The purpose of this report is to give the results of some simple experiments designed for the purpose of characterizing pathologically (on a histopathologic basis) the scorbutic condition. We have followed the histologic sequences in bone, connective tissue and teeth during the development of the absolute scorbutic condition and the immediate reparative processes following administration of antiscorbutics.

The pathology of human and experimental scorbutus has been extensively studied, and the main facts clearly established in a literature too extensive to be reviewed here. Hess, in his admirable book, gives a good review of the pathology up to 1920. Special mention, however, must be made of the monograph of Aschoff and Koch in 1919, though adequately quoted by Hess, and the monograph of Höjer. The work of Aschoff and Koch is based on human postmortem material, that of Höjer principally on the experimental disease in guinea-pigs. Aschoff and Koch review previous contributions, and their paper deals largely with the changes in bone and cartilage found at costochondral junctions, and at the junctions of diaphyses and epiphyses. From previous work reviewed by them and from their own observations, the important features in the bone pathology may be enumerated as follows: cessation of new bone formation and rarefaction of existing bone of cortex and spongiosa; irregularities, absorption and disappearance of cartilage columns, yielding of the bone under strain and a zone...
of fragmentation of bone trabeculae adjacent to the line of junction with cartilage. This is the "trummerfeld" zone and actual separation by fracture may occur here. Hemorrhages occur. Osteoblasts assume elongated shapes and apparently disappear from regions of bone formation.

Höjer's description of the bone changes does not materially differ from the foregoing, but he objects to Aschoff and Koch's hypothesis, and ascribes the deficient bone formation to ... "a degeneration, or rather a receding of the bone forming cells, these being changes so as to form a qualitatively more and more degenerate as well as quantitatively more and more reduced bone, till their activity eventually leaves altogether." He therefore attributed the pathologic condition to defective function of cells, and excludes the factor of materials available by the osteoblasts.

Höjer also demonstrates satisfactorily that in tuberculosis in scorbutic guinea-pigs there is much less collagen deposited by fibroblasts in the periphery of the tuberculous lesions. He also maintains without satisfactory presentation of evidence that there is in general an atrophy of collagen in connective tissue of various organs and in blood vessels, thus accounting for hemorrhages.

Our own work was formulated and begun before Höjer's monograph appeared. While we have studied every tissue and organ from our animals, the present account concerns only the following observations made on guinea-pigs in the state of absolute scorbutus and during early repair following the administration of antiscorbutics: (1) sequences in the incisor teeth, (2) sequences in bones of growing guinea-pigs, (3) sequences in the repair of soft tissues and (4) sequences in the repair of bone injury.
SUMMARY AND CONCLUSIONS

We have described the morphologic concomitants of the condition of complete scorbutus and the immediate responses in repair. Our work establishes the hypothesis of Aschoff and Koch and confirms some of the observations of Höjer, although our methods of procedure and resultant material give us few points of contact.

We characterize the condition of scorbutus as inability of the supporting tissues to produce and maintain intercellular substances. Direct proof of this conclusion has been obtained in study of teeth in regard to dentin, in the study of growth and repair of soft tissue in regard to the collagen of connective tissues. Our proof in regard to cartilage is incomplete.

The failure of capillary formation can be explained reasonably in the light of knowledge of other intercellular substances as due to failure of endothelial cells to form cement substance, an inference that Aschoff and Koch arrived at. We have at least shown that proliferative activity of the vascular endothelium is not at fault.

The proliferative power of epidermis, endothelium; fibroblasts and osteoblasts is not diminished in scorbutus. We are reasonably certain that it is augmented in the case of osteoblasts, which, however, undergo striking morphologic change.

Study of the sequences following antiscorbutic treatment has enabled us to control our observations at every stage in regard to the nature of cells contributing to the histologic ensemble of scorbutus. Osteoblasts, in spite of the great change in morphology, with complete similitude to fibroblasts, preserve their chemical potentialities and produce bone matrix.

Study of the sequences in teeth in progressive scorbutus, namely, the separation of the odontoblast layer from the dentin, led us to the theory that these cells continued to produce a liquid material. The same theory accounts for the edematous appearance of the fibrous-tissue-like structure in bones called gerüstmark. The theory as a whole is supported by the promptness and volume of matrix formation following antiscorbutic treatment.

We therefore advance the theory that the failure of cells to produce intercellular substance in scorbutus is due to the absence of an agent common to all supporting tissues which is responsible for the setting or jelling of a liquid product. Antiscorbutic substance is liberated in the destruction of tissues. The osteoporosis suggests further the hypothesis that this reaction is in some degree a reversible one.

We hope that the observations recorded in this report may suggest an approach to the study of the physiology of intercellular materials.
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