(3-4 h) than following intravenous administration (1-2
h). Increasing the dose of sufentanil by either route did
not significantly prolong analgesia, and is not recom-
mended because of the possibility of respiratory depres-
sion secondary to higher plasma concentrations. Al-
though epidural sufentanil has a relatively short dura-
tion of effect, its rapid onset makes it an ideal agent for
supplementing epidural local anesthetic analgesia (for
example, during exteriorization of the uterus during
cesarean section), or for initiating analgesia in patients
experiencing acute postoperative pain prior to adminis-
tration of a longer-acting narcotic. Our preliminary
data would suggest that epidural sufentanil, 30 μg, pro-
vides adequate postoperative analgesia with minimal
narcotic-induced side effects.

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Repeated Anesthesia for a Patient With Neuroleptic Malignant Syndrome

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Since Delay and Deniker first described the neuro-
leptic malignant syndrome (NMS) in the English lan-
guage as a potential complication of using neuroleptics,[1]
approximately 300 cases have been reported.[2,3] Signs of
NMS, which appear over a 24–72-h period, include
muscular rigidity, hyperthermia, altered level of con-
sciousness, and autonomic instability (manifested as
tachycardia, labile blood pressure, diaphoresis, and in-
continence). The syndrome occurs hours to months
after known exposure to neuroleptics, such as haloperi-
dol, fluphenazine, and thiothixene. It has been said that
NMS is underdiagnosed and that the frequency is as

high as 1.4% among patients exposed to neuroleptics.[4] Laboratory tests are usually helpful only for excluding other possible etiologies. Leukocytosis, rhabdomyolysis, and elevated CPK may be present. Treatment includes prompt recognition of the syndrome, discontinuing neuroleptics, and supportive measures. Dantrolene, bromocriptine, amantadine, anticholinergic agents, and electroconvulsive therapy have been used to treat several patients. Possible secondary complications of NMS include rhabdomyolysis, acute renal failure, respiratory failure, coma, and shock. The mortality rate is approximately 15%.[3]

NMS has many similarities to anesthetic induced malignant hyperthermia (MH). Because of this, several authors have suggested that known triggering agents of MH be avoided when anesthetizing a patient with NMS.[5,6]

We recently anesthetized a patient with NMS eight times for electroconvulsive therapy, using a technique which included succinylcholine, and MH did not result.

CASE REPORT

The patient was a 41-yr-old male. Eight months before admission to our hospital, he was briefly admitted to another hospital for pneumonia, which resolved with erythromycin therapy. Thioridazine was prescribed for agitation. At the time, a CT scan of the head and electroencephalogram were normal. His past psychiatric history was remarkable for two hospitalizations for acute psychosis, which were treated with various antipsychotic drugs.

One month before admission to our hospital, he was admitted to a nursing home for lethargy. At this time he was receiving haloperidol (9 mg daily), desipramine (150 mg daily), benztropine (2 mg daily), and lorazepam (2 mg daily). He was mute and unresponsive to verbal stimulation, but would grimace in response to pain. His neurologic examination was otherwise unremarkable. All medications were discontinued except lorazepam. Over the next 5 days, he became increasingly rigid. The rigidity was diffuse, but most apparent in the upper extremities. His baseline temperature climbed to 38° C. He developed persistent hypertension (150/100 mmHg), tachypnea (25 bpm), and tachycardia (120–150 bpm). Laboratory studies revealed no source of infection. His WBC was 10,800/mm³ and CPK was 523 U/1. Medical therapy for NMS was begun, including recommended doses of dantrolene (50 mg po q 6 h for 5 days) and bromocriptine (2.5 mg po bid for 13 days).[3] Despite treatment, there was little improvement in his condition over the next 2 weeks. He was transferred to our hospital for further evaluation.

On admission, a review of the patient's history revealed he had no allergies, his family history was negative for malignant hyperthermia or neuromuscular disorders, and he had received no previous anesthetics. He was receiving bromocriptine, but not dantrolene.

On physical examination, the patient was febrile (37.4° C), agitated, diaphoretic, and obtunded to the point he could only answer "yeah" to all questions. Muscle tone was diffusely increased, and he had to be physically restrained. Deep tendon reflexes were symmetric and brisk. Plantar responses were downgoing.

Chest and cervical spine radiographs, and serum electrolytes were normal. An EKG revealed a sinus tachycardia. His hematocrit was 39% and CPK was 113 U/1.

NMS was diagnosed because he clearly met published criteria for the disorder.[3] That is, he demonstrated three of the major manifestations

TABLE 1. Creatine Phosphokinase (CPK) Levels Before and After Electroconvulsive Therapy (ECT)

Day before ECT	113	U/1
5 min before ECT	205	U/1
5 min after ECT	209	U/1
40 min after ECT	192	U/1
75 min after ECT	203	U/1
5 h after ECT	159	U/1
11 h after ECT	185	U/1

Normal 1–90 U/1.

(rigidity, fever, and elevated CPK) plus six of the minor manifestations (tachycardia, abnormal blood pressure, diaphoresis, tachypnea, and altered consciousness). The onset of these signs and symptoms was temporally related to the use of neuroleptics and there was no other organic etiology to explain the syndrome.

The first and all subsequent ECT treatments were given in the recovery room with equipment and drugs to treat malignant hyperthermia immediately available. An EKG, oscillometric blood pressure cuff, precordial stethoscope, and rectal temperature probe were applied. Catheters were inserted into a vein and the radial artery. End-tidal CO_2 was not measured, because there was access to serial blood gas determinations, the anesthetic was to be brief, and the exhaled-arterial CO_2 gradient can be quite large during mask anesthesia. A second blood pressure cuff was applied and inflated prior to administration of a muscle relaxant. Because of the patient's severe rigidity and lack of cooperation, thiopental (75 mg) was given for sedation during application of monitors. Induction of anesthesia was accomplished with metocurine (2 mg), thiopental (350 mg), and succinylcholine (60 mg), intravenously. The patient was ventilated by face mask with oxygen. A brief electrical pulse stimulus was administered bilaterally to the brain with a frequency of 70 Hz, pulse width of 1.5 msec, and duration of 2.0 s. There was a 40-s motor seizure observed in an upper extremity and a 100-s seizure on the EEG. Spontaneous respirations resumed 5 min after induction of anesthesia, and the patient was awake and quiet in 40 min. There was a slight increase in arterial blood pressure with the shock which returned to baseline after 5 min. There was no change in body temperature, arterial blood gases, or serum potassium during or following ECT. At no time was there evidence of a metabolic acidosis. CPK values were essentially unchanged at 5, 40, and 75 min, and at 5 and 11 h after ECT when compared to pre-shock values (table 1).

The patient received ECT on seven subsequent occasions over the following 2½ weeks. Thiopental and succinylcholine were administered for each treatment without complications. Invasive monitoring was not employed, because of the lack of problems during the first treatment. The patient was discharged 3 weeks after admission with normal vital signs, and improved speech and motor abilities.

DISCUSSION

The etiology of NMS is unknown. Because there have been no consistent findings on cranial CTs, EEGs, CSF fluid assays, or autopsies, a molecular mechanism must be considered.[3]

Dopaminergic hypoactivity has been implicated in the pathogenesis of NMS.[7] Dopamine has been established as a central neurotransmitter affecting thermoregulation in the preoptic region of the hypothalamus. Intraventricular injections of dopamine or dopamine agonists generate changes of core body temperature in sev-

eral species. These temperature changes can be blocked by pre-treatment with neuroleptics.[8] Presumably, this occurs by dopamine receptor blockade which leads to altered thermoregulation and impaired heat dissipation. When combined with heat generation from rigid muscle contractions, an effect of neuroleptics on the basal ganglia, body temperature rises.[9] NMS has also occurred in patients withdrawing from anti-Parkinsonian medication,[10] and in a patient with Huntington's chorea taking alpha-methyltyrosine and tetrabenazine.[11]

No completely effective therapy for NMS has been found. Bromocriptine, a dopamine agonist, has been used to treat several patients with NMS, but there are occasional failures. Dantrolene has also been recommended.[2,3] In one instance, a patient's fever and rhabdomyolysis resolved after treatment with dantrolene, but his tremor, rigidity, and obtundation did not improve until treatment with bromocriptine was started.[12] Finally, ECT has been reasonably effective when supportive measures or drug therapy has failed.[13-17]

Because NMS is associated with rigidity, fever, diaphoresis, and hypermetabolism, NMS may be related to MH. However, MH is a genetically transmitted disease of muscle associated with an abnormality of excitation-contraction coupling and an abnormal calcium concentration in the myoplasm. Susceptibility to malignant hyperthermia is diagnosed by an elevated contracture tension of muscle exposed to halothane or caffeine *in vitro*. Muscle biopsy specimens from several patients with a diagnosis of NMS have exhibited an abnormal response to halothane, and these patients have been termed MH-susceptible.[18,19] Because of this finding it has been suggested that management protocols for MH (including the avoidance of known triggering agents) be used when anesthetizing patients with, or recovered from, NMS.[18] However, similar biopsy studies done on other patients with NMS have not yielded the same result,[20,21] and no case report of MH in a patient with NMS has appeared in the literature.

There are multiple reports of patients with NMS who have been treated with ECT.[13-17,22] In several instances, the type of anesthesia was not described. Complications were described in a few cases, but none could be directly attributed to an episode of MH. Including our case and those where it was clearly documented, there are now at least 16 patients who have received succinylcholine for multiple ECT treatments.[13,15,22] In only one instance was there a complication.[15] A patient sustained a cardiac arrest during the fifth of a series of ECT treatments. She was given three successive stimuli after thiopental and succinylcholine, and was quickly resuscitated after a period of asystole. The patient had no signs or symptoms of MH, there were no neurologic residua, and the patient subsequently underwent an enflurane general anesthetic and six ECT treatments, each with succinylcholine, and no cardiac problems or episodes of MH were apparent.

If NMS and MH have a similar clinical presentation and a few patients with NMS have *in vitro* evidence of MH susceptibility, then why does succinylcholine appear to be safe for patients undergoing ECT? First, the procedure is brief, and a single injection of succinylcholine may not be sufficient to trigger a clinically apparent MH response. In fact, animal data suggest that a single dose of succinylcholine is a weak trigger, particularly in the absence of a volatile anesthetic and in conjunction with the delaying action of thiopental.[23] Second, the two syndromes may have an entirely different etiology. NMS appears to be related to a metabolic derangement in the central nervous system, and MH is probably due to a defect in skeletal muscle metabolism. Third, pretreatment with dantrolene may be a prophylactic measure, although our patient did not receive any in the week preceding ECT. And fourth, both NMS and MH are heterogeneous syndromes without a definitive diagnostic test. While MH susceptibility can be diagnosed by muscle contracture responses to halothane or caffeine, the application of such testing to NMS may be suspect. Clinical experience suggests that "weak" MH triggers will not produce MH in patients with NMS. There is insufficient evidence to predict the response of NMS patients to "strong" triggers (such as halothane), but we suspect that MH susceptibility does not exist in NMS.

It would be an acceptable practice to avoid succinylcholine for ECT, as recommended by some authors, but to do so would unnecessarily complicate the procedure. A relatively long-acting non-depolarizing muscle relaxant must be used, and the patient kept anesthetized with more barbiturates, or an inhalation anesthetic, until the relaxant is reversed.

A recent report described a patient with NMS who developed hyperkalemia in response to succinylcholine.[24] Anesthesiologists must be alert for this complication. Though the data are limited, our case supports the conclusion of others[13,22,25] that the use of succinylcholine for ECT for patients with NMS is not associated with the development of MH.

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The Treatment of Reflex Sympathetic Dystrophy with Intravenous Regional Bretylium

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Reflex sympathetic dystrophy is a disorder characterized by chronic, refractory, severe pain, usually in a previously injured extremity.[1] The mechanism for the signs and symptoms of reflex sympathetic dystrophy is thought to be an abnormal reflex mediated by the sympathetic nervous system.[1,2] The exact pathogenesis remains obscure, but probably involves a self-sustaining reflex among sympathetic afferents, sympathetic efferents, and, possibly, sensory afferents, allowing for direct cross stimulation and pain-cycle formation.

In 1974, Hannington-Kiff reported the use of intravenous regional guanethidine for the treatment of causalgia.[3] Since then, there have been numerous clinical reports describing intravenous sympathetic blockade with guanethidine or reserpine for a number of syndromes in which sympathetic tone is implicated in the disease process.[4–9] These reports have demonstrated beneficial results, at least short term, for most of the patients studied. The beneficial response is attributed to a prolonged sympatholysis with the intravenous regional technique. Unfortunately, guanethidine is not available for intravenous use in the United States. Our experience, and that of others,[10] with intravenous regional reserpine has been less than satisfactory, since patients frequently experience undesirable side effects, including diarrhea, syncope, and prolonged depression.

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