all the cellular elements and to avoid hemolysis as much as possible. Alkaline phosphatase was determined by the method of King and Armstrong.⁸ The results are reported as phosphatase units per 100 ml of serum (*i.e.* mg of phenol liberated by the hydrolysis of disodium

monophenyl phosphate under standard conditions).

Results obtained with 5 pairs of animals are shown in Table I. They are typical of the values obtained with all 10 pairs. Although there was considerable variation in the phosphatase content both in the same rat over the experimental period and also in different animals, there was no evidence of any increase as the clinical symptoms of lathyrism developed, nor was there any significant difference between the values obtained with the control (white pea) and the experimental (sweet pea) groups. Certainly there was no indication of such a marked elevation of the alkaline phosphatase as has been reported by Rudra and Bhattacharya⁵ in human lathyrism.

Summary. No significant changes in the concentration of alkaline phosphatase of the serum were observed in rats in which experimental lathyrism was produced by feeding diets containing 50% of sweet pea (*Lathyrus odoratus*) seed. This does not confirm the observations of Rudra and Bhattacharya in which the phosphatase values were markedly increased in human lathyrism.

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⁸ King, E. L., and Armstrong, A. R., *Can. Med. Assn. J.*, 1934, **31**, 376.