

Anesthesiology  
1997; 86:1006-7  
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## Cardiovascular Collapse Resulting from Thiopental-induced Histamine Release

*To the Editor:*—Anaphylactic reactions to thiopental occur in approximately 1 of every 30,000 patients.<sup>1</sup> Nonimmunologically mediated anaphylactoid reactions are based on direct histamine release and are believed to be more common; reported incidence for methohexital is 1 in 1,630.<sup>2</sup> However, immunologic documentation of the etiology of such reactions is not always clear. Hirshman *et al.* demonstrated *in vitro* thiopental-induced histamine release from the leukocytes of a patient who developed cardiovascular collapse and cutaneous flushing but had no evidence of an immunoglobulin E-mediated hypersensitivity with thiopental administration.<sup>3</sup> We present a patient in whom we documented what is probably a nonimmunologically mediated reaction to thiopental.

Our patient was a man aged 65 years (81 kg) scheduled for abdominal aneurysm repair. Standard monitors and an arterial catheter were placed before induction of general anesthesia. The preoperative blood pressure was 160/80 mmHg, and the heart rate was 65 beats/min. Induction was accomplished with 300 mg of thiopental. Immediately after thiopental administration, the heart rate increased to 140 beats/min, and the blood pressure decreased to 50/20 mmHg, and the face and upper chest became erythematous. Auscultation of the lungs disclosed no wheezing. Blood pressure did not increase with 300  $\mu$ g of phenylephrine, but 150  $\mu$ g of epinephrine corrected the hypotension, which lasted for about 10 min. The blood was drawn 10 min after the event for the histamine levels and 45 min after the event for other immunologic variables: histamine plasma concentration was 43 nmol/l (normal, 0–6 nmol/l);  $\beta$ -tryptase serum concentration was less than 1 ng/ml (normal, less than 1 ng/ml);  $\alpha$ -tryptase serum concentration was 7 ng/ml (normal, 1–10 ng/ml); C<sub>3</sub> complement, 79 mg/dl (normal, 76–199 mg/dl); C<sub>4</sub> complement, 22 mg/dl (normal, 16–64 mg/dl); and complement deficiency assay, 37 U (normal, 40–126 U). The allergologist performed skin testing with thiopental 30 days after surgery; the result was negative.

Vigorito *et al.* demonstrated that intravenous administration of histamine to volunteers, which resulted in a serum histamine concentration of 4.6 ng/ml (48 nmol/l), caused significant decreases in blood pressure and vascular resistance and increases in heart rate.<sup>4</sup> The clinical symptomatology and serum histamine concentrations encountered in our patient agree with findings of Vigorito *et al.*

*In vivo* histamine is stored in mast-cells and basophils, while neutral protease, tryptase, is located in clinically significant concentrations only in the secretory granules of mast cells.<sup>5</sup> Therefore, increase in plasma histamine may reflect the degranulation of mast cells, basophils, or both types of cells, whereas increase in tryptase and histamine indicates specifically mast cells degranulation.<sup>5</sup> In our patient, the serum histamine concentration was elevated after thiopental without an elevated concentration of tryptase or abnormal complement concentrations. A similar clinical scenario was reported previously, although histamine levels were not measured.<sup>6</sup> It is possible that the cardiovascular collapse after thiopental administration resulted from histamine released from basophils, such as was described

by Hirshman *et al.*<sup>3</sup> During systemic anaphylaxis,  $\beta$ -tryptase levels in blood begin to increase 15–30 min after antigenic challenge, peak at 30 min to 2 h, and decrease at the half-life of around 2 h.<sup>7</sup> In insect sting-induced anaphylaxis, tryptase levels correlate closely to the severity of the hypotension.<sup>8</sup> Consequently, undetectable serum  $\beta$ -tryptase after a profound hypotensive event indicates that the mast cells were not the primary cell type involved. At the same time, histamine plasma half-life is under 2 min,<sup>7</sup> and its elevated serum concentrations return to normal in 20–60 min after immunologic or nonimmunologic stimulation.<sup>5</sup> Therefore, an elevated serum tryptase can be used to confirm the diagnosis of mast cell-dependent anaphylaxis for several hours after the event, depending on the clinical severity and magnitude of mast cell degranulation.

We conclude that in our patient, thiopental administration caused hypotension mediated by histamine that most likely was released from basophils rather than mast cells.

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(Accepted for publication January 6, 1997.)

Anesthesiology  
1997; 86:1007

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Lippincott-Raven Publishers

## Hypoglossal Nerve Palsy as a Complication of Transoral Intubation for General Anesthesia

*To the Editor:*—There have been isolated cases of hypoglossal nerve palsies after otolaryngologic procedures, such as prolonged direct laryngoscopy<sup>1,2</sup> or after aortic arch surgery<sup>3</sup> after use of a laryngeal mask airway.<sup>4</sup> We present a patient with a postoperative hypoglossal nerve palsy after uncomplicated intubation.

A healthy 35-year-old man was admitted for paranasal sinus surgery with nitrous oxide anesthesia induced by intravenous thiopental. The transoral intubation was performed with a McIntosh blade (No. 4, Heine, Germany) and an amoured tracheal tube (Silcolatex®, Rüsch, Germany) with an OD of 9.33 mm. The tube was inserted once atraumatically at the right oropharyngeal side and fixed to the right angle of the mouth. No laryngeal mask airway or throat packs were used. The head was dorsiflexed shortly for direct laryngoscopy. The whole operation (85') was performed in dorsal position, and the head was not extended. The next day, clinical examination revealed a hypoglossal nerve palsy on the left. The electromyographic (EMG) examination showed a clear decrease of the amplitude and a single nerve fiber activity without any degenerative potentials, indicating a transient nerve lesion. An oblique radiograph of the neck detected a calcified left ligamentum stylohyoideum. Serologic tests excluded infections, such as herpes viruses or borreliae, as possible causes of hypoglossal palsy. A neurologic examination and a computed tomography scan of the head revealed no abnormal findings. Four weeks later, the mobility of the tongue was back to normal.

All published cases have one of the following mechanisms in common: the nerve is exposed either to pressure or to stretching for a long interval. This case does not follow this pattern. Pressure to the left lateral root of the tongue occurred only for a short time during routine intubation using the McIntosh blade. A surgical injury is unlikely because the procedure was confined to the nose. We only detected the calcified ligamentum styloideum as pathologic findings. Thus, we conclude that the short compression of the nerve between

the blade and the calcified ligamentum was the event that caused the hypoglossal palsy. In addition, the nerve may have been stretched by the dorsiflexion of the head. If a hypoglossal palsy is noted postoperatively, we recommend radiography of the neck and an EMG investigation. If a calcified ligamentum is known preoperatively, ipsilateral pressure on the root of tongue should be avoided.

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(Accepted for publication February 4, 1997.)