

CORRESPONDENCE

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Cause of Hypotension after Isolated Limb Perfusion with Tumor Necrosis Factor

To the Editor:—Sigurdsson *et al.*¹ report an episode of hypotension, oxygen desaturation, and increasing pulmonary artery pressures requiring aggressive resuscitation. They attribute this episode to the effects of tumor necrosis factor (TNF) liberated after release of the tourniquet at the conclusion of the isolated limb perfusion. We believe that these symptoms may have been attributable to the dextran flush rather than toxic effects of TNF.

We have performed 40 hyperthermic isolated limb perfusions at the National Institutes of Health using TNF, melphalan, and interferon protocol with patients with sarcoma or melanoma. For only one of the early perfusions did we have a situation as described above, with rapid decompensation occurring with tourniquet release. We attributed it to the dextran flush because of the rapidity at which it occurred.

The toxic effects of systemic TNF and dextran anaphylaxis^{2,3} may appear similar. However, the effects of systemic TNF consistently manifest 3–4 h after tourniquet release, even in patients who have had up to an 8% recorded leak, assuming complete flush. The symptoms are treated with fluids and vasopressors until resolution and have never required ventilatory support. Furthermore, almost all patients have increased temperatures at the conclusion, which we attribute to preoperative interferon, external warming blankets for hyperthermia, and the perfusate drug.

We recommend that the authors reperfuse the isolated limb with

hetastarch or albumin rather than dextran to avoid this problem in the future.

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In Reply:—It is well known that dextran can cause allergic reactions in patients.^{1–3} However, severe anaphylactic reactions have become rare since hapten inhibition of dextran-reactive antibodies with dextran one (MW 1000 Dalton, Promiten) became a routine pretreatment in clinical practice.³ According to routine at our institution, the patient we described received hapten before administration of dextran.⁴ In addition, the patient received dextran on the 2nd and 3rd postoperative days with no reaction, which precludes dextran as a cause of the episode described. Thus, we still assume that the reaction in our patient was due to tumor necrosis factor (TNF) liberated after release of the tourniquet.⁴ Perhaps the reaction Wert-

heimer and Fraker mention and attribute to the use of dextran was caused by TNF as well. In fact, severe circulatory and respiratory reactions often have been described after TNF administration, in both humans and animals.^{4–8}

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