

of the involved lobe; however, sudden changes in compliance must be anticipated. This factor may have contributed to the refractory hypotension and carbon dioxide retention seen in the first case. Hypoventilation with carbon dioxide retention and acidosis is also undesirable since it may cause severe pulmonary vasoconstriction and may precipitate acute right-heart failure in a child with congenital heart disease or cause shunting of blood at the atrial or ventricular level. Finally, the surgeon should be present during induction of anesthesia, so that if there is catastrophic cardiovascular deterioration he may perform emergency thoracostomy. Compression atelectasis, decreased compliance, and mediastinal shift will occur earlier than pneumothorax, and therefore simple chest-tube drainage is not sufficient. Only thoracostomy to allow herniation of the overdistended lobe out of the thorax will allow cardiovascular stabilization; this was dramatic in the first case.

The management of bronchoscopy, which is necessary in older children to rule out mucous plug or foreign-body aspirations, is difficult, at best. Obviously, careful communication between surgeon and anesthesiologist is necessary to avoid high airway pressures while the bronchoscope is directed at the

involved lobe. Perhaps bronchoscopy and thoracotomy should be performed as a double set-up in order to avoid a second exposure to life-threatening anesthesia related events.

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### Implications of Masseter Spasm after Succinylcholine

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Isolated masseter muscle spasm is an abnormal response to succinylcholine (SCh).

Thiel,<sup>1</sup> Patterson,<sup>2</sup> and Cody<sup>3</sup> have described severe muscle spasm after SCh in some patients with pre-existing neuromuscular disease, including strabismus. An increased incidence of susceptibility to malignant

hyperthermia (MH) has been seen in patients with pre-existing muscle weakness.<sup>5-11</sup> Rigidity after SCh is often an early sign of MH.<sup>3,4</sup> Other early manifestations of MH include tachycardia, tachypnea, acidosis, and dark blood in the surgical field. Temperature elevation is often delayed as long as 45 minutes.

Masseter spasm with SCh occurs in myotonia congenita.<sup>3</sup> Recently, the clinical entity of isolated masseter spasm in response to SCh has been described to occur in children, in a setting of isolated muscle weakness<sup>12</sup> (strabismus). Barlow and Isaacs<sup>13</sup> report two fatal cases of MH in which the earliest abnormality was an intense masseter-spasm response to SCh. In both cases, when general anesthesia proceeded, fatal MH developed.

The following cases are presented to illustrate the course of isolated masseter spasm in response to SCh.

#### REPORT OF THREE CASES

*Patient 1.* An 8-year-old, 27-kg boy was scheduled for surgical correction of strabismus. Preoperative evaluation revealed a history

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of croup at age 2½ years, no previous surgical procedure, and no family history of problems with anesthesia. Physical examination was unremarkable; there was no increased muscle mass. Laboratory data were normal. Preoperative temperature was 36.7 C.

The patient received meperidine, 30 mg, im, atropine, 0.3 mg, im, and pentobarbital, 30 mg, per rectum, as premedication, with good effect. Routine monitoring, including monitoring of axillary temperature, was begun.

After thiopental, 75 mg, iv, halothane was administered by mask to a concentration of 4 per cent with nitrous oxide, 4 l/min, and oxygen, 4 l/min. Laryngoscopy was easily performed and provided good visualization. With the intubation attempt, laryngospasm developed. Succinylcholine, 20 mg, iv, was given, and although fasciculations were not seen, the laryngospasm was relieved and ventilation became easy. However, the jaw was definitely not relaxed, having clearly stiffened after SCh administration. The trachea was intubated with difficulty, but subsequently ventilation and chest compliance were good. The extremities remained flaccid. There was no mottling of skin or change in vital signs. Axillary temperature was 36.5 C. Approximately 30 minutes later, while the patient breathed 1 per cent halothane spontaneously, ventricular premature contractions (VPC's) appeared on the EKG monitor. It was felt that painful stimuli during light anesthesia and hypoventilation might have contributed to the cardiac irritability. Anesthesia was changed to 98.5 per cent oxygen and 1.5 per cent halothane. Arterial blood-gas analysis revealed  $P_{O_2}$  450 torr,  $P_{CO_2}$  77 torr,  $pH$  7.13, and  $K$ , 3.6 mEq/l. These values were interpreted to represent hypoventilation, and controlled ventilation was begun. The EKG reverted to a sinus rhythm. The circle system was intact and functioning. The soda lime was not discolored, and breath sounds were bilateral and equal. Controlled ventilation was maintained throughout the remainder of the operation, a sinus tachycardia (rate 136/min) persisted, but no further VPC activity was seen. Blood pressure was 125 torr systolic, the patient was pink and non-rigid, and temperature was stable at 37.5 C.

As the patient awakened at the end of the procedure, 70 minutes after induction of anesthesia, VPC activity reappeared on the EKG monitor. At this point the patient was breathing 100 per cent oxygen with spontaneous deep ventilations at 24/min, and both lungs were clearly well ventilated. It was impossible manually to take over control of ventilation. An arterial blood-gas analysis showed  $P_{O_2}$  447 torr,  $P_{CO_2}$  101 torr,  $pH$  7.05, and a base deficit of 6 mEq/l, consistent with respiratory acidosis and some metabolic acidosis. The cardiac irritability resolved during the next 10 minutes. Respirations became normal, and the patient remained pink, afebrile and non-rigid. Blood pressure was 125 torr systolic and pulse rate 132/min and regular. During the next two hours, rectal temperature remained 38 C, and EKG revealed normal sinus rhythm. An arterial blood-gas analysis of a sample drawn while the patient spontaneously breathed approximately 40 per cent oxygen by face mask showed  $P_{O_2}$  104 torr,  $P_{CO_2}$  45 torr,  $pH$  7.35,  $K$  3.4 mEq/l. The patient was awake, reactive and comfortable.

Serum creatine phosphokinase (CPK) in a sample drawn six hours later was 1,000 IU/l (normal 0-60). Laboratory values the next morning were: CPK 1,580 IU/l, lactate dehydrogenase (LDH) 126 IU/l (normal 34-76), serum glutamic oxaloacetic transaminase (SGOT) 220 IU/l (normal 10-40),  $K$  4.4 mEq/l, with urine negative for myoglobin. Except for some nausea and emesis in the morning, recovery was uneventful and the patient was sent home 28 hours after operation.

*Patient 2.* A healthy 20-year-old woman, weighing 58 kg, was scheduled for elective tonsillectomy. The patient was adopted, so family history was not available. After premedication with secobarbital, 100 mg, im, and atropine, 0.5 mg, im, she remained appre-

TABLE 1. Adenosinetriphosphatase Activity and Rate of Calcium Uptake in Fragmented Sarcoplasmic Reticulum Membrane

	Normal Range	Patient 2
Calcium uptake		
Initial ( $\mu\text{mol}/\text{mg}/\text{min}$ )	0.59-0.88	0.21
Total ( $\mu\text{mol}/\text{mg}$ )	1.7-4.8	0.57
ATPase activity		
Calcium-activated ( $\mu\text{mol}/\text{mg}/\text{min}$ )	0.51-0.82	0.30
Myofibrillar protein ATPase		
With EGTA ( $\mu\text{mol}/\text{mg}/\text{min}$ )	0.013-0.042	0.057
With calcium ( $\mu\text{mol}/\text{mg}/\text{min}$ )	0.20-0.36	0.11
Per cent increase with $\text{Ca}^{++}$	870-1,540	190

hensive and was given Innovar, 1 ml, iv. Before induction of anesthesia mobility of the jaw was good, without trismus. After induction with thiopental, 500 mg, iv, and succinylcholine, 100 mg, iv, normal fasciculations were evident, but the mandible was rigid and masseter spasm was felt. Endotracheal intubation was eventually performed with difficulty. During the next 30 minutes temperature remained 37.5 C, blood pressure was 120/90 torr, and pulse rate was 78/min. Results of arterial blood-gas analysis were normal; however, with the clearly abnormal reaction to succinylcholine, a decision was made to cancel the operation. Postoperatively it was learned that the patient had a history of severe muscle cramps in her legs when fatigued.

Two weeks later, using neuroleptanalgesia, a muscle biopsy was taken for study of calcium uptake and adenosinetriphosphatase (ATPase) activity. The results are presented in table 1.

*Patient 3.* A 36-year-old man, weighing 80 kg, known to be diabetic, with dyslexia, epilepsy, hypertension, and renal dysfunction, was scheduled for closed vitrectomy. He had a very muscular build but was not strong. He had "brittle" juvenile diabetes and was being treated with a 2,000-calorie diet and 44 units of NPH and 6 units of regular insulin each morning. Blood pressures in the range of 160/90 to 220/120 torr necessitated treatment with reserpine, 0.1 mg, b.i.d., and phenobarbital, 30 mg, h.s. Blood urea nitrogen (BUN) was 50 mg/100 ml and preoperative blood glucose was 341 mg/100 ml.

Premedication included demerol, 50 mg, im, pentobarbital, 100 mg, im, and atropine, 0.4 mg, im. After induction of anesthesia with thiamylol, 400 mg, iv, and succinylcholine, 100 mg, iv, it was noticed that "patient was difficult to intubate, unable to expose cords because jaw was stiff." After four attempts at endotracheal intubation and a repeat dose of succinylcholine, 100 mg, iv, blind oral intubation was finally achieved and the operation proceeded, using halothane, 2 per cent and 40 per cent oxygen with nitrous oxide for maintenance. About 45 minutes later the blood backed up in the iv tubing was seen to be very dark, the soda lime canister was changing color rapidly, and the patient's skin was warm and mottled. Nasal temperature was 38.9 C and rose to 40.3 C within 10 minutes. Blood pressure rose to 220/120 torr and pulse rate increased to 108/min. Arterial blood-gas analysis of a sample drawn shortly afterward showed  $P_{O_2}$  245 torr,  $P_{CO_2}$  180 torr,  $pH$  6.80,  $K$  4.8 mEq/l. Operation and anesthesia were discontinued. The patient was successfully treated with ice packs, iced Ringer's iv gastric lavage, fresh soda lime, hyperventilation with 100 per cent oxygen, furosemide, 30 mg, iv, sodium bicarbonate and a Foley catheter. He was observed for 24 hours in the intensive care unit, and, five days later, was sent home.

## DISCUSSION

The incidence of MH has been reported to be as high as 1:15,000 for children and 1:50,000 for adults, but higher in patients with muscle weakness.<sup>7</sup> Tammisto *et al.*<sup>14</sup> have reported unusually high CPK levels and an increased incidence of myoglobinuria in patients with strabismus given succinylcholine during halothane anesthesia. The masseter-spasm response to SCh, progressive intraoperative respiratory acidosis, tachycardia, and markedly elevated postoperative CPK are consistent with a hypermetabolic muscle derangement.

The persistent marked hypercarbia must be explained. Breath sounds were checked and found to be bilateral and equal. The  $P_{aO_2}$  of 450 torr is not consistent with the massive shunting expected with endobronchial intubation. Finally, with endobronchial intubation, controlled hyperventilation should restore  $P_{aCO_2}$  toward normal. In this case  $P_{aCO_2}$  continued to rise in spite of at least 30 minutes of controlled hyperventilation. The soda lime canister and circle system circuit and valves were checked and found to be functional. The anesthesia machine was used on previous and subsequent cases in the same operating room without problems. The levels of  $P_{CO_2}$  seen in the first case are much greater than those usually associated with some spontaneous hypoventilation during general anesthesia. The continued increase of  $P_{CO_2}$  even after a period of controlled hyperventilation suggests an overproduction rather than a failure to eliminate  $CO_2$  as a cause for the hypercarbia and acidosis.

The acidosis has both respiratory and metabolic components. Berman *et al.*<sup>15</sup> have shown in MH-susceptible Landrace pigs that before there is any significant temperature rise in MH, there is a mixed respiratory and metabolic acidosis with a base deficit of 7 mEq/l. Later, when the temperature rises several degrees centigrade, the metabolic acidosis becomes marked with the base deficit increasing to 22 mEq/l.

Serum CPK levels may be slightly elevated by stress, drugs, im injection, or muscle injury.<sup>16</sup> Succinylcholine has been shown by Innes *et al.*<sup>17</sup> to cause only a moderate increase in serum CPK. Therefore, it is unlikely that the postoperative CPK of 1,580 IU/l in this case could be due to succinylcholine, stress, eye surgery, or im injections. Although this patient did not become hyperthermic, many features of the case are sufficiently similar to MH to raise the question of whether the case represented: a) true MH that did not develop further due to the short duration of the procedure, or b) some variant of the classic MH syndrome. In some cases of MH the temperature may not become

elevated until 45 to 60 minutes after initiation of the syndrome. During this time a respiratory and metabolic acidosis is developing and causes cardiac irritability, tachycardia, and tachypnea.

The second case illustrates the prudence of postponing operation when a masseter-spasm response to succinylcholine occurs. No other clinical or chemical abnormality was present at the time. The patient remained afebrile and had a normal blood pressure and pulse rate; arterial blood-gas values and CPK were also normal. However, when a muscle biopsy study was done, the depressed calcium uptake, both initial and total, and the abnormally low myofibrillar calcium-dependent ATPase activity were consistent with similar findings in known cases of MH.<sup>19</sup>

In the third case, the isolated masseter spasm after succinylcholine contributed to difficulty in endotracheal intubation, but the operation proceeded. It was fully 45 minutes later before a clearly hypermetabolic, hyperthermic condition was recognized and treated. Had this been a brief 30-minute surgical procedure, this case might have been considered to pose no problem except difficulty of intubation.

A stiff jaw and cardiac irritability or tachycardia at the beginning of operation might be explained simply as responses to stimuli during light anesthesia in an otherwise clinically routine case. Only arterial blood-gas results or marked CPK elevation postoperatively may reveal the extent of the metabolic changes in muscle. Therefore, it is conceivable that many MH-susceptible patients have had some masseter spasm after succinylcholine but have been reported merely to have had "difficult intubation" and apparently have done well clinically during short procedures. Bernhardt<sup>19</sup> has reported a case where insufficient muscle relaxation after succinylcholine was followed by an uneventful 20-minute tonsillectomy with no change in body temperature. After operation marked myoglobinuria and CPK of 42,500 IU/l were seen.

Bloom *et al.*<sup>20</sup> discuss a case similar to our first case, in which a 10-year-old boy with strabismus had rigidity of the jaw after receiving succinylcholine. He remained afebrile during the 45-minute eye operation, but was tachycardic (130/min) and hypertensive. Postoperatively, hyperkalemia, myoglobinuria, and markedly elevated CPK were seen. He had had uneventful general anesthesia on one previous occasion. In fact, a third of patients in whom the complete syndrome develops have previously had "uneventful" general anesthesia one or more times.<sup>7</sup> However, except for patients who have had the fully developed syndrome or in whose cases caffeine tests of muscle biopsy speci-

mens are positive, we have no reliable criteria for identifying people as "MH-susceptible."

Regardless of whether isolated masseter spasm occurs after SCh in patients with pre-existing muscle disease or heralds the onset of MH, we believe that, because of the serious consequences of MH, with its associated 60 per cent mortality, continuation of anesthesia is contraindicated when isolated masseter spasm occurs after SCh. It is more prudent to postpone the operation until preparation can be made to treat MH if it develops. Subsequent anesthetics should be administered with careful monitoring using a neurolept-analgesia technique<sup>21,22</sup> and avoiding succinylcholine and all potent inhalational anesthetic agents.

In summary, MH can be insidious in its onset. Temperature elevation may be delayed, and the earliest sign of MH may be an abnormal muscle response to SCh, such as isolated masseter spasm. It is possible that in brief surgical procedures MH may go undetected in many patients who represent "difficult intubations" or are "resistant to SCh." Muscle biopsy data from patients having masseter spasm after succinylcholine are consistent with muscle abnormalities found in patients who have MH.<sup>18,23</sup> Therefore, in view of the present state of our knowledge, isolated masseter muscle spasm after SCh must be assumed to portend MH until proven otherwise. Consequent to this, surgical procedures should be postponed and subsequent use of anesthetics should be planned accordingly.

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