PLATELET KINETICS IN HEALTH AND DISEASE

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1. Radiochromate-labelled platelet concentrates were prepared following collection of blood into a solution of acid-citrate dextrose anticoagulant (ACD 'S') which resulted in a final whole blood pH of 6.5 - a more acidic form of anticoagulant than that customarily employed. Results were compared with those previously obtained in this laboratory using ACD 'A' and EDTA as anticoagulants for collection of blood. Platelet yield was greatest when EDTA was used but after transfusion relatively few platelets survived in circulation as viable units. In terms of overall efficiency both solutions of ACD were superior to EDTA. Platelet lifespan in circulation was unaffected by the anticoagulant used for the collection of blood. External scintillation counting showed that in man the majority of effete platelets is normally removed by the liver and that the spleen plays a secondary, but not unimportant role in this process.

2. It is an attractive theory that platelet encrustation is a contributing factor in the processes resulting in the development of atheroma. However, using chromium^{51}-labelled platelets, results of investigations carried out on 34 subjects with atheroma do not support the view that platelet lifespan is reduced and platelet turnover increased in these subjects. Furthermore, platelet survival was not prolonged

by the administration of the anticoagulant phenindione. Although platelet deposition on vascular endothelium may be a contributing factor in the pathogenesis of this disorder it is concluded that the techniques at present available are not sensitive enough to detect this phenomenon.

3. Studies using the Chandler apparatus have shown that the blood of patients suffering from myocardial infarction shows an increased tendency to abnormal spontaneous platelet aggregation and thrombosis in vitro. Thrombus size tended to be less in patients treated with anticoagulants and decreased with the passage of time after myocardial infarction. There was a direct relation between thrombus size and the plasma fibrinogen level in both healthy controls and in patients studied after myocardial infarction. There was no such relation between serum cholesterol and thrombus size. The incidence of abnormal platelet aggregation tended to increase with age in healthy controls. In patients with myocardial infarction, treatment with anticoagulants caused no significant decrease in the incidence of abnormal platelet aggregation. No conclusions can be drawn as to the significance of these findings. They may be the result of infarction rather than reflect a state existing prior to the clinical event. There is some evidence to suggest that there

is an increase in abnormal platelet behaviour with age and myocardial infarction may be the result of an exaggeration of this trend in some subjects. It is likely that the frequency for thrombosis to occur in subjects following such episodes may be in part related to this increased thrombotic tendency.

4. It has been demonstrated that reduced platelet survival indicative of increased random loss of a proportion of platelets from circulation occurs in some subjects following the insertion of Starr-Edwards prostheses for correction of valvular disease of the heart. This abnormality in platelet survival is directly related to the time after operation and occurs in those in whom the prosthesis has been in place the longest. Studies in subjects with uncorrected valvular disease were completely normal.

5. The results of studies in the Chandler tube in patients following the insertion of Starr-Edwards prostheses show that there is a significant increase in the frequency of abnormal spontaneous platelet aggregation in these subjects compared with normal control subjects. Furthermore, the frequency of abnormal spontaneous platelet aggregation was found to be greater in subjects with reduced platelet survival than in

subjects whose survival curve showed a normal contour. These findings in patients with Starr-Edwards prostheses had not previously been described by other workers.

6. Platelet survival in circulation was found to be reduced in some patients studied in the postoperative period and normal in others. Of the three subjects with reduced platelet survival two had suffered myocardial infarction some years previously, a factor which may be taken as additional evidence of an abnormal thrombotic tendency in these individuals.

7. Platelet survival studies in patients with thrombocytopenia showed a marked reduction of platelet lifespan in all cases studied. Surface counting data revealed that a more reliable prediction of the outcome of splenectomy may be made if there is an increased splenic uptake of labelled platelets. However, results of uptake studies should not be the only criterion to suggest operative intervention as favourable results may be obtained in subjects who show no increase in splenic localisation of radioactivity. Numbers in this series, however, are small - a limiting factor in the overall interpretation of data.

8. Studies on platelet sequestration using the sulphydryl inhibitor N-ethyl maleimide (NEM) have demonstrated that the site of sequestration of platelets is determined by the degree of damage they have sustained. Results are analogous to those found when red cells have been damaged by chemical and physical agencies and are comparable with the results of studies in which platelets have been damaged by either heat or immunological means. Minor damage causes platelets to be removed, principally by the spleen, and more severe damage results in platelet removal, mainly by the liver. These findings may be related to those in a number of disease states associated with increased platelet removal from circulation.