Anesthesiology
V 75, No 3A, Sep 1991

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Title: CPB INDUCES INCREASED LEUKOCYTE ADHESION RECEPTORS BUT NOT TNF-α

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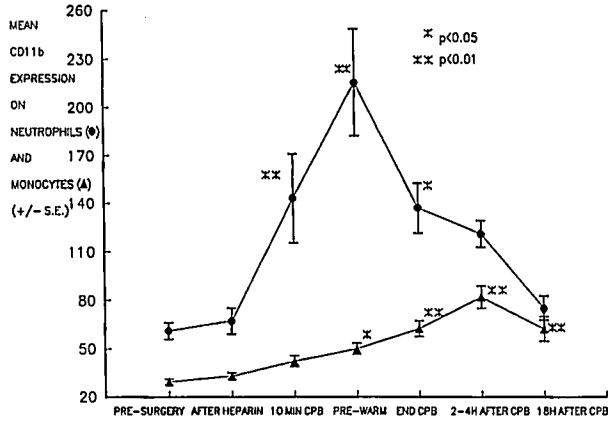
INTRODUCTION: Cardiopulmonary bypass (CPB) activates both platelets and the complement cascade. We hypothesized that CPB also activates monocytes (monos) and neutrophils (PMN), resulting in increased CD11b expression (a complement receptor induced by activation which mediates leukocyte-endothelial binding), and synthesis of the cytokine, tumor necrosis factor (TNF-α).
METHODS: After institutional approval, 28 patients undergoing elective surgery requiring CPB were studied. Whole blood samples were fixed at the times noted below, and using a fluorescent antibody, the density of CD11b on PMN and monos was measured by flow cytometry. In 11 patients, plasma TNF-α was also measured by ELISA pre-surgery, at end, and 6 hours after CPB. Data was analyzed by repeated measurement ANOVA.
RESULTS: CD11b expression on PMN and monos rose significantly during CPB (see Fig). PMN CD11b peaked prior to rewarming, then decreased promptly. Mono CD11b rose more slowly, but remained elevated 18 hours after CPB. However, in contrast to CD11b, plasma TNF-α did not change during or after CPB.
DISCUSSION: Activation of PMN and monos on CPB resulted in increased surface expression of CD11b, which can bind complement and mediate leukocyte-endothelial adhesion. PMN-mediated endothelial binding via CD11b has been implicated in reperfusion injury in animal models of ischemia. We found that maximal expression of CD11b occurred on PMN prior to rewarming, possibly contributing to reperfusion injury in incompletely protected areas of myocardium. The cytokine TNF-α is synthesized by activated PMN and monos and impairs vascular permeability and myocardial function in sepsis. Despite increased expression of CD11b, TNF-α levels did not increase significantly with CPB. We conclude that leukocyte expression of CD11b but not production of TNF-α may contribute to cardiorespiratory pathology found after CPB.



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TITLE: HIGHLY ELEVATED PLASMA HISTAMINASE (DIAMINE OXIDASE) DURING CARDIAC SURGERY

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Histamine released by drugs or cardiopulmonary bypass (CPB) is thought to be catabolized mainly via intracellular methylases (1,2). An alternative enzyme, histaminase, uses O_2 to deaminate substituted ethylamines such as histamine, putrescine and, possibly, drugs such as dopamine and aminocaproate. The potentially deleterious products are reactive aldehydes and H_2O_2. Plasma histaminase is usually low but is increased during pregnancy, in some neoplastic conditions, and upon heparin administration (3,4). Levels were thus examined in coronary revascularization patients receiving heparin (300 U/kg) for CPB.

With institutional approval, blood samples from eight patients were collected at indicated times and anticoagulated, and plasma was stored frozen. Histaminase was assayed by means of tritiated putrescine (1,4-diaminobutane) (4). Assay mixtures consisted of 50 μl plasma and 50 μl of buffer containing 20 μM [2,3-^{3}H]putrescine (350,000 cpm) and 40 mM HEPES-NaOH, pH 7.4, incubated aerobically at 23°.

As expected (3), heparin administration raised enzyme levels (Table). However, further large increases occurred during CPB in all patients examined. The observations pertain to catabolism of histamine and other amines, attempts to measure plasma histamine concentrations, and possible production of peroxide-derived free radicals during CPB.

The study was supported in part by NSF grant DMB 85-05498 awarded to Prof. R.H. Abeles, Brandeis U.

1. Anesthesiology 59, 330 (1983)
2. Anesthesiology 69, 92 (1988)
3. J. Clin. Invest. 52, 1985 (1973)
4. Proc. Natl. Acad. Sci. 74, 883 (1977)

	oxidase activity (pmol/h/ml plasma)
before induction	15 ± 9
after induction	11 ± 7
after heparin	80 ± 51
CPB, early	1,500 ± 510
CPB, late	30,000 ± 1,100
following CPB	31,000 ± 1,100
after protamine	460 ± 190