

THE INFLUENCE OF PURULENT INFECTION ON THE DEVELOPMENT OF EXPERIMENTAL SCURVY

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The relation of induced infection to experimental scurvy has been studied with reference to tuberculosis, and Höjer¹ found that this disease had no marked influence on the development and the extent of the scorbutic lesions in the different organs. In the course of an investigation of the regeneration of bone in scorbutic guinea-pigs, one of our animals developed an acute suppurative staphylococcus osteomyelitis. This animal was on a scurvy diet for 40 days, but developed no clinical signs of scurvy and at necropsy showed none of the cardinal lesions such as hemorrhages, beading at the costochondral junctions, and fractures. The abdominal fat was well preserved, the liver was large and fatty, and there was a splenomegaly of chronic infection. The animal weighed 322 grams when placed on the diet and 353 grams when killed. Its cage mates, which had been submitted to the same procedures, but which did not become infected developed severe acute scurvy after three weeks, and died with typical lesions within six weeks after the beginning of the experiment. This unusual result led me to gather more data on the possible relation between infection and scurvy.

Diet: This consisted of a soy bean flour base as used by Cohen and Mendel² and recently modified by Wolbach and Howe.³ The formula is as follows: soy bean flour, 50 parts; rolled oats, 29 parts; dried milk powder, 10 parts; brewer's yeast, 4 parts; butter, 5 parts; calcium carbonate, 1 part; and sodium chloride, 1 part. The soy bean flour, oats, and milk were mixed in these proportions and autoclaved at 15 pounds pressure for 45 minutes. The salts were then added. An adequate amount of this mixture, to which fresh yeast and butter were added, was fed daily. In addition the animals were given distilled water ad libitum and hay was given for roughage. This diet is deficient only in the antiscorbutic vitamin.

The Effect of the Scorbutic Diet on Normal Guinea-Pigs.—Twelve guinea-pigs weighing from 200 to 370 grams were fed this diet. Between the 13th and 18th day all manifested signs of scurvy such as

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¹ Acta paediat., 1924, suppl. 3, p. 8.

² J. Biol. Chem., 1918, 35, p. 427.

³ Wolbach, S. B., and Howe, P. R.: Arch. Path., 1926, 1, p. 1.

swollen and tender wrists, weakness, tender hind legs, and loosening of the teeth. Seven succumbed on or before the 30th day and by the 42nd day all had either died of scurvy or had been killed because they were moribund. A few animals were killed for necropsy between the 14th and 18th days, and on histological examination already showed well developed scorbutic changes in the costochondral junctions. The ribs best demonstrate the typical scorbutic changes, which have been described recently by Aschoff and Koch,⁴ Hess, Höjer,¹ and Wolbach and Howe.³

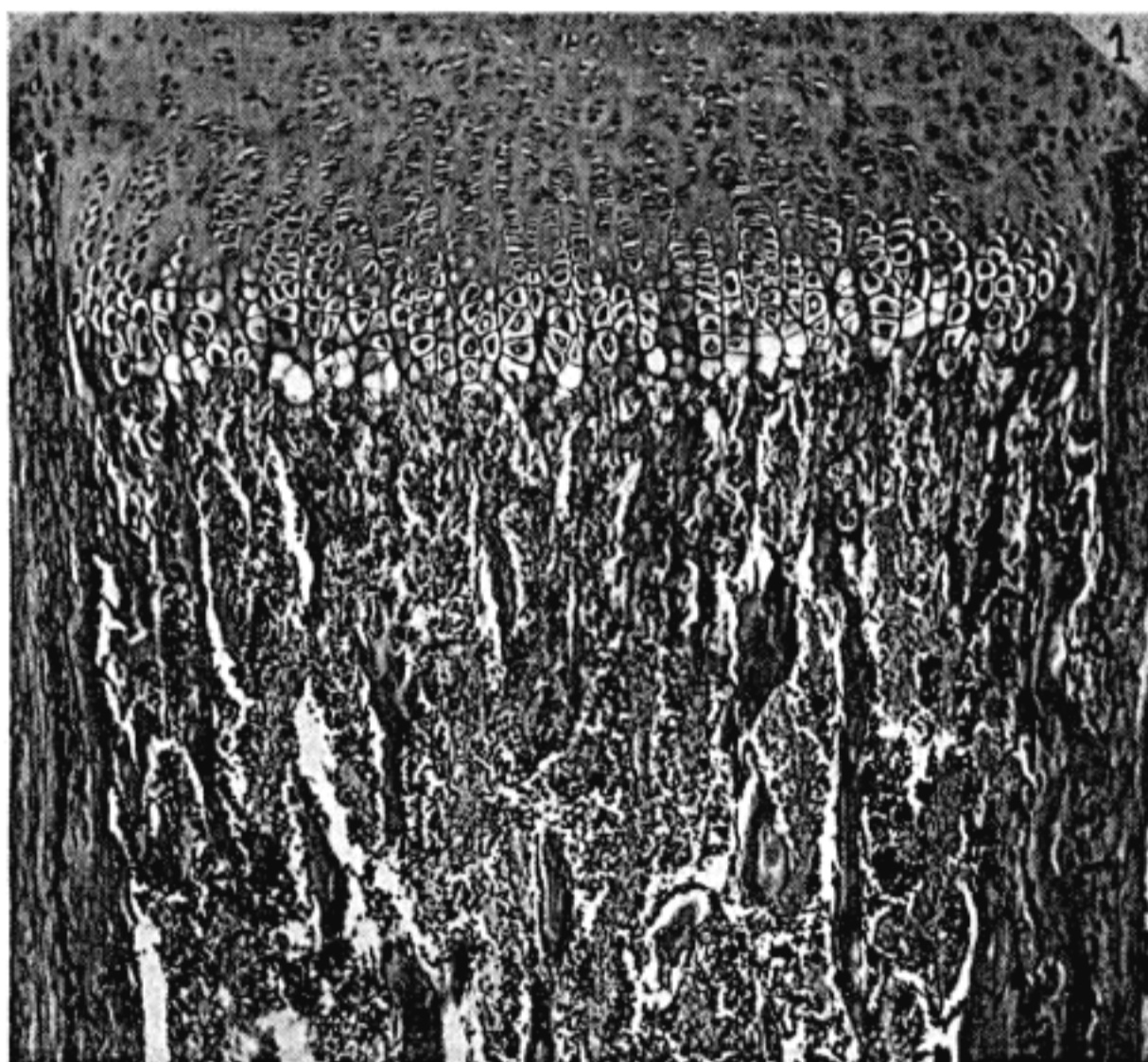


Fig. 1.—Costochondral junction of a normal guinea-pig, 47 days old.

They consist of cessation of new bone formation with diminution in the number of osteoblasts in the preparatory calcification zone, rarification of the existing cortex and spongiosa, irregularities and absorption and disappearance of the cartilage columns, and the formation of a zone of fragmented bone just distal to the costochondral junction, known as the Trümmerfeld zone. Fractures and hemorrhages frequently occur here. The marrow spaces of the shaft adjacent to the cartilage or Trümmerfeld zone, become filled with a loosely constructed fibrillar tissue on a

⁴ Skorbit, eine Pathologisch-Anatomische Studie, 1919.

⁵ Scurvy, Past and Present, 1920.

gelatinous appearing background ("Gerüstmark"). All our normal guinea-pigs fed on this diet for two weeks or more showed these changes, the severity varying with the length of time on the diet.

The Course of Scurvy in Infected Animals.—Eleven animals weighing between 198 and 428 grams were placed on the scorbutic diet and at the same time infected with 18 hour broth cultures of staphylococcus pyogenes albus by injecting a few minims of the culture into the marrow cavity of the tibia, muscles of the leg, or into an incised skin wound. In all, three injections were given at two or three day intervals. Six

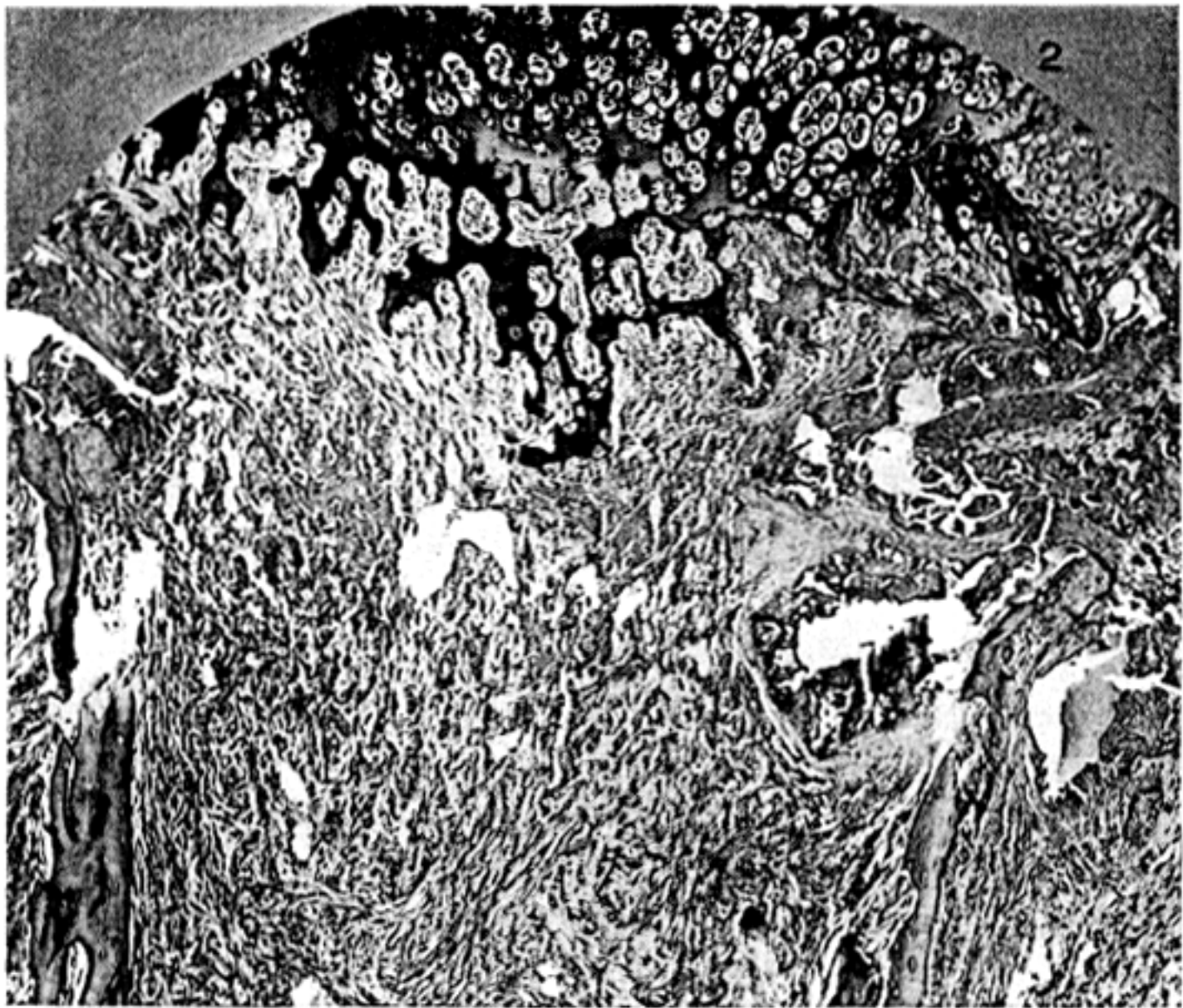


Fig. 2.—Costochondral junction of a guinea-pig 95 days old, on scurvy diet for 39 days, showing irregularity of the cartilage columns, Gerüstmark, Trümmerfeld zone, and fractures.

animals developed severe local infections with or without sepsis and when necropsied between the 19th and 40th days showed none of the classical changes of scurvy in either gross or histologic examination. The bones were somewhat brittle, due as shown on histologic examination to an osteoporosis. The livers were large and yellow and showed extensive fatty replacement of the liver cells, numerous areas of focal necrosis, and moderate leukocytic and lymphocytic infiltration in the peri-

portal spaces. The spleens were also large and pulpy, with markedly congested sinuses and prominent Malpighian corpuscles.

The remaining five animals died of scurvy between the 21st and 30th days. In none of these cases did the inoculations result in severe local infections, and the necropsies failed to reveal evidences of general infection or prolonged toxic absorption in the internal organs.

In this experiment severe infection prevented the appearance of scurvy in six of eleven guinea-pigs on a scurvy diet from 19 to 40 days. Normal animals on this diet developed scurvy after two weeks.

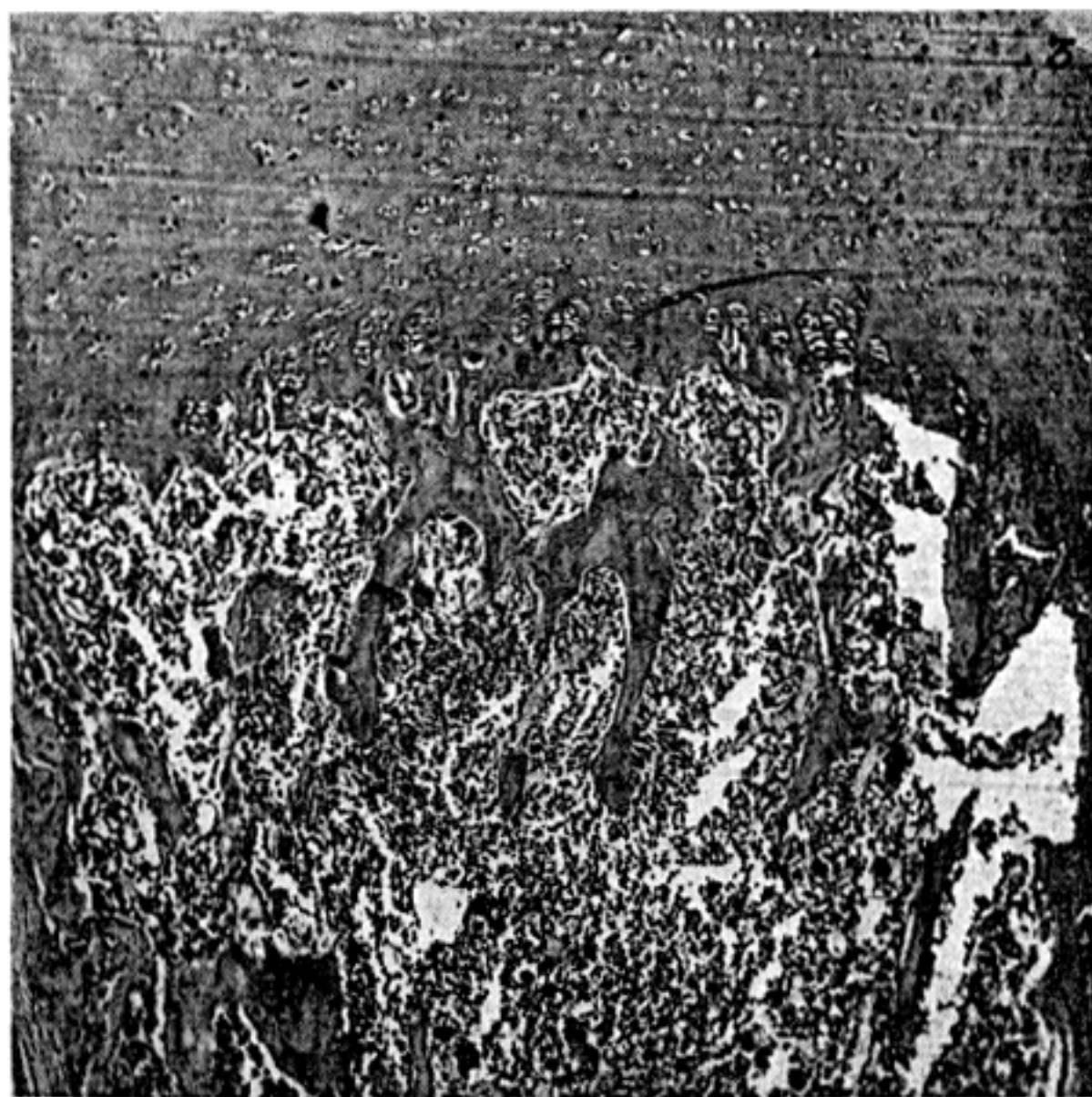


Fig. 3.—Costochondral junction of an infected guinea-pig 106 days old, on scurvy diet 40 days, showing atrophy and osteoporosis, but no scurvy.

The Effect of Infection on the Course of Scurvy Already Developed.—Six guinea-pigs weighing between 298 and 355 grams were placed on the scorbutic diet and ten days later, when signs of scurvy were first appearing, were injected with broth cultures of *Staphylococcus albus* as described before. In these animals death followed shortly after the development of the infections, three dying on the 7th day and the other three on the 12th day after the first injection.

The Influence of Staphylococcus Vaccine on the Course of Scurvy.—Four guinea-pigs each weighing about 250 grams were given four intraperitoneal injections of standard *Staphylococcus albus* and *aureus* vaccine containing one billion bacteria per cc. The inoculations began on the day the animals were placed on a scurvy diet, extended over a period of 11 days, and were graded from 0.5 to 2.5 cc. By the 15th day these animals had developed definite clinical signs of scurvy. Vaccine in the amounts we injected had no preventive effect on the disease.

DISCUSSION

All authors studying the pathologic anatomy of human or experimental scurvy emphasize the changes at the costochondral junctions as best indicating the progress and extent of the disease. I studied the costochondral junctions of our guinea-pigs and have interpreted the absence of "Gerüstmark," Trümmerfeld zone, fractures, and hemorrhages as indications of the absence of scurvy. Some degrees of osteoporosis developed in the infected guinea-pigs. This I interpreted as due to inanition.

I cannot explain why the onset and development of scurvy is delayed for a long time or entirely prevented in guinea-pigs on a scorbutic regime in the presence of a severe local staphylococcus infection, while noninfected guinea-pigs on the same diet develop clinical and anatomical evidences of scurvy regularly at about the 15th day. In conformity with the vast experience of human scurvy our findings show that the course of this disease is much more rapid if an infection is superimposed upon existing scurvy.

The antiscorbutic power of the infection is not due to antibody formation, for in our studies the course of scurvy was in no way influenced by vaccination. The possibility that vitamin C was produced by bacterial growth in the muscles must be considered. Although the production of vitamin C by bacterial growth has not been demonstrated, the production of vitamin A and B in this way has been proved.⁶ Another possibility is that protective substances were developed in the liver as the result of toxic absorption.

That infection does not cause scurvy has been proved beyond a doubt, but that a severe purulent infection present before the appearance of active scurvy may delay or prevent the development of this disease in guinea-pigs is suggested by these experiments.

⁶ Burrows, M. T., and Jorstad, L. H.: *Am. J. Physiol.*, 1926, 77, pp. 24, 37.

CONCLUSIONS

Six of eleven infected guinea-pigs on a scurvy diet developed severe purulent infections and did not develop scurvy within 19 to 40 days. Uninfected guinea-pigs on the same diet developed scurvy in 13 to 18 days.

The injection of *Staphylococcus albus* into animals with early signs of scurvy caused a rapid fatal termination. The course of scurvy was not influenced by the injection of standard staphylococcus vaccine.

These studies suggest the possibility that antiscorbutic substances may be developed by bacterial growth in the tissues or as a result of the action of absorbed toxins on the internal organs.