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In Reply:—I would like to make three points in respect to the comment made by Professor Kenneth E. Shepherd in his letter.

No doubt that there is more to postoperative metastasis risk than immunosuppression. Among other factors, the physical manipulation of the tumor may release tumor cells into the circulation,[1] and the sudden drop in levels of tumor-derived angiostatic agents may promote the development of existing micrometastases. These additional risk factors may indeed exacerbate the consequences of the suppression of natural killer cells evident in our study,[2] especially given the role of natural killer cells in controlling both the seeding of circulating tumor cells and the development of existing micrometastases.

Nevertheless, our study[2] was concerned with the effects of hypothermia, rather than tumor removal, on natural killer activity and resistance to metastasis. Angiogenesis inhibitors such as angiostatin are not expected to play a role in these respects, and certainly could not be implicated for the enhancement of metastasis seen in our study, as no primary tumor was removed. The study of natural killer cell-mediated resistance to metastasis under this condition is advantageous in discerning their unique role.

In accordance with the suggestion to couple the impact of angiostatic agents and immunosuppression in studying the pathobiology of perioperative metastasis, we have now begun to use surgical removal of spontaneously metastasizing tumors to better simulate the clinical setting, and study the interaction of immunosuppression with other factors that promote metastasis.

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Does Perioperative Antithrombotic Therapy Increase the Likelihood of a Postoperative Coagulopathy After Cardiac Surgery?

To the Editor:—Antithrombotic agents such as low molecular weight heparins and platelet glycoprotein IIb/IIIa inhibitors are increasingly being administered to cardiac surgical patients during the perioperative period. In the September 1999 issue of ANESTHESIOLOGY, Skubas and colleagues report a case of prolonged postoperative bleeding in a cardiac surgical patient treated preoperatively with the low molecular weight heparin, enoxaparin, and the platelet glycoprotein IIb/IIIa inhibitor, tirofiban.[1] Although Factor Xa or platelet function assays were not performed, the authors suggest that the preoperative use of enoxaparin and tirofiban may have contributed to the postoperative coagulopathy in this patient. Whereas perioperative antithrombotic therapy may increase the risk of a postoperative coagulopathy after cardiac surgery, we believe that several comments regarding this particular case are in order.

The half-lives of enoxaparin and tirofiban are 12 and 3 to 6 h, respectively.[2,3] In the case described by Skubas *et al.*, both tirofiban and enoxaparin were discontinued the evening before and on the morning of the operation, respectively. Yet, 30 h postoperatively this 56 kg patient continued to have significant bleeding (450 ml/h from the chest tubes) despite being transfused with packed erythrocytes (9 units), platelets (18 units), and fresh-frozen plasma (4 units). Thus, in the absence of assays for Factor Xa activity or platelet function, one has to wonder whether this patient's persistent coagulopathy was solely attributable to the preoperative use of tirofiban and enoxaparin. Regardless of the cause of this patient's postoperative bleeding, Skubas and colleagues do raise the interesting question as to whether a postoperative coagulopathy may be avoided in cardiac surgical patients treated preoperatively with antithrombotic agents such as tirofiban and enoxaparin. Both tirofiban and enoxaparin (molecular weight 2–8 kDa) are dialyzable molecules.[2,3] Hemofiltration during cardiopulmonary bypass may thus significantly reduce the plasma concentration of these agents. Thus, appropriate discontinuation of antithrombotic therapy in the preoperative period (based on knowledge of the drug half-lives) in association with intraoperative hemofiltration can minimize the likelihood of these agents causing a postoperative coagulopathy after cardiac surgery.

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In Reply:—We agree with Drs. Lewis and Collard that measurement of anti-Xa activity and platelet function would have provided important information. Nevertheless, in the presence of normal ACT, no detectable heparin by heparin concentration assay (Hepcon, Medtronic Blood Management, Parker, CO), no identifiable surgical source, and a borderline platelet count, possible explanations for this patients' excessive and protracted chest tube output that was unresponsive to hemostatic blood product transfusion, include either the persistent anticoagulant properties of low molecular weight heparin i.e., anti-Xa activity, or a platelet function abnormality that may be related to either of these agents, or a possible interaction between low molecular weight heparins and tirofiban. Previous anecdotal reports of increased bleeding when patients had received either low molecular weight heparin preparations[1,2] or platelet inhibitors[3–5] support our findings.

Furthermore, we are uncertain of the potential beneficial effects of hemofiltration, because we have previously shown that hemofiltration (using one specific filter) during cardiopulmonary bypass failed to remove the lower molecular weight fraction of unfractionated heparin (no anti-Xa activity in ultrafiltrate).[6] Factors related to the low molecular weight heparin molecule, such as, its linear shape, electrostatic charge, or binding to antithrombin III may account for these findings. Therefore, we would recommend that in patients receiving either enoxaparin or tirofiban, postponement of elective cardiac surgery should be considered for a period of time well over the five half-lives of either medication. Another alternative would be to switch patients from low molecular weight heparin to unfractionated heparin as soon as an operation is proposed. Further studies are needed to evaluate the efficacy of hemofiltration or plasma exchange filters with respect to removal of these agents.

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Inadvertent Misconnection of the Scavenger Hose: A Cause for Increased Pressure in the Breathing Circuit

To the Editor:—Condensation of water vapor and accumulation of water in the breathing circuit of anesthesia machines may cause an increase in resistance to gas flow and its associated complications. We present a case of steadily increasing pressure in the breathing circuit after drainage of the water that had accumulated in the 19-mm hose that leads from the breathing system adjustable pressure limiting valve (through the absorber pole) to the 19-mm terminal on the scavenger interface. After the drainage of the water, the hose was reconnected by mistake, not to the 19-mm hose terminal from which it had been disconnected, but to the 22-mm adjustable needle valve (ANV) terminal on the closed reservoir scavenger interface of a North American Drager Narkomed 2B machine (Draeger Medical, Telford, PA).

A 33-yr-old man was scheduled for retroperitoneal lymph node dissection under general anesthesia. Five hours after induction of anesthesia, during maintenance with isoflurane 1–2% in a 50:50 nitrous oxide:oxygen mixture with a fresh gas flow of 1 l/min, a gurgling sound was noted during the expiratory phase of ventilation. A survey of the machine revealed the cause to be accumulation of water in the 19-mm hose connecting the ventilator relief valve to the scavenger interface, "hose A" (fig. 1). To drain "hose A," the ventilation was switched from automatic to manual mode; but while the patient was being ventilated manually, similar sounds were heard again, but now were emanating from the 19-mm hose that leads from the breathing system adjustable pressure limiting valve (through the absorber pole) to the 19-mm terminal on the scavenger interface, "hose B" (fig. 1). The water was drained from "hose A" and the ventilation was switched back to automatic mode to drain "hose B." However, during emergence 3 h later, while attempting to restore spontaneous ventilation through manual ventilation of the patient, the end-expiratory pressure continued to increase from 1 cm H_2O to a maximum of 8 cm H_2O in spite of the fact that the adjustable pressure limiting valve was opened completely. As an immediate remedy for this situation and to decrease the risk of barotrauma, the breathing circuit was disconnected from the Y-piece. At this time it become apparent that after drainage of the water, "hose B" had been reconnected by mistake to the 22-mm ANV terminal on the scavenger interface (fig. 2). Such a mistake would not have been possible if the wing nut type of the ANV had been present instead of the screw type.

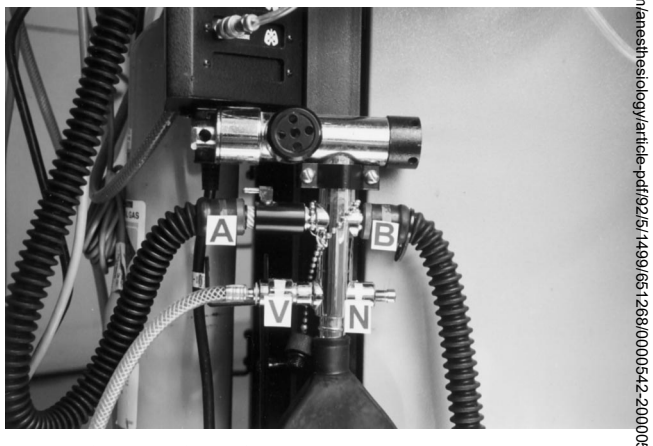

Fig. 1. Photograph of the scavenger interface for suction systems of the Narkomed 2B anesthesia machine with screw type adjustable needle valve (ANV). The 5/8 inches hexagonal lock nut has been removed to demonstrate the screw type ANV. A = hose A, the 19-mm hose connecting the ventilator relief valve to the scavenger interface; B = hose B, the 19-mm hose connecting the breathing system adjustable pressure limiting valve to the 19-mm terminal on the scavenger interface; N = the 22-mm terminal on scavenger interface for the ANV; V = the vacuum hose attached to vacuum source terminal.

Discussion

The "screw" type ANV in Narkomed machine was changed to "wing nut type" by North American Drager in 1982 to allow easier manual adjustment of gas flow through the scavenger system. This modification of ANV eliminates using a screwdriver for regulation of the waste gas exhaust flow. However, using the screw type ANV is still approved by North American Drager for scavenging system.

To increase the safety of anesthesia and to decrease the chance of inadvertent improper connection of scavenger hoses and the resulting complications, we recommend changing all screw type ANV to a wing nut ANV in all Narkomed machines. The wing type ANV has a large