with the majority of these patients appearing asymptomatic. Symptomatic hypotension in these patients resolved either during the infusion or within 30 min after its discontinuation.

Although a number of reports have noted the usefulness of esmolol in the treatment of supraventricular tachycardias, information specifically addressing its dose and therapeutic responses in the treatment of MAT are lacking.

In this report, MAT converted to sinus rhythm within 15 min after the initiation of esmolol infusion. The dosage at which conversion occurred was 50 \(\mu g/kg/min\). This was below the therapeutic dosage used for supraventricular tachycardias (97 to 115 \(\mu g/kg/min\)). Dose response, however, has been reported to range from 50 to 300 \(\mu g/kg/min\). The ease of titration of esmolol allowed for adequate antiarrhythmic effect without significant adverse side effects.

**References**


**Fatal Hyperthermia in a Quadriplegic Man**

**Possible Evidence for a Peripheral Action of Haloperidol in Neuroleptic Malignant Syndrome**

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A patient with a cervical cord transection isolating his hypothalamic thermoregulatory centers from peripheral effectors suffered a fatal hyperthermic episode after receiving haloperidol. This suggests that neuroleptic malignant syndrome is caused by a peripheral, not central, effect of haloperidol.

(Chest 1992; 101:1728-30)

NMS = neuroleptic malignant syndrome

There is debate whether neuroleptic malignant syndrome (NMS) is due to a central hypothalamic3-4 or peripheral muscular action5-7 of haloperidol. We encountered a patient with a complete cervical spinal cord transection and thus isolation of his central hypothalamic thermoregulators from his peripheral thermal effectors; nevertheless, this patient suffered a fatal hyperthermic episode following the administration of haloperidol. This implies that NMS is due to a peripheral and not central nervous system effect of haloperidol.

**Case Report**

A 30-year-old previously healthy man was brought to the Columbia-Presbyterian Medical Center emergency room after a single gunshot wound passed through his hand, entering his neck in the anterior midline. Physical examination revealed flaccid paralysis of all extremities. Cervical spine roentgenograms revealed disruption of the trachea and the seventh cervical vertebra with the bullet lying posterior to the vertebral column. During intubation with a stabilized neck and fiberoptic bronchoscopy, the patient suffered cardiac arrest. Reintubation through a criothyrotomy incision and the administration of epinephrine and atropine resulted in successful resuscitation. A chest tube was placed for treatment of a right pneumothorax.

Subsequent neurologic examination revealed the patient to be alert and responding appropriately to questions and commands with movements of his head. He demonstrated 3/5 strength of the right triceps and right and left deltoids but flaccid paralysis below this level. He had a sensory level consistent with a C-6 cord transection.

There was no personal or family history suggestive of muscular disorders, episodes of hyperthermia, or complications following anesthetics. The patient had not been receiving any medications, and illicit drug use was denied. He had no evident congenital anomalies.

Surgical debridement of the bullet tract, repair of the anterior cricoid ring, and creation of a pharyngostoma was performed. Anesthesia was obtained with Fentanyl, vecuronium, diazepam (Valium), nitrous oxide, and phenoxyphrine (Neo-Synephrine) hy-
The patient's temperature was less than 35.5°C throughout the operation. A CAT scan confirmed that the bullet had traversed the spinal canal at the level of the seventh cervical vertebra. The patient's postoperative medications consisted of methylprednisolone (until postoperative day 2), ranitidine, cefazolin, midazolam, morphine, and nystatin.

Despite a change in the patient's antibiotics to a ticarcillin-clavulanate combination, he was persistently febrile, with maximal rectal temperatures each postoperative day as follows: 38.9°C on day 1; 38.7°C on day 2; 38.9°C on day 3; and 39.6°C on day 4. Ambient temperature was 20°-22°C throughout. On the fifth postoperative day, the patient's temperature was recorded as 41.2°C (the maximal possible on a glass rectal thermometer and, therefore, representing only a lower limit to his actual temperature); there were no hemodynamic or mental status changes associated with this fever spike. A repeat CAT scan of the neck, local exploration of his wounds, and cultures of blood, urine, and sputum were unrevealing, except for an elevation of his white blood cell count of 18,000/μm³.

The patient had been lucid and coherent, but became progressively more agitated and depressed. During the fifth postoperative day, he received a single dose of haloperidol (3 mg IM). During the next 12 h, he became more lethargic, and again, a rectal temperature of 41.2°C was recorded. Simultaneously, the patient became hemodynamically unstable, with a systolic pressure of 70 mm Hg, pulse rate of 140 to 165 beats per minute, and a cardiac output of 16.9 L/min. A rectal probe (Hewlett-Packard) and the thermistor of a pulmonary artery catheter simultaneously recorded a core temperature of 43.4°C. Cooling by ice packs and gastric and rectal lavage reduced the patient's temperature to 38.8°C. His arterial lactate level was measured at 3.8 mM/L, and his oxygen consumption was calculated as 306 ml/min.

An electrocardiogram obtained immediately after this episode demonstrated severe global ischemia. A lumbar puncture was performed and demonstrated an opening pressure of 26 mm H₂O, a protein level of 320 mg/dL, glucose level of 34 mg/dL (serum glucose levels 132 mg/dL), WBC of 350/μm³ (polymorphonuclear leukocytes, 84 percent; lymphocytes, 14 percent; and monocytes, 2 percent), and RBC of 2,300/μm³. Gram stain and culture of the spinal fluid were again negative. The patient's CPK rose to 13,000 units/L. His chest roentgenogram did not reveal any infiltrates, and his white blood cell count persisted at 18,000/μm³. Blood and urine cultures were negative. Thyroid function tests were not performed. The patient remained persistently unresponsive. An EEG was severely abnormal due to a severe degree of attenuation and disorganization of the background. The patient developed multiple progressive electrolyte abnormalities, renal failure, and disseminated intravascular coagulopathy and died on the tenth postoperative day. An autopsy confirmed complete cord transection at the level of the seventh vertebral body; in addition, partial healing of the neck and hand wounds without abscesses and no infarcts or contusions of the brain were noted. There was evidence of consolidation of the lungs, possibly consistent with early pneumonia.

DISCUSSION

Information about the effects of central nervous system transection on thermoregulation in humans is, for obvious reasons, fragmentary; and there is much yet to be learned about human thermoregulation in general and the derangements causing hyperthermia in particular. The degree to which thermoregulatory control is disrupted in the spinal cord patient depends on the level of the transection. Efferents from the hypothalamus regulate responses involving vasomotor and sudomotor tone, nonshivering and shivering thermogenesis; mediated by descending noradrenergic and cholinergic fibers, these efferents exit the spinal cord below the seventh cervical segment. In cases such as the one reported with a complete transection of the cervical spinal cord, there is total disruption of all of the autonomic sympathetic outflow to the body which descends through the cord to T1; the patient is therefore unable to vasodilate, vasodilate, or sweat in response to central nervous system stimuli. Furthermore, the only muscles available for shivering thermogenesis are those innervated from above the lesion, in this patient the face, neck, and proximal shoulder girdle muscles. Therefore, the cervical spinal cord patient has lost most of the centrally controlled heat-conserving mechanisms, as well as the ability to increase temperature significantly through shivering.

It is not unusual to see fevers in spinal cord injured patients, but these temperature elevations are generally of low grade and attributable most commonly to a decreased ability to dissipate heat in the setting of elevated ambient temperatures but may also be due to infectious processes, pulmonary atelectasis or emboli, drug fevers, or brain or brain stem damage.

The patient described in this report is unique among quadriplegic subjects for the magnitude of his core temperature elevation in the setting of low ambient temperature and among previously reported cases of hyperthermia for having isolated his hypothalamus and brain stem from the spinal cord and peripheral thermal effectors by cervical cord transection. Malignant hyperthermia and thyrotoxicosis are the only hyperpyretic syndromes believed to occur through a purely peripheral mechanism. Malignant hyperthermia is due to a defective regulation of transmembrane calcium transport leading to muscle contraction and heat production. The absence of a personal or familial predisposition to febrile episodes, musculoskeletal abnormalities, the use of anesthetic agents known to precipitate episodes, and the delayed appearance until postoperative day 6 suggests that if this were a case of malignant hyperthermia, it would represent an atypical presentation. There does not seem to be any reason to suspect thyrotoxicosis, although in the absence of blood thyroid levels, it cannot be definitely ruled out.

It is possible (although unlikely) that the isolated segment of lower cord served as an independent thermoregulator. The hypothalamus is not believed to be the only source of control of effectors of thermoregulation but rather the highest controller of a series of redundant subhypothalamic negative feedback loops which include the spinal cord. Evidence derived from experiments involving hypothalamic lesions and transections of the brain stem and spinal cord (see Simon for references) and observations of paraplegic subjects suggest that the subhypothalamic CNS may be capable of receiving thermal input to produce efferent signals controlling thermoregulatory effectors, although in a largely disorganized and ineffective manner.

Most of the other causes of hyperpyrexia likely in this patient are believed to have central etiologies. Thermoregulatory instability may occur due to injury to central nervous system structures, such as with subarachnoid hemorrhage. Sepsis causes pyrexia; however, despite the lack of evidence that either endogenous or exogenous pyrogens or circulating...
ing IL-1*18,19 enters the thermoregulatory centers of the brain, infectious fever is believed to be due to the peripheral production of PGE2, which circulates centrally to act on the hypothalamus.* We are unaware of any data suggesting a peripheral pyretic action of endogenous pyrogens; however, the fact that quadriplegic patients have febrile episodes at all in response to sepsis indicates that a peripheral pyretic action may be the source. Cimetidine has been described as causing fever, probably through a blockade of the H2 receptors in the hypothalamus.20 Ranitidine, which this patient was receiving, may also have this effect.

This episode may represent a manifestation of NMS since hyperpyrexia and hemodynamic instability followed the administration of haloperidol by 12 h. Core features of NMS are pyrexia, altered consciousness, muscular rigidity, and autonomic dysfunction progressing over 24 to 72 h.21 The therapeutic action of neuroleptic drugs is believed to be through dopamine-receptor blockade in the basal ganglia and the hypothalamus; this central action is also believed by some to be the cause of NMS, a hypothesis that is supported by the occurrence in patients receiving dopamine-depleting drugs. A peripheral skeletal muscle mechanism similar to that seen with malignant hyperthermia has also been suggested,22 with support being provided by skeletal muscle pathology from victims demonstrating evidence of a toxic myopathy with absent muscular glycojen and lipid stores.23

In addition, dantrolene sodium, which acts peripherally on the contractile system of muscles, may be effective in some cases of NMS, and muscle contracture has been induced in vitro by another neuroleptic, chlorpromazine;7 however, muscle biopsy specimens from patients surviving episodes of NMS do not appear to give abnormal in vitro halothane-caffeine contracture tests.1

The argument for a haloperidol alone causing the hyperthermic episode is weakened by the record of a temperature of at least 41.2°C during the 24 h prior to the administration of haloperidol; because this episode was not accompanied by hemodynamic instability, it is likely that it was a continuation of his febrile course and not another hyperpyrexic event.

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Acute Myocardial Infarction Associated with Intravenous Injection of Pentazocine and Tripelemamine*

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This case report describes the evolution of an acute anteroseptal myocardial infarction in a 27-year-old man following intravenous injection of pentazocine and tripelennamine. Subsequent coronary angiography showed normal coronary arteries. Based on the known mechanism of action of these drugs, it is postulated that myocardial infarction resulted from coronary artery spasm secondary to excessive catecholamine stimulation.

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Acute Myocardial Infarction, IV Pentazocine and Tripelennamine (McGuer et al)