A 60-yr-old lady with HbM Saskatoon and congenital methemoglobinemia was scheduled for mastectomy. Clinical examination confirmed cyanosis but she had no symptoms due to methemoglobinemia and no history suggestive of cardiac or respiratory problems. Her electrocardiogram was normal and arterial blood gas (ABG) values on room air were: pH = 7.52, pO_2 = 104 mmHg, pCO_2 = 28 mmHg, BE = 0.9, lactate – within normal limits. We could not obtain details regarding oxyhemoglobin (oxyHb), reduced hemoglobin and MetHb from our co-oximeter. As the patient had good exercise tolerance and the normal lactate indicated adequate tissue perfusion[4] we planned to proceed with surgery. We monitored the patient by measuring serial ABGs through an indwelling arterial line in addition to routine monitors. Anesthesia was induced with fentanyl and propofol. A spontaneously breathing technique with a 1:1 mixture of oxygen/air and isoflurane was used. Intraoperatively, a representative ABG was as follows: pH = 7.47, pO_2 = 375 mmHg, pCO_2 = 32 mmHg, BE = 0.2; lactate = 1.1 $mmol \cdot L^{-1}$. The perioperative course was uneventful and the patient was discharged home two days later.

Severe MetHb is treated with methylene blue which rapidly reduces methemoglobinemia nonenzymatically.[3] The recommended dosage of methylene blue is 1–2 $mg \cdot kg^{-1}$ iv over a five-minute period. Doses > 15 $mg \cdot kg^{-1}$ can paradoxically cause methemoglobinemia.[1] It is known that methylene blue is ineffective in the presence of nicotinamide-adenine dinucleotide phosphate dehydrogenase and glucose-6 phosphate dehydrogenase deficiencies.[1,3] Methylene blue is not effective in the presence of HbM because HbM leads to the formation of an iron-phenolate complex that resists reduction. Co-oximeters are also misleading in the presence of HbM.[1] The HbM spectrum lacks the characteristic MetHb peak at 630 nm and has a peak near 600 nm. In the presence of HbM, co-oximeters may report normal fractions of MetHb, increased carboxyhemoglobin (COHb) or increased sulfhemoglobin.[1] Our ABG machine (Roche Omni S, Cambridge, UK) failed to record all types of hemoglobin (oxyHb, reduced Hb, MetHb and COHb). We raised this issue with our biochemistry department whose staff concluded that the HbM Saskatoon interfered with the algorithm of the co-oximeter and hence failed to record any form of hemoglobin.

The issues raised by this case include failure of methylene blue to treat methemoglobinemia in the presence of HbM and interference of HbM Saskatoon with the algorithm of the co-oximeter. In severe cases of methemoglobinemia with HbM, exchange transfusion or even hyperbaric oxygen[5] may have to be considered. The role of ascorbic acid in managing such cases remains uncertain.

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Adie syndrome associated with general anesthesia

To the Editor:
The sudden onset of anisocoria indicates the possibility of a life-threatening intracranial lesion. We describe a case of anisocoria which occurred in association with a hypertensive episode after anesthetic induction. Adie syndrome was subsequently diagnosed by a pilocarpine test.

A 61-yr-old previously healthy female was scheduled for a lung biopsy. She had no history of any ophthalmologic disorder, and she had no pupillary abnormalities preoperatively. Diazepam 5 mg *po* and pentobarbiturate 50 mg *po* were administered as premedicants 90 min before surgery. In the operating room a thoracic epidural was inserted following application of routine monitors. After documenting sensory loss in the T3-L1 dermatomes in response to 5 mL of epidurally injected 1.5% mepivacaine, anesthesia was induced with propofol 180 mg *iv* followed by vecuronium 6 mg *iv*. Immediately after laryngoscopy and tracheal intubation, the patient's blood pressure increased suddenly to 205/120 mmHg. Following several minutes of controlled ventilation with 3% inspired sevoflurane, the patient's heart rate

and blood pressure normalized, but marked anisocoria was observed. The diameters of her left and right pupils were 6 mm and 1 mm respectively, with noted absence of light reflex in the left eye. A hypertensive intracranial hemorrhage was considered in the differential diagnosis, hence surgery was postponed. Urgent computerized axial tomography was performed under sedation and mechanical ventilation, and the patient showed normal intracranial structures. Thus, she was awakened to demonstrate fully intact neurological findings and a normal level of consciousness. The patient was transferred to the ward without monitoring. The next day, an ophthalmologist diagnosed Adie pupil of the left eye based upon the clinical presentation and a positive pilocarpine test. Her anisocoria resolved within 24 hr.

Anisocoria associated with an Adie pupil is thought to originate from a peripheral mechanism involving parasympathetic postganglionic fibres, arising from a damaged ciliary ganglion.[1] In this syndrome, tonic pupillary movement (gradual pupil movement) and light-near dissociation (impaired light reflex with an intact convergence response) are the main diagnostic features.[2] To diagnose anisocoria, it is important to determine whether aniscoria is more pronounced in the dark or in the light, and whether light reflex or convergence responses, including neurological signs, are intact.[3] The pupillary size associated with physiological anisocoria (which exists in up to 10% of adults), is unchanged in both dark and light ambient lighting conditions. However, in unconscious patients under general anesthesia, the convergence response and neurological symptoms cannot be confirmed. The pilocalpine test, which is effective even in a vegetative state, appears to be useful for diagnosing whether anisocoria is caused by either a peripheral or a central lesion.

Pupillary constriction with a low concentration of pilocarpine implies denervation sensitivity for acetylcholine receptors. Thus, it induces pupillary constriction in an Adie pupil, while a normal eye is not affected. A constriction of more than 25% after 30 min following pilocarpine application is positive (positive in 80% of Adie's pupils). If pupil size does not change with a low concentration of pilocarpine (0.125%) but constricts with a higher concentration (0.5%), anisocoria is considered to be related to a central nervous system disorder such as a presynapse of the parasympathetic nervous system in the oculomotor nerve.[4]

In this case, the main factors contributing to the manifestation of the Adie pupil appear to have been parasympathetic dominance caused by sympathetic block induced by the thoracic epidural in the presence of anesthetics such as propofol and sevoflurane. Parasympathetic nerve stimulation causes contraction of the pupillary sphincter and hence pupillary constriction. The parasympathetic-dominant state induces rapid constriction in the normal eye, but much slower constriction in the Adie pupil, resulting in marked differences in pupillary diameter. Other possible risk factors for the development of Adie pupil include botulism, myasthenia gravis and dyshidrosis, all of which are associated with increased vulnerability of systemic cholinergic nerves.[5] The possibility of vecuronium having influenced autonomic tone in this patient cannot be excluded. In conclusion, Adie syndrome should be considered in the differential diagnosis of patients who develop anisocoria in the perioperative setting.

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