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Tocopherol Administration to Patients with Dupuytren's Contracture; Effect on Plasma Tocopherol Levels and Degree of Contracture.* (19692)

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Investigations of the effect of tocopherol administration on Dupuytren's contracture were initiated by Steinberg(1), who reported the results of treatment in 7 patients, who were given 300 mg of vit. E by mouth daily for periods ranging from one to 8 weeks. In 6 out of the 7 patients the contracture disappeared. More recent studies by Steinberg(2) on a larger group of patients have, on the whole, confirmed his original findings. Favorable results with this treatment have also been reported by Scott and Scardino(3) and by Thomson(4). In the group of patients studied by Thomson 10 hands were classified as early cases and 8 as late or chronic cases. Of the 10 early cases 8 had a definite extension defect, but in no instance were the fingers contracted closer than 90° to the palm. In these patients full extension of the fingers was restored following treatment with 200 mg of tocopherol daily for 12 to 20 weeks. The 8 chronic cases exhibited marked thickening of the palmar aponeurosis with fixation of the affected fingers in the palms; in these patients the tocopherol administration resulted in a softening of the palmar masses. On the whole, however, the improvement in the latter group was not very marked but nevertheless in 4 patients sufficient to make the hands suitable for surgical treatment.

In contrast to these rather favorable results are observations by Langston and Badre(5) and by King(6) who treated respectively 5 and 13 cases of Dupuytren's contracture with similar doses of tocopherol, but in no instance noted any benefit.

Experimental. The present investigation included 19 patients with Dupuytren's contracture, 14 men and 5 women, with a total of 26 contracted hands. The mean age of the men at the onset of the study was 74 years, and of the women 77 years. The lesion was bilateral in 6 of the men and one of the women. The right hand was affected in 16 cases (12 men, 4 women), the left hand in 10 cases (8 men, 2 women). In 5 of the 26 hands one or more of the fingers were contracted closer to the palm than 90°. In the remaining 21 hands the lesion could be characterized as moderately severe or slight. In none of the male patients was the coexistence of Peyronie's disease found. Treatment with 300 mg of dl-alpha-tocopherol acetate (Ephynal Acetate) daily was given to all the patients for a period of 300 days, and it was ascertained through supervision by a nurse that the patients swallowed the administered capsules. After discontinuation of treatment the patients were followed for another 350 days. Plasma tocopherol was determined before the onset of

* Vitamin studies in middle-aged and old individuals. IX.

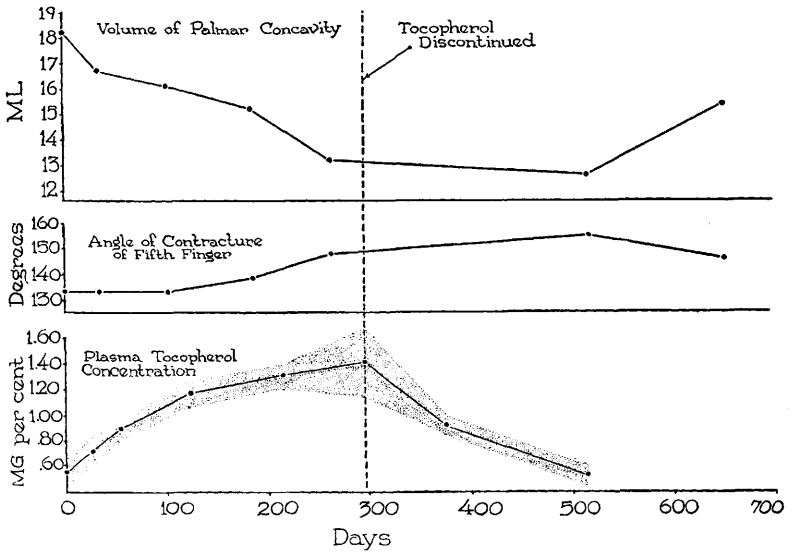

FIG. 1. Effect of alpha-tocopherol acetate administration (300 mg daily) and subsequent discontinuation on plasma tocopherol level and on degree of hand lesion in 19 old individuals with Dupuytren's contracture. The shaded area represents one s.d.

the treatment and at various intervals during and after tocopherol administration by the method of Quaife and Biehler(7). The procedure used for registering the degree of contracture was to make plaster casts of the hands under standard conditions. During the application of the plaster the patient's upper arm rested on a table with the elbow joint held in 90° flexion and the wrist in maximal dorsal flexion. A plaster bandage consisting of 3 layers of quick setting plaster gauze was then applied from a point proximal to the wrist to the finger tips. During this application, until the plaster had stiffened, a firm and constant pressure was exerted against the volar aspect of the distal part of the fingers, at the same time as the plaster gauze by a nurse was carefully molded against the surface of the palm and the individual fingers. These permanent casts obtained during maximal passive dorsal flexion of the wrist and fingers formed the basis for the evaluation of changes in the degree of contracture resulting from the tocopherol administration. For quantitative registration of the changes in the appearance of the hands 2 measurements were chosen, which give a fairly good impression of 2 of the main characteristics of the contracture, namely the degree of concavity of the palm and the angle formed between the fifth finger and the direction of the palm. Fine sand was applied to the palmar aspect of the plaster casts and the surface of the sand adjusted as accurately as possible to the plane formed by the thenar and hypothenar prominences. By subsequent weighing of the sand an estimate of the volume was obtained. This volume in normal individuals varies between 10 and 18 ml depending on the size of the hand. Tracings were made on paper directly from the casts and the angle formed between the volar surface of the 2 proximal phalanges of the finger and the general direction of the distal part of the volar aspect of the palm itself measured by a protractor. This measurement was possible in only 23 of the 26 hands. The angle in normal individuals usually varies between 190° and 205°.

Results. The effect of alpha-tocopherol administration on the plasma tocopherol concentration and on the hand measurements described above is illustrated in Fig. 1. The figure shows that the mean plasma tocopherol concentration before the onset of treatment was 0.55 mg %, a value which is significantly lower than the mean value of 1.02 mg % previously reported by the present authors(8) for this age group. Following the alpha-tocopherol administration the plasma level rose gradually and slowly to reach, after 300

days, a mean value of 1.37 mg %, or a concentration two and a half times as high as the original. After discontinuation of the alpha-tocopherol intake the plasma tocopherol concentration again decreased. As seen from the figure the mean value after 75 days had fallen to 0.88 mg % and, when measured after 215 days, had reached practically the same level as observed before the treatment was started, namely 0.53 mg %.

In no instance of moderately severe contracture did the treatment result in disappearance of the extension defect of the fingers. However, as seen in Fig. 1 a definite, though moderate improvement was noted during the prolonged alpha-tocopherol administration. In 23 of the 26 hands the palmar concavity became less marked. The determinations of the mean volume of the concavity in the 26 hands showed a decrease from 18.2 to 13.2 ml during the 300 days of alpha-tocopherol administration, a change which is statistically significant. In the first 215 days following discontinuation of the treatment a further slight improvement took place (mean volume 12.6 ml). On examination of the hands 250 days after discontinuation of therapy the amelioration had again regressed somewhat (mean volume 15.3 ml).

The angulation between the fifth finger and the direction of the distal part of the palm showed definite improvement in 15 of the 23 hands. In 7 of the remaining 8 hands the changes were only slight although with a tendency to an increase of the angle, whereas in one hand the angle remained constant. In none of the hands did the contracture of the fifth finger, when comparison was made between the first casts and the casts obtained at the end of the tocopherol treatment, became worse. A change in the mean value of the angle was not noticeable until after about 200 days of alpha-tocopherol administration, at which time the value had increased from 133.0° to 138.4°. This change is statistically significant. After 300 days of treatment the value had increased further to 147.7°, and this improvement continued during the first 215 days after discontinuation of the alpha-tocopherol therapy, at which time the value of 154.0° was reached, corresponding to a total mean increase in the angle of 21°. In the subsequent 135 days the mean value for the contracture angle of the fifth finger again decreased to 146.3°.

No untoward symptoms were noted during the prolonged alpha-tocopherol administration. A few of the patients volunteered the information that they could move their fingers and hands a little better; on the whole, however, the moderate objective improvement was not registered by the senile patients, who also before the onset of the treatment seemed unconcerned about the condition of their hands.

Discussion. In view of the fact that the lesion in the present group of patients on the whole was less severe than in the cases studied by Thomson, the smaller and slower response to alpha-tocopherol administration observed in our group becomes notable. In spite of this difference in the degree of improvement observed, the results of the present investigation would, nevertheless, support the contention of Steinberg and of Thomson that the administration of alpha-tocopherol in large daily doses has an effect on the lesion in Dupuytren's contracture.

It is possible that the smaller effect observed in the present group of patients may be due to the advanced age of the patients. Since the contracture in our cases probably had existed for a far longer period than in the patients treated by Thomson it seems further likely that the less marked effect noted by us on the degree of contracture of the fifth finger may have been conditioned by the existence of degenerative arthritic changes in the finger joints. Such changes are known to occur in contractures of long standing, and, if present, would tend to obscure an eventual therapeutic effect on the connective tissue of the palmar aponeurosis.

Summary. 1. Treatment with 300 mg of alpha-tocopherol acetate daily was given to 19 old patients with Dupuytren's contracture (26 contracted hands) for a period of 300 days. Following discontinuation of the treatment the patients were followed for another 350 days. Before therapy and at various intervals during and after alpha-tocopherol administration determinations were made of the

plasma tocopherol concentration and permanent plaster casts prepared of the affected hands in maximal passive dorsal flexion. 2. The alpha-tocopherol administration resulted in a slow but steady rise of the mean plasma tocopherol level from 0.55 to 1.37 mg %; after discontinuation of the treatment the concentration again fell to the original level. A moderate, but statistically certain effect of the therapy was observed on the condition of the hands. Thus, during the treatment the volume of the palmar concavity decreased from 18.2 to 13.2 ml, and the angle between the fifth finger and the palmar surface increased by 14.7°. The improvement continued for some time after discontinuation of the therapy, but some regression had taken place on examination 350 days after the end of the alpha-tocopherol treatment.

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Effects of Potassium on the Guinea Pig after Barbiturate Administration. (19693)

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Lamson and coworkers(1) have demonstrated that glucose and other organic substances can modify the anesthesia produced by barbiturates in various animal species. The well-known relation of potassium to glucose in the movements of the latter in and out of cells, and the implication of this cation in carbohydrate metabolism and neuromuscular processes(2) suggested a trial of potassium under conditions similar to those described for glucose. Preliminary work indicated that potassium could reinduce deep levels of anesthesia in guinea pigs recovering from hexobarbital anesthesia. The results of the investigation which followed are the subject of this report.

Methods. Guinea pigs were used throughout the study. Hexobarbital sodium† was used as the anesthetic agent, fresh solutions being made up for each experiment. Potassium chloride (KCl) and sodium chloride (NaCl) were administered as isotonic solutions (1% and 0.85% respectively). All doses of anesthetic or inorganic salt were injected intraperitoneally.

Results. The first experiments were attempts to reinduce deep anesthesia in guinea

TABLE I. Effect of KCl on Guinea Pigs Recovering from Barbiturate Anesthesia.

Guinea pig	Hexobarbital, mg/kg	Duration of anesthesia, min	KCl, mg/kg	Additional anesthesia, min
1	60	32	100	7
2	60	35	100	6
3	60	31	200	8
4	60	33	200	7
5	40	13	20	2
6	40	9	25	3½
7	40	14	50	5
8	40	15	50	5
9	40	26	400	13
10	40	20	400	10

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