mal degree of radioactivity; in untreated animals under these conditions, spinal ganglion neurons give a less intense autoradiograph than nerve cells within the neuraxis (*1*). These observations provide evidence that, in cats treated with fluoroorotic acid, the ability to incorporate labeled methionine into the protein of nerve cells and glia within the neuraxis is impaired but that the ability to incorporate it into the protein of spinal ganglion neurons is not.

Several considerations make it seem likely that the effects of intracisternal injection of 5-fluoroorotic acid in cats result from an interference with pentose nucleic acid metabolism. The chromatolysis of Purkinje neurons itself represents a quantitative reduction of cytoplasmic pentose nucleic acid (*6*). The course of this syndrome—that is, the symptom-free latent period, gradual onset, and progressive worsening—resembles the toxic effect of nucleic acid antimetabolites on bone marrow, liver, intestinal mucosa, and tumors (*3*). The apparent diminution in incorporation of labeled methionine into nerve and glial cell protein furnishes further support for this hypothesis, since pentose nucleic acid plays an important role in protein synthesis (*7*). The significance of this evidence is enhanced by the finding that spinal ganglion cells show little reduction in incorporation of labeled methionine; 5-fluoroorotic acid would be expected to have much less effect on these cells because they incorporate orotic acid into pentose nucleic acid at a relatively slow rate (*1*). Possible mechanisms of action of 5-fluoroorotic acid include: (i) competitive or noncompetitive blocking of the incorporation of normal precursors into pentose nucleic acid, leading to depletion of the acid; and (ii) the incorporation of the fluorinated pyrimidine analog or its derivatives into pentose nucleic acid, rendering it metabolically ineffective or harmful. The proximity of the cerebellum to the site of injection and its active turnover of pentose nucleic acid probably account for the early and severe derangement of this portion of the neuraxis. The production of neurological deficit, neuronal lesions, and impairment of protein metabolism in nerve and glial cells by a nucleic acid antimetabolite indicates the possibility that some "degenerative" and other disease processes which occur within the central nervous system may be caused by biochemical or other disturbances in nucleic acid metabolism (*8*).

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2 January 1958

Relation of Structure to Adsorption of Substances during Crystallization of L(−) Tyrosine

The incorporation of impurities into growing crystals has attracted considerable attention for a long time. Whereas the prevailing emphasis has been directed toward modification of crystal growth or habit, virtually nothing has been said of the relationship between chemical structure and incorporation.

With L(−)tyrosine as the parent substance, and chemically related substances as the impurities, the incorporation by the growing crystals was studied by the use of the spectrophotometric method of Goodwin and Morton (*1*). The data, illustrated in Fig. 1, demonstrate that the incorporation of the various substances used is specific. No incorporation was observed with hydrocinnamic acid (not shown) up to 0.016*M*, where solubility difficulties are encountered. In the case of L(−)alanine (not shown), a concentration of 0.047*M* was required before incorporation could be detected [0.041*M* L(−)alanine per mole of tyrosine].

The adsorption process is clearly evident in the cases of L(−)histidine, D(+)-phenylalanine, and L(−)phenylalanine. The amount of impurity incorporated is seen to be related not only to the structural similarity of the mother substance and the impurity but also to the spatial relationships of the two substances, as evidenced by the stereoisomeric specificity of the phenylalanine isomers.

For L(−)phenylalanine, the adsorption empirically resembles that of Henry's law or a simple Langmuir isotherm, which is indistinguishable from it at small adsorptions. It is possible to conceive of the growing crystal, because of its ability to present a changing surface to its surrounding medium, as obeying the Langmuir isotherm for a given surface and Henry's law for the sum total of surfaces generated, resulting in what is known as a solid solution. In this instance the heat of adsorption and the adsorption capacity of each new surface would have to remain constant. When this does not occur, deviations from linearity would be expected. This, perhaps, is part of the exacting requirements necessary for specificity of a stereoisomeric adsorption.

Additional information concerning this specificity is obtained from the examination of the molecular models of the interacting substances. These are shown in Fig. 2. Models with the same configuration are depicted as L. The stereoisomer of this configuration is arbitrarily designated D. If we assume that the complementary charged groups of the two interacting substances are active in the adsorption process, the charged amino group of one is placed in the position of closest approach to the carboxylate ion of the other, the rings of both molecules being in the same plane. In the case of L(−)tyrosine and D(+)phenylalanine, the two carboxylate ions are capable of very close approach, and hence one would anticipate an inhibitory effect from the resulting repulsion. This is actually reflected in the decreased adsorption at higher concentrations (Fig. 1). In the case of L(−)phenylalanine and L(−)tyrosine, this proximity of the carboxylate ions does not exist. In fact, it is possible that there is a hydrogen bond between the two carboxylate ions, thus enhancing the adsorption.

These experiments indicate that no one bond type is responsible for the adsorption by tyrosine. The ionic bonds, which are the most important in the crystal, as evidenced by the high melting points of dipolar ions generally, must be supplemented by other forces. With the exception of hydrocinnamic acid, all the substances studied may be looked upon as derivations of alanine. Hence, if the

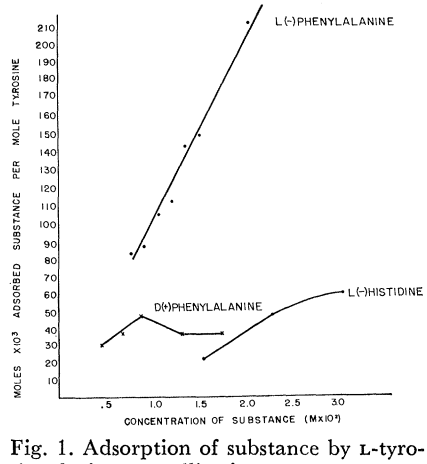

Fig. 1. Adsorption of substance by L-tyrosine during crystallization.

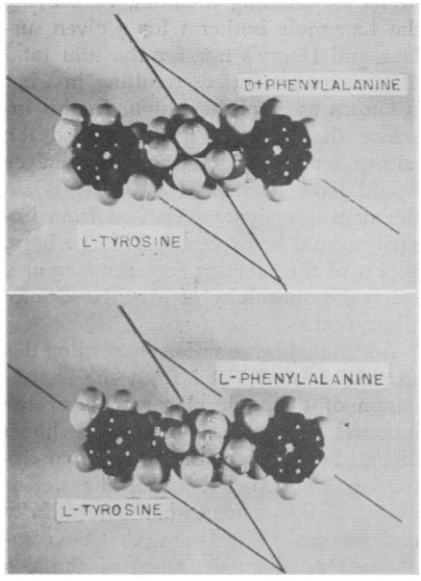

Fig. 2. (Top) Molecular models of L-tyrosine and D(+)phenylalanine with complementary charged groups in juxtaposition. Note the close approach of the two negative carboxylate oxygens (labeled O). (Bottom) Molecular models of L-tyrosine and L-phenylalanine. Note the separation of the carboxylate oxygens made possible by a hydrogen bond.

complementary charged groups alone were responsible for the adsorption, one would anticipate no differences among the reactants, or possibly even a stoichiometric relationship. The fact that this is not observed indicates that other factors, such as steric relationship and hydrogen bonding, must be present to supplement the initial binding of the charged groups (*2*).

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16 December 1957

Differential Staining of Connective Tissue Fibers in Areas of Stress

During the course of investigations of age changes in connective tissues, sections of formalin-fixed human jaws and teeth were oxidized in peracetic acid for 30 minutes and subsequently stained with aldehyde fuchsin. Many fibers of the periodontal membrane stained a brilliant purple; others remained unstained (Fig. 1). The fibers that remained unstained were birefringent and therefore are believed to be collagen. The purple-stained fibers were interspersed between collagen fibers and were not birefringent. They were round, elliptical, or flattened on cross section and varied from 3 to less than 0.5 μ in diameter, the larger ones exceeding 2 mm in length.

In the mid and apical portions of the roots of teeth, these fibers were anchored either in the cementum or bone on one end, and they frequently ramified while they followed the course of the principal fibers. It was not possible to trace a single fiber that extended from the tooth to the bone. In the area of the cementoenamel junction, the fibers were anchored in the cementum and either curved upward into the gingiva, along with the collagen fibers, or joined with the transseptal group. In addition, at all levels of the periodontal and gingival tissues in mesiodistal sections, numerous fibers were seen, cut crosswise or tangentially; this indicated their many-directional course.

These fibers were also found in tendons (Fig. 2), in ligaments, in the adventitia of blood vessels, in the connective tissue sheath surrounding hair follicles, and in the epineurium and perineurium in the human being. In sections of tendons and ligaments they were found internally as well as surrounding the collagen bundles, taking the same course as the collagen fibers.

The fibers were found in the periodontal membranes of human beings, mice, rats, and guinea pigs and in the Achilles tendons or patellar ligaments, or both, of human beings, monkeys, mice, rats, guinea pig and a turkey. In the guinea pig periodontium, some of these fibers were flattened like a ribbon and were oriented in an apical-occlusal direction, as they were in the periodontal membranes of developing human teeth.

With the usual staining procedures, connective tissue fibers of periodontal membranes, tendons, and ligaments appear to be composed almost entirely of white collagen. Fine elastic fibers have been described in tendons (*1*), and a few elastic fibers are found in human periodontal membranes, associated with blood vessels and nerves and not arranged to support the teeth during mastication. The fibers described in this report do not stain with any of the elastic tissue stains and were not dissolved in formalin or alcohol-fixed sections by elastase, as elastic tissues were in comparably treated skin sections. Reticular fibers of the spleen and lymph nodes were not stained by this method, and reticulum stains did not differentiate these fibers.

Undoubtedly these fibers have been called collagen heretofore and further investigation may reveal them to be a form of collagen that develops in areas of stress. Since they were not found in skin or in granulation tissue, it is unlikely that they are a form of procollagen or aged collagen.

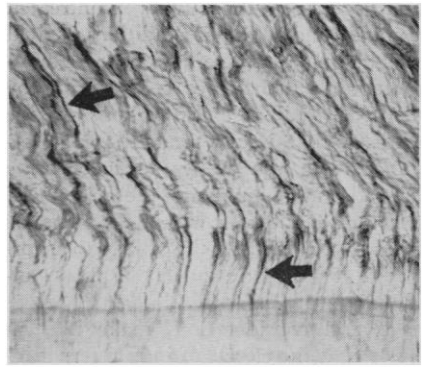

Fig. 1. Section of tooth and periodontal membrane from a white male, aged 20. Arrows point to the special fibers reacting with aldehyde fuchsin after peracetic acid oxidation. Neighboring collagen fibers are unreactive and pick up the counterstain. Horizontal band at bottom, cementum; remaining area, periodontal membrane. (about × 650)

Fig. 2. Section of Achilles tendon from a white male aged 53. Arrows point to special fibers reacting with aldehyde fuchsin after peracetic acid oxidation. (about × 225)

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24 December 1957

Natural and Fission-Produced Gamma-Ray Emitting Radioactivity in Soil

The gamma-ray spectrum emitted by present-day surface soil reveals the presence of several lines which do not pertain to either the thorium or uranium series or to K^{40}. These additional gamma-ray lines come from radioactive fission products in fallout, and previous investigations at Argonne National Laboratory have shown that these gamma-ray spectra may be gotten *in situ* by placing a