

THE LESIONS IN THE SKELETAL MUSCLES IN EXPERIMENTAL SCORBUTUS

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PLATE 13

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This report describes a lesion observed in the skeletal muscles of scorbutic guinea pigs and seeks to clarify its relationship to the scorbutic process as well as to demonstrate a factor modifying its distribution.

The voluminous literature bearing on scorbutus contains relatively little reference to the skeletal muscles. With two exceptions those authors who have described muscle lesions have merely mentioned that thinning and waxy degeneration of the fibers are occasionally to be found. Reports of degeneration of the muscles occur in the early studies of the disease in man by Hayem (1), Nambu and Sato (2), and recently in a study of experimental scurvy by Meyer (3).

The first report to emphasize the importance of the lesions in muscles was the monograph of Aschoff and Koch (4), containing observations of the disease in Balkan soldiers during the recent war. These authors studied the thigh muscles but were primarily interested in the hemorrhages, and chose hemorrhagic areas for study. They found changes similar to those previously reported by other workers. They believed the hemorrhages were largely responsible for the degenerative change and the thinning and atrophy the result of the cachexia in their cases.

Subsequently Höjer (5) described lesions in the muscles in experimental scorbutus which he regarded as an intrinsic part of the disease. His observations conform with our own on several points.

The material on which this report is based consists of seventy-one guinea pigs of which forty-eight were scorbutic. Many of the animals were studied in cooperation with Dr. Walter H. Eddy of Teachers College, Columbia University, who was conducting feeding experiments, and these were partially protected with canned vegetable or fruit. Most of the animals were submitted to us for diagnosis, without

record of their weight curve, behavior or diet. In some cases only selected tissues were received. The examination was chiefly of ribs and long bones, where characteristic changes occur in scurvy.

The diagnosis of scurvy is not difficult. The criteria employed were cessation of bone growth, irregularities, spreading and fragmentation of the cartilage columns and the development of the so-called "gerüstmark," a lax, delicate connective tissue which appears at the junction of bone and cartilage. Other elements in the histo-anatomical picture are hemorrhages and separation of bone and cartilage or pathological fracture of bone. The lesions are not uniformly disposed and many samples are at times necessary to estimate properly the extent of the disease or even its presence. The latter fact is especially true in animals which receive a diet only partially deficient in anti-scorbutic material.

In our routine examination of the ribs we commonly found a lesion of the intercostal muscles. Its nature varied with the characteristics of the bone lesion.

When the disease is very marked and active in the bones one finds that a variable number of muscle cells have become opaque, strongly eosinophilic and fragmented. The lines of recent fractures run directly across the fibers, paralleling the striations. Usually, however, the striations have disappeared. The segments of the muscle cells may be rectangular, square or discoid. In the latter case a series of these discoid fragments resembles blood rouleaux. Some muscle cells have been seen in which there were regular, deep clefts on only one side of the cell. The degenerate portions lose their affinity for acid dyes and appear swollen. Some show crevices and loculi within. These fibers are surrounded by large endothelial cells which engulf them and form foreign body giant cells.

Two other kinds of cells may be distinguished. Rows of spindle shaped fibroblasts with delicate fibroglia form between the muscle cells and large cells with clear acidophilic cytoplasm appear, singly and in clusters, near the point of fracture and even between the muscle fibers. These latter cells resemble young muscle cells and many are in process of mitotic division. A further study of these cells is under way to determine if possible their exact nature.

In chronic scorbutus, that is, where the lesion in the bone appears

inactive and the diseased costo-chondral junction is largely fortified by a connective tissue scar, and the "gerüstmark" has become passive, its cells no longer dividing actively, the muscles present a different picture. In such cases densely stained hyaline fragments, few in number, will be found lying in a lax, collagen-poor connective tissue. This stroma is identical with the "gerüstmark" in its cellular structure with the single exception that in the latter case dead islands of calcified cartilage or other remnants of past osteoid function are embedded within it, while in the former, fragments of muscle fibers remain.

It will be noted that in many features the lesion described resembles hyaline or Zenker's degeneration as seen in infectious and toxic diseases. Indeed the resemblance to that variety of degeneration as Forbus (6) has found it in guinea pigs is very close. Our animals were carefully searched for evidence of infectious disease but in none of those appearing in this series was there reason to suspect infection.

After some experience with this material it appeared that animals with scorbutic changes in the bones invariably presented lesions in the muscles. Indeed, in cases where the first preparations showed muscle involvement but no bone changes, further sampling regularly disclosed the presence of lesions in other bones. The intercostal muscles were invariably involved. A search for similar changes in the extensors of the thighs and forelegs and in the psoas muscle disclosed no comparable changes. Only an occasional darkly stained muscle cell was seen. It is of interest to note that in a general way within the intercostal muscles the lesions tended to favor certain locations. They were most frequent near the junction of cartilage and bone, or when present throughout the muscle they were more pronounced in these regions.

Several facts suggest that the muscle lesion is an intrinsic part of the scorbutic process. It occurs regularly in the scorbutic animals and never in the controls. It bears a definite and constant relationship to the scorbutic lesion in the bones, being active when bone changes are active, and inactive when the bone lesions are inactive. Moreover, we have not been able to find any other cause for the condition.

The selectivity of the lesion for the thoracic wall seemed to call for an explanation. It was suspected that possibly another factor other than the scurvy determined the location of the lesion and that this factor might be the activity of the thoracic muscles. The weakened

scorbutic guinea pig spares the muscles of the skeleton except those necessary to vital functions, as the respiratory muscles. If the conception just mentioned is correct the diaphragm and possibly the masseter muscles should show some degeneration as well as the intercostals. In most of our specimens these muscles had not been preserved but of eight cases in which material was available for examination the masseter muscles were found to be degenerate in three instances and the diaphragmatic muscles in five.

To further test this point of view several animals with advanced scorbutus were placed in a large barrel which could be rotated slowly with a motor so that the animals were required to exert themselves to stay on their feet. The animals were given 1 hour of this exercise every day and were then sacrificed. In each instance, florid, extensive lesions were found in the several muscles of the hind and fore legs and psoas muscles. In five non-scorbutic animals no muscle lesions were found. In all, seven scorbutic guinea pigs have been so tested. The records of three are given below.

DISCUSSION

The earliest clinical evidence of scurvy in a guinea pig is a change in attitude. At times this is represented by the elevation and sparing of one leg or by a tendency to squat quietly for long periods. Later in the disease the animals become nearly helpless and may lie on one side, apparently unable to move. In human cases an early sign of the disease (7) is loss of vigor with a tendency to tire quickly. Scorbutic infants exhibit marked tenderness in their thighs and commonly keep their extremities slightly flexed. These well known phenomena have been explained as the result of hemorrhages. The tenderness in the thighs of scorbutic infants has been said to be the result of subperiosteal hemorrhages. Observation of our guinea pigs suggests that muscle lesions may be largely responsible for both the tenderness and weakness. Moreover we have seen tenderness and the characteristic muscle degeneration develop in muscles which had been bruised.

The selective development of the muscle degeneration at points of exercise and trauma is in accord with other features of scorbutus. A causal relationship exists in the case of the hemorrhages. As was

emphasized by Aschoff and Koch, hemorrhages occur in places exposed to trauma. Bleeding about vessels and nerves was noted by these authors only when the vessel or nerve was in an exposed location, never when it was protected by bone.

A less marked relationship exists in the case of the bone lesions but here a causal connection between stress and lesion is suggested. In the thoracic wall, for example, lesions are most common in the more active and exposed ribs being relatively uncommon in the first two or three of these bones. I have noted that guinea pigs kept in separate cages, which remain quiet throughout the disease, show less marked lesions than animals which have been kept active by crowding or excitement. A special observation of the sort was made in the case of six animals sent to us while alive and which had been necessarily much shaken in transit. Some of the most striking muscle and bone lesions were present in this group.

Wolbach and Howe (8) believe that the underlying change in the bones is a deficiency in the intercellular substances. Aschoff and Koch and others have supposed that the hemorrhages were the result of altered cement substances in the vessel walls which predispose to rupture or leakage. We have noted rupture in the striated muscle. Whether a related underlying cause is responsible is not apparent from our material. We have seen cells which had ruptured but which appeared otherwise normal. If degeneration of the muscle fiber does not precede separation it follows it closely, for the usual fragmented cell is hyaline.

CONCLUSIONS

1. Muscle degeneration was constantly found in the intercostal muscles of scorbutic guinea pigs.
2. It has likewise been found in the masseter and diaphragmatic muscles.
3. Exercise will produce an identical lesion in other skeletal muscles in scorbutic animals.
4. The lesions appear to be an intrinsic part of the scorbutic process.
5. It is suggested that the tenderness over muscles in scorbutic animals and in man may be due to this myopathy.

Specimen Histories of Exercised Animals

Animal A.—Had been on basal diet plus 2 gm. canned tomato for 90 days. The weight at the beginning of the experiment was 315 gm. The weight on the 90th day was 422 gm. On the 91st and 92nd days the animal was exercised $\frac{1}{2}$ hour, on the following 4 days 1 hour each day. The following day the animal was sacrificed. There was much pale fat throughout. The joints were easily dislocated, the bone crackled like egg shell, the teeth were loose. The costochondral junctions showed broad zones of "gerüstmark." A few, small, superficial hemorrhages were present in the muscles of the extremities. In the microscopic preparations all of the muscles of the extremities as well as the psoas and intercostal muscles showed extensive and severe degeneration.

Animals B and C.—Were practically identical. They were receiving 2 gm. canned peas daily and had gained weight. Both had the attitude of scorbutic animals and had joint tenderness. Each was exercised on 3 successive days for 1 hour per day. In both there was widespread muscle degeneration and abundant evidence of scorbutus in the bony system.

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EXPLANATION OF PLATE 13

Fig. 1. Degeneration in an intercostal muscle with active proliferation of young muscle cells (?). Two of these cells are in process of mitotic division. Many fibroblasts and endothelial cells are likewise present.

Fig. 2. A late stage in muscle degeneration in scorbutus. A few muscle fiber fragments lie in a collagen poor connective tissue stroma.

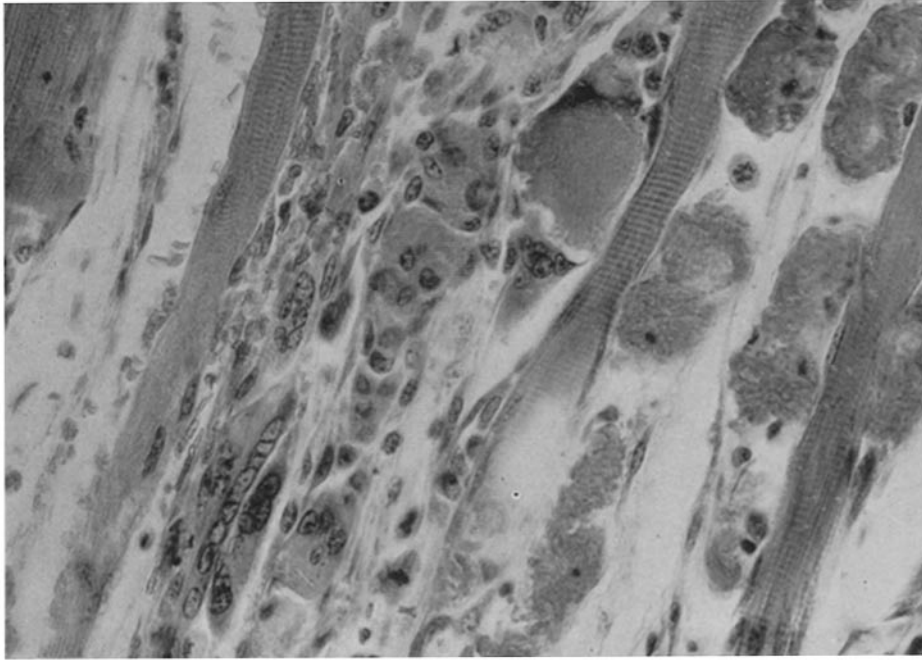


FIG. 1

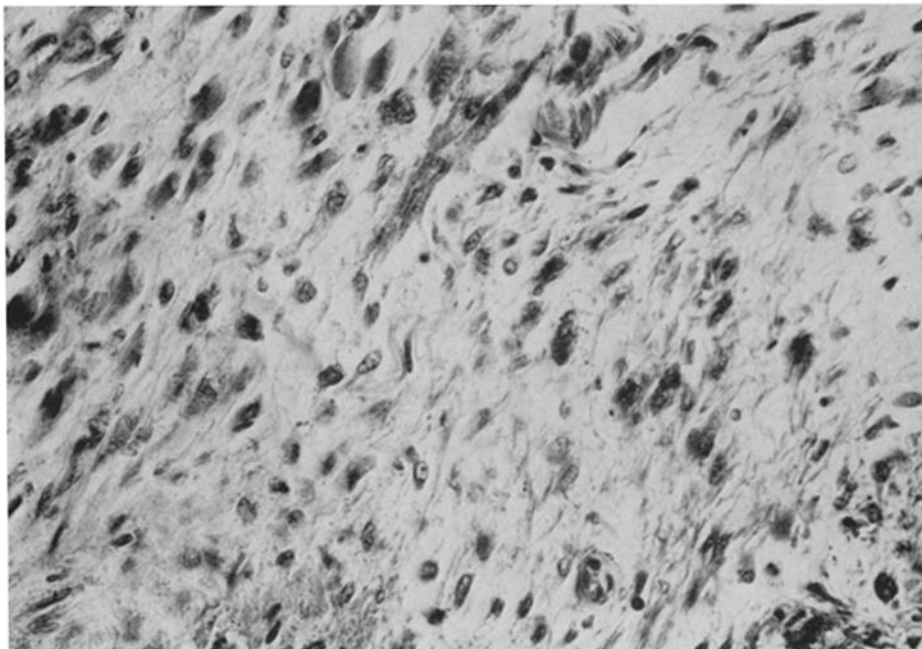


FIG. 2

(Dalldorf: Lesions in experimental scorbutus)