

Most anaphylactic reactions are mediated by IgE; reactions mediated by IgG and other immunoglobulins are termed "anaphylactoid" and do not require previous sensitization.<sup>6</sup> This patient possessed no IgE antibodies to protamine. Subclass 4 of IgG may be responsible for anaphylactic reactions as they can bind to mast cells and release histamine; this is not true of other IgG subclasses.<sup>7</sup> The authors do not state whether IgG detected in their patient was of this subclass.

The author's second contention is that IgG antibodies to protamine produce severe reactions to protamine. Most diabetic patients receiving protamine-containing insulin preparations develop IgG antibodies to protamine;<sup>8</sup> yet few diabetic patients with prior exposure to protamine suffer intraoperative anaphylactic reactions to protamine.<sup>9</sup>

Third, this patient had two opportunities to produce antiprotamine antibodies: his vasectomy and his exposure to intravenous protamine during catheterization. The authors do not state why his vasectomy should be the culprit. If the patient indeed had circulating antiprotamine antibodies prior to his catheterization, he apparently escaped anaphylaxis when given 45 mg protamine at catheterization but not when given 50 mg protamine 6 weeks later at operation.

In summary, the case report identifies a patient with a previous vasectomy, antiprotamine IgG antibodies, and two hypotensive episodes after receiving protamine. The association, if any, among these observations remains speculative. Two prospective studies of 8 and 20 vasectomized men did not detect any untoward responses to intraoperative protamine.<sup>9,10</sup> Current evidence, this case report included, remains inadequate to implicate prior vasectomy as a risk factor for severe reactions to protamine.

**Samuel Metz, M.D.**

Associate Professor of Clinical Anesthesiology  
Department of Anesthesiology  
Hahnemann University  
Broad and Vine Streets  
Philadelphia, Pennsylvania 19102-1192

Anesthesiology

79:618-619, 1993

© 1993 American Society of Anesthesiologists, Inc.

J. B. Lippincott Company, Philadelphia

*In Reply:*—Metz is concerned with three issues that he believes we raised in our recent case report.<sup>1</sup>

First, he questions whether we should call the reactions to protamine "anaphylactic" because the patient responded to medical treatment, did not have pulmonary edema or bronchospasm, and had protamine-specific IgG (not IgE) antibodies in his serum. Anaphylaxis is a descriptive term delineating a severe, abrupt, life-threatening reaction manifested by cardiovascular, pulmonary, or cutaneous signs.<sup>2</sup> This patient experienced severe hypotension characterized by a decrease in systolic blood pressure from 95 to 40 mmHg in the operating room, within minutes after receiving protamine and again during cardiac catheterization in the radiology department 2 weeks later. Cardiovascular collapse or severe hypotension often is seen in the absence of skin signs and bronchospasm during anesthesia,<sup>3,4</sup> and many such patients respond promptly to treatment.<sup>5</sup> Furthermore, these reactions may be associated with complement activation

## References

1. Adourian UA, Champagne EL, Hirshman CA, Fuchs E, Adkinson NF: High-titer protamine-specific IgG antibody associated with anaphylaxis: Report of a case and quantitative analysis of antibody in vasectomized men. *ANESTHESIOLOGY* 78:368-372, 1993
2. Lowenstein E, Johnston WE, Lappas DG, D'Ambra MN, Schneider RC, Daggett WM, Akins CW, Philbin DM: Catastrophic pulmonary vasoconstriction associated with protamine reversal of heparin. *ANESTHESIOLOGY* 59:470-473, 1983
3. Morel DR, Zapol WM, Thomas SJ, Kitain EM, Robinson DR, Moss J, Chenoweth DE, Lowenstein E: C5a and thromboxane generation associated with pulmonary vaso- and bronchoconstriction during protamine reversal of heparin. *ANESTHESIOLOGY* 66:597-604, 1987
4. Horrow JC: Heparin reversal of protamine toxicity: Have we come full circle? *J Cardiothorac Vasc Anesth* 4:539-542, 1990
5. Horrow JC: Protamine allergy. *J Cardiothorac Vasc Anesth* 2: 225-242, 1988
6. Stoelting RK: Allergic reactions under anesthesia. *Anesth Analg* 62:341-356, 1983
7. Levy JH: *Anaphylactic Reactions in Anesthesia and Intensive Care*. Boston, Butterworth-Heinemann, 1992
8. Kurtz AB, Gray RS, Markand S, Nabarro JD: Circulating IgG antibody to protamine in patients treated with protamine-insulins. *Diabetologia* 25:322-324, 1983
9. Levy JH, Schwiager IA, Zaiden JR, Faraj BA, Weintraub WS: Evaluation of patients at risk for protamine reactions. *J Thorac Cardiovasc Surg* 98:200-204, 1989
10. Vezina D, Sheridan P, Blain R, Roberts KD, Bleau G: Safety of protamine sulfate administration in vasectomized men. *Contraception* 41:605-616, 1990

(Accepted for publication June 4, 1993.)

through interaction of protamine and complement-fixing antiprotamine IgG antibody.<sup>6</sup> This type of reaction is defined as an "anaphylactic reaction" in the major textbook in this field.<sup>2</sup>

Second, Metz is apparently unaware that diabetic patients receiving protamine-containing insulin preparations are at risk for life-threatening reactions to protamine<sup>7,8</sup> and that antibody-mediated mechanisms are the likely cause for the increased risk.<sup>9</sup>

Third, vasectomy is thought to disrupt the blood testes barrier, after which 20-33% of such men develop hemagglutinating auto-antibodies against protamine-like compounds.<sup>10</sup> It is possible that 45 mg protamine, given 6 weeks earlier at cardiac catheterization, may have contributed to the increased IgG level.

Our publication was a case report and did not address the issue of whether vasectomized males with high titers of antiprotamine IgG are at risk for developing life-threatening reactions to protamines. However, the demonstration of life-threatening cardiovascular re-

## CORRESPONDENCE

sponses on two separate occasions after protamine administration suggests that the relationship between the elevated IgG and the reactions was more than coincidental.

**Carol A. Hirshman, M.D.**

The Johns Hopkins School of Hygiene  
and Public Health, Room 7006  
615 North Wolfe Street  
Baltimore, Maryland 21205

## References

1. Adourian UA, Shampaine EL, Hirshman CA, Fuchs E, Adkinson NF: High-titer protamine-specific IgG antibody associated with anaphylaxis: Report of a case and quantitative analysis of antibody in vasectomized men. *ANESTHESIOLOGY* 78:368-372, 1993
2. Wasserman SI, Marquardt DL: Anaphylaxis in Allergy: Principles and Practice. Edited by Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW. St. Louis, Mosby, 1988, pp 1365-1376
3. Fisher MM, More DG: The epidemiology and clinical features of anaphylactic reactions in anaesthesia. *Anaesth Intensive Care* 9: 226-234, 1981
4. Weiss ME, Hirshman CA: Anaphylactic reactions and anesthesia, Principles and Practice of Anesthesiology. Edited by Rogers MC, Tinker JH, Covino BG. St. Louis, Mosby Year Book, 1993, pp 2457-2481
5. Levy JH: Anaphylactic Reactions in Anesthesia and Intensive Care. Boston, Butterworth-Hanemann, 1992, pp 161-203
6. Lakin JD, Blocker TJ, Strong DM, Yocum MW: Anaphylaxis to protamine sulfate mediated by a complement-dependent IgG antibody. *J Allergy Clin Immunol* 61:102-107, 1978
7. Gottschlich GM, Gravlee GP, Georgitis JW: Adverse reactions to protamine sulfate during cardiac surgery in diabetic and nondiabetic patients. *Ann Allergy* 61:277-281, 1988
8. Stewart WJ, McSweeney SM, Kellelt MA, Faxon DP, Ryan TJ: Increased risk of severe protamine reactions in NPH insulin-dependent diabetics undergoing cardiac catheterization. *Circulation* 70:788-792, 1984
9. Weiss ME, Nyhan D, Peng Z, Horrow JC, Lowenstein E, Hirshman CA, Adkinson NF Jr: Association of protamine IgE and IgG antibodies with life-threatening reactions to intravenous protamine. *N Engl J Med* 320:886-892, 1989
10. Samuel T: Antibodies reacting with salmon and human protamines in sera from infertile men and from vasectomized men and monkeys. *Clin Exp Immunol* 30:181-187, 1977

(Accepted for publication June 4, 1993.)

Anesthesiology

79:619-620, 1993

© 1993 American Society of Anesthesiologists, Inc.  
J. B. Lippincott Company, Philadelphia

## A Normal Cervical Spine X-ray Does Not "Clear" the Patient with Suspected Cervical Spine Injury

*To the Editor:*—A recent study reported in the trauma literature<sup>1</sup> may be of substantial import and concern to anesthesiologists managing trauma patients and casts a revealing light on Hastings and Kelley's report<sup>2</sup> of neurologic deterioration after airway management in a patient with an unsuspected cervical spine injury.

Woodring and Lee studied 216 consecutive patients who had suffered cervical spine injuries proven by computed tomography (CT).<sup>1</sup> Although 87% of the patients had signs or symptoms of cervical spine injury at presentation, 5% were asymptomatic with an intact mental status (a further 8% were also asymptomatic but had mild closed head injuries or were intoxicated). Sixty-eight percent of the asymptomatic patients harbored unstable cervical spine injuries. Most importantly, the full cervical spine x-ray series (cross-table lateral (CTL), anteroposterior, and odontoid) missed 23%, and the CTL view 32%, of the cervical spine injuries, half of which were unstable. Furthermore, the CT scan often demonstrated abnormalities of a far greater extent and severity than those demonstrated on the plain x-rays. These data strongly suggest that clinical examination and cervical spine plain films are inadequate for "clearing" the cervical spine in a patient with a known injury mechanism and in particular a patient with an altered mental status. This is cause for much concern because a recent

survey of 125 North American hospitals found that one-third of responding institutions relied solely upon the CTL for radiologic evaluation of possible cervical spine injury.<sup>3</sup>

In Hastings and Kelley's report, the patient did initially complain of neck pain, and left arm weakness may have been a further sign of cervical spine injury (as opposed to brachial plexus injury). Woodring and Lee's study suggests that this patient should thus have undergone CT scanning, even though his cervical spine films initially were read as normal.

It has long been routine practice that all patients with a known mechanism of cervical spine injury undergo radiologic imaging, whether or not signs or symptoms are present. Woodring and Lee's report supports this and further suggests that, regardless of plain film results, CT should be added to the imaging evaluation whenever a patient has signs or symptoms of cervical spine injury. Additionally, patients with abnormal x-rays should undergo CT scanning to determine the true extent of the cervical spine injury.

Thus, in airway management of patients with known mechanisms of injury, unless CT scanning has ruled out cervical spine injury, it would seem prudent to initially treat all patients as if the cervical spine was unstable, even if plain films are normal.