

splenic vein into the rest of the portal system.

Twenty-seven patients were submitted to splenectomy at Mercy Hospital in Baltimore, during the past twelve years. Nine cases of idiopathic thrombocytopenic purpura were operated upon with complete recovery in six of these patients, one recurrence in another and mild conservatively controlled recurrences in the remaining two patients.

Four patients preoperatively diagnosed as Banti's disease underwent operation for removal of their spleens. Satisfactory improvement followed in one case, another died on the sixth postoperative day of pneumonia while the remaining two cases proved to be mistaken diagnoses. One turned out to be a case of myelogenous leukemia and the other was eventually shown to be an example of agnogenic megakaryocytic myeloid metaplasia. This latter patient while unimproved, survived operation and has persistently shown a marked thrombocytosis ranging between 1,500,000 and 5,000,000 thrombocytes per cubic millimeter of blood.

Two cases of hypoplastic anemia were operated upon, one congenital and the other acquired. No benefit followed splenectomy in the former condition while the results in the latter were excellent.

A case of agnogenic myeloid metaplasia was confirmed by splenic biopsy.

Splenectomy was performed for each of the following: gun-shot perforation of the spleen, glandular spread from a carcinoma of the splenic flexure of the colon, and in one case to facilitate repair of a left diaphragmatic hernia.

Seven members of two interesting families underwent splenectomy for congenital hemolytic jaundice. Excellent results were obtained in each instance. Associated gallstones were noted in two of the adult cases and a dermoid cyst of the left ovary was an incidental finding in one patient.

Accessory spleens were noted in two of the twenty-seven patients or 7.4 of the cases.

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### A NEW CONCEPT IN THE TREATMENT OF PEYRONIE'S DISEASE\*

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#### INTRODUCTION

Largely as the result of the reported clinical effectiveness of the tocopherols in the treatment of certain forms of fibrositis, such as Dupuytren's contracture, the authors were prompted to try these substances in the treatment of Peyronie's disease. Initially, we were unaware that Dupuytren's contracture and Peyronie's disease may coexist and were surprised to find six instances of Dupuytren's contracture in twenty-three patients with Peyronie's disease.

Plastic induration of the penis, chronic cavernositis, Peyronie's disease, are all terms used to describe a condition of the penis first reported by Ephemerides<sup>1</sup> in 1687 and more fully defined

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by La Peyronie<sup>2</sup> in 1743. In 1832, Dupuytren<sup>3</sup> wrote his account of contracture of the palmar aponeurosis. Kirby,<sup>4</sup> in 1850, was the first to describe the occurrence of both Peyronie's disease and Dupuytren's contracture in the same individual. Since then others have reported the association of the two conditions. Polkey<sup>5</sup> in an excellent review of the literature to 1928 found reports of 549 (five hundred and forty-nine) cases of Peyronie's disease; twenty-two of these had had Dupuytren's contracture. However, since 1928 reports of either condition have failed to mention the association of the two.

Peyronie's disease is characterized by fibrous infiltration of the intercavernous septum of the penis. This fibrosis may extend into Buck's fascia and the tunica albuginea on either side of the septum and result in the formation of plaques. The corpus spongiosum is never involved. Owing to the formation of these plaques, a fibrous chordae is produced often resulting in curvature of the penis on erection and making intromission difficult or impossible. Occasionally pain may be pronounced.

Most authors state that the etiology of Peyronie's disease is unknown. Others, particularly the earlier writers, ascribe the condition to inflammatory fibrosis or vascular disease. Still others believe that plaque formation results from fibrous replacement of elastic fibers. Gout and diabetes mellitus have been considered as etiologic factors.

Heretofore, treatment has consisted of surgical removal of the offending plaque, radium and x-ray irradiation, diathermy and the injection of fibrolysin, thiosinamine and autogenous vaccine.

#### TOCOPHEROL THERAPY IN MUSCULAR DYSTROPHY AND FIBROSITIS

Encouraged by reports of successful use of vitamin E in the treatment of certain of the muscular dystrophies, Steinberg<sup>6</sup> in 1941 began a clinical investigation of the use of the tocopherols in the treatment of cases of fibrositis. Of 30 cases of "primary fibrositis," improvement occurred in every instance. In a more recent communication, Steinberg<sup>7</sup> called attention to the striking similarity in pathology between "nu-

tritional muscular dystrophy" and "primary fibrositis." Chemical evidence of similarity was the finding of increased urinary creatine in both conditions. A lowering of urinary creatine to normal levels was observed in cases of "nutritional muscular dystrophy" showing clinical improvement and in cases of primary fibrositis treated with mixed tocopherols. Such findings lead Steinberg to believe that "primary fibrositis" is a metabolic disorder concerned with the deprivation of vitamin E.

In 1946, Steinberg<sup>8</sup> reported 6 cures in a series of 7 patients with early and moderately advanced Dupuytren's contracture. No surgery was required in these cases. The one failure case was complicated by an alcoholic history and an early portal cirrhosis. These patients received 300 milligrams of vitamin E daily in divided doses until maximum improvement occurred and were maintained thereafter on 1 milligram per kilogram of body weight. No untoward effects were observed with this dosage in spite of continuing the maintenance dose for periods ranging to four years.

Because of the possibility that Peyronie's disease, a fibrositis, like Dupuytren's contracture, a fibrositis, might be a manifestation of a simple human vitamin E deficiency, a study was initiated to determine the effects of both natural and synthetic tocopherols on this condition. With this introduction the authors wish to present a brief report of the promising results obtained so far.

#### METHOD OF TREATMENT

Since January, 1947, we have treated 23 cases of Peyronie's disease at the Brady Urological Institute. These patients have been observed monthly for periods ranging from a minimum of five to a maximum of nine months. Treatment has consisted of the oral administration of a total daily dose of 300 milligrams of mixed tocopherols\* or 200 milligrams of synthetic alphatocopherol.<sup>†</sup> (One hundred milligrams of the

\*The mixed tocopherols used in this study, in the form of "ergolin" were supplied by Eli Lilly and Company, Indianapolis, Indiana, through the courtesy of Dr. C. E. Roach. "Each gaseal contains distilled tocopherols, natural type, equivalent by spectrophotometric analysis to 100 mg. of alphatocopherol."

†The synthetic tocopherol used in this study in the form of "epbynal," were supplied by Hoffmann-LaRoche, Inc., Nutley, New Jersey, through the courtesy of Dr. R. J. Floody. Each tablet contains 100 mg. of synthetic d.l. alpha-tocopherol acetate.

mixed tocopherols were given three times each day at meals or one hundred milligrams of the synthetic alpha-tocopherol were given twice each day.) This dosage was somewhat arbitrary and probably represents more than is necessary. In this connection as a first approximation based on animal studies, Hickman and Harris<sup>9</sup> give a value for the "safe minimum prophylactic dose" (S. M. P. D.) of 0.84 milligrams per kilogram body weight for a mixture of alpha, beta, and gamma tocopherols that occur in diet. For a 70 kilogram human this would amount to 59 milligrams per day. The S. M. P. D. for synthetic racemic alpha-tocopherol has been calculated to be 0.7 milligrams per day per kilogram body weight. According to these authors other means of calculation lead to a lesser estimate. Clinically either the oral or parenteral routes of administration appear to be equally effective.

#### PRE-TREATMENT SYMPTOMS AND SIGNS

Analysis of our data in 23 cases of Peyronie's disease reveals that the most common symptom was penile curvature (*Tables 1 and 2*). Curvature occurred in twenty of twenty-three cases and varied from a moderate bend to extreme angulation. Frequently, intromission was impossible. Pain on erection occurred in twelve cases, loss of potentia in sixteen and loss of libido in four. Six patients presented complaints referable to Dupuytren's contracture. Like Dupuytren's contracture, Peyronie's disease usually manifests itself for the first time during

the latter part of the fourth and early part of the fifth decade. Both are uncommon in young people. In this series the ages ranged from 35 to 63 years and averaged 50 years.

Typical penile plaques, varying in consistency from firm to stony, were found in all but one patient. This individual (BUI No. 40019) had a firm to hard collar-like lesion located at the base of the penis. Six patients showed evidence of moderate Dupuytren's contracture. Both hands were involved in three cases, the right hand in two and the left hand in one.

Eight of the twenty-three patients with Peyronie's disease had been treated previously, four with radium and four with diathermy. Two of the four treated with radium had suffered burns.

#### RESULTS

At the risk of oversimplification, we feel that the results we have observed are best presented in tabular form (*Table 2*). An evaluation in each case was made by comparing pre-treatment symptoms and signs with those elicited and observed with treatment. The results of tocopherol therapy are summarized according to symptoms and signs in *Table 3* (data taken from *Table 2*). Complete disappearance of curvature was noted in four cases, a marked decrease in four, a moderate decrease in ten and no change in two. Data are absent for this symptom in three. Pain disappeared in every instance (twelve in twelve). Sexual intercourse was described as normal in ten cases and unsatisfactory in three.

Softening and a decrease in the size of the penile plaque was described as marked in six cases, moderate in fifteen and unchanged in two.

In the six patients with Dupuytren's contracture, marked improvement was seen in one case, moderate improvement in three and no change in two. One of the two patients showing no change in palmar contracture presented a far advanced lesion and probably falls into the group best treated by a combination of surgery and tocopherol therapy.

In our overall evaluation, we have rated the

THE INCIDENCE OF SYMPTOMS AND SIGNS BEFORE TREATMENT IN TWENTY-THREE CASES OF PEYRONIE'S DISEASE

Symptoms	Incidence	Signs	Incidence
Penile curvature		Penile plaques	
Severe	11	Severe	6
Moderate	9	Moderate	16
Not present	3	(Collar)	1
Pain on erection	12	Dupuytren's contracture	6
Loss of libido	4		
Loss of potentia	16		
Palmar contracture	6		

Table 1

BUJ No.	AGE	PRE-TREATMENT			POST-TREATMENT			Results
		Symptoms	Signs	Type of Therapy	Mot. of Therapy	Symptoms	Signs	
31081	48	Penile curvature, severe. Loss of libido and potentia. Palmar contracture, moderate, right and left	Penile plaques, moderate. Dupuytren's, moderate	Mixed and synthetic tocopherols	9	Penile curvature, no change	Moderate softening, penile plaques changed	No change
30712	55	Penile curvature, moderate. Pain on erection. Loss of potentia	Penile plaques, severe	Mixed tocopherols	8	Marked decrease of penile curvature. Disappearance of pain. Sexual intercourse normal	Moderate decrease, penile plaques	Good
30930	62	Penile curvature, severe. Pain on erection. Loss of libido and potentia. Palmar contracture, moderate. Previous treatment, diathermy	Penile plaques, moderate. Dupuytren's, moderate	Mixed tocopherols	9	Disappearance of penile curvature. Disappearance of pain. Sexual intercourse normal	Marked decrease, penile plaques. Moderate improvement in Dupuytren's	Good
30948	48	Penile curvature, moderate. Pain on erection. Loss of potentia. Palmar contracture, right. Previous treatment, diathermy	Penile plaques, moderate. Dupuytren's, moderate	Mixed and synthetic tocopherols	9	Moderate decrease of penile curvature. Disappearance of pain. Sexual intercourse unsatisfactory	Moderate decrease, penile plaques. Moderate improvement in Dupuytren's	Fair
36277	60	Penile curvature, severe. Pain on erection. Loss of potentia. Previous treatment, diathermy	Penile plaques, severe	Mixed tocopherols	7	Disappearance of penile curvature. Disappearance of pain. Sexual intercourse normal	Moderate decrease, penile plaques	Good
9837	58	Penile curvature, severe. Pain on erection. Loss of potentia	Penile plaques, moderate	Mixed tocopherols	9	Moderate decrease of penile curvature. Disappearance of pain. Sexual intercourse normal	Moderate decrease, penile plaques	Good
30828	63	Penile curvature, moderate. Pain on erection. Loss of potentia. Palmar contracture, right and left	Penile plaques, moderate. Dupuytren's, moderate	Mixed and synthetic tocopherols	9	Moderate decrease of penile curvature. Disappearance of pain. Palmar contracture, no change	Moderate decrease, penile plaques. Dupuytren's no change	Fair
30846	36	Penile curvature, severe. Loss of potentia. Previous treatment, diathermy	Penile plaques, moderate	Mixed and synthetic tocopherols	8	Disappearance of penile curvature. Sexual intercourse normal	Marked decrease, penile plaques	Good
30949	50	Penile curvature, severe. Loss of potentia. Palmar contracture, right and left	Penile plaques, moderate. Dupuytren's, moderate	Mixed tocopherols	8	Marked decrease of penile curvature. Sexual intercourse markedly improved	Moderate decrease, penile plaques. Dupuytren's markedly improved	Good
30962	62	Penile curvature, moderate. Loss of potentia	Penile plaques, moderate	Mixed tocopherols	8	Moderate decrease of penile curvature. Sexual intercourse unsatisfactory	Moderate decrease, penile plaques	Fair
30950	52	Penile curvature, severe. Pain on erection. Loss of potentia. Palmar contracture, right	Penile plaques, moderate. Dupuytren's, moderate	Mixed tocopherols	8	Marked decrease of penile curvature. Sexual intercourse normal. Palmar contracture moderately improved	Moderate decrease, penile plaques. Dupuytren's moderately improved	Good
30952	39	Penile curvature, moderate. Pain on erection. Loss of potentia	Penile plaques, severe	Mixed tocopherols	8	Marked decrease of penile curvature. Disappearance of pain. Sexual intercourse normal	Marked decrease, penile plaques	Good
34503	41	Penile curvature not present. Previous treatment, radium with burn	Penile plaques, moderate	Mixed tocopherols	7	Penile curvature, moderate	Marked decrease, penile plaques	Good
36476	57	Penile curvature, moderate. Previous treatment, radium with burn	Penile plaques, moderate	Mixed tocopherols	7	Moderate decrease of penile curvature	Moderate decrease, penile plaques	Fair

39429	46	Penile curvature, moderate. Previous treatment, radium	Mixed tocopherols	7	Moderate decrease of penile curvature	Moderate decrease, penile plaques	Fair
40019	35	Penile curvature not present. Loss of potentia	Mixed tocopherols	6	Sexual intercourse normal	Moderate decrease, penile plaques	Fair
40244	52	Penile curvature, moderate. Loss of libido and potentia	Mixed tocopherols	6	Penile curvature, no change	Penile plaques, no change	No change
40300	57	Penile curvature, severe. Pain on erection. Loss of potentia. Previous treatment, radium	Synthetic tocopherols	5	Disappearance of curvature, no change. Disappearance of pain. Sexual intercourse normal	Marked decrease, penile plaques	Good
40402	51	Penile curvature, severe. Pain on erection. Loss of potentia	Mixed tocopherols	5	Moderate decrease of penile curvature. Disappearance of pain	Penile plaques, no change	Fair
40350	49	Penile curvature, moderate. Pain on erection	Mixed tocopherols	5	Moderate decrease of penile curvature. Disappearance of pain	Moderate decrease, penile plaques	Fair
40379	36	Penile curvature not present. Sexual intercourse unsatisfactory	Synthetic tocopherols	5	Sexual intercourse partially unsatisfactory	Moderate decrease, penile plaques	Fair
40246	59	Penile curvature, severe	Mixed tocopherols	6	Moderate decrease of penile curvature	Moderate decrease, penile plaques	Fair
40031	55	Penile curvature, severe. Pain on erection	Mixed tocopherols	7	Moderate decrease of penile curvature. Disappearance of pain	Marked decrease, penile plaques	Good

Table 2

THE INCIDENCE OF CHANGE IN SYMPTOMS AND SIGNS IN TWENTY-THREE CASES OF PEYRONIE'S DISEASE TREATED WITH TOCOPHEROLS

Symptoms	Incidence	Signs	Incidence
Penile curvature		Penile plaques	
Disappearance	4	Marked decrease	6
Marked decrease	4	Moderate decrease	15
Moderate decrease	10	No change	2
No change	2		
No mention	3		
Pain on erection		Dupuytren's contracture	
Disappearance	12	Marked improvement	1
		Moderate improvement	3
Sexual intercourse		No change	2
Return to normal	10		
Unsatisfactory	3		

Table 3

response as good in eleven cases, fair in ten cases and unchanged in two.

The authors recognize that an occasional case of Peyronie's disease improves without treatment. In this regard, the values of Burford<sup>10</sup> are of interest. In his series of nineteen untreated cases, spontaneous improvement was noted in only one. We feel that our results with tocopherol therapy cannot be explained on the basis of spontaneous improvement, and that continued use of these substances is indicated. Further work is necessary to establish the cause of Peyronie's disease; but the promising results obtained so far with the administration of substances possessing vitamin E activity, plus the similarity of Peyronie's disease to other forms of fibrositis, justify the consideration that Peyronie's disease is secondary to vitamin E deficiency.

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