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(Accepted for publication July 18, 1996.)

Anesthesiology
1996; 85:1209

Lack of Tolerance to Propofol

To the Editor:—We read with interest the report of Setlock *et al.*[1] concerning the lack of tolerance to repeated doses of propofol used for sedation in pediatric radiation therapy patients. We, like Setlock *et al.*,[1] and in contrast to Deer and Ridi,[2] have not seen tolerance to propofol develop in these patients. Specifically, in two recent patients accounting for more than 50 treatments, there was no increase in the induction and maintenance doses for sedation. We would like to add this experience to that of the authors.

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(Accepted for publication July 30, 1996.)

Anesthesiology
1996; 85:1209-10

Anaphylactoid Reactions to Protamine

To the Editor:—Some aspects of the interesting case report by Takenoshita *et al.*[1] merit, in our opinion, further discussion.

Acute reactions to protamine vary from mild reactions, such as erythema, urticaria, and transient mild elevations in pulmonary artery pressure to more severe reactions, which include bronchospasm, hypotension, and, although rare, cardiovascular collapse and death.[2] Protamine is also hypothesized to be a potential cause of fulminating noncardiogenic pulmonary edema after cardiopulmonary bypass.[3] The exact mechanisms by which protamine produces these adverse reactions are not completely understood and include direct, nonimmunologic release of histamine, immunoglobulin E (IgE)-mediated release, complement-fixing antiprotamine immunoglobulin G (IgG) antibodies, and protamine-heparin complexes that activate complement.[2]

The case report, as presented, contributes only partially to the understanding of adverse reactions to protamine. The acute facial edema and marked increase of tryptase in the described patient indicate a significant skin mast cell degranulation. However, an antibody-mediated mechanism is the likely cause for the increased risk of life-threatening reactions to protamine in patients with diabetes who receive neutral protamine Hagedorn insulin.[4] Binding of protamine to specific IgE or possibly to subclass 4 of IgG on mast cells or basophils may result in a release of histamine and tryptase. Unfortunately, neither IgE nor IgG antibodies to protamine were determined in this case. The positive skin tests to protamine after the incident do not necessarily confirm the hypersensitivity to protamine and may only indicate previous exposure to protamine. In addition, a recent study has established a poor specificity of protamine skin tests.[5] Intradermal injections of protamine with concentrations between 100 and 1,000 μg/ml induce irritative skin responses in healthy subjects[6]; 10 μg/ml might have been a nonirritative concentration, although Takenoshita *et al.*[1] did not have control subjects to test. However, the recommended protamine test dose concentration is 1 μg/ml.[5] In addition, out of the 11 patients taking neutral protamine Hagedorn insulin who had severe anaphylactoid reactions to protamine, only one of four patients studied by cutaneous testing had clearly positive results.[2]

In summary, the case report identifies a patient with neutral protamine Hagedorn insulin-dependent diabetes mellitus who suffered a

severe anaphylactoid reaction during open heart surgery probably caused by protamine. The findings of an elevated tryptase and positive protamine skin tests remain inadequate to answer questions concerning the mechanism of this severe reaction.

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(Accepted for publication August 6, 1996.)

Anesthesiology
1996; 85:1210

In Reply:—As Kindler and Bircher correctly point out, immunoglobulin E and immunoglobulin G antibodies to protamine were not measured, and, therefore, the precise mechanism underlying our observations remains uncertain. Although I did not have control subjects, I do not think the protamine with concentrations between 10 and 100 μg/ml used in our report induced irritative skin responses. Weiler *et al.*[1] reported that out of 85 patients who were skin tested with 0.001–0.1 mg/ml protamine, only 3 were positive, and the protamine concentration at which these 3 patients showed positive reactions was 0.1 mg/ml.

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(Accepted for publication August 6, 1996.)

Anesthesiology
1996; 85:1210–1

Fiberoptic Tracheal Intubation Using a Nipple Guide

To the Editor:—Fiberoptic tracheal intubation of the infant may be assisted *via* a laryngeal mask airway (LMA), a standard mask, or a ventilating mask.[1] Of these devices, only the LMA acts as an oropharyngeal-laryngeal conduit, through which a flexible fiberoptic bronchoscope may be placed directly above the vocal cords. Unfortunately, the LMA is poorly tolerated by the awake infant. We describe an alternate device that facilitated fiberoptic bronchoscopic tracheal intubation of an infant with an unstable cervical spine who could not be safely anesthetized before intubation.

A 7-month-old expremature infant with a history of bronchopulmonary dysplasia, apnea and bradycardia of prematurity, and chronic respiratory failure that required prolonged intubation was admitted with rapidly progressive upper extremity weakness. A magnetic resonance imaging (MRI) examination was indicated to rule out a space-occupying lesion that involved the spinal cord. The combination of the patient's medical history and his remote position while in the MRI scanner necessitated tracheal intubation with controlled ventilation. Because of his progressive paralysis, we were compelled to assume that his cervical spine was unstable, and that direct laryngoscopy might result in permanent neurologic damage. In summary, we were confronted with a 7-month-old boy with an unstable cervical spine who could not sustain more than mild sedation for the fiberoptic placement of an endotracheal tube.

Fiberoptic bronchoscopy was performed in the operating room