LATHYRISM: A REVIEW OF RECENT DEVELOPMENTS*

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LATHYRISM has been defined by Selye,\textsuperscript{38} in his excellent article on the subject, as “a disease induced by the ingestion of certain Lathyrus pulses or treatment with the toxic principles of such pulses and related compounds most of which are aminonitriles.” The name is derived from the Greek lathros, vetchlings. Its Greek root is thought to be thouros, exciting, impetuous. The name lathyrism was applied to the clinical disease by Cantani in 1873, though the disease had not escaped the attention of Hippocrates.

The classical form of the disease is one affecting the nervous system, termed neurolathyrism by Selye. The clinical syndrome\textsuperscript{11} usually consists of an acute onset of weakness of the lower extremities, sometimes with prodromal sensory manifestations of pain or paresthesia, progressing to spastic paraplegia. Symptoms indicative of involvement of the sensory tracts of the spinal cord are not unusual. Loss of sphincter control and impotence are often present. Finally, there may be muscular atrophy. The upper extremities are less frequently affected than the lower. Symptomatic regression is uncommon and no effective therapy is known. The disease is said to be more common in young males. In addition to man, cattle, horses, swine, ducks, peacocks and elephants are subject to neurolathyrism. The human disease tends to occur during periods of famine and has been associated with the ingestion of considerable quantities of one of the following pulses: \textit{L. sativus} (dog-tooth pea), \textit{L. cicera} (chick pea), \textit{Vecia sativa} (tares or acta), \textit{Erviua ervi:Va} (bitter vetch). The common pea, \textit{Pisum sativum}, is benign. Numerous epidemics of the disease have occurred in India and there have been occasional outbreaks in Spain, France, Italy, Algeria, Syria and Russia. None has been reported in North America, though domestic animals have been affected by the foliage of \textit{L. sylvestris}.

The pathology of the disease in man is lacking in many details. It is summarized as follows: “Partial degeneration of the motor tracts of the spinal cord,” “Microgliosis in the anterior horns and the lateral cords,” “Anterolateral sclerosis in the dorsolumbar spinal cord.” Buzzard and Greenfield\textsuperscript{9} described a single lesion thus: “The lesions were very similar to those seen in ergotism, i.e., a pseudo-systematised degeneration of the long ascending and descending tracts of the cord. This was particularly marked in

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\textsuperscript{†} The original sources of articles published prior to 1957 may be found in Selye’s paper.

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the pyramidal tracts, both lateral and ventral, in the direct cerebellar tracts, and in the dorsal columns. In the lumbar and thoracic regions the margins of the cord showed the same loose, honeycombed structure as is seen in the more rapid cases of 'subacute combined degeneration,' with oedema at the point of entrance of the dorsal roots. The nerve roots showed a definite increase of connective tissue, and in the peripheral nerves a similar increase was seen, chiefly in the epi- and peri-neurium. These changes are all of the same character as those found in ergotism, and it is probable that the two diseases are closely connected."

The foregoing is a brief summarization of the accumulation of knowledge of lathyrism over about 2,500 years. However, in the early 1930’s, Beatrice Geiger,14 at the University of Wisconsin, undertook for her Ph.D. thesis the study of the effect of sweet peas in the diet of young rats. The results, published in 1933, included retardation of growth, lameness, spinal curvature, sternal curvature, enlargement of the costochondral junctions, mal-formation of the long bones, and hernia formation. Thus emerged experimental osteolathygism. These findings were soon corroborated. Ponseti and co-workers31,32 have made extensive studies of the mesodermal deformities produced by L. odoratus seeds. The basic pathology appears to be loss of cohesion of the cartilage matrix of the epiphyseal plates in young rats, with loosening and detachments of osseous insertions of tendons and ligaments. There resulted the following abnormalities: Slipped epiphyses, metaphyseal fibrous defects, kyphoscoliosis, thoracic deformities, detachments of the tibial tuberosity, subluxations and dislocations of the shoulder, diastasis of the sacro-iliac joints, degeneration of the intervertebral discs, disc herniations, Legg-Perthes-like disease of the femoral head, periosteal detachments with new bone formation, and degenerative arthritis. As a final damnation of the otherwise sweet pea, they found a very high incidence of dissecting aneurysms of the thoracic aorta. It appears obvious that L. odoratus is meant to be smelled, not eaten. In full justice, it must be admitted that it does not produce primary lesions of the nervous system. However, fatal fetal edema and absorption are among its effects.

The year 1954 ushered in the chemical phase of lathyrism. From numerous reports there emerged three aminonitriles capable of producing osteolathygism. The basic chemical structure seems to be an amino group separated from the terminal cyanide group by one or two methyl linkages. The three osteolathyrogens are: Aminoacetonitrile, β aminopropionitrile, and methyleneaminoacetonitrile. Many closely related compounds have been found to be non-lathyrogenic. However, one of special interest is β,β′-iminodipropionitrile which produces a form of "neurolathyism"26 to be described later. A considerable number of chemicals, including a series of antioxidants, have been tested for possible neutralizing effects upon the osteolathyrogens without success.

We arrive now at the pathophysiological phase of lathyrism, where Selye36 has made major contributions. Several "conditioning factors" have