Venous Thrombosis—Newer Diagnostic and Therapeutic Approaches

A CLINICAL CONFERENCE on venous thromboembolism is published elsewhere in this issue of THE WESTERN JOURNAL OF MEDICINE. Dr. Arthur J. Silvergleid of Stanford University School of Medicine describes newer techniques for the diagnosis of venous thrombosis, considers the problem of prophylactic therapy and discusses methods for using heparin in the treatment of established thrombosis. Since venous thrombosis occurs as a complication of a wide variety of medical and surgical illnesses, physicians in many branches of medicine should find the transcript of this conference worth their review.

Dr. Silvergleid summarizes the advantages and limitations of five diagnostic procedures for venous thrombosis: venography, the Doppler ultrasound flow study, impedance phlebography, radionuclide venography with technetium-sulfur labeled macroaggregates of albumin and external scanning of the legs after administration of ^{125}I-fibrinogen. The newer techniques are still under investigation and not generally available. The oldest procedure, venography, is widely available but probably under-utilized because of some degree of patient discomfort. In experienced hands[1] venography provides a reliable evaluation of the deep venous system, and it serves as the standard for comparing the accuracy of the newer methods. Venography has proven particularly valuable in patients with superficial thrombophlebitis in whom physical findings suggest associated deep venous involvement. It may also provide very useful information in a patient with minor leg signs suggestive of deep venous thrombosis who has a relative contraindication to the use of anticoagulants. In addition, Dr. Silvergleid advocates venography for patients with proven pulmonary embolism in order to define risk potential for future emboli. I suspect, however, that most physicians will settle for the pragmatic approach of administering anticoagulant therapy for from three to six months to such patients without delineating the extent of underlying venous disease.

The Doppler procedure should become increasingly available as diagnostic methods using ultrasound spread throughout the practicing community. As Dr. Silvergleid points out, this simple, rapid, non-invasive test helps particularly in the evaluation of a patient with an acutely swollen lower leg. Further data are needed to compare the findings obtained by the Doppler technique with the results of venography in patients who have minor leg signs suggestive of posterior tibial or superficial femoral vein thrombosis.

Studies with ^{125}I-fibrinogen scans, primarily in Britain, have added remarkably to our understanding of the incidence, pathogenesis, and therapy of venous thrombosis. Because of the risk of transmitting hepatitis with fibrinogen, use of this technique has been limited in the United States to a few clinical studies such as those currently in progress at Stanford. Although obviously destined for an expanded role in the clinical investigation of venous thrombosis, the place of ^{125}I-fibrinogen scans as a diagnostic method for general use in patient care has not yet been defined.

The ^{125}I-fibrinogen technique has revealed a startlingly high incidence of thrombi in small calf veins in surgical patients, orthopedic patients and patients with myocardial infarction. Such thrombi will develop in about 30 percent of patients over 40 years of age after major operations, and in a small but significant number of patients these small thrombi will extend cephalad to give rise to clinically significant thrombosis in the posterior tibial and superficial femoral veins. Understandably, attention has turned to an evaluation of prophylactic therapies capable of reducing the incidence of positive postoperative scans. Drugs impairing platelet function have been without such prophylactic effect to date, whereas small doses of heparin have been strikingly effective. These results support the pathologic studies of Sevitt,[2] which strongly suggest that accumulation of activated clotting factors in areas of stasis, rather than accumulation of platelets upon areas of injured endothelium, represents the key pathogenetic event triggering the formation of venous thrombi.

A low dose heparin schedule which has proven prophylactically effective in the general surgical patient—5,000 international units given subcutan-

eously two hours before operation and every 12 hours for the next five to seven days—does not increase clinical bleeding and does not prolong the activated partial thromboplastin time test beyond the normal range. Thus, the obvious question arises: Should surgical patients routinely receive prophylactic heparin? Although this question is discussed in the Stanford clinical conference, a conclusion is not reached. An editorial by Wessler and Yin[3] is quoted; the physician attempting to answer this question for his own patients should read that excellent editorial carefully. A very recent report by Gallus, Hirsh and Gent[4] raises the possibility that a short preoperative activated partial thromboplastin time test will help to identify which surgical patients should receive prophylactic heparin. I believe that prophylactic low dose heparin should be given to a patient over 40 years of age undergoing thoracic, abdominal or pelvic surgery if (1) the patient has a history or physical findings suspicious in any way of venous disease of the legs, or (2) the patient is grossly overweight, or (3) the patient has a short preoperative partial thromboplastin time, for example, a time of less than 36 seconds by the kaolin-activated technique. Unfortunately, small doses of prophylactic heparin will not prevent venous thrombosis in some groups of high-risk patients—namely, patients undergoing open prostatectomy or reconstructive hip procedures and patients with fractured hips. Full anticoagulation with warfarin has been recommended as the best method of providing effective prophylaxis against thromboembolism for these groups of patients.[5]

One must never confuse prophylactic and therapeutic heparin dosage schedules. When a thrombosis has already formed, much more heparin must be given, and it should be given intravenously, not subcutaneously. Either an intermittent or a continuous intravenous technique may be used. Basu and coworkers[6] have clearly shown that a continuous intravenous method provides effective therapy for venous thrombosis with minimal risk of bleeding. Jick and associates[7] in an earlier paper, which summarizes experience in three hospitals with an intermittent technique, reported a higher incidence of bleeding. Whatever method is used, two taboos must not be broken if bleeding is to be kept at a minimum. First, the heparinized patient must not receive intramuscular injections. Second, the heparinized patient must not be given drugs containing aspirin because such drugs impair platelet function. No data have yet appeared in which the same investigators, keeping all other factors constant, have compared intermittent and continuous intravenous heparin administration for therapeutic effectiveness and incidence of bleeding. Hence the results of the study described by Dr. Silvergleid which is currently in progress at Stanford are awaited with much interest.

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"Trauma Rounds"

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We present "Trauma Rounds" in the confident expectation that they will make an important contribution to the medical literature in this field.