CORTISONE THERAPY IN DUPUYTREN'S CONTRACTURE*†

HAMILTON BAXTER, CARL SCHILLER, LOUIS H. JOHNSON, JOHN H. WHITESIDE AND ROBERT E. RANDALL

Department of Plastic Surgery and University Clinic, Royal Victoria Hospital and McGill University, Montreal, Canada

During the past two years a great deal of interest has been developed in the study of various diseases of obscure etiology through the availability of ACTH and Cortisone for experimental and clinical research. A considerable volume of investigation (1, 2, 3, 4, 5, 6, 7) indicates that these hormones retard the development of all elements of connective tissue and inhibit the growth of granulation tissue in wounds in experimental animals and a number of workers have confirmed the results of animal experimentation on man (8, 9, 10, 11). Hench and Ragan were among the first to observe the increased range of motion in patients with rheumatoid arthritis treated with ACTH or Cortisone. It occurred to us that patients with Dupuytren's contracture of the hand might be benefited by treatment with these hormones.

It is well known that in Dupuytren's contracture there is a pathological involvement of the palmar fascia, the etiology of which is unknown. Bunnell (12) has admirably described the disease: "Apparently the condition is associated with a diathesis which leads to overgrowth and thickening and contracture of ligamentous tissue. Part or all of the palmar fascia and its vertical components undergo various degrees of thickening and contracture. On microscopic examination the active phase is represented by a well vascularized, proliferating fibroblastic tissue with numerous vesicular nuclei. At a later stage nothing but dense cicatricial tissue is seen which has squeezed out all the fat and deeper structures of the skin." Clinically he has been impressed by the fact that people with this condition show a marked tendency towards limitation of motion of their joints on slight provocation. In our investigation of the effect of cortisone on Dupuytren's contracture we divided the study into three phases: (1) Injection into hypertrophied palmar fascia; (2) Systemic administration; (3) Operation followed by systemic administration.

1. INJECTION INTO HYPERTROPHIED PALMAR FASCIA

It has been shown (4, 5, 13) that cortisone exerts an inhibitory effect on granulation tissue formation when applied topically to wounds. We injected cortisone acetate into hypertrophied palmar fascia in five patients. The duration of the condition varied from one to twenty years and the severity of the involvement from mild to severe. Two patients received only 2 injections at weekly intervals while the remaining three received 7 injections, usually twice a week. The first

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Fig. 1 (top) Case 7: Control: Biopsy of a nodule in the palm of left hand. Whorls of actively growing fibrous tissue are shown. Some older, dense fibrous tissue may be seen at the right upper corner.

Fig. 2 (bottom) Case 7: Local Therapy: Biopsy, 4 days after last injection of palmar fascia following two injections of 25 mg. of cortisone acetate at weekly intervals. The edge of an active nodule is shown in the upper right corner. A typical collection of cortisone crystals (arrow) is present with a slight granulomatous reaction about the edge. No effect of cortisone is seen on the adjacent tissue.
dose of cortisone was 12.5 mg. in a volume of half a cc. Subsequently, injections were of 25 mg. in a volume of one cc. The material was injected into tendon-like contracted cords of hypertrophied palmar fascia or into discrete nodules when these were the major pathological feature. The hormone was not injected into one spot, but was spread through the nodule or contracted cord as much as was feasible. In the latter instance considerable pressure was required to force the solution into the firm scar-like tissue. Biopsies of the hypertrophied palmar fascia were taken; in two cases, before and after treatment and in one, after treatment only. Case 7 (Figs. 1 and 2).

Plaster models were made prior to injection in three patients and also following cessation of therapy.

**Results**

Clinically no significant decrease in the size of the nodules or increase in ability to extend the fingers was noted. The patients observed no change and this was confirmed by our careful observation and by comparison of plaster casts. There was no appreciable difference between comparable areas of the control biopsies and biopsies of the treated areas which showed crystals of cortisone in proximity to the dense fibrous tissue seen in Dupuytren's contracture. No deposits were noted in immediate contact with areas of actively proliferating fibroblasts although these were often situated nearby.

**2. SYSTEMIC ADMINISTRATION**

In view of the failure of local administration of cortisone we tried the effect of cortisone administration intramuscularly and orally. In one patient, cortisone was administered intramuscularly for two weeks and in another orally for three weeks. Biopsies, photographs and plaster casts were taken before and after treatment. In case No. 3, treated intramuscularly, the tips of the little and ring finger on the right hand both lacked one half centimeter of full extension and large nodules were present in the palm. The fingers of the left hand could be completely extended and a few small nodules were present. He had not noticed these changes in the right hand until six months previously or in the left hand until one month before admission. A biopsy was taken and a single injection of 200 mg. of cortisone was given daily for two weeks. Fasciectomy was then performed on the left hand.

**Results**

Neither symptomatic nor clinically observable improvement was noted in the hand as a result of systemic cortisone therapy. Comparison of the pre-treatment biopsy and the palmar fascia removed at operation failed to reveal any significant changes (Figs. 3 and 4).

In case No. 2 treated orally, the tips of the little and ring fingers of the left hand lacked 1 and 2 cm. of extension respectively and nodules were present in the palm. The right hand showed minimal changes in the palm without contracture of the fingers. Changes in the hands characteristic of Dupuytren's
Fig. 3 (top) Case 3: Control: Biopsy prior to systemic treatment shows relatively actively proliferating fibroblasts above and older collagenous tissue at lower left.

Fig. 4 (bottom) Case 3: Systemic therapy with 200 mg. of cortisone acetate daily for 14 days by intramuscular injection pre-operatively. Biopsy shows typical whorls of active fibroblasts with some older, less cellular fibrous tissue at lower left. No significant difference from control is seen.
contracture had been observed by the patient for 5 years. Joint swelling and pain on movement of the fingers suggestive of rheumatoid arthritis had been present for 4 years.

In this patient prior to administration of cortisone a biopsy of the contracted palmar fascia of the left hand was taken and a total dose of 200 mg. of cortisone was given daily by mouth in four equally divided doses for three weeks. At the end of this period fasciectomy was performed.

![Image](image-url)

**Fig. 5** Case 2: Systemic therapy with 200 mg. of cortisone acetate daily, in tablet form, for three weeks pre-operatively. Biopsy shows relatively active proliferation of vascular connective tissue with a band of older collagenous tissue running diagonally from the upper left side to the centre of the field.

**Results**

There was marked improvement in the rheumatoid arthritis manifested by decrease in size of the swollen joints and relief of pain on movement of fingers. On clinical examination, no improvement could be observed in the hypertrophied palmar fascia. It was assumed that the increase in range of movement of the left hand was due primarily to improvement in the arthritic condition and not to change in the palmar fascia. Sections taken after cortisone therapy showed no obvious change (Fig. 5).

Under the conditions of our study, it seems to be apparent that local or systemic therapy with cortisone does not cause improvement in Dupuytren's
contracture of the hands. Of course, complete fasciectomy usually will relieve the condition, but a considerable percentage of patients experience a rather prolonged convalescence following operation. Those with a history of arthritis undergoing operations on the hand are particularly susceptible to post-operative stiffness of joints. As a logical development of our problem we decided to employ cortisone following fasciectomy. Under these circumstances there is complete removal of the hypertrophic palmar fascia leaving a wound of considerable extent beneath the skin flaps, which heals by the usual method of granulation tissue formation. An ever increasing volume of clinical and experimental research supports the hypothesis that cortisone may delay the formation of all elements of granulation tissue. It should be noted that treatment early in the stage of granulation tissue formation is thought to be more effective, just as acute systemic collagen diseases usually respond more readily than do many chronic collagen diseases after formation of scar tissue. Therefore, it was hoped that post-operative complications due to formation of scar tissue as well as stiffness and limitation of mobility of joints would be reduced.

3. OPERATION FOLLOWED BY SYSTEMIC THERAPY

By administration of this hormone at varying periods following fasciectomy we were able to observe its effect on formation of adhesions and stiffening of joints. In two patients therapy was started immediately post-operatively with doses of 200 mg. daily. Another, received 100 mg. daily commencing on the seventh post-operative day while the fourth case received cortisone as an adjunct to physiotherapy three and a half months after operation.

Case 1

J. J. aged 40. Both hands of this white male were involved by Dupuytren's contracture. His father, uncle and two siblings had the same condition. Involvement of the right hand was first observed ten years before admission. The ring finger lacked one half cm. of complete extension and the distal part of the palm was involved. Changes began in the left hand six years before admission, but progressed more rapidly so that both little and ring fingers lacked 1 cm. of full extension. Large nodules of hypertrophic tissue were situated in the distal part of the palm over the fourth and fifth metacarpals and proximal phalanx of the little finger. Immediately after operation on the right hand he was started on 200 mg. of cortisone orally in four equally divided doses daily. Three days later, fasciectomy was performed on the left hand and therapy continued as before until sixteen days after the second operation.

The appearance of the hands pre-operatively is shown in Fig. 6 and the extent of movement on the 10th and 13th day post-operatively is seen in Fig. 7 and 8.

Results. A free range of extension and flexion of this patient's hands was demonstrated on the 10th and 13th days respectively after operation. This complete range of movement did not cause discomfort or separation of the wound edges.
Case 2

H. S. aged 48. Both hands of this white male were involved with Dupuytren's contracture, the right very slightly and the left more extensively. Family history was non-contributory. The extent of involvement of the hands is described under case 2 receiving systemic administration. This patient had suffered from rheumatoid arthritis affecting the hands and right wrist for the past four years. The disease started in the left hand first and the fingers were quite deformed. No other joints have been involved. He first noticed firm nodules forming in the palm of the left hand five years ago and shortly afterward in the right palm. The left hand became progressively worse but the right hand was only slightly involved. Immediately following fasciectomy, oral cortisone in dosage of 200 mg. daily was continued for 2 weeks post-operatively and then was gradually discontinued. It should be recalled that this patient had also received the same dosage for three weeks prior to operation.

Results. This patient was one in whom a prolonged period of post-operative stiffness of the hand might be anticipated because of the extensive degree of
involvement of the hands by rheumatoid arthritis. In spite of the apparently poor prognosis a wide range of movement of the fingers without pain was obtained by the fifteenth day, and union of the wound margins had occurred.

Fig. 9 (left) Case 3: The extent of flexion of the fingers and appearance of nodules can be seen.
Fig. 10 (top right) Case 3: Operation followed by cortisone therapy. 14 days post-operatively an almost complete range of flexion and extension of the fingers can be obtained.
Fig. 11 (bottom right) Case 3: 23 days after operation a complete range of motion and a firm grip was present.

Case 3

G. P. aged 42. The family history was negative for Dupuytren's contracture. The little and ring fingers of the right hand could not be completely extended, each of these fingers lacking about one half cm. of full extension (Fig. 9). In addition, large nodules and scar bands were present over the distal half of the fourth and fifth metacarpals and first phalanx of the little finger. He claimed that the first appearance of the condition had started about seven months previously. A fasciectomy was performed. One week post-operatively parenteral injection of 100 mg. of cortisone was given for two weeks. Two weeks after operation complete flexion, with the exception of the little finger which lacked one half cm. of flexion and a range of almost complete extension was obtained (Figs.
Fig. 12 (top left) Case 4: Maximum amount of extension of fingers which was possible when the patient was admitted to hospital 3½ months after operation. Photograph was taken one day prior to commencement of cortisone therapy.

Fig. 13 (top right) Case 4: Cortisone as an adjunct to other therapy. The marked improvement in range of extension of the middle, ring and little fingers following 2 weeks of cortisone therapy may be noted.

Fig. 14 (bottom left) Case 4: Cast of hand taken with fingers extended as fully as possible one month after cessation of hormone treatment. The improvement obtained during the 2 weeks of cortisone therapy was not only maintained but also further continued.

Fig. 15 (bottom right) Case 4: Complete flexion and almost complete extension of all fingers was obtained 1 year later.

10 and 11). On the twenty-third day a complete range of movement and firm grip was present.
Results. This patient with only moderate involvement of short duration obtained a rapid return of complete functional movement which quite probably might have occurred without hormone therapy.

Case 4

R. A. aged 45. Both hands of this white female were involved by Dupuytren's contracture, the right ring and little finger lacking one half and one cm. respectively of full extension, with firm cords and nodules in the vicinity of the distal flexion crease. The condition had been present for about six months. The family history revealed a strong hereditary predisposition, since the patient's maternal grandfather, father and two brothers had become similarly affected. A fasciectomy was performed by another surgeon. Following operation there was some delay in healing of the skin incision which probably stimulated the development of excess scar tissue in the palm with subsequent limitation of extension of the little, ring and middle fingers. Seven weeks post-operatively, intermittent elastic traction splinting of the hand was carried out for three weeks. Upon discontinuing the use of this splint the fingers contracted markedly. Nine weeks postoperatively 400 mg. of vitamin E was given daily for one month, and
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since no improvement occurred as a result of this therapy 15 mgm. of desoxycorticosterone acetate and 300 mgm. of vitamin C were given daily for one week, without benefit.

Three and a half months after operation the patient was admitted to the Royal Victoria Hospital. The maximum amount of extension which could be obtained is shown in Fig. 12. There was dense scarring in the region of the incision on the hypothenar eminence and along the distal flexion crease of the midpalm. Beginning on May 11th, cortisone acetate was administered intramuscularly in doses of 100 mgm. daily for one week. The dose was then increased to 200 mgm. daily for another week because the eosinophil count had not shown an adequate drop. Physiotherapy, consisting of whirlpool baths and massage, was started on May 15th, and five days later an elastic extension splint was applied. During the two-week period of cortisone therapy there was marked improvement in the degree of extension of the little, ring and middle fingers (Fig. 13). The systemic manifestations were as follows: the eosinophils decreased to 10 at the conclusion of treatment and there was an increase in body weight of 5 pounds.

During the two-month period prior to cortisone therapy, elastic extension splinting had been used for several weeks without visible improvement. Therefore, it was considered that the addition of cortisone therapy to physiotherapy and active splinting, largely contributed to the rapid improvement which took place during the two-week period. One month after cessation of hormone treatment the degree of extension of the fingers had improved still further (Fig. 14). One year later the range of movement is shown (Fig. 15). The clinical data and timing of the various types of treatment are summarized in Fig. 16.

DISCUSSION AND CONCLUSIONS

We have shown that healing of donor areas in man is neither delayed nor accelerated by ACTH therapy (11). Also it was noted in man and in the rabbit that in hormone treated experimental wounds, although epithelial proliferation and union had occurred, the deeper parts of the wound frequently revealed inhibition of fibroblastic proliferation.

Numerous clinical observations have been made in man of delay in wound healing following surgical procedures: Furthermore, reports of sudden perforation of peptic ulcers (14), leakage of intestinal anastomoses and quantitative reduction of granulation tissue in some patients while receiving ACTH or cortisone therapy, is evidence that in some cases there is a marked inhibition of granulation tissue formation.

The marked relief from pain and free movement of joints following such therapy in rheumatoid arthritis, suggests its use in patients with Dupuytren's contracture who require fasciectomy (15) and in those who have a tendency to arthritis or stiff joints. The ultimate indication for using hormone therapy, is of course in patients who are afflicted with both rheumatoid arthritis and Dupuytren's contracture.

In one case we delayed hormone therapy until one week postoperatively, but
subsequent experience in these cases shows that even with early therapy, epithelial union is not delayed to an extent which would precipitate the risk of separation of the wound edges. As a precaution the stainless steel sutures may be left in for two weeks or more if necessary. Parenteral injection of cortisone acetate was employed at first but was superseded by cortisone tablets (16).

A fall in the level of the circulating eosinophils is commonly used as an index in treatment of patients with cortisone. It cannot be stated with certainty that when a fall of eosinophils occurs that a dose adequate for the treatment of the condition concerned has been attained. However, it is the most convenient method available at present and a marked fall does indicate the dose of cortisone has had some effect. Oral administration, three or four times daily, has many advantages including: freedom from painful injections, rapid absorption and rapid action. There is freedom from prolonged effect should dangerous reactions occur. The effective oral dose is similar to that usually given intramuscularly.

Hormone therapy should be withdrawn gradually for several reasons. Administration of cortisone inhibits the output of endogenous corticotropin by the pituitary gland and as a result there is some degree of adrenal cortical atrophy which requires a week or ten days to overcome. It is possible that sudden complete withdrawal may cause stiffness of joints of the hand and oedema, particularly if there has been a history of rheumatoid arthritis.

A history of active peptic ulcer, previous psychotic state or tuberculosis should exclude treatment with ACTH or cortisone.

Since it is difficult to find patients who exhibit the same degree of involvement with Dupuytren's contracture of both hands, on whom a controlled study may be carried out, it is obvious that a large number of cases must be treated by fasciectomy and hormone before statistical improvement in result over fasciectomy alone can be proved. While we have treated only a limited number of cases, from clinical and pathological data it appears that local injection and even systemic therapy without operation offers little promise. In a few patients, combination of operation and hormone therapy seemed to facilitate the early return of a free range of extension and flexion. Perhaps the greatest practical use of hormone therapy will be for those in whom for one reason or another, stiffness of joints may be anticipated post-operatively.

We fully realize that the number of cases studied is small, but submit this preliminary report hoping that other investigators will make their experiences known.

714 Medical Arts Bldg.
Montreal P.Q., Canada

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