HEPARIN IN ACUTE MYOCARDIAL ISCHEMIA: DOSE AND SOURCE DEPENDENT EFFECTS. M.J. Saliba, Jr. University of California, San Diego, School of Medicine, La Jolla, California, U.S.A.

Because conventional anticoagulant doses of nonspecified source heparin used in myocardial ischemia had produced controversy, studies with larger doses of heparin from intestine and lung source were initiated. In dogs, control occlusion for 20 minutes of the left anterior coronary artery, with intestinal electrocardiographic recordings, was followed after one hour of reperfusion with a second occlusion plus a 60,000 unit heparin infusion. The ischemic S-T segment elevations on control occlusions (64.5 ± 8.5 mV) were lowered 84% in intestinal heparin added occlusions (10.4 ± 3.0, $p < .00005$). Lung heparin lowered S-T segments a lesser 36% ($p < .008$). The difference between intestinal and lung heparin was significant ($p < .0007$). Myocardial adenosine triphosphate levels at 90 minutes of occlusion were 31% higher in intestinal heparin dogs than in lung ($p < .01$). At 24 hours, myocardial necrosis was 32% less, and myocardial creatine phosphokinase levels were 15% higher, in dogs with 110,000 total units of intestinal heparin added, than in control dogs. Lung heparin has not been tested. Thus, large dose of both heparins significantly modified myocardial ischemia, and intestinal was significantly better than lung. Lung and intestinal heparin are probably functionally and structurally different. Then, in 18 acute myocardial infarction patients, anticoagulant doses of intestinal heparin significantly lowered S-T segments, but did not clearly improve cardiac enzyme levels. Optimal human heparin dose is probably larger than conventional anticoagulant dose. These studies may explain partially the controversy regarding heparin use in myocardial ischemia, and through increased dose of specific source heparin produce new therapy. They may eplain other paradoxical findings with heparin in other studies. More animal studies seem indicated prior to large dose heparin use in humans.

INTERLABORATORY ORAL ANTICOAGULANT QUALITY ASSESSMENT BY THE NETHERLANDS FEDERATION OF THROMBOSIS SERVICES. C.A. van Dijk-Wierda, J. Hermans, E.A.Loeliger and J.Roos. Netherlands Federation of Thrombosis Services, The Hague, The Netherlands.

The 50 laboratories of the Netherlands Federation of Thrombosis Services have participated since 1974 in a voluntary external and internal quality control program. The external program comprises a monthly distribution to the member laboratories of a series of artificially prepared control blood samples, two of which are identical. The overall variation of the coagulation times found were 10% (CV) in 1974 and 8% (CV) in 1975 and 1976. Performance improved rather abruptly at the beginning of 1975, after the application of a tight methodological standardization and improvement by the manufacturer of the thromboplastin preparation (Thrombotest) used by the great majority of the laboratories involved. The main source of variation was found to be random error in the Thrombotest determination, approximating 6%. Interbatch variation of Thrombotest and inter-aliquot variation of control blood samples both do amount to approximately 3%.

AN IN VIVO MODEL FOR THE STUDY OF ANTITHROMBOTIC DRUGS. C.J.L.Strachan, R.J.Hawker, and J. Fejfar. Department of Surgery, Queen Elizabeth Hospital Birmingham, U.K.

A series of experimental animal models have been developed (a) to produce a model for double blind crossover assessment of new and existing antithrombotic drugs, and (b) to investigate the nature of the initiating factor in venous thrombosis. The following table describes results from 4 models in 80 dogs and 8 baboons.

Type	Injury		Control (no electrodes)	
I.	Electrode + stasis cuff	= thrombus	No cuff	= no thrombus
II	Electrode + stasis cuff	= thrombus	Cuff only	= late thrombus
III	Electrode, no stasis cuff	= no thrombus	Cuff only	= thrombus
IV	Jugular electrode	= no thrombus	Femoral cuff	= thrombus

Types I, II, III involved bilateral femoral vein dissection but type IV was unilateral, jugular and femoral and allowed crossover studies. The 2.5 milliamps for 10 minutes was standard but if no current passed in Type IV with jugular electrodes in situ, no thrombus was produced in the femoral vein indicating a third factor is required i.e. circulatory, as in Virchow's triad. Partial thromboplastin time, euglobulin lysis, white blood count, haematocrit, platelet count, fibrinogen and fibrinogen turnover were followed for 7 days and reflected the clinical response. Low dose heparin prevented and an anti-factor XIII inhibited, thrombus formation. A series of anti-platelet drugs had little or no effect on thrombogenesis. We conclude that Types III and IV models reproduce the 3 factors in Virchow's triad with minimal trauma.