Clinic Workshop

would have run the risk of receiving the medication on another occasion. This case stresses the importance of thorough investigation and complete genotypic classification of an individual who has experienced apnea or prolonged muscular paralysis associated with administration of succinylcholine. Correct information regarding succinylcholine-sensitive individuals and subsequent family follow-up studies warrant this expense in order to preclude further exposure and risk to the patient or to other susceptible family members.

The authors gratefully acknowledge the technical assistance of Mrs. Patricia Ford and the assistance of Mrs. Kristy Stone in preparation of the report.

References


Drug-induced Heat Stroke

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Malignant hyperthermia is not the only thermoregulatory disorder which may require the attention of the anesthetist. Drug-induced "heat stroke" is not uncommon, and its treatment may necessitate emergency airway management and intensive care. Awareness of this cause of heat stroke is necessary for proper management. Two patients recently admitted to San Francisco General Hospital during

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Received from the Department of Anesthesia, University of California, San Francisco, California 94122. Accepted for publication January 17, 1973.

"heat spells" in which ambient temperatures exceeded 90°F illustrate the problems in treatment.

Report of Two Cases

Patient 1. A 48-year-old Negro man was brought to the emergency room after having collapsed on the street. He was deeply comatose, and no history was immediately available. His skin was hot and dry. Physical examination of the chest disclosed no abnormality, and there were no focal neurologic signs. The blood pressure was 180/120 torr, pulse 120/min, and respirations 50/min. Rectal and axillary temperatures were above 108°F. Ventilation was 60 l/min. Arterial blood gas values with the patient breathing
oxygen were \( P_{\text{ao}} > 200 \) torr, \( P_{\text{aco}} \), 64 torr, and 
\( pH \), 7.02 (values corrected to 108 F).

Treatment consisted of intubation of the trachea and administration of oxygen. The patient’s body was covered with wet towels, over which ice water was continually poured. During cooling he vomited a massive amount of recently ingested food. Rectal temperature was continuously monitored, and when it reached 101 F the towels were removed. Serum electrolyte values were normal.

The patient awakened 12 hours after admission, at which time the temperature was 99 F, and he was able to report that he had been taking chlorpromazine, 1 g, and benztropine mesylate (Cogentin), 6 mg, daily, for treatment of a mental disorder. He did not report experiencing any prodomata prior to losing consciousness. He made an uneventful recovery and was discharged from the hospital after two days after admission.

**Patient 2.** A 33-year-old Caucasian man was admitted after being found unconscious in a hotel room. Again, there was no immediate history. Like the first patient, he had hot, dry skin, rapid, deep respiration, and normal lungs. He was unresponsive to painful stimuli. His treatment was similar to that of the first patient. Although the rectal temperature decreased from more than 108 F to normal in two hours, coma persisted. Ten days later, without regaining consciousness, the patient died from multiple causes, including circulatory insufficiency, pneumonia, respiratory failure, and thrombosis of the superior sagittal sinus. He, too, had been taking chlorpromazine, 1 g, and Cogentin, 6 mg, daily, as prescribed by a local outpatient mental health facility.

**DISCUSSION**

Reports such as these are not rare. Every “heat wave” precipitates a number of such cases, some of which are fatal. That atropine and atropine-like compounds and phenothiazines may disturb thermal homeostasis was recognized more than 20 years ago. Despite this, most reports of heat stroke fail to report the patients’ drug histories. It is therefore impossible to estimate the number of cases induced orabetted by drugs, but it is probably larger than appreciated. Four of the last five patients admitted to the emergency room of San Francisco General Hospital with temperatures exceeding 106 F had histories of taking phenothiazine and atropine-like drugs.

Although it is widely appreciated that the phenothiazines may interfere with temperature regulation, the effect is generally thought to be to decrease body temperature. While this is true when ambient temperatures are low, core temperature will increase at high ambient temperatures. It has been shown that “chlorpromazine abolishes all mechanisms of temperature regulation for both heat and cold.” This is also true of the other commonly used phenothiazines, the magnitudes of thermal disruption roughly paralleling tranquilizing potency. Mepazine, now seldom used, has a profound effect on temperature regulation when used in high doses, and was associated with heat stroke epidemics and fatalities. The main mechanism is thought to be inhibition or depression of the thermoregulatory center of the anterior hypothalamus.

When large doses of phenothiazines are prescribed, an atropine-like agent such as benztrapine mesylate is frequently added to prevent extrapyramidal side-effects. Anticholinergic agents disturb temperature regulation as well by inhibiting sweating. Combining the anticholinergic depression of a peripheral thermoregulatory mechanism with the central disruption of hypothalamic thermal responsiveness by a phenothiazine sets the stage for inability to adjust to high ambient temperatures.

Emergency medical care for heat stroke includes support of ventilation and circulation, prevention of aspiration, and restoration of body temperature to normal. Because affected patients may be comatose, vomiting and aspiration are major concerns and necessitate intubation of the trachea with a cuffed tube. Use of supplemental oxygen is rational, because oxygen consumption is high.

The need for intravenous fluids depends upon the cause of the hyperthermia. In classic heat stroke with dehydration and secondary failure of the sweating mechanism, fluid replacement is vital to successful treatment. Since patients on phenothiazines and anticholinergics do not sweat, they are not usually dehydrated. Neither patient reported here required more than maintenance fluids to maintain urinary output and fluid and electrolyte balance.

Acidosis may be severe and must be corrected. The first patient in our report had a base deficit of \(-21\) mEq/L, which spontaneously reverted to normal as he was cooled. The second patient was similarly acidic and did need bicarbonate therapy and controlled ventilation to restore acid-base status to normal. However, before selecting a plan of
management that involves controlled ventilation, the anesthetist must be certain that a ventilator capable of delivering the high minute ventilations that this situation necessitates is available.

Basic to treatment, of course, is reduction of core temperature. Favorite methods for cooling rapidly vary from immersion in ice water to alcohol sponging, but the primary goal is to maintain a substance of low temperature and high specific heat next to the skin. Ice-water lavage of the stomach through a nasogastric tube has been used. Feed intravenous solutions have been advocated for malignant hyperthermia during anesthesia, but are seldom available in the emergency ward setting. Immersion of the patient in ice water and constant irrigation of the skin with towels soaked in ice water are the most convenient available methods for rapid cooling. Constant, accurate monitoring of the temperature is vital, and the site of the monitor must be free from local effects of the cooling solution. A well-placed nasopharyngeal thermometer or tympanic membrane probe is dependable; these two approaches probably give the best reflections of brain temperature. Salicylates and steroids may be helpful in the treatment of drug-induced hyperthermia, but their specific value is undocumented.

A variety of other complications can occur during recovery, particularly when hyperthermia has been present for some time before treatment. Convulsions, clotting disorders, renal failure, hepatic failure, and high-output cardiac failure can all occur. They are discussed at length by several authors.10, 12-16

With widespread use of drugs which impair thermoregulatory capability, it is important that this cause of hyperthermia be considered when such patients are seen in the emergency ward, particularly during periods of high environmental temperatures. These patients must be given intensive care, usually without the benefit of an accurate history. Under such circumstances, treatment will usually include maintaining an adequate, protected airway, administering a high inspired concentration of oxygen, restoring acid-base status, rapid cooling, and avoidance of excessive fluid administration.

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