Published online: 2019-04-16

FREE COMMUNICATIONS XIX

Thrombosis: Treatment of Arterial and Venous Disease.

HEPARIN TOLERANCE DETERMINATING FACTORS EVALUATED BY THE HEPARIN THROMBIN CLOTTING TIME. P. Andersen and H.C. Godal. Haematological Research Laboratory, Department IX, Ullevål Hospital University Clinic, Oslo, Norway.

The anticoagulant effect of heparin in test systems composed of purified antithrombin III, fibrinogen and thrombin, proved by far more sensitive to heparin than was whole plasma, indicating that components of platelet poor plasma (besides antithrombin III and fibrinogen) strongly interfere with the anticoagulant effect of heparin. Among the so-called acute phase proteins, orosomucoid and α_1 -antitrypsin were especially active, probably acting as competitive inhibitors of the heparin-antithrombin III formation. Thus, inhibition of heparin by orosomucoid (final concentration 1 mg/ml) was stronger than the heparin-neutralizing effect of crude platelet factor 4 (PF-4) obtained by freezing and thawing of a platelet suspension containing 200×10^3 platelets/ul. Since orosomucoid and α_1 -antitrypsin are both markedly increased in various clinical situations associated with increased frequency of thrombosis, these glucoproteins may prove important contributors to the increased heparin tolerance observed under these circumstances.

METHODOLOGICAL PROBLEMS RELATING TO THE ELIGIBILITY OF CLINICAL OUTCOMES IN CARDIOVASCULAR INTERVENTION STUDIES. M. Gent. McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada.

Many patients in long-term cardiovascular clinical trials fail to complete the study according to the original protocol and this raises questions of what should be done with the results from such patients. Examples of protocol failures would include (1) patients dropping out of the trial for reasons which may, or may not, be related to their treatment or clinical condition, (2) interruptions in treatment which may be patient- or physician-initiated, and (3) patients entered into the study who were subsequently found not to meet entry criteria. In practice, the decision to include an observed clinical outcome in the final analysis has usually depended on whether the outcome occurred before or subsequent to the patient leaving the study, and on whether or not the patient was on the allocated treatment at the time of the event.

However, this approach is too simplistic and it can be shown that this will often lead to considerable bias in the evaluation of the treatment under study. The need for more specific decision procedures will be illustrated by examples in previously published trials of anticoagulants, platelet suppressive drugs, and thrombolytic agents.

Recommendations for dealing with these problems will be made which would be pertinent to the several major intervention studies in myocardial infarction and stroke which are currently in progress.