THROMBOANGIITIS OBLITERANS

A Summary of Recent Trends and Treatment

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DURING the past three or four years several new methods for the treatment of thromboangiitis obliterans have been suggested. The most promising have been the anticoagulants, histidine and vitamin C, sympathectomy, tetraethyl ammonium chloride, and caudal anesthesia or lumbar sympathetic block. These, however, should be considered only as supplements to the well-established principles and methods used in the management of thromboangiitis obliterans, namely, elimination of tobacco, careful hygiene and care of the extremities, and proper physical therapy measures.

Anticoagulants

Following the introduction of heparin and dicumarol as anticoagulants to be employed in the treatment of thromboembolic disease, it was suggested that these preparations might be helpful in thromboangiitis obliterans. Comparatively little coordinated or extensive work has appeared in the literature concerning such use for these anticoagulants. In 1942 Allen *et al.*[1] reported the use of dicumarol in 2 cases, but significant conclusions as to its value could not be drawn. LeFevre[2] employed the same substance in 8 cases in 1945 but, noting no definite changes, believed that dicumarol had little effect upon the course of the disease. In 1946 Aggeler[3] reported that the anticoagulants had been given in chronic occlusive arterial disease but that their benefits had not yet been determined. Barker[4] in 1945 stated that dicumarol was beneficial after acute peripheral arterial thrombosis from any cause and that possibly it might prevent an extending arterial thrombosis such as that present in thromboangiitis obliterans. In 1946 Barker *et al.*[5] reported the treatment of acute arterial occlusion of the e tremities with special reference to anticoagulant therapy. Three cases of thromboangiitis obliterans were recorded in which both heparin and dicumarol were employed. Recovery of the limb ensued in each case, indicating that progressive thrombosis and gangrene do not develop while anticoagulant therapy is being given. In 1944 Gefter[6] treated 2 cases of thromboangiitis obliterans with dicumarol and noted partial improvement. In 1947 Allen[7] summarized the present status of the anticoagulants in the chronic occlusive arterial diseases by stating that the results have not been satisfactory.

Method of Treatment. The administration of heparin and dicumarol depends upon the acuteness of the disease state. In the acute thrombotic processes, heparin and dicumarol therapy should be started simultaneously. Fifty milligrams of heparin solution is drawn into a syringe containing about

15 to 20 cc. of a physiologic saline solution and given intravenously every four hours for ten doses. On the first day the prothrombin time is recorded and the patient is given 300 mg. of dicumarol orally. One hundred and fifty milligrams of dicumarol is again given on the second day. Following this the dosage of dicumarol is adjusted to keep the prothrombin time between 20 and 30 per cent of normal. We have found this to vary with each patient. The prothrombin time should be observed daily. Caution should be used to take the prothrombin time at least three hours after heparin has been given, as it has been shown that heparin will affect the prothrombin time. In the chronic occlusive states, the heparin can be omitted.

Comment. Although the exact role that heparin and dicumarol will play in the treatment of thromboangiitis obliterans has not yet been determined, conservative evaluation indicates that the anticoagulants should be employed in acute cases. The occurrence of venous thromboses and rapidly progressive arterial thromboses, such as in acute thromboangiitis obliterans, appears amenable to the action of the anticoagulants. In the chronic forms of Buerger's disease where there is no active thrombotic process the administration of anticoagulants hardly seems justified.

Histidine and Vitamin C

Considerable interest has been centered about the treatment of occlusive vascular disease with histidine and vitamin C. As in all these newer methods, the primary aim is to increase the supply of blood to the affected extremity. Up to the present time only one reference to treatment with these materials has appeared in the literature.[8] Two cases of thromboangiitis obliterans were treated by histidine and vitamin C, and the observers noted a rapid response with relief of pain, a sensation of warmth, and an increase in temperature of the affected extremities.

Egeberg[9] used histidine and ascorbic acid in 50 patients, 11 of whom had thromboangiitis obliterans. Three of the 11 had osteomyelitis and underwent amputation. Three cases were mild and showed improvement; 5 were severe and were improved by these substances. Egeberg believes that two to three months of continuous therapy may be necessary before favorable results are apparent.

Technic. The patient is given 500 mg. of sodium ascorbate. This is followed immediately by the intramuscular injection of 5 cc. of a 4 per cent aqueous solution of histidine monohydrochloride and the simultaneous injection of 100 mg. of sodium ascorbate subcutaneously. Care is taken to inject these substances in different locations. This treatment is given every four hours. In addition, 600 mg. of ascorbic acid is given by mouth daily. Results should be evident within a few days. The length of therapy has not been established, although Egeberg believes two to three months should be the average duration of therapy.

Comment. In 2 typical cases of thromboangiitis obliterans treated at the Clinic in this manner for ten days improvement could not be established.

Despite this, we believe that further work along this line is justified, considering Egeberg's views regarding the length of time necessary for a favorable response.

Tetraethyl Ammonium Chloride

Tetraethyl ammonium chloride has been shown to block the autonomic ganglia. Because of this effect it was believed that this substance might be beneficial in relieving the neurogenic vasoconstriction which is frequently present in thromboangiitis obliterans.

In 1946 Berry *et al.*[10] reported the treatment of 18 cases of thromboangiitis obliterans with tetraethyl ammonium chloride. Of 11 which were treated conservatively over a period of two weeks to six months, 5 became symptom-free. Intermittent claudication was relieved, and the exercise tolerance improved in all members of the group. A sympathectomy was performed on 3 of these patients. Three of the patients received only single injections for the purpose of producing a sympathetic block.

In 1947 Lyons *et al.*[11] reported the effects of blockade of the autonomic ganglia by tetraethyl ammonium in man. This report included cases of thromboangiitis obliterans, and it was concluded that patients with Buerger's disease experienced continued relief of pain and a decrease in the inflammatory process. Lyons' group also felt that the use of tetraethyl ammonium chloride was a diagnostic agent helpful in evaluating neurogenic vasoconstriction and therefore of aid in determining the importance of lumbar sympathectomy in cases of thromboangiitis obliterans. This preparation was believed to be as reliable as paravertebral blocks or local nerve blocks.

Technic. All of the material we have used was supplied through the courtesy of Parke Davis and Company. The material is furnished as a powder which is dissolved in highly distilled water so that each cubic centimeter of solution contains 100 mg. This preparation can be given either intravenously or intramuscularly, although with this concentration we used only the intramuscular route. We used an average daily dosage of 3 cc. intramuscularly for three to six weeks. The intravenous route should be used more cautiously and the solution given very slowly, as the blood pressure may drop precipitously. With both modes the blood pressure should be watched for at least forty-five minutes.

Comment. We have treated 4 patients with thromboangiitis obliterans in this manner. One was an acute case and did not show significant improvement following therapy. Three chronic cases of thromboangiitis obliterans were treated over a period of three months with evidence of increase in the peripheral circulation and relief of symptoms. We have concluded that tetraethyl ammonium is a promising drug in treatment of thromboangiitis obliterans. Too few cases have been reported for final evaluation. Further investigation is indicated.

Sympathectomy

Sympathectomy has been recognized for several years as a procedure of importance, and more recently it has been possible to draw conclusions con-

cerning the success of this operation. Recent reports in the literature continue to stress its importance. In 1944 DeTakats[12] discussed the value of sympathectomy in the treatment of Buerger's disease in 50 patients. Thirty-seven were able to resume full-time work, 7 returned to part-time work, and 6 remained invalids. It was his opinion that sympathectomy deprived the extremities of vasoconstrictor tone. He did not think that it influenced the course of Buerger's disease but felt that when the disease is in an inactive phase and when adequate preoperative tests reveal the presence of sufficient collateral vascular supply, sympathectomy would be of value. In 1943 Shumacker[13] reported the treatment of peripheral vascular disease by sympathectomy. He included 17 cases of thromboangiitis obliterans, and it was his impression that sympathectomy did not accomplish a great deal for the intermittent claudication associated with the disease. He stressed the importance of adequate preoperative selection of cases, particularly those demonstrating significant vascular spasm. In 1947 Freeman[14] observed good results following sympathectomy in 34 cases. Of his series 31 improved, although 5 required minor amputation; 3 failed to improve, 2 of these requiring amputation. Hildenbrand[15] advised that a candidate for sympathectomy should demonstrate the presence of an adequate collateral vascular bed and should be in a quiescent stage of the disease rather than in an acute one. The disease should also not show any visceral extension. Grimson[16] stated that sympathectomy may help patients with thromboangiitis obliterans, believing that such benefits may be largely related to an increase in temperature of the extremity, slight improvement of circulation, and to elimination of the constant fluctuation of tone ordinarily induced by vasomotor nerves. He believed that the lower extremities respond to sympathectomy better than the upper extremities because the legs appear to be more actively influenced by sympathetic vasomotor tone of proprioceptive origin. Sympathectomy effects its greater benefit by interrupting this vasomotor tone and also, during changes of posture, may produce an uncompensated passive vascular exercise.

In 1946, we treated 8 patients with bilateral sympathectomy. Five received definite benefit and returned to normal activities, 2 were uninfluenced, and in 1 case the disease process was apparently slowed but a minor amputation was necessary. We believe that lumbar sympathectomy is one of the most effective methods of treatment for thromboangiitis obliterans. In our experience the procedure has been of little help in the treatment of acute thromboangiitis obliterans but valuable in chronic cases and those without active inflammatory involvement, such as thrombophlebitis or ulceration.

Definite evidence of vasoconstriction should be present before operation is performed. This evidence can be demonstrated by the use of lumbar procaine hydrochloride nerve block or tetraethyl ammonium chloride.

Lumbar Sympathetic Nerve Block

Injection of procaine hydrochloride into the lumbar sympathetic nerve ganglion has been employed for several years in the treatment of peripheral vascular disease. It is helpful in thromboangiitis obliterans, particularly in

relieving associated pain. A series of nerve blocks carried out over several weeks often produces enough additional circulation to reduce the inflammation and to assist in the healing of ulcers. We recommend its use in the acute cases and as a diagnostic method for predicting the effectiveness of sympathectomy.

Caudal Anesthesia

We have recently employed caudal anesthesia as a means of relieving the exquisite pain of acute thromboangiitis obliterans. We have not found any reference in the literature to the use of this method in Buerger's disease. Caudal anesthesia has the added value of blocking not only the autonomic nerve fibers but also the sensory nerve fibers. We believe that this break in the pain cycle is very beneficial.

The procedure was first tried recently in a case in which the pain had been resistant to paravertebral block. The patient obtained his first relief with the caudal block and enabled us to proceed with further measures. In the past few months we have used the caudal block instead of the paravertebral block in all cases of occlusive peripheral vascular disease, including Buerger's disease and arteriosclerotic vascular disease. A preliminary survey reveals that in some cases this has been more effective than paravertebral block.

Summary

1. Abstinence from tobacco, careful foot hygiene, and various modes of physical therapy remain the important basic features of treatment of thromboangiitis obliterans.

2. The anticoagulants, heparin and dicumarol, appear to be of value for venous thromboses and rapidly progressive arterial thromboses. Anticoagulants do not seem to be helpful in chronic forms of Buerger's disease.

3. The evidence concerning histidine and vitamin C in thromboangiitis obliterans is inconclusive.

4. Tetraethyl ammonium chloride apparently has more value in chronic than in acute cases and may be a valuable drug.

5. Sympathetic nerve block and caudal anesthesia are helpful in relieving symptoms and in predicting the value of sympathectomy.

6. Sympathectomy helps in chronic cases of Buerger's disease but is of little use in acute cases.

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