

ture was higher than that in the operating room by approximately 3 C. However, the increases above saturated humidity at room temperature were very similar in the two settings (7.5 mg H₂O/l in the laboratory and 7.25 mg H₂O/l in the operating room).

The soda lime used in all our experiments was Soda-Sorb,††, which probably accounts for the low stabilized humidity output of the regular circle system compared with values obtained in a previous study conducted with barium hydroxide lime USP.⁵ In fact, temperatures in the center of the canister did not exceed 34 C in the present study, whereas they were of the order of 42 C when barium hydroxide lime was used. This no doubt indicates that we could have obtained even higher humidities in the present study had we used a different type of lime.

A loss of humidity still occurs in the unheated portion of the MCS, which includes the part of the

tube in the center of the canister that emerges above the lime (fig. 1), the inspiratory dome valve, and its connection with the circuit. It is obvious that water of condensation occurs in this area, since we noticed fogging of the inspiratory dome valve in all our experiments. Thermally insulating that section would no doubt increase the humidity of inspired gas.

REFERENCES

1. Weeks DB, Broman KE: A method of quantitating humidity in anesthesia by temperature control. *Anesth Analg (Cleve)* 49:292-296, 1970
2. Chalon J, Ramanathan S: Water vaporizer heated by the reaction of neutralization by carbon dioxide. *ANESTHESIOLOGY* 41:400-404, 1974
3. Berry FA, Jr., Hughes-Davies DI: Methods of increasing the humidity and temperature of inspired gases in the infant circle. *ANESTHESIOLOGY* 37:456-462, 1972
4. Ramanathan S, Chalon J, Turndorf H: A compact, well humidified breathing circuit for the circle system. *ANESTHESIOLOGY* 44:238-242, 1976
5. Chalon J, Kao ZL, Dolorico VN, Atkin DH: Humidity output of the circle absorber system. *ANESTHESIOLOGY* 38:458-465, 1973

†† Dewey and Almy Chemical Division, W. R. Grace & Co., Cambridge, Massachusetts.

Anesthesiology
48:146-148, 1978

Anesthesia-induced Rhabdomyolysis in a Patient with Duchenne's Muscular Dystrophy

EDWARD D. MILLER, JR., M.D.,* DONALD B. SANDERS, M.D.,† JOHN C. ROWLINGSON, M.D.,‡
FREDERIC A. BERRY, JR., M.D.,§ MICHAEL D. SUSSMAN, M.D.,¶ ROBERT M. EPSTEIN, M.D.**

Tachycardia during general anesthesia is a non-specific response of the body to a variety of stimuli. Pain, hypercarbia, hypoxia and pyrexia are important differential diagnoses that must be considered when tachycardia occurs. We report a case in which a young child in whom severe tachycardia with multifocal premature ventricular contractions developed was subsequently found to have acidosis, hypercarbia, myoglobinuria, and markedly elevated creatinine phosphokinase, without an elevation in body temperature or evidence of increased heat production. Subsequent clinical investigation and muscle biopsy revealed that the patient had Duchenne's muscular dystrophy.

REPORT OF A CASE

A 4-year-old boy, an only child (20 kg), was scheduled for elective calcaneal osteotomy to repair "flat feet." Halothane anesthesia given without the use of succinylcholine for tonsillectomy at another hospital four months previously had been uneventful. The child was brought to the operating room without premedication. Rectal temperature prior to operation was reported to be 36 C. Induction of anesthesia by mask through a circle system with CO₂ absorber with halothane, N₂O and oxygen was accomplished without difficulty in this cooperative child. A #20 intravenous line was established. The heart rate was 120/min, with normal sinus rhythm. Succinylcholine, 20 mg, was administered. Rigidity was not seen, and ventilation was controlled briefly with 1.5 per cent halothane (Dräger Vapor vaporizer) and oxygen. Insertion of the laryngoscope resulted in a transient slowing of the heart rate to 70/min, and 0.1 mg atropine was given. The heart rate then returned to 120/min. The larynx was difficult to visualize but muscular relaxation seemed adequate. After two attempts at intubation, the succinylcholine effect had worn off, and the child breathed spontaneously. Heart rate was 120/min. A second dose of succinylcholine (20 mg) was administered after an additional 0.2 mg atropine, and a #5 orotracheal tube was inserted. The breath sounds were equal over each hemithorax.

The surgical preparation of the patient began approximately 20 minutes after induction of anesthesia. Manual ventilation with 50 per cent N₂O and 2 per cent halothane did not slow the pulse rate of 140/min. Oropharyngeal temperature was 36.6 C.

* Assistant Professor of Anesthesiology.

† Associate Professor of Neurology.

‡ Resident in Anesthesiology.

§ Professor of Anesthesiology and Pediatrics.

¶ Assistant Professor of Orthopedics.

** Professor of Anesthesiology.

Received from the University of Virginia Medical Center, Charlottesville, Virginia 22903. Accepted for publication August 9, 1977.

Address reprint requests to Dr. Miller.

Because of the persistent tachycardia (heart rate 150–160/min), blood gases were analyzed. Radial and femoral pulses, although palpable, diminished. Anesthesia was discontinued and 100 per cent O₂ administered. The EKG, which had shown sinus tachycardia, now evidenced heightened T waves and multifocal premature contractions. The systolic blood pressure (Doppler) was 50 torr. The heart rate increased to 160–180/min. Blood gases were reported to be P_{O₂} 63 torr, P_{CO₂} 57 torr, pH 7.15; base deficit, 9. Oropharyngeal temperature remained 36.6 C. Sodium bicarbonate, 20 mEq, and lidocaine, 20 mg, were given iv for rapid treatment of the multifocal premature contractions. A portable chest x-ray showed both lung fields well inflated, heart size normal, and the endotracheal tube 2 cm above the carina. Ten minutes after drug administration systolic pressure was 90 torr, heart rate 140/min, temperature 36.8 C orally, and analysis of arterial blood showed P_{O₂} 440 torr, P_{CO₂} 38 torr, pH 7.36; base deficit, 3. Dexamethasone, 2 mg was given iv. Thirty minutes after discontinuation of anesthesia, the patient showed signs of awakening. Respirations were adequate. The trachea was extubated and the patient taken to the recovery room. No surgical procedure had been performed. A total of 250 ml 5 per cent dextrose in lactated Ringer's solution had been given iv.

On arrival of the patient in the recovery room, systolic pressure was 90 torr, pulse rate 140/min, respiratory rate 32/min, and temperature 37.2 C rectally. The serum creatinine phosphokinase (CPK) concentration in a sample drawn two hours after the beginning of anesthesia was reported to be 77,600 international units (IU) (normal is less than 200). Isoenzyme studies were not done. Additional fluids and 7 g mannitol were given iv. Shortly after this, the patient voided brown urine, which tested 4⁺ for myoglobin. Serum K⁺ was 4.8 mEq/l, hematocrit 45 per cent, Ca⁺⁺ 8.6 mEq/l, and PO₄ 5.6 mEq/l at this time.

The patient was sent to the intensive care unit and monitored overnight. He showed no sign of elevated temperature. A repeat CPK value was 165,500 IU. The heart rate slowly declined over the night to 120 beats/min, and an EKG showed only an abnormal T vector. The urine became clear. The patient was discharged from the hospital two days later without other sequelae.

Creatine phosphokinase values in sera of the mother and father were found to be 176 and 100 IU, respectively. Thirteen days after anesthesia, the patient's CPK was 8,100 IU. The EKG again showed an abnormal T vector. Subsequently, the parents stated that the child had not walked until quite late, but that it had been believed that this was due to his "flat feet." He had also complained of muscle cramps when he ran with the other children.

Creatine phosphokinase determinations at monthly intervals showed persistent elevations, with values between 8,000 and 12,000 IU. Four months after the previous admission, the patient was readmitted for a diagnostic work-up of his muscle disorder. During that admission CPK was 10,000 IU. Electromyography was consistent with a myopathic process. A muscle biopsy of the left quadriceps muscle was done using triclofos sodium, 100 mg/kg, as a premedicant and 1.5 per cent procaine for infiltration. No untoward effect was seen. The muscle biopsy showed features diagnostic of Duchenne's muscular dystrophy.

A separate portion of the muscle biopsy specimen was sent to Dr. Frank Sreter at the Boston Biomedical Research Institute to examine halothane sensitivity and compare with biopsy specimens obtained from patients with known malignant hyperpyrexia. The two tests performed (calcium uptake of sectioned muscle and muscle contraction with halothane) gave normal results, suggesting that this was not an atypical case of malignant hyperpyrexia.

DISCUSSION

This case report emphasizes the need to find the cause of tachycardia during general anesthesia. Light anesthesia was our first concern, but the anesthesia vaporizer appeared to work normally and had done so during a previous operation that morning. Two per cent inspired halothane should produce adequate anesthesia for surgical skin preparation in a 4-year-old child. The intravenous doses of atropine given prior to the succinylcholine to this child did not seem excessive for his weight, and they did not cause tachycardia at the time they were given.¹

Hypoxia and hypercarbia may also cause tachycardia, but we felt we had hyperventilated the patient, and there was no evidence of mechanical difficulty with the endotracheal tube. The only abnormality readily apparent besides tachycardia was the severe metabolic acidosis. Once these more common causes of tachycardia had been ruled out, malignant hyperthermia was entertained as a diagnosis, but in the absence of temperature elevation, it seemed unlikely.

In order to help confirm this diagnosis, CPK levels and urinary myoglobin samples were obtained. These were both markedly abnormal, and repeat samples showed the same results. No intramuscular injection had been given, and succinylcholine reportedly does not cause such large elevations in CPK or the release of massive amounts of myoglobin.² This finding suggested for a while that a *forme fruste* of the malignant hyperthermia syndrome might have been responsible.

As more cases of malignant hyperthermia have been reported, a spectrum of manifestations has appeared.³ Carbello reports an aborted case of malignant hyperthermia that was diagnosed immediately after the injection of succinylcholine when the patient became rigid.⁴ Our case differs from Carbello's in two important respects: first, no muscle rigidity was seen with the succinylcholine, and second, the temperature never exceeded 37.3 C even though active cooling was not instituted. Furthermore, the muscle biopsy specimen tested for sensitivity to halothane (not N₂O or succinylcholine) gave a negative result. Whether

this case represents one end of the spectrum of the malignant hyperthermia syndrome cannot be defined at present, but it seems unlikely.

At the time of operation we did not know of the underlying muscle disease in this patient. However, anesthesia for the patient with muscular dystrophy has not been associated with significant problems. Cobham and Davis reported a series in which anesthesia was administered 100 times to 76 patients with various forms of muscular dystrophy; they found that when the general physical status of the patient was good there was a favorable response to anesthesia.⁵ In six patients receiving cyclopropane, tachycardia occurred but responded to decreasing the anesthetic concentration.

Cardiac dysfunction with Duchenne's muscular dystrophy is, however, not uncommon. Perloff and co-workers reported an abnormal electrocardiogram in 91 per cent of patients with Duchenne's muscular dystrophy.⁶ In the few patients undergoing cardiac catheterization, they found that the patients appeared unduly susceptible to cardiac arrhythmias with catheter manipulation; the arrhythmias ceased when the catheter was withdrawn. Boba,⁷ Wislicki,⁸ Berenbaum and Horowitz,⁹ and Kepes *et al.*¹⁰ have emphasized the importance of arrhythmias in patients with Duchenne's muscular dystrophy, but these few reports have discussed older children with the disease clinically present for some time and without myoglobinuria. What effect this patient's cardiac involvement had in the syndrome that occurred is unknown. However, this patient's disease represents the very early form of muscular dystrophy, and gross involvement of the heart at this stage is unlikely. Subsequent examination has revealed only the abnormal T vector. There is no evidence of congestive heart failure or persistent tachycardia.

The appearance of myoglobin in the urine signifies extensive muscle damage. Berenbaum and co-workers¹¹ have estimated that at least 200 g of muscle must be damaged to increase serum myoglobin high enough for myoglobin to appear in the urine. With such damage, there is a cellular release of potassium, protein, and other ionic substances, which may explain the arrhythmias, the acidosis, and relative hypoxia seen in our patient.

Myoglobinuria in patients with Duchenne's muscular dystrophy has not been reported.¹² However, Walton and Adams have suggested that any muscle disease, when sufficiently acute and sufficiently severe, could be followed by myoglobinuria.¹³ Perhaps our use of succinylcholine in this case was the stress needed to cause extensive rhabdomyolysis.

There have been two recent reports by Moore and co-workers¹⁴ and Schaer and co-workers¹⁵ of cases

in which myoglobinuria without temperature elevation occurred. In the case reported by Moore *et al.*, myoglobinuria was noticed four hours after anesthesia with halothane, N₂O, and succinylcholine, which had occurred without complication. The patient was subsequently found to have a subclinical myopathy characterized by elevated CPK. The report of Schaer *et al.* discusses a 9-year-old boy who had similar anesthesia and suffered two cardiac arrests intraoperatively. Subsequently, this patient was found to have paroxysmal myoglobinuria as a result of a clinically inapparent myopathy.

In summary, we report a case of acute rhabdomyolysis associated with severe cardiac arrhythmias in a child with unsuspected Duchenne's muscular dystrophy. Children undergoing corrective orthopedic surgery or other operations where muscle disease may be present are at risk to develop such problems. The possibility of underlying muscle disease in such patients should be carefully considered before the use of succinylcholine is assumed to be safe.

REFERENCES

1. Danchot P, Gravenstein JS: Effects of atropine on the electrocardiogram in different age groups. *Clin Pharmacol Ther* 12: 274-280, 1971
2. Innes RK, Stromme JH: Rise in serum creatinine phosphokinase associated with agents used in anaesthesia. *Br J Anaesth* 45:185-189, 1973
3. Bloom DA, Fonkalsrud EW, Reynold RC: Malignant hyperprexia during anesthesia in childhood. *J Pediatr Surg* 11: 185-190, 1976
4. Carballo A: Aborted malignant hyperthermia: Case report. *Can Anaesth Soc J* 22:227-231, 1975
5. Cobham IG, Davis HS: Anesthesia for muscle dystrophy patients. *Anesth Analg (Cleve)* 43:22-29, 1964
6. Perloff JK, de Leon AC, O'Doherty D: The cardiomyopathy of progressive muscular dystrophy. *Circulation* 33:625-648, 1966
7. Boba A: Fatal post-anesthetic complications in two muscular dystrophic patients. *J Pediatr Surg* 5:71-75, 1970
8. Wislicki L: Anesthesia and post-operative complications in progressive muscular dystrophy. *Anaesthesia* 17:482-487, 1962
9. Berenbaum A, Horowitz W: Heart involvement in progressive muscular dystrophy. *Am Heart J* 51:662-627, 1956
10. Kepes E, Martinez L, Andrews C: Anesthetic problems in hereditary muscular abnormalities. *NY State J Med* 1: 1051-1053, May 1972
11. Berenbaum M, Birch C, Moreland J: Paroxysmal myoglobinuria. *Lancet* 1:892-895, 1953
12. Rowland L, Penn A: Myoglobinuria. *Med Clin North Am* 56: 1233-1256, 1972
13. Walton J, Adams R: *Polymyositis*. Baltimore, Williams and Wilkins, 1958
14. Moore W, Watson R, Summary J: Massive myoglobinuria precipitated by halothane and succinylcholine in a member of a family with elevation of serum creatinine phosphokinase. *Anesth Analg (Cleve)* 55:680-682, 1976
15. Schaer H, Steinmann B, Jerusalem S, et al.: Rhabdomyolysis induced by anaesthesia with intra-operative cardiac arrest. *Br J Anaesth* 49:495-499, 1977