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THE COMBINATION OF INCREASED FIBRINOLYTIC ACTIVITY AND REDUCED PLATELET NUMBER AND FUNCTION CONTRIBUTES TO POSTOPERATIVE BLEEDING IN CARDIOPULMONARY BYPASS PATIENTS. D.S. Holloway, L. Summaria, J. Sandesara, J.P. Vagher, J.C. Alexander, and J.A. Caprini. Evanston Hospital, Evanston, IL, and Northwestern University Medical School, Chicago, IL, USA.

Both increased fibrinolysis and reduced platelet number and function have been reported postoperatively in cardiopulmonary (CP) bypass patients, but correlations with postoperative bleeding often have not been found. We simultaneously evaluated platelet and fibrinolytic parameters to assess their individual and combined contributions to postoperative blood loss. Plasminogen (plg) concentration, alpha-2-antiplasmin (AP) concentration, free protease activity (fPA), platelet count, and platelet aggregability were measured in nine patients undergoing cardiopulmonary bypass surgery. Hematocrit was also measured in order to determine the degree of blood dilution during CP bypass. Chest tube drainage was used as the measure of postoperative blood loss. Plg and AP concentrations decreased with hemodilution during bypass. fPA did not decrease with dilution but remained at pre-bypass levels. Platelet count decreased during bypass but aggregability to ADP and arachidonic acid (AA) did not change significantly. Following protamine administration there was a large increase (83%) in fPA, the platelet count showed a further drop (from 61% to 50% of pre-bypass levels), and platelet aggregability decreased significantly (from 95% to 34% of pre-bypass levels). Early chest tube drainage (1st 4 hrs postoperatively) correlated positively ($p[0.05$) with the combination of increase in free protease activity and decrease in platelet count. Total chest tube drainage correlated positively ($p[0.05$) with the combination of increase in free protease activity and decrease in platelet aggregability to ADP. None of the measured parameters individually showed significant correlation with chest tube drainage. In this patient sampling, however, the combination of changes in fibrinolytic activity and changes in platelet function did correlate significantly with chest tube drainage. These data indicate that the increased fibrinolytic activity and the decreased platelet number and function have a synergistic effect on postoperative blood loss in CP bypass patients.

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THROMBOXANE AND PROSTACYCLIN GENERATION IN CHILDREN UNDERGOING CARDIAC BYPASS SURGERY. M. McLaren (1), C. Shiach (2), B. Gibson (2), J. Pollock (2), G.D.O. Lowe (1) and C.D. Forbes (1). University Department of Medicine, Royal Infirmary, Glasgow, Scotland, U.K. (1) and Royal Hospital for Sick Children, Yorkhill, Glasgow, Scotland, U.K. (2).

Children undergoing surgery involving cardiac bypass frequently have problems with post-operative bleeding, more so than children having the same length of surgery but without cardiac bypass. Although the platelet count is known to fall during bypass surgery it also falls in other groups of surgical patients in whom post-operative bleeding is not a problem. The passage of blood through the bypass machine may cause damage to the platelets which may therefore be functionally abnormal after surgery and thus promote bleeding. We studied eight patients undergoing cardiac bypass surgery aged between 4 and 14 years. All had similar operating conditions and non-pulsatile, membrane oxygenatory bypass. Each patient was sampled immediately prior to surgery after being anaesthetised and 30 minutes and 24 hours post-operatively. Platelet count, antithrombin III and protein C levels fell significantly consistent with activation of platelets and coagulation. Plasma levels of beta-thromboglobulin, thromboxane B_2 and prostacyclin metabolites (all measured by radioimmunoassay) were elevated in most patients 30 minutes after surgery, but had usually returned to normal levels 24 hours later. We conclude that cardiac bypass in children causes transient activation of platelets and the thromboxane/prostacyclin pathways: the relationship to bleeding requires further study.

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FRAGMIN VS HEPARIN AT RECYCLING OF HUMAN BLOOD IN HEART-LUNG MACHINE (HLM). L. Bagge (1), E. Holmer (3), S.O. Nyström (1), H. Tydén (2) and T. Wahlberg (3). Departments of Thoracic Surgery (1) and Anaesthesiology (2), University Hospital, Uppsala, Sweden and Kabi Vitrum AB (3), Stockholm, Sweden.

During cardio-pulmonary bypass (CPB), Heparin inhibits FXa (FXaI), thrombin and platelet activity and is also reported to induce fibrinolysis. Fragmin (Frag) has 25% thrombin inhibition capacity as related to that of Heparin (Hep). An in vitro study was performed to compare Frag with Hep by circulating blood in a pure artificial system. In 20 experiments, 400 ml of freshly collected blood with Frag or Hep were recycled for 2 h. HLM was primed with 400 ml of Ringeracetate. Blood sampling: donor, blood pack and every 20 min from the oxygenator. Variables/assay/:ACT/Hemochron/; APTT, TT and NT/Nyegaard/;FXaI, FVIII and ATIII (ATA)/amydolytic/; ATIII (ATAg) and vWF/IEP/;Plasminogen (Plg) and albumine/immunodiffusion/;FDP/Wellcome/;Platelet function/Adeplat S/;Fibrinogen (Fbg)/clottable/;Hemolysis (HL)/photometric/;β-Thromboglobulin (βTG)/RTA/;EVF, Hb, platelet count (PC) and Leucocyte count (LC)/conventional). Corrections for hemo-/plasma dilutions were calculated. Dosages (n): Frag: 750 (1), 1500 (3), 2100 (4), 2500 (4) FXaI-U (U); Hep: 1000 (3), 1500 (6) IU clinical level. Clotting only occurred at Frag 750 (1) and 1500 (2) U, when ACT, APTT, FVIII, Fbg and ATA were significantly lowered. Generally, PC fell 75% during the recycling, while PF was constant ~20% and βTG increased. Neither presence of FDP nor Plg consumption were detected. FXaI, ACT, APTT, TT and NT were dose dependent for both drugs. ATA was directly dose-related to Frag but inversely to Hep. LC decreased with the Frag-dose but inversely to that of Hep. HL increased generally. Several proteins increased (clotting excl): Fbg 30%, ATAg 25%, ATA 45% and vWF 60%. Conclusions. Prevention of clotting required about the double dosage of Frag. Shortened ACT and APTT predicted clotting while the levels of FXaI, TT and NT did not. Thus, an effective thrombin inhibition is needed under this conditions. Consumptions of FVIII, Fbg and ATA but no further drop in PC at clotting, indicate weak platelet aggregation involvement. Absence of fibrinolytic signs supports that the fibrinolysis seen at CPB, is not a genuine effect of Hep (or Frag). Increases in some proteins may be caused by cytolysis. The rise in vWF is probably due to release from platelet surfaces.

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INDICATORS OF INCREASED RISK FOR EXCESSIVE BLEEDING AFTER CARDIOPULMONARY BYPASS SURGERY. W.A. Rock (1), C.W. Pearce (2) R.F. Weichert (2), W. Johnson (1), LSU Medical Center, New Orleans, LA, USA (1), Touro Infirmary, New Orleans, LA, USA (2)

A prospective study of 565 consecutive cases of cardiopulmonary (CP) bypass surgery (in 26 months) was made to identify indicators for excessive postoperative bleeding ("bleeders" defined as greater than 400 ml from 1st to 3rd hours in recovery). Patients were studied before, during,and after surgery, with data recorded on a computerized format for analysis (Table). Preoperative indicators of increased postop bleeding risk included surgical complexity; complex-valve or coronary artery bypass graft (CABG) ($X^2, P<.01$), preop use of any antibiotic ($P<.001$), nefedipine ($P<.05$), and use of aortic balloon pump ($P<<.001$). Previous myocardial infarction, diabetes mellitus, hypertension, obesity, smoking history, use of verapamil, digoxin, antihypertensive drugs, preop hematocrit, platelet count, and fibrinogen did not predict bleeders.

Percent of Bleeders By Operation Excluding Reoperation:

CABG (N=440)	Valve (N=26)	Valve +CABG (N=32)	Total (N=498)
8%(33)	15%(4)	22%(7)	44

Percent of Bleeders Including Reoperation:

	Bleeder (N=65)	Non-bleeder (N=500)	Total (N=565)
One op	8%(44)	86%(487)	531
Reop	4%(21)	2%(13)	34

Intraoperative indicators for increased risk included poor tissue strength ($P<.01$) and blood added to pump ($P<.001$). Intraoperative pump run time, cross-clamp time, hematocrit, platelet count, and fibrinogen were not indicators for increased risk for bleeding. Postoperative indicators included bleeding into leg and chest bandages ($P<.005$), chest tube drainage with clots ($P<.001$), platelet count (t-test, $P<.05$); and fibrinogen (t-test, $P<.05$). The postop hematocrit and prolongation of aPTT did not characterize bleeders. This analysis suggests that the intrinsic health of the patient, the strength of the heart, the complexity of the surgery, and the use of certain medications may be better indicators of a risk for bleeding than are factors related only to CP bypass surgery.