

VENOUS THROMBOEMBOLISM: A COMPARISON OF TREATMENT WITH INTERMITTENT CONSTANT DOSAGE HEPARIN AND CONTINUOUS INFUSION WITH LABORATORY CONTROL. M.J. Mant, B. O'Brien and M.G. Grace. University of Alberta and University of Alberta Hospital, Edmonton, Alberta, Canada.

We are conducting a prospective randomized trial comparing the treatment of venous thromboembolism for 10 days with constant dosage intermittent (I) I.V. heparin 5000 u 4 hrly and with continuous (C) I.V. heparin in comparable dosage with daily dosage adjustment designed to maintain thromboplastin times between $1\frac{1}{2}$ and $2\frac{1}{2}$ x control values. Patients with massive pulmonary embolism are excluded. Fifty-five patients have now received I heparin and 50 C heparin. Age and sex distributions, clinical diagnoses and factors potentially predisposing to hemorrhage were similar in the 2 groups. The clinical diagnosis was radiologically confirmed in 80 of the 105 patients. Although no patients have had a certain pulmonary embolus during treatment 5 in each group had suggestive clinical and/or radiologic findings. Pain or tenderness occurred at a new site or in an asymptomatic leg in 7 patients on I heparin and in 13 on C heparin. Hemorrhage occurred in 18 patients on I and 16 on C heparin. Major bleeding occurred in 7 patients and was spontaneous in 5 of these, in each group. Minor bleeding occurred in 15 patients on I heparin and 12 on C heparin. Some of these also had major bleeding. No patients have died of bleeding. One patient has died from progressive respiratory failure due to the original emboli. These preliminary results demonstrate that, although mortality is low, both hemorrhage and clinical features suggestive of recurrent thromboembolism are common during the first 10 days of heparin therapy. They also suggest that continuous administration of heparin with laboratory control may have no significant advantages over the simpler intermittent constant dosage treatment regimen.

VASOACTIVE SUBSTANCES IN PULMONARY EMBOLISM. M.H. Todd, J.B. Forrest and J. Hirsh. McMaster University, Hamilton, Ontario, Canada, L8S 4J9.

Embolisation of the pulmonary vasculature with microspheres releases prostaglandin-like substances, PGLS (Piper and Vane, N.Y. Acad. Sci. 180: 363, 1971) but the capacity of autologous blood clots (ABC) to release pulmonary vasoactive substances is disputed. Ten normal mongrel dogs were anesthetized with pentobarbitone sodium and instrumented. Pulmonary venous blood was continuously superfused over isolated tissues for bioassay and then returned to the animal. Injection of ABC into the right atrium increased pulmonary artery pressure from 21 ± 6.5 mm Hg to 38 ± 15 mm Hg (mean \pm S.D.), increased arterial pCO_2 and decreased arterial pO_2 . No significant changes in heart rate, systemic arterial blood pressure or cardiac output occurred. In three animals contractions of the blood superfused assay tissues occurred following embolism. This effect was produced in normal assay tissues and those pretreated with antagonists of ACh, Serotonin, Histamine and Catecholamines and could therefore be attributed to PGLS. No cardiovascular or assay tissue tension changes were observed when equivalent volumes of saline or clot lysate were injected into the right atrium. Therefore, pulmonary embolism with ABC can release PGLS which may contribute to the pulmonary artery pressure rise. Vasoactive substances may normally be inactivated in the lung but in some animals appear in pulmonary venous blood.

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THE ORGANIZATION OF DUTCH THROMBOSIS SERVICES. C.A. van Dijk-Wierda and J.L. van Dijk. Netherlands Federation of Thrombosis Services, The Hague, The Netherlands.

In the Netherlands the prevention and treatment of thrombotic diseases by means of coumarin derivatives are carried out by "Thrombosis Services", which cover a territory of 9 million inhabitants where they perform more than 2 million prothrombin estimations a year. A thrombosis service is an institute with the object to an appropriate treatment of patients with oral anticoagulants by means of: providing dosage and other advices by expert doctors attached to the service; venapuncture by skilled nurses at the patients home or at out-patient departments and standardized laboratory work. The Thrombotest of Owren is used for the laboratory assay, aiming at therapeutic levels of 5-10%. In a well organized thrombosis service a score of 83% of the laboratory results within the target limits are made. In 1971 the thrombosis services were united in a federation which set itself to quality control and improvement by means of standardization of techniques in laboratory control, directives for dosage, instruction to patients, external quality control, etc. This highly privileged condition seems one of the reasons that the Netherlands do not share the negative attitude towards the efficiency of coumarin described in many other countries.