FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF LUND
MALMÖ GENERAL HOSPITAL
HEAD: HELGE B. WULFF, PROFESSOR OF SURGERY

PREVENTION OF EXPERIMENTAL TENDON ADHESIONS BY CORTISONE

A Preliminary Report

By

NILS CARSTAM

Cortisone has been shown to inhibit the formation of granulation tissue and of connective tissue (1, 2, 3, 4, 5), and experimental studies have been carried out to determine the value of the agent in the prophylaxis of peritoneal, pericardial and pleural adhesions (6, 7, 8). It has also been used in arthroplasty to prevent too strong a reaction of the soft parts (9).

As the success of tendon operations is jeopardized by the subsequent production of adhesions about the tendon, it was decided to try to find out whether such formation could not be obviated by the use of cortisone.

The purpose of the present investigation was to gain an idea whether cortisone is of any value in the prevention of adhesions about tendons experimentally injured without loss of continuity.

MATERIAL AND METHODS

Rabbits weighing 2–2,3 kg. were used.

The tendon of the extensor hallucis longus was selected as a test object, because a long section of this tendon extending down the lower leg is muscle-free and straight. It lies adjacent the antero-medial surface of the tibia and is covered by thin fascia, which to a certain extent acts like a tendon sheath.

The animals were anaesthetized with Nembutal and ether.

An incision was made about 2 cm. from and parallel to the tendon, which was dissected free and traumatized. In some cases the tendon was rubbed with dry gauze, clamped with haemostats, and incised across about one quarter of its width (Fig. 1), in others this injury

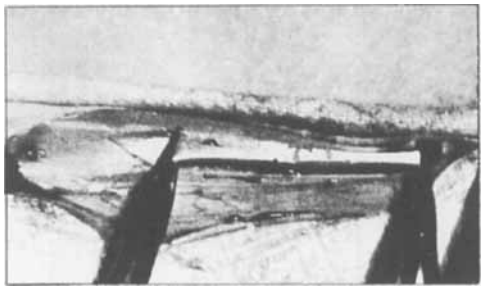


Fig. 1.
Traumatized extensor hallucis longus. The tendon was traumatized by clamping with haemostats and incised across one quarter of its width.

to the tendon was increased by rubbing its bed too, i.e. the inner surface of the fascia and the periosteum-lined surface of the tibia. All the injuries were inflicted by one and the same surgeon, care being taken to produce lesions of each type as uniform as possible. After traumatization the fascia was closed with a couple of nylon stitches. Both hind legs were treated in this manner, and the animals were operated on in pairs. One of each pair–as afterwards decided by the toss of a coin–then received cortisone, the other animal served as a control.

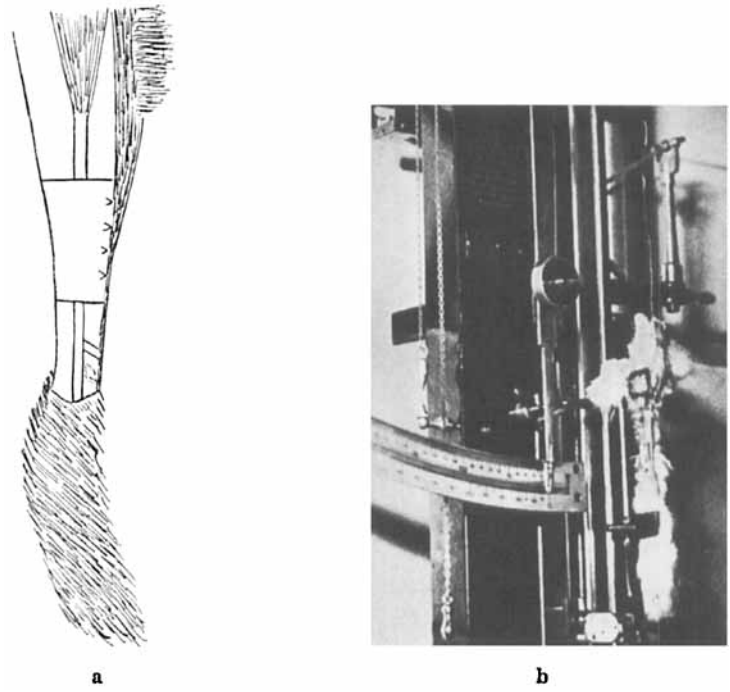
As comparison of the reaction and adhesions by visual inspection must to a certain extent be unreliable, attempts were made to find a method for judging the adhesions objectively. With this in mind the traction necessary to pull a section of the tendon out of its bed was measured with a thread tester.

Measuring technique.–The hind legs of the killed animals were removed. The leg was prepared in such a manner that a bridge of skin 2½ cm. wide was left intact over the most severely damaged part of the tendon (Fig. 2 a). Proximal to this bridge the tendon was dissected free and divided, after which a steel wire was fastened to the now free proximal end of the tendon. The leg was then mounted in a thread tester (Fig. 2 b). The tendon was cut through with a razor blade at the distal end of the intact skin. The 2½ cm. long section of the tendon was now pulled out of its bed by the wire, the force applied being shown on the dial of the thread tester. The traction thus noted was regarded as a good relative measure of the effect of the adhesions formed.

The force required to pull out a similar section of tendon of a normal rabbit not previously traumatized was found to be about 50 gm.–150 gm.

The use of this method requires the employment of an agent capable of pro-

ducing a strong inhibitory effect, otherwise the amount of adhesions in the cortisone-treated rabbits will not differ appreciably from those in the controls. The lesions must also be severe, otherwise, even in the controls the amount of adhesions will give small or even unrecordable values and, of course, be of no use for appraising any inhibitory effect of cortisone on the formation of adhesions.



a b

Fig. 2.
a. Sketch of the prepared hind leg.
b. The hind leg mounted in the thread tester.

Sixty rabbits (120 tendons) were used. Half of them were not damaged severely enough to satisfy the requirements just described, although they showed essentially the same type of reaction. Therefore only 30 rabbits (60 tendons) were used for the traction tests.

The animals were sacrificed after a varying interval of 7, 14 and 21 days, during which they received cortisone[1]. The dose administered was 10 mg. daily (half of the dose in the morning and the other half in the evening).

In order to bring out any effect of the drug more distinctly, the dose employed was fairly large. The dose, as calculated per kilogram body weight, corresponds to 250–300 mg. daily in man.

[1] Cortisone-acetate, Ciba, generously placed at my disposal by Ciba Produkter Aktiebolag, Stockholm.

RESULTS

After 7 days.–In the controls the fascia covering the tendons was thickened, it was no longer transparent and showed grey-red loose granulation tissue. This was also seen about the tendons, which had not recovered their lustre. In the cortisone-treated animals the fascia

Traction necessary to pull the severely traumatized tendons out of their beds.

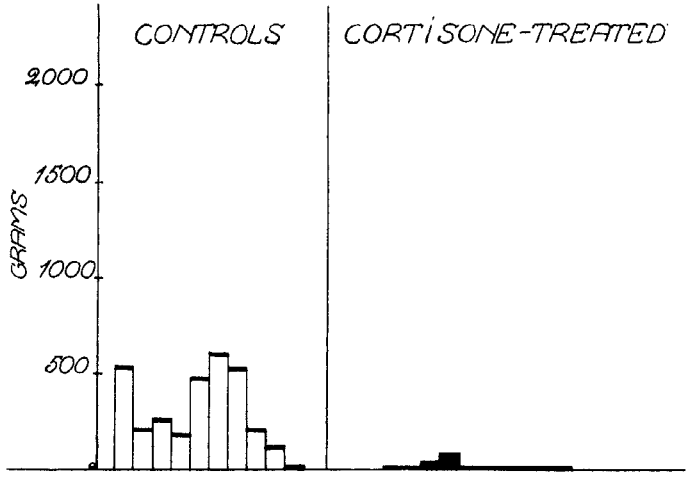


Fig. 3.

After 7 days.
Every column represents the force applied to pull one tendon out of its bed.

was still thin and almost transparent. The tissue often showed slight, fresh imbibition of blood, but no marked haemorrhages or haematomas were seen. Despite the fairly strong reaction in the controls, the adhesions were loose and slight traction was sufficient to pull the tendons out of their beds. However, in the cortisone-treated animals the pull required was still less and sometimes too small to be recorded. This difference is apparent from Fig. 3.

After 14 days.–In the controls the fascia was still thickened and the persistent granulation tissue about the tendons was no longer of such fresh appearance. The tendons were now more intimately connected to the surrounding tissue. In the cortisone-treated animals the picture was about the same as it was after 7 days: though still persistent the imbibition was less marked and the tendons had almost recovered normal lustre.

The values now recorded for the controls were appreciably greater

than those noted after 7 days, while the values for the cortisone-treated rabbits showed only a slight increase (Fig. 4).

After 21 days.–In the control animals the tendons were now nearly always so adherent to their surroundings that they could not be pulled out of their beds. The fascia, tendon and bone were usually fused

Traction necessary to pull the severely traumatized tendons out of their beds.

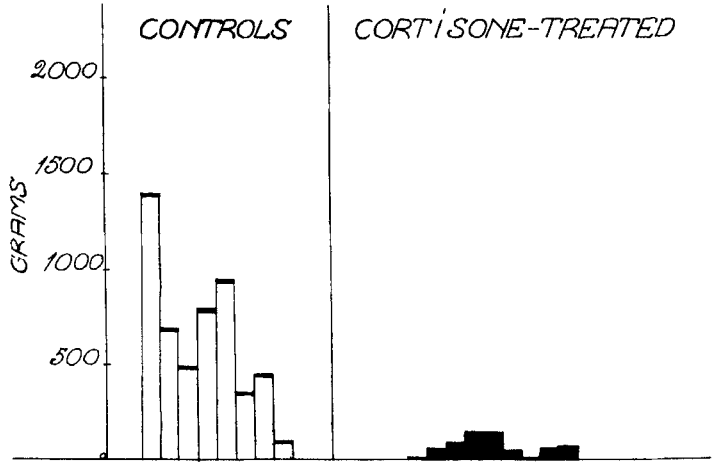


Fig. 4.

After 14 days.
Every column represents the force applied to pull one tendon out of its bed.

together by firm, fibrous tissue. In the cortisone-treated animals the fascia was still thin and showed no signs of haemorrhage, and–except for the rounded notches produced by the incisions–the tendons had recovered normal appearance.

Fig. 5a shows the tendon of a control rabbit after three weeks: it is adherent, its outline is somewhat irregular, and in the embedded part it is "woolly". In the cortisone-treated rabbit (Fig. 5b) the outline of the tendon is well preserved and the adhesions are only thin.

In most cases the control tendons were so firmly adherent to their surroundings that on application of traction they were torn by the wire to which they were fastened in the thread tester. In these cases the pull recorded was naturally a minimum value. In the cortisone-treated animals the traction required to pull the tendons out of their beds was only relatively slight, on the average 230 gm. as measured in eight tendons (Fig. 6).

MICROSCOPIC EXAMINATION

Controls.–After 7 days abundant, richly cellular granulation tissue was seen about the tendons. After 14 days and after 21 days the cells were less abundant and the in-growth of fibroblasts had turned the granulation tissue into fibrous scar tissue, which was often so

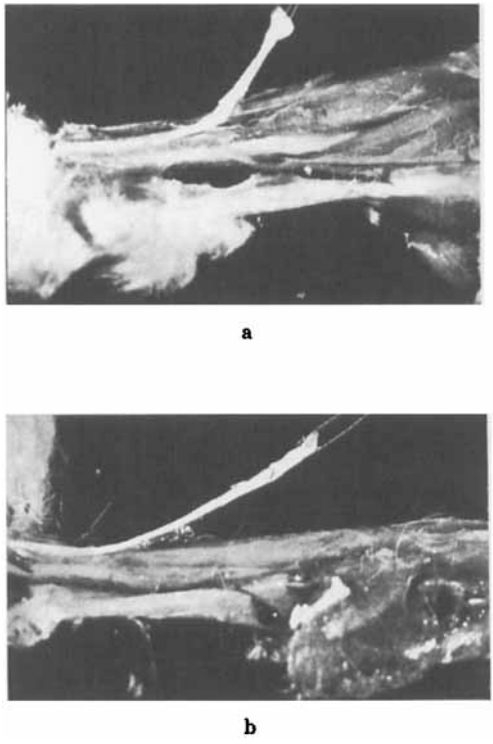


Fig. 5.
a. Tendon of a control rabbit three weeks after operation.
b. Tendon of a cortisone-treated rabbit three weeks after traumatization. Note the clear outline and the thinness of the adhesions.

intimately fused with the tendon that the outline of the latter was no longer recognizable.

Cortisone-treated animals.–After 7 days the tendons showed only a mild histiocytic reaction with only a slight increase in the number of vessels and no lymphocytes. Hardly any cicatrization followed this reaction, and even after three weeks the surface of the tendons seemed to be well preserved. They were connected to their surroundings by only thin adhesions poor in cells.

Complications.–The rabbits seemed to tolerate cortisone well. They ate as usual. Slight increase and decrease in weight were noted both among the cortisone-treated rabbits and among the controls, but the groups did not differ appreciably from one another in this respect.

Cortisone did not manifestly influence the healing of the skin wounds.

In a few instances in both groups necrosis or infection occurred near the distal end of the wound.

Traction necessary to pull the severely traumatized tendons out of their beds.

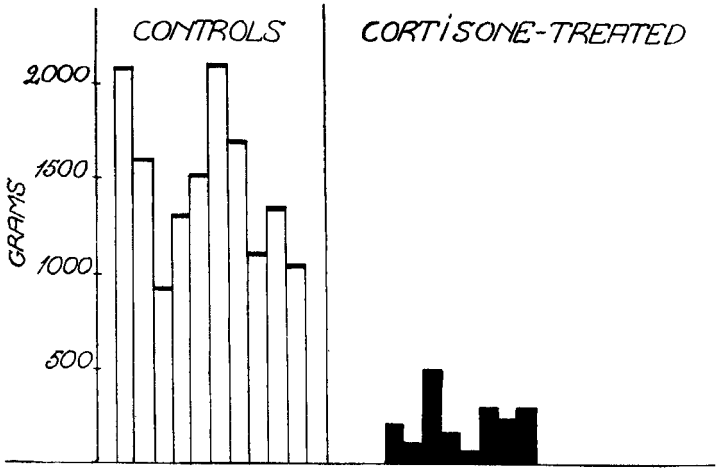


Fig. 6.

After 21 days.
Every column represents the force applied to pull one tendon out of its bed.

Among the animals that received cortisone for three weeks the fur was somewhat moulty in appearance and renewal of the hair in the operative field was delayed.

COMMENTS

Observations made in these preliminary experiments show that the parenteral administration of cortisone inhibits the formation of granulation tissue and of adhesions about tendons experimentally injured without loss of continuity. However, the dose of cortisone used was twice as large as that employed in the clinic and the animals were not followed up long enough to judge the late results.

The procedure adopted does not correspond to conditions met with in the clinic. The favourable inhibitory effect of cortisone on the formation of granulation tissue and adhesions may, for example, also have an appreciable, undesired effect on the healing of sutured tendons.

The experimental conditions did not even parallel clinical tenolysis: such experiments would require traumatization and, after a period sufficient for adhesions to form, re-operation with freeing of the tendon in combination with the administration of cortisone.

Local treatment with cortisone has experimentally been proved to produce a similar effect on the formation of granulation tissue and connective tissue (3, 10, 11) and it has also been used, for example, in eye diseases. On account of the risk of complications attending parenteral administration, it would be of value if a method could be devised to obtain a similar favourable effect of such local treatment in tendon surgery, too. Although it is still too early to say anything definite, experiments suggest that a single local application of ordinary cortisone acetat during operation is less suitable. For local treatment to be successful, cortisone must probably be obtainable in a fairly non-irritating and less readily absorbable preparation.

Summarizing, despite the sources of error attending the method used, and the differences between the experimental and clinical conditions, observations hitherto made are promising and justify continued research. Further investigation under conditions approaching those met with in the clinic are in progress.

SUMMARY

A daily dose of 10 mg. cortisone administered parenterally markedly inhibited the formation of granulation tissue and adhesions about tendons traumatized without loss of continuity. This macroscopic observation was confirmed microscopically. Attempts were made to estimate the degree of the adhesions by measuring the traction necessary to pull a certain section of the tendon out of its bed. This force, as measured three weeks after the traumatization, was found to be 100–500 gm. (average 230 gm.) for the cortisone-treated animals as against 1000–2000 gm. for the controls, in which the tendon was sometimes too strongly adherent to its surroundings to be pulled out.

ZUSAMMENFASSUNG

Tägliche Verabreichung von 10 mg. Cortisone auf parenteralem Wege verhinderte die Bildung von Granulationsgewebe und Adhäsionen an

Sehnen, die ohne Kontinuitetsverlust geschädigt worden waren. Diese makroskopischen Beobachtungen wurden mikroskopisch bestätigt. Versuche wurden gemacht den Grad der Adhäsionen zu bestimmen mit Hilfe der Feststellung des Zuges der notwendig war, um einen gewissen Abschnitt der Sehne aus ihrem Bett zu heben. Diese Kraft war, 3 Wochen nach der Schädigung gemessen, 100–500 gm (durchschnittlich 230 gm) für die mit Cortisone behandelten Tiere, während sie in den Kontrolltieren 1000–2000 gm betrug. Bei den letzteren waren die Sehnen manchmal so stark mit ihrer Umgebung verwachsen, dass sie überhaupt nicht herausgezogen werden konnten.

RESUME

Une dose journalière de 10 mg. de cortisone administrée parentéralement diminue considérablement la formation de tissu granulé et d'adhérences autour des tendons traumatisés, sans perte de continuité. Cette observation macroscopique a été confirmée par l'examen microscopique. Des essais ont été faits pour évaluer la force des adhérences en mesurant la traction nécessaire pour retirer un certain segment du tendon hors de son lit. Mesurée trois semaines après le trauma, on a constaté que cette force était de 1200 à 500 gm (en moyenne 230 gm) pour les animaux traités au cortisone, tandis que chez les animaux de contrôle les tendons adhéraient si fortement qu'il était probablement impossible de les arracher ou qu'il fallait en tout cas une force de 1000 à 2000 gm.

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