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Experimental Lathyrism in the White Rat.*

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Lathyrism, associated with the consumption of considerable amounts of certain species of legumes of the genus *Lathyrus*, has been a common disease of man in India, northern Africa, and occasionally in other countries.[1] Lathyrism has also been observed to occur in domestic animals and has been produced experimentally in laboratory animals. The outstanding symptoms are muscular weakness and paralysis of the extremities.

Neither Zagami,[2] McCarrison,[3] nor Visco[4] was able to produce experimental lathyrism (*Lathyrus sativus*, L., and *Lathyrus cicera*) in white rats, although impaired growth and failure of normal organ development, particularly of the reproductive and skeletal systems, were observed. Geiger and coworkers[5] produced lathyrism in rats by feeding diets which contained *Lathyrus odoratus*, the flowering sweet pea, at levels of 80, 50, and 25% of the diet. Characteristic symptoms were lameness, paralysis, and curvature of the spine and sternum.

Our experiments were carried out with finely ground meal (20 mesh sieve) prepared from decorticated sweet peas (*Lathyrus odoratus*) and as a control, with similar meal from the edible split pea of commerce† (*Pisum sativum*, subspecies *arvense*). These were incorporated into the diets of young white rats as follows: pea meal, 50%; casein (Labco, vitamin-free), 10%; corn starch, 27%; sucrose, 5%; salt mixture (modified Osborne-Mendel), 4%; cod liver oil, 2%; corn oil, 2%. Each rat received approximately 200 mg of a dried yeast tablet (Mead Johnson and Co.) daily. The casein was added to the diet to insure a satisfactory protein content, since the proteins of many legumes are known to be inadequate if fed as the sole source of protein. The total protein of the mixed diet was calculated to be 26% (16% derived from the peas).

Young white rats, 50-80 g in weight, in litter units, were paired as to sex and weight. The paired feeding method was employed; one rat of each pair received the sweet pea diet *ad libitum*, while the intake of the paired litter mate fed the edible pea diet was limited by the food intake of the mate fed sweet peas.

In the first series in which 9 pairs were fed, all of the rats fed the *Lathyrus* pea diet showed definite symptoms of lathyrism (incontinence, lameness, paralysis of limbs, spinal curvature of the thoracic region, etc.), symptoms being observed in from 2 to 7½ weeks. No control (edible pea diet) animals showed any abnormalities during the period of observation. In addition, 2 pairs received extra casein to give a total dietary protein content of approximately 41% (25% of casein), the extra casein replacing an equivalent amount of starch. The presence of larger amounts of a superior

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1 Stockman, R., *J. Pharm. and Exp. Therap.*, 1929, **37**, 43.

2 Zagami, V., *Atti della Reale Accademia Nazionale dei Lincei*, Ser. 6, Rendiconti 1931, **14**, 218; abstracted in *Chem. Abs.*, 1932, **26**, 3823.

3 McCarrison, R., *Ind. J. Med. Res.*, 1928, **15**, 797; McCarrison, R., and Krishnan, B. G., *Ibid.*, 1934, **22**, 65.

4 Visco, S., *Arch. farmacol. sper.*, 1923, **35**, 39; **37**, 1; **47**, 269; abstracted in *Chem. Abs.*, 1923, **17**, 1983; 1924, **18**, 1345, 2544.

5 Geiger, B. J., Steenbock, H., and Parsons, H. T., *J. Nutrition*, 1933, **6**, 427.

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animal protein in the diet did not prevent or delay the onset of lathyrism, since characteristic symptoms were observed in 3½ to 5 weeks.

In a second series the effect of cold water extracts of the peas was studied. *Lathyrus* peas were extracted overnight at 0° with distilled water, the fluid decanted and extraction repeated 3 times. The combined extracts were evaporated to a thick syrup *in vacuo*. Edible split peas were similarly extracted. To the split pea residue was added the extract of the *Lathyrus* peas and to the *Lathyrus* residue, the split pea extract. The combined extract and residue in each case were dried in thin layers at 80°, ground finely and incorporated into the diets, as described above. All of the rats receiving the *Lathyrus* extract-split pea residue developed acute lathyrism in from 2½ to 4½ weeks, while none of the rats receiving the split pea extract-*Lathyrus* pea residue diet showed any symptoms in 7 to 8 weeks. It thus appears that the toxic substance is readily extracted from *Lathyrus* meal by cold water and that the extracted residue is relatively non-toxic. This is in accord with the findings of Geiger,[5] who extracted peas with boiling water.

Pathological studies of the bones made with the cooperation of Professor Carl V. Weller revealed changes in the long bones of the leg similar to those observed in acute scurvy. The rat is believed to be able to synthesize ascorbic acid and does not require the preformed dietary vitamin. It was believed that the toxic principle of *Lathyrus odoratus* might either affect the synthesis of ascorbic acid or in some way increase the requirement beyond the capacity of synthesis of the organism. In a third series, rats fed the sweet pea diet were paired, one animal of each pair receiving in addition 12 mg of ascorbic acid. All of the animals showed symptoms of acute lathyrism within the usual period of time. No preventive effect of the ascorbic acid could be demonstrated.

Further experiments designed to determine the nature of the toxic principle are in progress.

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Role of the Premotor Cortex in Human Motor Activity.

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The collateral systems (thalamus, basal ganglia, cerebellum, and premotor cortex) which play such a prominent role in human motor activity are particularly refractory to experimental manipulation, due to the fact that complex motor dysfunction is peculiarly human and has no certain counterpart in lower mammals. It is desirable, therefore, to employ human material for information relative to the motor complex. This report serves to clarify certain points concerning the anatomy and function of the human premotor region.

A patient (aged 38 years) was subjected to bilateral (2-stage) premotor cortical excision (Klemme)[1] for the relief of generalized tremor in both upper extremities, moderate tremor and rigidity of the left lower extremity, and tremor of the tongue. The right side was operated first with relief of the contralateral tremor. The left side was operated 9 months later, the patient expiring on the seventh post-operative day. At no time was there loss of volitional movement, the residua being generalized weakness, more marked on the left, and inability to do finely coördinated movements with the left hand. Degeneration studies with the Swank-Daven-

[1] Klemme, R. M., *Res. Publ. Assn. Nerv. Ment. Dis.*, 1940, **21**, 596.