Diets containing ground Lathyrus odoratus seeds fed to rats produce kyphoscoliosis, epiphysial slipping with fibillation and rents in the epiphyseal plate cartilage, loosening and detachments of tendon and ligament insertions, osteoarthritis, and other skeletal deformities. Some rats develop dissecting aneurysms of the aorta and hernias. (The SCAP indicates that this paper has been cited in over 210 publications since 1955.)

This paper stimulated the study of human disorders resembling the experimental lesions observed in rats. Thus it was found that the pathology of dissecting aneurysm of the aorta in patients with Marfan’s disease, and in some of the Ehler-Danlos syndromes, is similar to the pathology seen in the experimental animals. The incidence of dissecting aneurysm of the aorta in human patients with skeletal deformities and with Marfan’s disease was further explored by us in 1955. The epiphyseal plate lesion seen in lathyric rats is similar to the lesion observed in children with slipping of the upper femoral epiphysis, with Legg-Perthes disease, and with juvenile kyphosis. The pathology of “idiopathic” scoliosis in humans, however, remains to be elucidated.

The cause of the loss of strength of the newly formed connective tissue and cartilage in lathyric animals intrigued biochemists. The observations on lathyism laid the groundwork for the study of cross-linking in collagen. In the mid-1950s an active principle was isolated from the sweet pea and identified as β-aminoapropionitrile (BAPN). In 1959 C.J. Levene and J. Gross discovered that in lathyric animals the newly synthesized collagen fibrils were soluble in cold neutral physiologic salt solution. After much work by many researchers for the elucidation of the collagen cross-linking mechanism, S.R. Pinnell, J. Gross, and R.C. Siegel found the enzyme lysyl oxidase responsible for converting the specific lysine residue to an aldehyde and discovered that the lathyrogen BAPN functions by inhibiting the enzyme.

Patients with a type of Ehler-Danlos syndrome have a genetic deficiency of this enzyme.

For this and related work, I received the Kappa Delta Award for Outstanding Orthopaedic Research in 1956. Robert Shepard wrote his thesis on the muscle physiology of lathyrysm and vitamin E deficient animals and is now professor of physiology at Wayne State University.