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MORPHOLOGICAL CHANGES IN STRIATED MUSCLE DURING ISCHAEMIA

A clinical and histological study in man

By

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Ischaemia is a prerequisite for modern surgery of the hand. However, ischaemia is an unphysiological condition which leads to anoxia of tissues and initiates changes of cellular death. Opinion varies as to how long ischaemia can be maintained without endangering the tissues, from 1 to 3 hours being the time usually suggested.

Fishback & Fishback (1932) investigated muscle degeneration following ischaemia. According to them, the first change is slight granular clouding with dimming of cross striations of muscle. This is followed first by oedema of fibres with prominent longitudinal fibrils and then by vacuolization, granular, albuminous and fatty degeneration and further waxy degeneration and disruption of the tissues. *Harman* (1947) made an experimental study of muscle ischaemia in the rat and in the rabbit. He observed increased cross striations, while the longitudinal striations decreased and the muscle fibres were more clearly distinguishable from one another than usual as a result of ischaemia. Prolonged ischaemia was followed by so-called Bowman's discoid degeneration. In their electron microscopical studies, *Moore, Ruska & Copenhauer* (1956) concluded that in post-ischaemic degeneration of the muscles, the extent of degeneration is not directly a function of time, but depends on whether the muscle is stretched or not, and on its content of mitochondria. They saw severely damaged and almost normal fibres as early as 20 minutes and as late as 16 hours after the circulation had been restored. *Dahlbäck & Rais* (1966) investigated the morphological changes in cross-striated muscle of the rabbit after

ischaemia of varying duration and after post-ischaemic periods of varying length. On gross examination they found that oedema of the muscle was already visible after 30 minutes' ischaemia. These workers found that the degenerative changes became more marked with increasing duration of ischaemia and such changes were demonstrable after ischaemia of 30 min. The changes were slight as long as the muscle was ischaemic but increased rapidly when the circulation was restored.

Our aim was to elucidate by a histological method the changes occurring in human cross-striated muscle during ischaemia, a search of the literature having failed to reveal any investigation on human material.

MATERIAL AND METHOD

The material was obtained at operation on the hands of 17 patients aged 2 to 46 years. These were reconstructive operations after injuries sustained in accidents, which in the majority of cases required tendon reconstruction with the aid of free tendon grafts, but in some cases also transposition of tendons.

Exsanguination was achieved in the usual manner by raising the limb and applying Esmarch's bandage, and ischaemia was maintained with a tourniquet. The tourniquet pressure was 280–300 mm Hg. In 13 cases the specimen was taken from the palmaris longus muscle, in 3 from the superficial flexor digitorum muscle and in 1 from the extensor carpi ulnaris. The muscle and its tendon were always entirely undamaged and functioning and there was no scar tissue. The specimen was taken from the distal end of the muscle together with the transplant; grasping the tendon, the muscle was carefully lifted and severed with a sharp knife, while the region of the specimen remained untouched by any instrument. When the tendon had been divided from the specimen, the latter was immediately fixed in a 4 per cent neutral formol. Paraffin blocks were made in the usual way. Sections from each specimen were stained with haematoxylin-eosin, van Gieson and Gomori's trichromic staining.

At histological examination particular attention was paid to degenerative and reactive changes (Figures 1, 2, 3, 4).

We did not consider quantitative measurement of the changes possible except by rough estimation. The changes were thus classified as follows:

0 no changes.
1 slight changes.
2 moderate changes.
3 severe changes (cf. *Dahlbäck et al.*).

RESULTS

On gross inspection nothing abnormal, *e.g.* no oedema was seen in the specimen.

The histological findings have been compiled in Table 1.

Table 1. Histological changes.

Case number	Age in years	Period of ischaemia in minutes	Degeneration			Changes of msucle striation	Inflammatory cell reaction	Increase of sarcolemmal nuclei
			Granular	Vacuolar	Hyaline			
1	2	30	0	0	0	0	0	0
2	46	35	1	0	0	0	0	0
3	36	40	1	1	0	1	0	0
4	35	40	1	1	0	0	0	0
5	26	43	1	0	0	3	0	0
6	37	45	2	1	0	1	0	0
7	39	50	1	1	0	1	0	1
8	10	50	1	1	0	2	0	0
9	16	50	1	0	0	1	0	0
10	38	55	1	1	0	1	1	1
11	33	60	1	1	0	1	1	1
12	25	65	2	1	0	2	1	1
13	25	74	2	1	0	2	1	2
14	18	75	1	1	1	3	0	1
15	18	80	1	1	0	2	1	2
16	27	90	2	2	1	3	2	2
17	40	135	2	2	0	3	1	3

DISCUSSION AND CONCLUSIONS

No macroscopic changes were visible in the specimens taken during ischaemia.

After a short period of ischaemia, degeneration is at most slight. Granular degeneration was noticed in all except case no. 1 with ischaemia of only 30 minutes. The degree of degeneration varied and it had a tendency to increase with the period of ischaemia. Vacuolization and hyalinization did not appear before 40 minutes' ischaemia. After ischaemia of 1 hour or more signs of degeneration became numerous even before the circulation was restored.

The inflammatory cell reaction was seen first after 55 minutes' ischaemia. It was always slight, but clearly increased with longer periods of ischaemia.

No haemorrhages were seen. Slight erythrocyte extravasation might have been the result of pressure by Esmarch's bandage. In ischaemia of more than 1 hour, an observation pointing to oedema was separation of the muscle fibers and an increased space between the fibrils, while

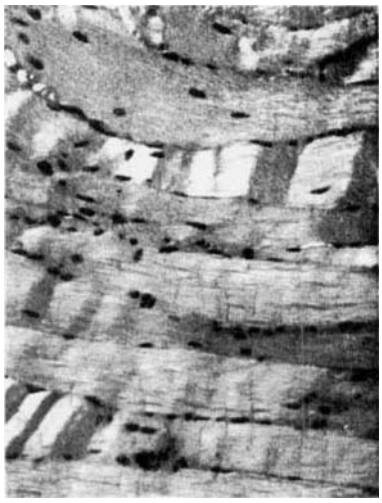

Figure 1. (Case 10)—Muscle specimen after 55 minutes' ischaemia. Variation of striation and early degenerative changes. × 120. Photographed in polarized light.

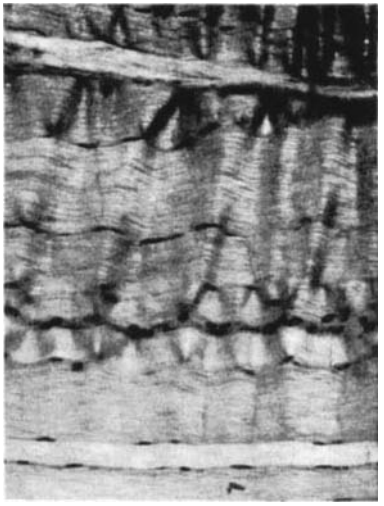

Figure 2. (Case 13)—Muscle specimen after 74 minutes' ischaemia. Variation of striation and degeneration. × 120. Photographed in polarized light.

cross-striation simultaneously increased. These changes were also a function of time.

The amount of sarcolemmal nuclei increased with increasing duration of the ischaemia.

We may conclude that capillary and cell damage caused by ischaemia become histologically demonstrable after ischaemia of more than 30 minutes' duration. The changes are mild, however, until about 2 hours after the onset of ischaemia. It should be mentioned that in none of the patients were there any postoperative signs indicative of irreversibility of the changes occuring during or after ischaemia.

The aggravation of the changes occurring after restoration of the circulation which, according to earlier reports and clinical observations (hyperaemia, oedema), seem probable, could not be investigated in this connexion.

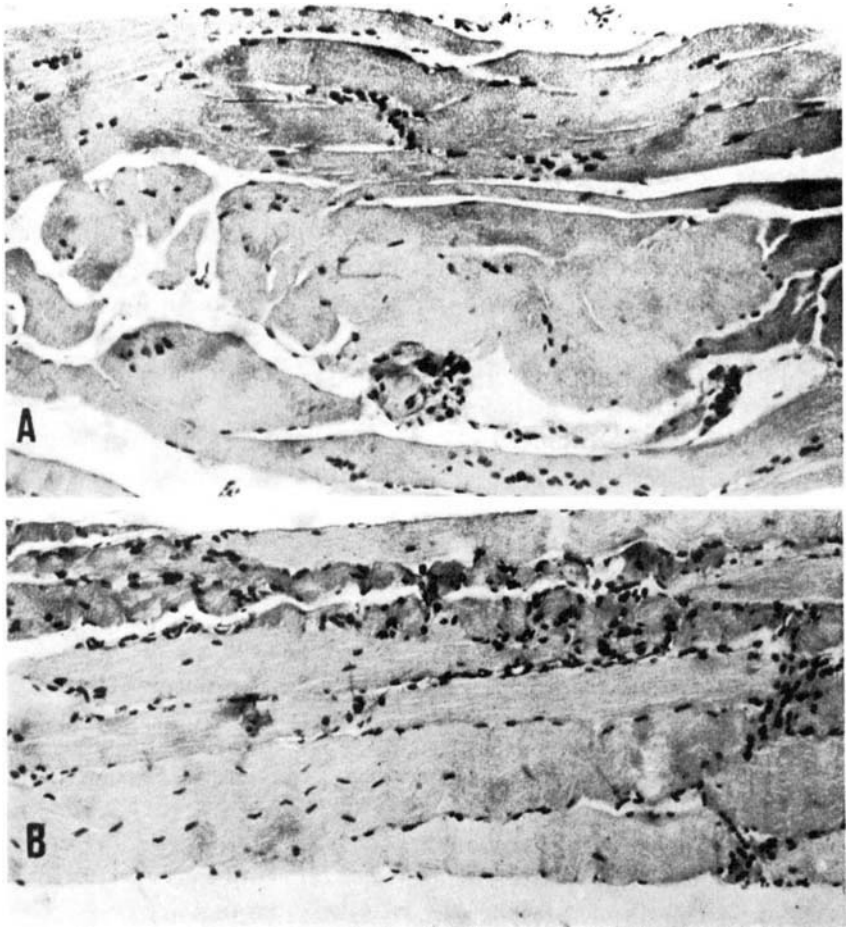

Figure 3. (A-B) (Case 17)—Severe degenerative changes in striated muscle after 135 minutes' ischaemia. Note loss of striation and increase of nuclei. × 120.

SUMMARY

A study was made of the histological changes visible in muscle specimens taken from 17 patients undergoing surgery of the hand, after tourniquet ischaemia of varying duration.

It appeared that degenerative changes of the muscular tissue, oedema and the inflammatory cell reaction, as well as the number of nuclei, increased with prolonged ischaemia.

The changes were slight at first but increased when the ischaemia

had been maintained for about 35 minutes and became more marked with time.

Postischaemic changes were not investigated.

RESUME

Il a été procédé à une étude des altérations histologiques visibles dans des spécimeens de muscles, prélevés chez 17 malades ayant subi une intervention chirurgicale dans la main après ischémie au tourniquet de durée variable.

Il est apparu que les altérations dégénératives du tissu musculaire, l'oedème et la réaction inflammatoire des cellules, de même que le nombre des noyaux, augmentent loorsque l'ischémie est prolongés.

Les altérations étaient légères au début, mais augmentent lorsque l'ischémie est maintenue pendant environ 45 minutes, devenant plus marquées avec le temps.

Il n'a pas été fait de recherches sur les altérations post-ischémiques.

ZUSAMMENFASSUNG

Eine Studie der histologischen Veränderungen in Muskelproben wurde an 17 Patienten vorgenommen, die während handchirurgischen Operationen Blutleere verschiedener Dauer unterworfen waren.

Es zeigte sich, dass die degenerativen Veränderungen des Muskelgewebes, Ödem und entzündliche Zellreaktion, und auch die Zahl der Zellkerne, mit der Verlängerung der Blutleere zunahmen.

Die Veränderungen waren im Beginn nur leicht, nahmen aber zu wenn die Blutleere für ungefähr 45 Minuten aufrechterhalten wurde und wurden mit der Zeit mehr ausgesprochen.

Postischaemiche Veränderungen wurden nicht untersucht.

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