the fluid on two occasions was less than 7.20 in the malignant variant of BPM. This low pH may be of diagnostic and prognostic value in separating localized malignant mesotheliomas from the more common benign type of BPM.34

An 85-year-old man was admitted with a four-month history of a dry, non-productive cough associated with exertional dyspnea. Although there was recent weight loss and fatigue, he denied chest pain, hemoptysis, fever, chills or sweats. His past medical history included congestive heart failure, 40 pack-years of smoking cigarettes, and work as a sculptor without asbestos exposure. His only chronic medications were digoxin and dyazide.

Physical examination was significant for tachypnea at 40 bpm, tachycardia at 110/min and marked decrease in breath sounds on the right, with dullness to percussion. There was an S2 gallop. No cyanosis or clubbing was present.

Admission laboratory data was remarkable for a chest roentgenogram (CXR) which demonstrated right pleural effusion with pleural and pericardial calcifications. These were new findings compared to a CXR taken three years earlier. The complete blood count and serum chemistries were normal. A computerized axial tomography of the chest supported the CXR abnormalities. Malignancy was suspected and a right thoracentesis was performed, with 800 ml of serosanguinous fluid removed. The following day, a repeat thoracentesis was performed. Chemistries of the fluid revealed an LDH of 786 IU/ml and 701 IU/ml on respective days. Fluid pH was 7.02 and 7.16, with corresponding blood pH of 7.49 and 7.46, respectively. Three days after admission, the patient continued to have marked shortness of breath requiring mechanical ventilatory assistance. On the fifth hospital day, fatal cardiopulmonary arrest occurred. At autopsy, the pertinent findings were limited to the thoracic cavity. The right pleura, both visceral and parietal, had been replaced by leathery, gray, firm, non-granular tissue which measured up to 15 mm in thickness. The right lung was atelectatic, adherent to the thickened visceral and parietal pleura. The leathery pleural tissue extended by contiguity extension into the pericardial sac, replacing in areas the visceral and parietal pericardium.

Histologic studies revealed the thickened pleura to be the result of a proliferation of benign fibrous tissue with nuclei of equal size. In some areas, the proliferating fibrous tissue was relatively cellular, but there was no evidence of mitotic activity and there was no variance in nuclear size. Broad areas of hyalinization of the proliferating connective tissue was seen. Within the pericardial sac, this proliferating fibrous tissue extended into the superficial myocardium. Stains for bacteria, fungi, and acid-fast bacilli were negative. All cultures at eight weeks were negative for fungi and mycobacterium.

BPM has been recognized to have an aggressive malignant variant which, unlike the benign form, usually proves to be fatal.4 The rarity of effusions in BPM has limited the description of the fluid in the literature to two patients with the benign variant. One had an exudative effusion by LDH and protein criteria,4 and the other an effusion with a pH of 7.5.4 Our patient with the malignant variant of BPM had a pleural fluid pH of less than 7.20 on two occasions. His rapid demise is in keeping with the grave prognosis of histologically-proven malignant effusions with a pH less than 7.30.5 More reports of the characteristics of the fluid are necessary to substantiate our contention that a low pH (<7.30) supports the presence of the malignant variant of BPM, and implies a poor outcome.

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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-cardiomyotomy 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


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 acetylsalicylic 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 proteolytic 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, dipyridamole, 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.

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