

tine of teeth and the matrix of bone. The characterization applies to cartilage and connective tissue, and, by inference, to other intercellular substances, including that of blood vessels. The hypothesis is entertained, based upon the study of repair in incisor teeth of scorbutic guinea pigs, that in the formation of intercellular substances there is a change of the material from a liquid to a solid or jell state, and that the missing factor in the scorbutic condition is one affecting the jelling or setting of a liquid product.

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#### The epithelial tissues in experimental Xerophthalmia.

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Standard strains of white rats obtained from the Wistar Institute were employed in this study. The diet employed was practically that of Mendel, as used by Yudkin and Lambert<sup>1</sup>: Casein, 18 grams; mineral salts (Mendel's mixture), 4 grams; starch, 54 grams; lard, 24 grams; yeast extract (Harris), 0.1 gram. Control rats on the same diet, but with fresh butter in place of lard, have been maintained in a healthy condition since August, 1924. On the deficient diet, rats exhibited the usual external evidences of the xerophthalmic condition in from seven to sixteen weeks, according to their age. The rats which died in advanced xerophthalmia, or which were sacrificed, presented a few very striking gross pathological changes, in addition to the pathology of the eyes, which is so well known. Most conspicuous among these changes are the presence of cavities at the base of the tongue and in the pharynx filled with a yellow cheesy material, and similar abscess-like cavities in the sub-maxillary glands. In male rats, very striking changes are to be observed in the prostate glands and seminal vesicles. These organs may be shrunken, yellowish in color, and filled with opaque yellowish spots. These gross changes are readily accounted for by the microscopic examination. The cavities described are in reality cysts lined with a stratified keratinizing epithelium, and the cheesy contents is a

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<sup>1</sup> Yudkin and Lambert, *J. Exp. Med.*, xxxviii, 1.

mixture of desquamated keratinized cells and leucocytes. A careful microscopic study of rats killed at different stages in the development of advanced xerophthalmia shows that the morphological concomitants in the condition are limited practically to epithelial structures. While interesting transitional stages may be observed, and are being studied, the condition of xerophthalmia results in the transformation of various epithelia into a stratified squamous keratinizing epithelium. This change is practically constant in the upper respiratory tract, including the whole of the nasal passages, larynx, trachea, and bronchi. In the digestive tract, the stomach and intestines have so far exhibited no change, but all the salivary glands and the accessory salivary glands are affected, and frequently show cavities resulting from the retention of desquamated keratinized epithelial cells. Similar changes occur late, in the pancreas. In the genito-urinary tract, this transformation into keratinized epithelium is found in the renal pelvis, bladder, seminal vesicles, epididymis, and prostate gland. In all of the glands noted above there is a considerable degree of atrophy before the change in character of the epithelium takes place.

Other changes observed include a striking atrophy of the thyroid gland, testes, and paraocular glands. The complete histological sequence involved in this change in structure of epithelium has not been worked out. In most instances in glands, the earliest changes are noted in the ducts. The change is an abrupt one, beginning in foci and spreading. This change is attended by the acquisition of intense basic staining properties on the part of the cells, and these cell clusters lie in the lowest layer of the mucosa and have at the first the appearance of minute independent new growths. Gradually, however, the whole of the normal mucosa becomes replaced by the new type of epithelium. Preliminary mitochondrial studies indicate that there is no intimate relationship between the maintenance of mitochondria and the transition in type of epithelium.

#### *Conclusions:*

Deprivation of the anti-xerophthalmic vitamine (fat soluble A) affects specifically epithelial tissues. This effect is manifested in cells having presumably widely different chemical (secretory) functions, and terminates in the complete loss of specific function and the transformation into a common type of chemically inactive (non-secretory) epithelium.