

The resistance of the bacilli contained in the brain was tested by injecting cultures of X₂ and X₁₀ strains intraperitoneally into normal guinea pigs. The animals died in 24 to 48 hours, having developed septicemia, fibrinopurulent peritonitis and hemorrhagic splenitis—a pathological picture wholly different from that induced by the pure typhus virus. The brain, which yielded cultures of *Proteus bacilli*, was cut into fragments, immersed in 1 and 50 per cent glycerol and kept in the ice-box. Interval cultures of this glycerolated brain showed profuse growths of the *Bacillus proteus* for as long as 3 weeks. After one month the material in the 1 per cent glycerol yielded a sparse growth of *Bacillus proteus*, and that in the 50 per cent glycerol gave no growth.

In conclusion, *Bacillus proteus* X₂ and X₁₀, either in culture or in the brain of *Proteus*-infected guinea pigs, is quite resistant to the action of glycerol, and differs markedly in this respect from the typhus virus. Under these experimental conditions the infective and immunizing properties of the pure virus are very susceptible to the destructive action of glycerol.

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The effect of the scorbutic state upon the production and maintenance of intercellular substances.

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Guinea pigs in the condition of absolute scorbutus, *i. e.*, complete deprivation of anti-scorbutic substances in the diet, have been studied, and the effects of the administration of anti-scorbutics noted. The diet employed was: Soy beans, 50 grams; rolled oats, 28 grams; dried skimmed milk (Klim), 10 grams; yeast, 4 grams; butter, 5 grams; calcium carbonate, 1 gram; sodium chloride, 1 gram. For roughage, the guinea pigs were liberally supplied with filter paper. Control guinea pigs, which received the same diet, with the liberal administration of orange-juice, or green vegetables, remained healthy.

The effects have been studied in growing guinea pigs and in the repair of lesions of bone experimentally made. The earliest

effect of the scorbutic state is to be found in the incisor teeth, and is evidenced by the manner in which the formation of dentine is affected and in changes in the layer of odontoblasts. The earliest changes may be observed in six to seven days, while a few days later very striking conditions are found, among the most noticeable of which is the separation of the layer of odontoblasts from the dentine. This space is presumably filled by liquid. The odontoblasts undergo striking changes in regard to size, arrangement and staining reaction. The effect of the administration of an anti-scorbutic upon this condition is apparent within forty-eight hours, and results in the prompt formation of dentine so as to fill the space caused by the separation of the layer of odontoblasts. In the bones, formation of bone ceases immediately, while osteoblasts in certain locations, particularly beneath the periosteum, continue to proliferate. This applies both to flat bones and long bones. Accumulations of osteoblasts of considerable size may occur before hemorrhages take place. That the cells under consideration are osteoblasts is proved by the effect of the administration of a single dose of an anti-scorbutic substance, because it is followed by the prompt appearance of bone matrix between the cells. A single administration of orange juice produces an effect which is easily demonstrable forty-eight hours later. In the incisions through the cortex of bone in the scorbutic state there is no bony repair, while controls operated on in the scorbutic state, but given anti-scorbutic substances after the operation, show new bone formation very promptly. The repair of soft tissues is likewise very markedly affected. Proliferation of fibroblasts is apparently but little affected by the scorbutic state, but there is a marked diminution in the amount of intercellular substance formed. There is also a very marked effect seen in the retardation of new blood vessel formation in the organization of lesions, etc.

Other observations were made on the effect of the scorbutic state upon bone previously formed and upon cartilage.

Summary and Conclusions.

The scorbutic state may be characterized as one affecting supporting tissues in which the cells are unable to produce and maintain intercellular substances. This condition affects various supporting substances to a different degree, and is most marked in those in which the intercellular substance is calcified, as the den-

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 Lambert¹: 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

¹ Yudkin and Lambert, *J. Exp. Med.*, xxxviii, 1.