

LOCALISATION OF THROMBOTIC PROCESSES WITH IN-111 LABELED THROMBOCYTES. M.R.Hardeman, J.Vreeken & J.B.van der Schoot. Departments of Internal and Nuclear Medicine, Wilhelmina Gasthuis, University of Amsterdam, the Netherlands.

Human platelets were labeled with In-111 oxinate in order to establish their *in vivo* kinetics as well as their possible use for the detection of the early events in various thrombotic, i.e. platelet consuming, processes. Autologous platelets were incubated at room temperature with 250-500 uCi In-111 oxinate; the labeling-efficiency was 75-90 %. *In vivo* survival of In-111 labeled platelets was found to be equal to that of Cr-51 labeled platelets: 8-10 days, while the *in vivo* recovery was 60-70 % (in the presence of a spleen) indicating that nearly all of the injected platelets were viable. Injected, not platelet-bound radio-activity disappeared rapidly from the plasma during the first day after injection; on the following days, plasma as well as urine activities were negligible. Thrombotic processes could be visualized in renal artery thrombosis, DVT, atherosclerotic and dissecting aneurysms, rejecting kidney-transplants and shunt-thrombosis. Most results correlated well with those of other techniques, i.e. angiography and clinical, histological and biochemical parameters. A false negative result, however, was found in a patient with an a.carotis thrombus, existing for longer time. Pathological accumulation of radio-activity seen at scintigraphy could always be correlated with an increased rate of disappearance of circulating radio-active platelets. Thus, using In-111 oxinate, platelets can be labeled with a high efficiency, a high *in vivo* recovery and maintenance of normal *in vivo* kinetics. These platelets are suitable for scintigraphic detection of thrombotic processes. The method seems to be limited to new, growing thrombi.

ALTERATIONS OF PLATELET MORPHOLOGY IN HUMAN ISCHEMIC HEART DISEASE AND IN AN ACUTE THROMBOSIS RABBIT MODEL. M.M. Frojmovic, J.G. Milton, W. Yung, Physiology, McGill University, Montreal, Canada, J. Burgess, C. Rose, Cardiology, Montreal General Hospital, Canada, M. Buchanan and J. Hirsh, Pathology, McMaster University, Hamilton, Canada.

Methods are needed for screening patients at risk for thrombo-embolic diseases. We present an assessment of the relative usefulness of platelet shape distribution and mean volume measurements for probing abnormalities in ischemic heart disease (IHD). Platelet morphology in whole blood (WB) from the antecubital vein and/or abdominal aorta, and citrated platelet-rich plasma (PRP), which have been fixed by 4 volumes 0.8% glutaraldehyde-Tyroses, pH 7.4, is compared for 17 healthy and 13 IHD donors: (I) 6 post-myocardial infarction (2-16 days), 1 acute coronary insufficiency (7 days) and (II) 6 angiographically characterized coronary artery disease. Platelets were examined under phase contrast microscopy classified as discocytes (D), disco-echinocytes (DE) and spherocytocytes (SE). WB of IHD donors has fewer D than WB from healthy donors (27(5-57)% vs 71 (65-80%); *mean (range)) and more SE (24(6-65)% vs 1(0-8) %). Although platelet morphology in PRP from healthy donors was similar to that of WB, PRP from TED donors contained fewer SE (3(0-11)%) and D (52(20-87)%) than WB. Platelet mean volumes, measured by microscopy, were increased by < 7% for IHD donors. Rabbits with induced acute thrombosis (indwelling catheter model) studied at 2 hrs, 24 hrs, 1 day and 5 days showed no alterations in platelet morphology distribution evaluated in fixed whole blood, from either normal (4) or sham-operated (4) rabbits. The distributions in morphologies were essentially identical to those seen for normal human donors. These results indicate that changes in platelet morphology in IHD (i) are best measured in whole blood, (ii) probably do not reflect acute thrombo-embolic events and, (iii) are much larger than the changes in platelet mean volume, suggesting that morphology is the more sensitive probe for abnormalities in IHD.

PLATELET AGGREGABILITY IN HEALTHY AND ISCHEMIC HEART DISEASE (IHD) DONORS: A UNIQUE AGGREGOMETRY PARAMETER PRACTICALLY INDEPENDENT OF PLATELET COUNT OR DRUGS SUCH AS ACETYSALICYLIC ACID. M.M. Frojmovic, J. Milton, W. Yung, J. Brandwejn and T. Wong, Physiology, McGill University, Montreal, Canada, and J. Burgess, C. Rose, Cardiology, Montreal General Hospital, Canada.

We report on a uniquely useful parameter of platelet aggregation derived from aggregometry tracings for adenosine diphosphate (ADP)-induced aggregation in citrated platelet-rich plasma, pH 7.4, 37°C., for 13 healthy and 13 IHD donors (6 post-myocardial infarct (2-16 days), and 1 acute coronary insufficiency (7 days) (group I) and 6 angiographically characterized coronary artery disease (group II)). A double reciprocal (L-B) plot of [ADP] (1-100 μ M) against the velocity of light transmission increase associated with platelet aggregation obtained for the initial velocity (V) or for the maximal velocity (V*) was usually linear only at high ADP ($\geq 5 \mu$ M), from which a Vmax value could be extrapolated. We then derived [ADP]^{1/2}:- [ADP] yielding V=1/2 Vmax, from a Hill-type plot ((log (V/Vmax-V) vs log [ADP])). Only [ADP]^{1/2} values derived from V* allowed a highly significant (P < 0.001) distinction to be made between healthy and IHD donors (2.4 \pm 0.4 μ M (n=13) vs 1.3 \pm 0.3 μ M (n=7, group I; n=4/6, group II)). Other parameters such as extent of primary or maximal aggregation did not distinguish IHD from normal donors, and could not be normalized for varying platelet counts. 2/6 donors in group II (coronary artery occlusions) and 4 donors with normal angiographs had "normal" [ADP]^{1/2} = 2.5 \pm 0.4 μ M. One recall of a 7 day post-myocardial infarct donor after 7 weeks still exhibited "abnormal" [ADP]^{1/2} = 1.0 vs 1.4 μ M. This new parameter appears independent of normal hematocrit-citrate/platelet count variations, or of drug type including aspirin, and promises to be useful for classification of diseases according to platelet aggregability.

ALTERATION IN PLATELET FACTOR 3 ACTIVITY IN PLASMA IN ASSOCIATION WITH CIGARETTE SMOKING. F.C. Chao, D.M. Kenney, J.L. Tullis, C.A. Alper and J.E. Silbert. Center for Blood Research, Boston, MA 02115 and the Veterans Administration Outpatient Clinic, Boston, MA 02108.

Changes in blood coagulation and platelet functions *in vivo* in healthy smoking and non-smoking individuals of different age groups were studied. Blood samples were obtained on four different occasions (6 months apart during 1978-1980) from each of the 21 smokers and 42 non-smokers (age range 35-79), and analyzed. Statistically significant changes (p < 0.03) associated with cigarette smoking are: 1) increases in platelet count and fibrinogen in plasma; 2) elevation in a platelet procoagulant, platelet factor-3 (PF-3) activity in platelet-poor plasma (PPP); 3) increases in serum levels of α_1 -antitrypsin, orosomucoid, haptoglobin and properdin factor B; and 4) shortening of the lag period of collagen-induced platelet aggregation. Filtration through Millipore filters removed membrane vesicles which are enriched with PF-3 activity from the PPP. The difference in PF-3 activity in filtered plasma between the smoking and non-smoking groups were no longer statistically significant. The results are consistent with the interpretation that enhanced PF-3 activity in plasma occurs in association with cigarette smoking and results from the liberation into plasma of platelet membranes enriched in PF-3 activity.