Post-Thrombotic Sequelae Preventable with Anticoagulant Therapy

By Harry Zilliacus, M.D.

After five years of duty as a military physician in the war, I felt a strong urge to carry on some research investigation. As conditions for this were very poor in Finland at that time, I left for Stockholm, where my former teacher of physiology, Prof. R. Granit, working at the Karolinska Institutet, did me the great favor of introducing me to Prof. Erik Jorpes in December 1944. By that time Professor Jorpes was well along in the development of the concept that thromboembolism could be controlled in large measure by the use of anticoagulants. Favorable results for prophylaxis and treatment with heparin had been reported in Sweden by Jorpes, Crafoord, Watterdal, Bauer, Simon, Suve, and Linde. On the other side of the Atlantic encouraging results were reported by Best, Murray, and McKenzie. Similar advantages had been reported following the use of Dicumarol by Wright, Prandoni, Meyer, Allen, Barker, Nygaard, Walters, Priestly, Waugh, Butsch, and Stewart, in the United States, and by Lehmann and Bruzelius in Sweden.

In 1945, Bauer, reporting a series of 103 patients, drew attention to the possibility of preventing post-thrombotic sequelae by treating the very early stages of deep venous thrombosis with heparin. As these observations were based on relatively few patients there remained some doubt about the specificity and effectiveness of the anticoagulants. I felt, therefore, very fortunate to be asked by Professor Jorpes to organize a study, based on a large number of patients, to evaluate anticoagulant therapy in the control of acute deep vein thrombosis and reduction of the risk of pulmonary emboli and other post-thrombotic sequelae. Through the courtesy of the Chiefs of Staff of 15 leading hospitals in Sweden and Finland it was possible to review the material on 1,158 cases of deep thrombosis of the veins of the legs. This report was published under the title, "On the specific treatment of thrombosis and pulmonary embolism with anticoagulants, with particular reference to the post-thrombotic sequelae" (Supplementum Acta Medica Scandinavica, 1946). It was found that specific therapy with anticoagulants shortened the time the patient had to stay in bed to about one fifth of that required by conservative therapy. The thrombotic process could usually be limited to the vein in which it was first diagnosed. It was also established that under anticoagulant therapy the frequency of pulmonary embolism in thrombotic cases decreased from approximately 30 to 0.5 per cent, and that the earlier high mortality from this much dreaded complication was reduced to almost nil. In the course of follow-up examinations of 609 patients who had suffered from an acute deep venous thrombosis from 1 to 5 years previously, it was found that post-thrombotic sequelae, including chronic edema, induration, eczema, pain, and leg ulcer, occurred in 4 out of 5 patients conservatively treated. In those patients in whom early diagnosis was still limited to the calf, and anticoagulants were administered, post-thrombotic symptoms were mostly absent or very mild. One decade later, in 1946, Gjöres (Acta Chirurgica Scandinavica, Suppl. 206) found in a follow-up study of 303 patients an incidence of post-thrombotic sequelae very similar to the corresponding figures in my investigation.

In the discussion of my thesis I had stressed that thrombosis, probably due to anatomic reasons, was found much more frequently in the left than in the right leg, and that this was reflected in the more frequent occurrence of post-thrombotic sequelae in the left leg. I
had pointed out that this correlation could be confirmed by watching ladies' legs in the street, and soon thereafter I received a telegram in which congratulations were sent by The Society for Saving the Beauty of Ladies' Legs. I have always suspected that this originated from Professor Jorpes!

The great number of thrombotic cases examined in the course of this investigation established the fact that anticoagulant therapy for thromboembolism was about as specific as insulin therapy for diabetes. The evidence clearly demonstrated that with the aid of anticoagulants thrombosis could be controlled in the acute stage, and post-thrombotic sequelae thus avoided. My additional studies in this field are found in the reference list of this article.

This early experience with the problems of coagulation and thrombosis has been of the greatest value in the prevention and treatment of thrombosis on my obstetrical service, where 5,000 obstetrical and 1,000 gynecological patients enter the I. University Hospital for Women in Helsinki annually.

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