

HEPARIN THERAPY IN AMBULATORY, OUT-PATIENT HUMAN SUBJECTS BY CONTINUOUS, LONG TERM, INTRAVENOUS INFUSION EMPLOYING A PORTABLE PUMP. A.J. Samuels, M.D., University of California, Center for the Health Sciences, Los Angeles, California and R.D. Sullivan, M.D., University of California, Irvine, California, USA.

A method is described for continuous, long term, ambulatory, out-patient, heparin therapy in human subjects. A portable light-weight pump originally designed for ambulatory, continuous intravascular chemotherapy in patients with malignant neoplastic disease was employed for this purpose. Six studies in four patients have been conducted to date. Diagnoses included: carcinoma of the breast, 65 year old female, thrombophlebitis of the ilio-femoral veins and inferior vena cava thrombosis; carcinoma of the tonsil, 49 year old female, pulmonary emboli; carcinoma of the lung, 51 year old male; carcinoma of the lung, 47 year old female. In one patient, three individual courses of therapy were conducted for 56, 105 and 111 days. In the remainder, intravenous therapy was continuous for 58, 39 and 26 days respectively. The anticoagulant effect was almost continuously optimal and free of unusual bleeding. There have been no adverse effects from the use of heparin in this fashion. Infection did not occur at the site of insertion of the intravenous catheter. The method is recommended for trial in selected patients with recurrent thrombotic disease and for experimental therapy in patients with malignant neoplastic disease where a trial of such adjuvant therapy may be indicated and feasible, on an ambulatory, out-patient basis.

STANDARDIZATION OF HEPARIN THERAPY IN MYOCARDIAL INFARCTION. J. Zahavi and S. Smetana. University of Tel-Aviv School of Medicine, Tel-Aviv, Israel.

Sixty patients with myocardial infarction were randomized for intravenous 10 days heparin therapy, 400 U/ kg/ 24 hrs. In 20 of them, sodium heparin was injected every 6 hours and in another 20, by a continuous infusion preceded by a bolus of 50 U/kg. The remaining 20 patients were used as controls. Blood was drawn pre and 1-4 hours post heparin injection and then twice daily for the following tests: heparin tolerance, activated partial thromboplastin time (APTT), heparin half life and level. During continuous drip, therapeutic anticoagulation (TA), 1.5-2.5 time control APTT levels, was maintained most of the time with daily and interindividual variations. When heparin was injected intermittently (I), TA was achieved only in the first 3-4 hours. In addition, a significant negative correlation between plasma fibrinogen and APTT, as well as a positive one between APTT and plasma heparin level, were found. These results suggest that heparin dose should be individualized during continuous infusion and when it is injected I, frequency of injections should not exceed 4 hours and the daily dose must presumably be higher than 400 U/kg. Plasma fibrinogen seems to be an important factor influencing negatively the heparin activity and should be considered during anticoagulant therapy with heparin.

PLATELET FACTOR 4 (PF<sub>4</sub>) AND PROTAMINE NEUTRALISATION OF HEPARIN IN PLASMA. R. Michalski, D.A. Lane, D. Pepper\*, and V.V. Kakkar. Thrombosis Research Unit, King's College Hospital Medical School, London and \*S.E. Scotland Blood Transfusion Centre, Edinburgh.

The ability of PF<sub>4</sub> and protamine sulphate to neutralise heparin in plasma has been studied using a specific anti-Factor Xa assay and a KCCT assay to measure residual heparin. When heparin is added to plasma in vitro PF<sub>4</sub> and protamine neutralise almost equivalent amounts of heparin on a weight basis, 1.0 unit of heparin being neutralised by approximately 20 µg of PF<sub>4</sub> and 15 µg of protamine. Similar results are obtained using either of the heparin assays. However, following intravenous injection of heparin only about one half of the circulating heparin could be neutralised in vitro by PF<sub>4</sub> or protamine when it was measured by anti-Factor Xa assay. Total neutralisation was obtained with both neutralising agents in the KCCT assay system. These results demonstrate that the choice of assay is important when a protamine titration is used to measure plasma heparin levels, and that PF<sub>4</sub> and protamine are unable to totally neutralise circulating antithrombotic heparin activity.