

true that our initial abstracts were sometimes prepared without the assistance of the anesthesiologist(s) involved, most adverse events were self-reported by that practitioner.<sup>13</sup> Also, the involved anesthesiologist(s) were generally present for the discussion and error analysis. Finally, the suggestion by Gauge that this peer review mechanism would be corrupted, if it were applied to patient compensation, is an interesting speculation. Perhaps, Gauge would be more comfortable with a no-fault system of medical liability. The stability with which all adverse outcomes occur suggests that this may also be a viable alternative.<sup>1,8</sup>

Hogan and Lavaruso wish to preserve and modify the present malpractice tort system. Their argument that the tort system should be preserved because it is our "best weapon in the battle for autonomy against managed care" must raise a smile on the faces of those who see similar value in both. As for their remaining arguments, the principles of scientific medicine are part of every medical school curriculum in the United States, and a stronger focus is being made on evidence-based medicine as we struggle to be cost effective. Increasing public exposure to courtroom proceedings, however, demonstrates that the legal system does not suffer from the same imposed cost constraints, nor does it adhere to the same scientific rigors. The lack of a response to the growing body of evidence that the tort system falls short of its goals is a good example. The suggestions for a Specialty Board of Legal Medicine and a Medical Malpractice Bar appear to offer a niche for a new breed of practitioner, but the legal profession should test these remedies with the same scientific principles and cost consciousness that the medical profession applies consistently.

**Robert S. Lagasse, M.D.**

Associate Professor of Clinical  
Anesthesiology  
Montefiore Medical Center and  
Albert Einstein College of Medicine  
Bronx, New York 10461  
BobLagasse@aol.com

Anesthesiology  
2000; 92:1498-9  
© 2000 American Society of Anesthesiologists, Inc.  
Lippincott Williams & Wilkins, Inc.

## Postoperative Metastasis Risk: More Than Immunosuppression

*To the Editor:*—An increase in the rate of development of tumor metastasis, controversially attributed to immune suppression related to various aspects of surgery and anesthesia, has been reported for years and is discussed in an article<sup>1</sup> and commentary<sup>2</sup> that appeared in the September 1999 issue of *ANESTHESIOLOGY*. However, it is important to point out that facilitation of metastasis can occur independent of immune mechanisms. Indeed, metastasis can be stimulated by the removal of an angiogenesis inhibitor (such as angiostatin) along with the primary tumor (as reviewed in Cramer<sup>3</sup>). (Angiostatin is a naturally occurring protein shown in animal experiments to strongly suppress metastasis.<sup>4</sup>)

## References

1. Edbril S, Lagasse R: Relationship between malpractice litigation and human errors. *ANESTHESIOLOGY* 1999; 91:848-55
2. Cheney FW, Posner K, Caplan RA, Ward RJ: Standard of care and anesthesia liability. *JAMA* 1989; 261:1599-603
3. Brennan TA, Sox CM, Burstin HR: Relation between negligent adverse and the outcomes of medical-malpractice litigation. *N Engl J Med* 1996; 335:1963-7
4. Localio A, Lawthers A, Brennan T, Laird N, Hebert L, Petersen L, Newhouse J, Weiler P, Hiatt H: Relation between malpractice claims and adverse events due to negligence. Results of the Harvard Medical Practice Study III. *N Engl J Med* 1991; 325:245-51
5. Brennan TA, Leape LL, Laird NM: Incidence of adverse events and negligence in hospitalized patients: Results of the Harvard Medical Practice Study I. *N Engl J Med* 1991; 324:370-6
6. Leape L, Brennan T, Laird N, Lawthers A, Localio A, Barnes B, Hebert L, Newhouse J, Weiler P, Hiatt H: The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. *N Engl J Med* 1991; 324:377-384
7. Liang B, Cullen D: The legal system and patient safety: Charting a divergent course. *ANESTHESIOLOGY* 1999; 91:609-11
8. Lagasse RS, Steinberg ES, Katz RI, Saubermann AJ: Defining quality of perioperative care by statistical process control of adverse outcomes. *ANESTHESIOLOGY* 1995; 82:1181-8
9. Mish F: Webster's Ninth New Collegiate Dictionary. Springfield, MA, Merriam-Webster, 1984
10. Liang B: Clinical assessment of malpractice case scenarios in an anesthesiology department. *J Clin Anesth* 1999; 11:267-79
11. Levine RD, Sugarman M, Schiller W, Weinshel S, Lehning EJ, Lagasse RS: The effect of group discussion on interrater reliability of structured peer review. *ANESTHESIOLOGY* 1998; 89:507-15
12. Goldman R: The reliability of peer assessments of quality of care. *JAMA* 1992; 267:958-60
13. Katz R, Lagasse R: Factors influencing the reporting of adverse outcomes to a quality management program. *Anesth Analg* 2000; 90:344-56

(Accepted for publication January 10, 2000.)

It seems imperative that continued research into the traditional areas of immune suppression/modulation must be coupled with more recent findings (e.g., angiogenesis inhibitors) if we are to truly understand the pathobiology of perioperative metastasis. Such integrated research seems necessary if we are to devise effective clinical strategies to decrease the incidence of postoperative metastasis.

**Kenneth E. Shepherd, M.D.**

Assistant Professor of Anesthesia  
Harvard Medical School  
Department of Anesthesia and Critical Care

## CORRESPONDENCE

Massachusetts General Hospital  
Boston, Massachusetts 02114  
KShepherd@partners.org

## References

1. Ben-Eliyahu S, Shakhar G, Rosenne E, Levinson Y, Beilin B: Hypothermia in barbiturate-anesthetized rats suppress natural killer cell

Anesthesiology  
2000; 92:1499

© 2000 American Society of Anesthesiologists, Inc.  
Lippincott Williams & Wilkins, Inc.

*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,<sup>1</sup> 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,<sup>2</sup> 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<sup>2</sup> 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

activity and compromises resistance to tumor metastasis. ANESTHESIOLOGY 1999; 91:732–40

2. Klein HG: Immunomodulatory aspects of transfusion: A once and future risk? ANESTHESIOLOGY 1999; 91:861–5

3. Cramer DA: Applied vascular biology: Can angiogenesis inhibitors help control malignant growth? Ann Intern Med 1998; 129:841–3

4. O'Reilly M, Holmgren L, Shing Y, Chen C, Rosenthal RA, et al: Angiostatin: A novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma. Cell 1994; 79:315–28

(Accepted for publication January 12, 2000.)

setting, and study the interaction of immunosuppression with other factors that promote metastasis.

**Shamgar Ben-Eliyahu, Ph.D.**  
Professor  
Department of Psychology  
Tel Aviv University  
Tel Aviv 69978  
Israel  
shamgar@post.tau.ac.il

## References

1. Motomura K, Koyama H, Noguchi S, Inaji H, Kasugai T, Nagumo S: Malignant seeding of the lumpectomy cavity upon breast-conserving surgery. Oncology 1999; 57:121–6

2. Ben-Eliyahu S, Shakhar G, Rosenne E, Levinson Y, Beilin B: Hypothermia in barbiturate-anesthetized rats suppresses natural killer cell activity and compromises resistance to tumor metastasis: A role for adrenergic mechanisms. ANESTHESIOLOGY 1999; 91:732–40

(Accepted for publication January 12, 2000.)

Anesthesiology

2000; 92:1499–1500

© 2000 American Society of Anesthesiologists, Inc.  
Lippincott Williams & Wilkins, Inc.

## 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 in-

hibitor, tirofiban.<sup>1</sup> 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.