Prophylaxis for Post-perfusion CABG Bleeding

To the Editor:

DelRossi et al. reported a double-blind, randomized study utilizing epsilon aminocaproic acid (EACA) for prophylaxis against post-perfusion cardiopulmonary bypass bleeding. Several other investigators have also demonstrated the efficacy of EACA for the reduction of post-cardiotomy bypass bleeding. However, several important issues were raised by this article which, we believe, should be addressed before the routine application of EACA for cardiac surgical patients.

Of the group of 350 patients, 61 percent consisted of elective myocardial revascularization procedures. It is implied, though not stated, that only saphenous vein grafts were used. There was no mention of the role of the internal mammary artery as a conduit which could possibly alter the outcome, especially with the use of bilateral internal mammary arteries since more extensive chest wall dissection and hence postoperative bleeding is encountered.

Cardiopulmonary bypass times were not mentioned. The coagulopathy and cellular destruction associated with extended cardiopulmonary bypass perfusion may certainly alter total blood loss postoperatively.

Several other important factors related to post-perfusion hemorrhage are clinically relevant but were not mentioned. These include: 1) the use of aspirin and/or heparin immediately preoperatively; 2) the number of units of platelets, fresh frozen plasma and cryoprecipitate that may have been transfused postoperatively; 3) the use of desmopressin acetate; 4) the utilization of autotransfusion devices intraoperatively and postoperatively. Perhaps the authors could state whether any of these variables were used and whether there was any statistical difference between the control and the EACA-treated group.

In the placebo group there is a 3.3 percent reoperation rate for bleeding. It is not stated whether the patients exhibited any laboratory finding indicative of a hyperfibrinolytic state since no obvious bleeding site was identified at the time of re-exploration.

Finally, the study concludes that EACA should be utilized to decrease the total blood loss and the number of blood transfusions in routine elective cardiac operations. We think the ultimate test of EACA efficacy to reduce post-perfusion bleeding would probably be in patients with myocardial failure requiring the use of intraaortic balloon, emergency operations, reoperative myocardial revascularization, and reoperative valve replacements. We believe that EACA should not be utilized routinely but only in selected patients at higher risk for post-perfusion bleeding. In that regard, we are curious if the authors currently routinely treat all of their patients undergoing elective, low-risk cardiac operations requiring cardiopulmonary bypass with EACA, or if it is utilized only in selected circumstances, as we have indicated above. We would certainly appreciate hearing from the authors on this very controversial paper.

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REFERENCES
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To the Editor:

We appreciate the interest of Drs. Cohn and Jones in our article. Our results indicated that prophylactic use of EACA may reduce the blood loss and transfusion requirements after operations using cardiopulmonary bypass (CPB), presuming that hyperfibrinolysis is one of the most important, although not unique, factors of post bypass bleeding. We did not concentrate our discussion on the procedure itself since 75 percent (not 61 percent) of the patients have undergone CABG (alone or combined with valve replacement) and 37 percent have had valvular procedures. To our knowledge, this is the first study where EACA is used prophylactically in a variety of operations necessitating CPB and not only in CABGs. However, we mentioned clearly in the Methods that we included in the study only those patients in whom saphenous vein bypass was used. We did not use EACA in other series when the internal mammary artery would be employed for bypass so we could not comment more. Although not mentioned in the article, the CPB times were similar in both groups and no statistical difference was observed. As specified, we presented only relevant data.

Since acetyl salicylic acid (ASA) mechanism on platelet function is different (it covalently acetylates cyclooxygenase, blocking its activity and subsequent formation of thromboxane A2 from that of EACA which inhibits the plateletolytic activity of plasmin and the conversion of plasminogen to plasmin by plasminogen activator), we feel that the administration of ASA would have no impact on those patients receiving EACA, so there should be no distinction made in this regard. This could also be valid regarding the concomitant and/or preoperative use of sulfipyrazone, diprydiamole, ticlopidine, some penicillins, furosemide, and other drugs that may induce platelet dysfunction.

The purpose of the study, as stated, was to compare EACA vs placebo and not against other pharmacologic manipulations (desmopressin, aprotinin, etc) which have been shown to conserve blood loss post-CPB. However, their mechanism of action is not established with certainty and there is only limited experience with these drugs. We certainly agree that a well-controlled, randomized study comparing all these agents would be of value.

In both groups, the contents of the oxygenator was returned to each patient at the end of the procedure as centrifuged blood. As stated, "blood transfusion" refers to packed red blood cells. Six patients (3.3 percent) in the control group required reoperation for diffuse bleeding. All of them have exhibited different degrees of hyperfibrinolysis manifested as consumptive coagulopathy with thrombocytopenia, hypofibrinogenemia, and increased fibrinogen split products in the plasma.

We do not advocate the prophylactic use of EACA as the only definitive treatment for post-CPB bleeding and we agree that certain subgroups of patients, particularly those who are prone to bleed more, would benefit most from this therapy. However, we subscribe to the concept that even in low risk elective operations using CPB, efforts should be directed toward decreasing blood loss. In our practice, we use EACA prophylactically in all cases with predetermined reasons for increased bleeding, and in approximately 70 percent of the elective cases.
Bronchoalveolar Lavage in Sarcoidosis and HIV Infection

To the Editor:

We read with great interest the case presented by Coots and Lazarus concerning a young black man who was found to be HIV positive on routine military screening and developed bilateral hilar lymphadenopathy compared to a chest film taken two years previously. Gallium uptake in the hilar lymph nodes performed one year later on reevaluation led to a diagnostic thoracotomy, with noncaseating granuloma found in the lung and lymph node biopsy. This case raises clinical questions about discerning of sarcoidosis from advanced HIV infection. We have diagnosed a similar case and wish to report the utility of bronchoalveolar lavage and flow cytometry in patients with both these diseases.

A 37-year-old white man was referred for evaluation of positive HIV serology and sarcoidosis. Medical history revealed a diagnosis of stage I sarcoidosis made in 1977 by mediastinal lymph node biopsy, high risk behavior for HIV infection, and a 30 pack-year smoking history. The patient was asymptomatic at the time of initial presentation and had received no therapy. A follow-up chest roentgenogram (CXR) in 1985 showed bilateral hilar and right paratracheal lymphadenopathy without parenchymal disease. HIV-positive serology was detected on routine military screening in June, 1987. The patient’s physical examination was normal except for bilateral axillary lymphadenopathy. Laboratory evaluation revealed cutaneous anergy and a stable CRX film. Pulmonary function tests (PFTs) performed in June, 1987 revealed a normal forced vital capacity of 4.62 L (89 percent of predicted), a one-second forced expiratory volume of 3.89 L (97 percent of predicted), and a diffusion capacity for carbon monoxide 90 percent of predicted. The patient presented in February, 1988 with increasing dyspnea on exertion and fatigue. Physical examination, PFT, and CXR (Fig 1) film were unchanged. He was referred for evaluation of advanced HIV infection progression of sarcoidosis. Laboratory evaluation revealed a peripheral white blood cell count of 3.8 x 10^9/L (total lymphocyte count 1,100/L mm), and a CD4 lymphocyte count of 120/µL with a CD4/CD8 ratio of 49 percent. Bronchoscopy with bronchoalveolar (BAL) was performed. BAL fluid showed 28 percent lymphocytes with a CD4/CD8 ratio of 34 percent. Special stains and cultures for pathogens were negative. The patient was not treated and received only close follow-up. A repeat bronchoscopy eighteen months later with BAL showed 32 percent lymphocytes with a CD4/CD8 ratio of 28 percent. The patient has remained free of symptoms to date.

Clinical features of this case are typical for both advanced HIV infection and sarcoidosis. Advanced HIV infection is suggested with a reversed CD4/CD8 ratio in both the lung and peripheral circulation. Bronchoalveolar lavage has shown utility in the staging and diagnosis of both disease. Flow cytometric analysis of lymphocyte subsets has been helpful in characterizing lymphocytic alveolitis with high CD4/CD8 ratios (ie, sarcoidosis and berylliosis) or low CD4/CD8 (ie, hypersensitivity pneumonitis). The differentiation of sarcoid alveolitis and HIV infection has therapeutic implications concerning the use of corticosteroid therapy and can be made with BAL and flow cytometry.

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To the Editor:

We read with interest the recent report by Coots et al entitled, “Sarcoidosis diagnosed in a patient with known HIV infection” (Chest 1989; 96:201-202) concerning the diagnosis of sarcoidosis in a patient with previously known HIV infection.

A 25-year-old bisexual black man was evaluated with a history of one week of pleuritic chest pain, non-productive cough, chills, and night sweats. Subsequent radiographic examination showed a 30 percent right pneumothorax, and serology for HIV antibody test was positive. The patient subsequently presented with bilateral hilar adenopathy, and the differential diagnosis included the possibility of lymphoma, granulomatous disease, histoplasmosis, tuberculosis, and other inflammatory conditions. On mediastinoscopy, however, the lymph node biopsy showed noncaseating granulomatous lymphadenitis without evidence of opportunistic infection and no evidence of malignancy. All special stains for the lymph nodes for mycobacteria and fungi were negative.

The patient also had evidence of a skin rash with epidermal changes of ichthyosis, and on biopsy this skin lesion revealed numerous non-caseating granulomas in the superficial and deep dermis.

We would like to call attention to this additional case as previously reported in the Virginia Medical Journal (1989; 3:122-24).

We would like to reiterate that a positive HIV antibody titer need not imply the presence of an opportunistic lung infection nor the existence of an immunodeficiency state and that tissue diagnosis should be pursued in patients who present in this setting.

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