SIMULTANEOUS ^{51}Cr AND ^{14}C -SEROTONIN PLATELET SURVIVAL MEASUREMENTS. S. Hanson and L.A. Harker, University of Washington School of Medicine, Seattle, Washington, U.S.A.

In vivo platelet reactions resulting in platelet utilization or release of constituents without platelet destruction have been studied in baboons by measuring isotopic disappearance of doubly labeled platelets using ^{51}Cr as the cytoplasmic label to detect destruction and ^{14}C -serotonin as a granular label to detect release. In 25 normal animals, the ^{14}C -serotonin platelet survival (^{14}C -SPS) was 6.0 days $\pm$ 0.2 compared with a ^{51}Cr platelet survival (^{51}Cr -PS) of 5.5 days $\pm$ 0.2, suggesting about 10% reutilization of the ^{14}C label. Platelet labeling in vivo with ^{14}C -serotonin showed that only 13% - 2% of the injected activity became platelet bound; the remainder was cleared from the plasma within three hours. The platelets labeled in vivo survived normally (6.0 days $\pm$ 0.4). These results indicate that in vivo reutilization of serotonin is not extensive and that the process of labeling platelets with ^{51}Cr in vitro does not appreciably shorten their survival in vivo. In other studies, animals with doubly labeled platelets received intravenous infusions of thrombin, ionophore R02-2985, arachidonic acid, ADP, collagen, plasmin, streptokinase, endotoxin, bovine factor VIII, and air bubbles. Thrombin or collagen infusions produced rapid, equivalent disappearance of both labels that correlated closely with decreases in platelet counts indicating that platelet destruction is not associated with reuptake of released ^{14}C -serotonin by ambient circulating platelets. In contrast the infusions of R02-2985, plasmin or some studies with endotoxin induced selective disappearance of ^{14}C -serotonin while ^{51}Cr -PS was normal, reflecting platelet release in vivo without platelet destruction. With ADP, arachidonic acid, streptokinase and air bubbles platelets disappeared from the circulation transiently without loss of either label indicating transient platelet sequestration. We conclude that doubly labeled platelet survival studies are useful in characterizing platelet reactions and their pharmacologic alterations in vivo.

THE EFFECT OF A COMBINATION OF SULFINPYRAZONE (SUL) & ASPIRIN (ASA) ON PLATELET SURVIVAL & THROMBUS SIZE IN AN EXPERIMENTAL THROMBOSIS MODEL. A.R.Giles, M.R.Buchanan and J.Hirsh. Dept. Pathology, McMaster University, Hamilton, Ontario, Canada.

Platelet survival (PS) may be decreased in some thromboembolic disorders. Treatment of patients with drugs that suppress platelet function may or may not be associated with normalization of PS. It is uncertain, however, whether a lack of influence on PS necessarily indicates lack of an antithrombotic effect. We have examined this problem in an arterial thrombosis model in rabbits. A non-occlusive mural thrombus was produced in the aortic arch and PS studied using ^{51}Cr -labeled homologous platelets. Thrombus size was assessed by measuring ^{51}Cr accretion. Three groups of 15 animals were studied as follows: group A - thrombus induced 30 min prior to start of PS, group B - as for group A but animals treated with SUL (25 mg/Kg) and ASA (25 mg/Kg) prior to thrombus induction and 12 hrs thereafter and group C - sham operated controls. Animals in group B showed a 45% reduction in thrombus size when compared with group A ($p < 0.05$). The platelet $\text{TI}/2$ in groups A, B, and C were 25.7, 25.6, and 33.8 hrs respectively. The difference between groups A and C and between groups B and C was significant ($p < 0.01$). Thus, treatment with SUL and ASA reduced thrombus size but did not modify the change in PS associated with thrombus induction. Re-examination of PS data by 7 different analytical methods established that all were equally sensitive in discriminating thrombosis but all failed to detect a drug effect. It is concluded that failure to modify platelet survival does not necessarily exclude an antithrombotic effect and that this apparent lack of sensitivity does not relate to the method of data analysis used.

PLATELET SURVIVAL AND PLATELET SEROTONIN RELEASE IN VIVO IN VARIOUS ANIMAL MODELS. D.I. Cargill and R.J. Ryan. Research Dept., CIBA-GEIGY, Ardsley, N.Y. U.S.A.

Decreased platelet survival is a clinically accepted indicator of increased platelet consumption, and in some cases may reveal "hyperthrombotic" states. Decreased platelet survival has also been demonstrated in the homocystinuric baboon and the hypercholesterolemic rhesus monkey (Ross and Harker). Treatment with antiplatelet drugs does increase platelet survival in patients as well as in experimental animals.

We have found platelet survival to be decreased in both uricemic and hypercholesterolemic guinea pigs. However, platelet survival in the atherosclerotic rabbit and the streptozotocin diabetic rat was normal. When atherosclerotic rabbits or diabetic rats were given platelets labeled with ^{51}Cr and ^{14}C -serotonin, they were found, five days after receiving the platelets, to have higher $^{51}\text{Cr}/^{14}\text{C}$ ratios than did their corresponding controls. This suggests a higher serotonin release from circulating platelets in these models.

The $^{51}\text{Cr}/^{14}\text{C}$ ratio in platelets may be a more sensitive measure of platelet activity in vivo than is platelet survival alone.