lar collapse at arterial concentrations between 21 and 34 mg/100 ml. Of the remaining four patients whose arterial blood halothane concentrations rose above 20 mg/100 ml, all had significant reductions in blood pressure. The highest arterial blood concentration without cardiovascular collapse was 28 mg/100 ml; this was associated with a 40 per cent decrease in systolic blood pressure.

The closed-system technique employing programmed injection of liquid halothane was found to produce a blood halothane concentration of 10–20 mg/100 ml, based on 59-kg body weight and a normal distribution of blood flow. With this technique, as well as with any technique employing halothane as the major agent, the patient's respiratory and cardiovascular responses are critical for evaluation of the appropriateness of the selected dose.

The case reported here had several interesting features. For one, although the patient had organic heart disease manifested by paroxysms of atrial tachycardia, with an electrocardiogram showing premature atrial contractions and digitalis effect, her only arrhythmia while under anesthesia occurred during induction, before a substantial blood concentration of halothane was achieved. Second, in spite of a sustained high concentration of halothane in the blood, blood pressure did not fall below 80 per cent of the previous day's value. Third, in the absence of atropine, the pulse rate did not fall below 60/min and, during most of the anesthetic course, remained between 90 and 110/min. Inspiratory effort, which was maximally assisted, was retained even at the patient's highest concentration of halothane in blood, the arterial Pa_{CO_2} never rising above 30 mm Hg. The only sign of circulatory instability was the facial flush which occurred when the halothane concentration rose above 32 mg/100 ml. Even in the presence of this flush there was brisk capillary filling.

In this case, the usual cardiovascular signs of depth of halothane anesthesia could not be relied upon. Furthermore, it has been demonstrated that one individual sustained a halothane blood concentration of 35 mg/100 ml without severe cardiovascular depression.

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Hyperthermia under Anesthesia with Regional Muscle Flaccidity

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The development of severe hyperpyrexia in patients under general anesthesia has recently been reported.[1, 2, 3] The etiology of the syndrome is still obscure, but it has been suggested that genetic factors may play a role,[4, 5] or that pathological biochemical mechanisms, such as the uncoupling of oxidative phosphorylation,[6, 7] may occur. Increased muscle tone with hyperpyrexia following the administration of succinylcholine has been a frequent finding.[8, 9, 10]

In a study undertaken to relate the degrees of muscle fasciculation and muscle pain after the administration of succinylcholine, as measured by an increase in muscle enzyme activity, there was a sevenfold increase in enzyme activity when halothane was used.[11] This enzyme, creatine kinase (creatine phosphokinase) is generally assumed to be elevated when muscle cells are injured. In conjunction with these biochemical findings the case reported here suggests that muscle enzyme function may be altered peripherally in susceptible patients by depolarizing muscle relaxants and/

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or general anesthetic agents. Heredity may be significant in determining the stability of the substrate.

Case Report

A 33-year-old woman was admitted for emergency repair of laceration of the tendons of the right forearm. Preoperative temperature was 98.4 F, pulse rate 82 beats/min, respiration 22, packed cell volume 34, and blood pressure 115/80 mm Hg. Physical examination was noncontributory, except for the injury to the patient's arm. Demerol, 25 mg, Vistaril, 50 mg, and atropine, 0.4 mg, were given intravenously in the operating room for premedication, following which the pulse rate rose to 120 beats/min and the blood pressure to 130/78 mm Hg. Thiopental, 175 mg, was given at 6:15 AM for induction, which was smooth and rapid. Succinylcholine, 60 mg, was given intravenously at 6:20 AM to facilitate intubation. Sustained contracture of the jaw which did not allow adequate exposure for intubation developed. Another 40 mg was given intravenously without any evidence of muscle relaxation. Marked muscular fasiculation followed the first injection of succinylcholine, but not the second.

Anesthesia was maintained with nitrous-oxide–halothane. The airway was maintained satisfactorily with an oral pharyngeal airway. A tourniquet was applied to the right upper extremity at 6:30 AM and maintained at 275 mm Hg. At 7:30 AM the patient's face felt hot. The rectal temperature was 38.5 C. At this time the pulse rate was 140 beats/min and the blood pressure had risen to 140/70 mm Hg. Cooling measures were instituted. By 7:45 AM the rectal temperature was 39 C, the blood pressure and pulse remaining unchanged. Anesthesia was discontinued, and 100 per cent oxygen was given by controlled ventilation. The surgeons were asked to close as rapidly as possible. The patient's entire body was rigid except distal to the tourniquet, in which pressure was still maintained. Complete flacidity of the fingers, hand, wrist and elbow was present. At 7:50 AM the rectal temperature was 39.5 C, an oral endotracheal tube was inserted without using succinylcholine, an EKG monitor was applied, and the patient was completely immersed in an ice bath without anesthesia. At 7:55 AM the rectal temperature was 40 C. The tourniquet had been released immediately before body immersion and the surgeons again commented on the absolute flaccidity of the muscles distal to the tourniquet while all other muscles were rigid. Despite the ice the patient's temperature continued to rise, and at 8:10 AM short clonic convulsive episodes occurred. Intravenous fluids were given more rapidly and urinary output was measured at 40 ml/hr through the urethral catheter. The pulse rate rose to 150 beats/min, systolic blood pressure fell to 70 mm Hg. A 5 per cent sodium bicarbonate infusion was begun and sodium bicarbonate, 7.5 gm, was given rapidly intravenously. A decrease in compliance was noted during manual compression of the reservoir bag, and increased positive pressure was required for ventilation. The temperature continued to rise; at 8:30 AM it was 42 C. Pulse and blood pressure were not obtainable. The lungs developed rales and frequent suctioning was required. Isuprel drip was started, another 7.5 gm of sodium bicarbonate given, and administration of a second 500 ml of 5 per cent sodium bicarbonate begun. At 8:50 AM the electrocardiogram showed no cardiac function. Closed-chest compression was instituted, with prompt success. Aramine drip replaced the Isuprel. At 9:05 AM a percutaneous pacemaker was placed, and Solumedral, 250 mg, was given intravenously. A nasogastric tube was inserted and grossly bloody fluid returned, which continued until the patient's death. Throughout this entire episode, the right upper extremity which had been distal to the tourniquet remained flaccid. However, the right shoulder, which was proximal to the tourniquet, did show resistance to motion. The temperature did not rise further, and at 9:30 AM it dropped to 41.5 C. From this point on the pacemaker required progressive increases in milliamperage to maintain myocardial pacing. The temperature continued to fall. At 9:45 AM it was 40.5 C, but at this time pupillary dilatation was noted. At 10:00 AM the temperature was 40 C, and at 10:05 AM the pacemaker was no longer effective.

During the course of resuscitation, blood was drawn for study. The following data obtained: serum glucose 300 mg/100 ml; BUN 15 mg/100 ml; potassium 7 mEq/l; sodium 192 mEq/l; carbon dioxide (bicarbonate) 41 mEq/l; venous pH 7.23; base excess +15; P_{CO_2} in excess of 50 mm Hg; PBI 3.5 μg/100 ml. Urinary 5-hydroxy-indolacetic acid was 4.9 mg/l. An autopsy was performed, but the only significant findings were severe pulmonary congestion and edema and gastrointestinal hemorrhage.

Comment

An apparently-healthy young adult under general anesthesia developed sudden, fulminating hyperpyrexia, preceded by an atypical response to succinylcholine, and died. The exact etiology of the hyperpyrexia remains obscure. The unusual aspect of this case was the persistent flaccidity distal to the surgical tourniquet while all other muscle groups had increased tone. That circulation to this area was interrupted by the tourniquet suggests that basic muscle metabolic processes may be altered peripherally by 1) circulating halogen concentrations affecting muscle metabolism, or 2) the modification of depolarizing muscle re-

laxants by circulating halogen concentrations in susceptible patients.

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Surgery

CARBON MONOXIDE Severe carbon monoxide poisoning can produce several types of lesions of the skin. The lesions vary in degree from areas of erythema and edema to marked blister and bulla formation. These lesions can easily be mistaken for burns or trauma. The bullous lesions heal by eschar formation. The scalp lesions of edema and erythema evolve into areas of alopecia. (*Long, P. I.: Dermal Changes Associated with Carbon Monoxide Intoxication, J.A.M.A. 205: 50 (July) 1968.*)

HEPATIC DISEASE Metabolic deficiencies in hepatic failure are reflected in hypoalbuminemia, clotting aberrations, vitamin depletion, inability to oxidase glucose and fat, intolerance to opiates and anesthetics, antidiuresis, sodium retention, abnormal immune responses, and abnormal metabolism of proteins, endocrines, bile pigments and ammonia. Prognosis for survival in cirrhotics cannot be predicted from available clinical and laboratory data. Most anesthetic drugs are protoplasmic poisons and either affect hepatic function or must be excreted by the liver. Narcotics, especially morphine, thiopental, and succinylcholine, should be avoided or used in minimal doses. Pre-existing hepatic disease increases the chances of postoperative hepatic complications more than 500-fold. Choice of anesthesia is minimal doses of thiopental and meperidine with nitrous oxide and tubocurarine or gallamine for muscle relaxation. (*Jackson, F. C., and others: Preoperative Management of Patients with Liver Disease, Surg. Clin. N. Amer. 48: 907 (Aug.) 1968.*)