Correspondence

Complications of Ketamine

To the Editor:—After a year's experience with ketamine hydrochloride, it seems timely, for the purpose of documentation, to add our department to what is probably a growing group of dissenters to the original claims made for the drug. For ease of administration and analgesic properties, there is no question of its excellence. We can now document, however, a number of complications from which ketamine hydrochloride was claimed to be free.

In the approximate order of their occurrence, we have encountered severe laryngospasm and respiratory arrest in neonates. Hypoxic cardiac arrest secondary to respiratory depression has been observed in a debilitated adult. Severe airway obstruction has occurred in a child under ketamine anesthesia and, most recently, vomiting with aspiration occurred in an infant with a full stomach. In addition, we have observed a hysterical postanesthetic reaction in a child following ketamine. We have noted increased tolerance to its effects in alcoholics and in a number of patients who received several ketamine anesthetics.

Our current recommendation would be that the candidate for ketamine anesthesia be as carefully selected and prepared as any other patient for general anesthesia.

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State of Contracture in Malignant Hyperthermia

To the Editor:—The case report, "Malignant Hyperthermia Associated with Hypocalcemia," by Pollock and Watson (ANESTHESIOLOGY 34: 188, 1971) presented an excellent theoretical discussion of the roles of the cyclic AMP system and psychotropic drugs in producing hyperthermia, but did not mention the possible *role of succinylcholine in initiating* the chain of events. Their patient was probably in a state of muscle contracture after incomplete relaxation with succinylcholine. The term "contracture" signifies mechanical shortening of muscle maintained without muscle action potential and independent of transmission at the neuromuscular junction.

The prolonged relaxation phase that some patients have in the contraction–relaxation cycle of striated muscle deserves mention in any discussion of the etiology of malignant hyperthermia. Some patients with slow relaxation develop progressive muscle stiffness with exercise, leading to a state of contracture.[1] There are metabolic diseases with specific enzyme defects, such as McArdle's disease (muscle phosphorylase deficiency)[2] and phosphofructokinase deficiency,[3] in which exercise-induced contractures occur. According to current concepts, in order for a skeletal muscle to relax, the sarcoplasmic reticulum must actively reaccumulate calcium ions from the aqueous sarcoplasm, thereby depriving the myofibrils of the calcium necessary for contraction.[4, 5] It takes energy in the form of ATP and enzymatic activity to relax a contracted muscle —it is not a passive process. The term "relaxing factor" is used to refer to the ability of the sarcoplasmic reticulum to accumulate calcium. The activity of relaxing factor can be measured, and a patient with a normal contraction phase but a slow relaxation phase and

muscle contractures induced by exercise has been reported.[1] This patient had a demonstrable selective defect of microsomal uptake of calcium (25 per cent of normal).

Abnormalities of relaxing factor along with other intracellular degenerative changes have been reported in muscular dystrophy,[6, 7] myotonic dystrophy,[7] myositis,[6] neurogenic atrophy,[6] and experimental denervation.[8] Aching muscle cramps and myoglobinuria due to exercise or fasting have been associated with a possible defect of lipid metabolism.[9] These two patients had a selective defect in the metabolism of long-chain free fatty acids. Even at rest, fatty-acid oxidation provides more than 50 per cent of the energy requirement of skeletal muscle. We suggest that patients with a slow muscle relaxation phase and subsequent muscle cramps or contractures may be very susceptible to the muscular activity induced by succinylcholine, or even the increased muscle tone seen in light anesthesia. The prominence of young muscular patients, musculoskeletal disorders, and muscle symptoms among reports of malignant hyperthermia tends to support this concept. Malignant hyperthermia is probably a metabolic disorder, but the metabolic diseases mentioned here with selective enzyme defects in fat and carbohydrate metabolism and in the muscle relaxation phase have received little consideration. We propose that the above metabolic disorders involving muscle may be a reasonable prototype defining some of the patients susceptible to malignant hyperthermia.

Orndahl and Stenberg[10] have reported that patients with myotonia are less sensitive to the stimulating action of depolarizing muscle relaxants when gallamine or *d*-tubocurarine is given before succinylcholine. The dangers of giving *d*-tubocurarine before succinylcholine to modify the stimulating action are minuscule, and administering it to all patients might be good practice.

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To the Editor:—Patients susceptible to development of malignant hyperthermia appear to have a disorder of muscle: a few patients complain of muscle cramps[1] of the lower extremities; other susceptible individuals have clinical evidence of latent myopathy[2]; many suffer muscle rigidity during reaction to anesthesia[1]; and still others have been found to have altered serum calcium levels. These findings have led numerous investigators to suspect defective function of the sarcoplasmic reticulum.

Preliminary studies of calcium uptake and binding in a small number of Landrace and Poland China pigs[3, 4] and an even smaller number of susceptible humans[5] suggest that calcium accumulation by sarcoplasmic reticulum may be abnormally low. Expanded studies are under way at several centers. The role played by this apparent disturbance of calcium balance remains to be elucidated.

Hoech and Jones suggest that other myopathies may be prototypes of the disorder in