REFERENCES

1. Hull CJ: Electrocution hazards in the operating theatre. Br J Anaesth 50:647-657, 1978
2. Starmer CF, Whalen RE: Current density and electrically induced ventricular fibrillation. Med Instrum 7:158-161, 1973
3. International Electromechanical Institution: General safety requirements for electrical equipment used in medical practice. British Standards Institute, 1978.

"Heparin Allergy" and Cardiopulmonary Bypass

To the Editor:

Our Cardiac Anesthesia Service was recently involved in the care of a woman presenting for emergent myocardial revascularization. In addition to a number of more common medical problems, the patient had a well-documented history of clinical anaphylaxis and shock following prior exposure to heparin years earlier for the treatment of deep venous thrombosis. These reactions are extremely rare and are believed to be due to either the heparin compound itself or the preservative, chlorocresal, used in the formulation. Antibodies can be developed to each of the two types of heparin available, bovine or porcine. Antigenic testing and immunodiffusion studies may be used to define the exact allergen but these were impossible on this emergent basis.[1,2] The planned surgical procedure required full cardiopulmonary bypass, hence complete systemic anticoagulation. The newer low molecular weight heparin formulation was not available on such short notice, and, therefore, the administration of a full dose of regular heparin was required. Fortunately, the product currently in use in this institution does not contain chlorocresol as a preservative, thus eliminating this substance as a potential antigenic problem. Which type of heparin to use, bovine or porcine derived, remained an issue. After consultation with the Pharmacy Department, it was decided to use the pure beef extract because the patient's prior exposure would most likely have been to the porcine preparation. Using a derivative to which the individual has not been previously exposed may offer an advantage in such situations,[2] though this is controversial. The patient was premedicated with methylprednisolone, 125 mg, diphenhydramine, 50 mg, cimetidine, 300 mg, and an epinephrine infusion (5 μg/min) as prophylaxis prior to the administration of the bovine heparin. Then a 100 U test dose was given. No adverse response was evident and an anticoagulant dose (300 U/kg) was administered in incremental allotments. This was likewise uneventful and the rest of the procedure continued without incident.

The question as to whether this patient was truly allergic to porcine heparin or rather had experienced an anaphylactoid reaction to the preservative it was contained in could not be answered at the time she presented for emergency care. However, a very severe response had occurred upon previous exposure and efforts were made to avoid a recurrence. The patient was given a heparin formulation to which she had not been previously exposed (in this case bovine-derived heparin with a benzyl alcohol preservative), and premedication to ameliorate any reaction that might have still developed despite the antigen change. No problems were encountered. Which step was actually effective in preventing the adverse response is unknown, but a serious problem was avoided.

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REFERENCES

1. Coon W, Willis P: Some side effects of heparin, heparinoids and their antagonists. Clin Pharmacol Ther 7:379-398, 1966
2. Curry N, Bandana E, Pirofsky B: Heparin sensitivity: Reported case. Arch Intern Med 132:744-745, 1973

Commentary to Letter by J.G. Bray

To the Editor:

Dr Bray's experience raises several issues. First, do any currently marketed formulations of heparin use chlorocresal as preservative? All those listed in the 1992 Physicians' Desk Reference (Montvale, NJ: Medical Economics Data) use benzyl alcohol. Second, would a low molecular weight heparin (LWMH) compound have been a superior choice? Not likely. Cross-reactivity is not assured. Because skin tests yield many false positives, a provocative trial similar to the one Dr Bray describes with bovine heparin would probably have occurred with LWMH. Unfortunately, the anticoagulant effect of

LWMHs cannot be monitored in the operating room and they are poorly neutralized by protamine, resulting in excessive postbypass bleeding.

Third, did the prophylactic cocktail provide protection or was it unnecessary? As Dr Bray states, this remains unknown in the absence of further immunologic investigation of the patient's previous adverse response to heparin. Measurement of plasma histamine concentrations would have aided this distinction: normal levels would suggest prior allergy to the preservative or to porcine heparin, whereas substantially increased concentrations would occur with an allergic response blocked with histamine antagonists. Steroid inhibition of histamine release provides an exception to this logic.

Fourth, should cimetidine play a role in protection from anaphylactoid reactions? Theoretically, it may exacerbate an anaphylactic response by blocking H_2 feedback receptors on mast cells. Its use for this purpose remains controversial. Finally, do the potential deleterious effects of epinephrine infusion (tachycardia and hypertension in this woman with coronary artery disease) outweigh any protective effect on anaphylaxis? Most likely so, because the treatment of anaphylaxis requires very large doses of epinephrine compared to the dose administered, 5 μg/min. However, that dose does substantially increase heart rate.

Dr Bray describes the successful management of a suspected lethal intervention. Many of the measures undertaken will prove useful to others placed in a similar situation.

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Use of Inhaled Nitric Oxide to Reduce Pulmonary Hypertension After Heart Transplantation

To the Editor:

Right ventricular dysfunction is a relatively frequent complication of heart transplantation, often due to preexisting pulmonary hypertension in the recipient. It has been noted that a transpulmonary gradient (TPG = mean pulmonary artery pressure minus pulmonary capillary wedge pressure) greater than 15 mmHg and/or a pulmonary vascular resistance (PVR) greater than 400 dynes · sec · cm^{-5} is associated with right ventricular dysfunction and a significant increase in perioperative mortality.[1-3] Isoprenaline and sometimes prostacyclin have been used to overcome this problem. Neither of these drugs, however, is a selective pulmonary vasodilator and may induce or worsen an already existing systemic hypotension. Recent reports, however, suggest that inhaled nitric oxide (NO) is a selective pulmonary vasodilator,[4-6] devoid of significant effects

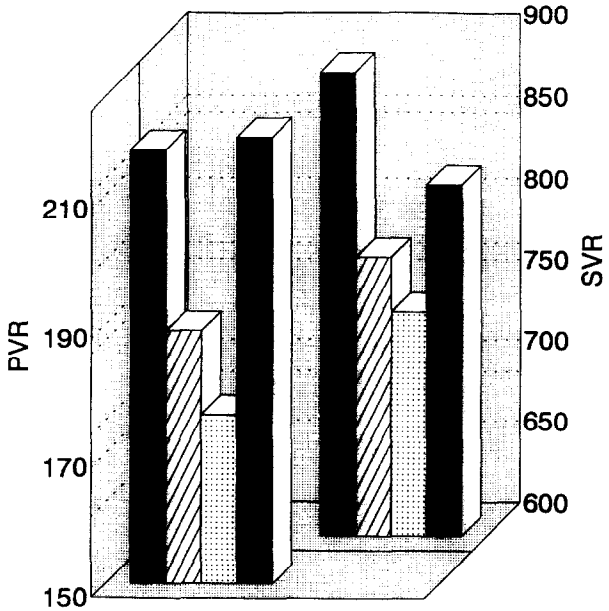

Fig 1. ■, baseline; ▨, 10 minutes NO; □, 20 minutes NO.