CHAPTER 52

Thermoregulation, Hypothermia, & Malignant Hyperthermia

KEY CONCEPTS

1. When there is no attempt to actively warm an anesthetized patient, core temperature usually decreases 1– 2°C during the first hour of general anesthesia (phase one), followed by a more gradual decline during the ensuing 3–4 h (phase two), eventually reaching a point of steady state.
2. In the normal, unanesthetized patient the hypothalamus maintains core body temperature within very narrow tolerances, termed the interthreshold range, with the threshold for sweating and vasodilation at one extreme and the threshold for vasoconstriction and shivering at the other.
3. Anesthetics inhibit central thermoregulation by interfering with these hypothalamic reflex responses.
4. Postoperative hypothermia should be treated with a forced-air warming device, if available; alternately (but less satisfactorily) warming lights or heating blankets can be used to restore body temperature to normal.
5. Nearly 50% of patients who experience an episode of malignant hyperthermia (MH) have had at least one previous uneventful exposure to anesthesia during which they received a recognized triggering agent. Why MH fails to occur after every exposure to a triggering agent is unclear.
6. The earliest signs of an MH episode during anesthesia are succinylcholine-induced masseter muscle rigidity (MMR) or other muscle rigidity, tachycardia, and hypercarbia (due to increased CO_2 production).
7. Musculoskeletal diseases associated with a relatively high incidence of MH include central-core disease, multi-minicore myopathy, and King–Denborough syndrome. Duchenne's and other muscular dystrophies, nonspecific myopathies, and osteogenesis imperfecta have been associated with MH-like symptoms in some reports; however, their association with MH is controversial.
8. Treatment of an MH episode is directed at terminating the episode and treating complications such as hyperthermia and acidosis. The mortality rate for MH, even with prompt treatment, ranges from 5% to 30%. First and most importantly, the triggering agent must be stopped; second, dantrolene must be given immediately.
9. Dantrolene, a hydantoin derivative, directly interferes with muscle contraction by inhibiting calcium ion release from the sarcoplasmic reticulum. The dose is 2.5 mg/kg intravenously every 5 min until the episode is terminated (upper limit, 10 mg/kg). Dantrolene should be continued for 24 h after initial treatment.
10. Propofol, thiopental, etomidate, benzodiazepines, ketamine, opiates, droperidol, nitrous oxide, nondepolarizing muscle relaxants, and all local anesthetics are nontriggering agents that are safe for use in MH-susceptible patients.

THERMOREGULATION & HYPOTHERMIA

Hypothermia, usually defined as a body temperature less than 36°C, occurs frequently during anesthesia and surgery. Unintentional perioperative hypothermia is more common in patients at the extremes of age, and in those undergoing abdominal surgery or procedures of long duration, especially with cold ambient operating room temperatures; it will occur in nearly every such patient unless steps are taken to prevent this complication.

Hypothermia reduces metabolic oxygen requirements and can be protective during cerebral or cardiac ischemia. **Nevertheless, hypothermia has multiple deleterious physiological effects (Table 52–1).** In fact, unintended perioperative hypothermia has been associated with an increased mortality rate.

Core temperature is normally the same as the central venous blood temperature (except during periods of relatively rapid temperature change as can occur during extracorporeal perfusion). When there is no attempt to actively warm an anesthetized patient, core temperature usually decreases 1–2°C during the first hour of general anesthesia (phase one), followed by a more gradual decline during the ensuing 3–4 h (phase two), eventually reaching a point of steady state (phase three). With general, epidural, or spinal anesthesia redistribution of heat from warm "central" compartments (eg, abdomen, thorax) to cooler peripheral tissues (eg, arms, legs) from anesthetic-induced vasodilation explains most of the initial decrease in temperature during phase one, with actual heat loss from the patient to the environment being a minor contributor. Continuous heat loss to the environment appears to be primarily responsible for the slower subsequent decline during phase two. At steady state, heat loss equals metabolic heat production (Figure 52–1).

TABLE 52–1 Deleterious effects of hypothermia.

Cardiac arrhythmias and ischemia
Increased peripheral vascular resistance
"Left shift" of the hemoglobin–oxygen saturation curve
Reversible coagulopathy (platelet dysfunction)
Increased postoperative protein catabolism and stress response
Altered mental status
Impaired renal function
Delayed drug metabolism
Impaired wound healing
Increased risk of infection

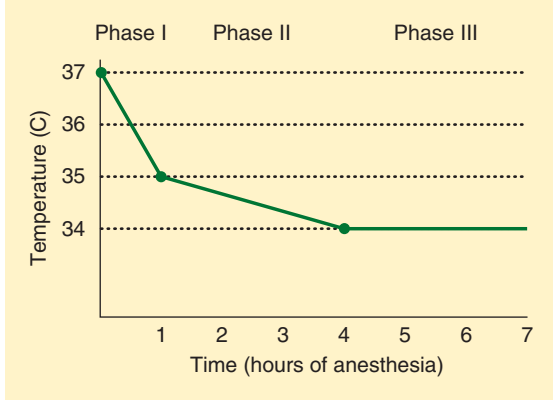

FIGURE 52–1 Unintentional hypothermia during general anesthesia follows a typical pattern: a steep drop in core temperature during the first hour (phase one, redistribution), followed by a gradual decline during the next 3–4 h (phase two, heat loss), eventually reaching a steady state (phase three, equilibrium).

In the normal unanesthetized patient the hypothalamus maintains core body temperature within very narrow tolerances, termed the *interthreshold range,* with the threshold for sweating and vasodilation at one extreme and the threshold for vasoconstriction and shivering at the other. Increasing core temperature a fraction of a degree induces sweating and vasodilation, whereas a minimally reduced core temperature triggers vasoconstriction and shivering. Anesthetic agents inhibit central thermoregulation by interfering with these hypothalamic reflex responses. For example, isoflurane produces a dose-dependent decrease in the threshold temperature that triggers vasoconstriction (3°C decrease for each percent of inhaled isoflurane). Both general and regional anesthetics increase the interthreshold range, albeit by different mechanisms. Spinal and epidural anesthetics, like general anesthetics, lead to hypothermia by causing vasodilation and internal redistribution of heat. The accompanying thermoregulatory

impairment from regional anesthetics that allows continued heat loss is likely due to altered perception by the hypothalamus of temperature in the anesthetized dermatomes rather than a central drug effect, as with general anesthetics.

Intraoperative Considerations

A cold ambient temperature in the operating room, prolonged exposure of a large wound, and the use of large amounts of room-temperature intravenous fluids or high flows of unhumidified gases can contribute to hypothermia. **Prewarming the patient for half an hour with convective forced-air warming blankets prevents phase one hypothermia by eliminating the central–peripheral temperature gradient.** Methods to minimize phase two hypothermia from heat loss during anesthesia include use of forced-air warming blankets and warm-water blankets, heated humidification of inspired gases, warming of intravenous fluids, and increasing ambient operating room temperature. Passive insulators such as heated cotton blankets or so-called space blankets have limited utility unless virtually the entire body is covered.

Postoperative Considerations

Shivering can occur in postanesthesia care units (PACUs) or critical care units as a result of actual hypothermia or neurological aftereffects of general anesthetic agents. Shivering is also common immediately postpartum. Shivering in such instances represents the body's effort to increase heat production and raise body temperature and may be associated with intense vasoconstriction. Emergence from even brief general anesthesia is sometimes also associated with shivering. Although the shivering can be part of nonspecific neurological signs (posturing, clonus, or the Babinski sign) that are sometimes observed during emergence, shivering is most often associated with hypothermia and volatile anesthetics. Regardless of the mechanism, shivering appears to be more common after longer durations of surgery and the use of greater concentrations of a volatile agent. Occasionally it is intense enough to cause hyperthermia (38–39°C) and metabolic acidosis, both of which promptly resolve when the shivering stops. Both spinal and epidural anesthesia lower the shivering threshold and vasoconstrictive response to hypothermia; shivering may also be encountered in the PACU following regional anesthesia. Other causes of shivering should be excluded, such as sepsis, drug allergy, or a transfusion reaction. Intense shivering may increase oxygen consumption, CO_2 production, and cardiac output. These physiological effects are often poorly tolerated by patients with preexisting cardiac or pulmonary impairment.

Postoperative shivering may increase oxygen consumption as much as fivefold, may decrease arterial oxygen saturation, and may be associated with an increased risk of myocardial ischemia. Although postoperative shivering can be effectively treated with small intravenous doses of meperidine (12.5–25 mg) in adults, the better option is to reduce the likelihood of shivering by maintaining normothermia. Shivering in intubated and mechanically ventilated patients can also be controlled with sedation and a muscle relaxant until normothermia is reestablished and the effects of anesthesia have dissipated.

4 Postoperative hypothermia should be treated with a forced-air warming device, if available; alternately (but less satisfactorily) warming lights or heating blankets can be used to restore body temperature to normal. Hypothermia has been associated with an increased incidence of myocardial ischemia, arrhythmias, increased transfusion requirements, and increased duration of muscle relaxant effects, the latter of which can be especially harmful in the recently extubated patient.

MALIGNANT HYPERTHERMIA

Malignant hyperthermia (MH) is a rare (1:15,000 in pediatric patients and 1:40,000 adult patients) genetic hypermetabolic muscle disease, the characteristic phenotypical signs and symptoms of which most commonly appear with exposure to inhaled general anesthetics or succinylcholine (triggering agents). MH may occasionally present more than an hour after emergence from an anesthetic, and rarely may occur without exposure to known triggering agents. Most cases have been reported in young males; almost none have been reported in infants, and few have been reported in the elderly.

Nevertheless, all ages and both sexes may be affected. The incidence of MH varies greatly from country to country and even among different geographic localities within the same country, reflecting varying gene pools. The upper Midwest appears to have the greatest incidence of MH in the United States.

Pathophysiology

A halogenated anesthetic agent alone may trigger an episode of MH (Table 52–2). In many of the early reported cases, both succinylcholine and a halogenated anesthetic agent were used. However, succinylcholine is less frequently used in modern practice, and about half of the cases in the past decade were associated with volatile anesthetics as the only triggering agents. Nearly 50% of patients who experience an episode of MH have had at least one previous uneventful exposure to anesthesia during which they received a recognized triggering agent. Why MH fails to occur after every exposure to a triggering agent is unclear. Investigations into the biochemical causes of MH reveal an uncontrolled increase in intracellular calcium in skeletal muscle. The sudden release of calcium from sarcoplasmic reticulum removes the inhibition of troponin, resulting in sustained muscle contraction. Markedly increased adenosine triphosphatase activity results in an uncontrolled increase in aerobic and anaerobic metabolism. The hypermetabolic state markedly increases oxygen consumption and CO_2 production, producing severe lactic acidosis and hyperthermia.

One early focus of investigations into the mechanisms of MH has been the gene for the ryanodine (Ryr_1) receptor, located on chromosome 19. Ryr_1 is an ion channel responsible for calcium release from the sarcoplasmic reticulum and it plays an important role in muscle depolarization. Subsequent reports linked MH with mutations involving the sodium channel on chromosome 17. An autosomal recessive form of MH has been associated with the King–Denborough syndrome. Most patients with an episode of MH have a history of relatives with a similar episode or with an abnormal halothane–caffeine contracture test (see below). The complexity of genetic inheritance patterns in families reflects the fact that MH can be caused by mutations of one or more genes on more than one chromosome. To date genetic studies in humans have revealed at least five different chromosomes and more than 180 individual mutations associated with MH. Genetic testing, although available, currently screens for less than 20% of recognized mutations. A patient with a *bona fide* clinical history of MH has about a 30–50% chance of testing positive.

TABLE 52–2 Drugs known to trigger malignant hyperthermia.

Inhaled general anesthetics
Ether
Halothane
Methoxyflurane
Enflurane
Isoflurane
Desflurane
Sevoflurane
Nondepolarizing muscle relaxants
Succinylcholine

Clinical Manifestations

The earliest signs of MH during anesthesia are succinylcholine-induced masseter muscle rigidity (MMR) or other muscle rigidity, tachycardia, and hypercarbia (due to increased CO_2 production) (Table 52–3). Two or more of these signs greatly increase the likelihood of MH. Tachypnea is prominent when muscle relaxants are not used. Overactivity of the sympathetic nervous system produces tachycardia, arrhythmias, hypertension, and mottled cyanosis. Hyperthermia may be a late sign, but when it occurs, core temperature can rise as much as 1°C every 5 min. Generalized muscle rigidity is not consistently present. Hypertension may be rapidly followed by hypotension if cardiac depression occurs. Dark-colored urine reflects myoglobinemia and myoglobinuria.

Laboratory testing typically reveals mixed metabolic and respiratory acidosis with a marked base deficit, hyperkalemia, hypermagnesemia, and reduced mixed-venous oxygen saturation. Some case reports describe isolated respiratory acidosis early in the course of an episode of MH. Serum ionized calcium concentration is variable: it may initially increase before a later decrease. Patients typically have increased serum myoglobin, creatine

TABLE 52–3 Signs of malignant hyperthermia.

Markedly increased metabolism
Increased CO_2 production
Increased oxygen consumption
Reduced mixed venous oxygen tension
Metabolic acidosis
Cyanosis
Mottling
Increased sympathetic activity
Tachycardia
Hypertension
Arrhythmias
Muscle damage
Masseter spasm
Generalized rigidity
Increased serum creatine kinase
Hyperkalemia
Hypernatremia
Hyperphosphatemia
Myoglobinemia
Myoglobinuria
Hyperthermia
Fever
Sweating

kinase (CK), lactic dehydrogenase, and aldolase levels. When peak serum CK levels (usually 12–18 h after anesthesia) exceed 20,000 IU/L the diagnosis is strongly suspected. It should be noted that succinylcholine administration to some normal patients without MH may cause serum myoglobin and CK levels to increase markedly.

Much of the problem in diagnosing MH arises from its variable presentation. Fever is an inconsistent and often late-presenting sign. An unanticipated doubling or tripling of end-tidal CO_2 (in the absence of a ventilatory change) is one of the earliest and most sensitive indicators of MH. If the patient survives the first few minutes, acute kidney failure and disseminated intravascular coagulation (DIC) can rapidly ensue. Other complications of MH include cerebral edema with seizures and hepatic failure. Most MH deaths are due to DIC and organ failure due to delayed or no treatment with dantrolene.

7 Susceptibility to MH is increased in several musculoskeletal diseases. These include central-core disease, multi-minicore myopathy, and King–Denborough syndrome. The latter syndrome is seen primarily in young boys who exhibit short stature, mental retardation, cryptorchidism, kyphoscoliosis, pectus deformity, slanted eyes, low-set ears, webbed neck, and winged scapulae. Duchenne's and other muscular dystrophies, nonspecific myopathies, heat stroke, and osteogenesis imperfecta have been associated with MH-like symptoms in some reports; however, their association with MH is controversial. Other possible clues to susceptibility include a family history of anesthetic complications, or a history of unexplained fevers or muscular cramps. There are several reports of MH episodes occurring in patients with a history of exercise-induced rhabdomyolysis. Prior uneventful anesthesia procedures and absence of a positive family history are notoriously unreliable predictors of lack of susceptibility to MH. Any patient who develops MMR during induction of anesthesia should be considered potentially susceptible to MH.

Intraoperative Considerations

8 Treatment of an MH episode is directed at terminating the episode and treating complications such as hyperthermia and acidosis. The mortality rate for MH, even with prompt treatment, ranges from 5% to 30%. Table 52-4 illustrates

TABLE 52–4 Protocol for immediate treatment of malignant hyperthermia.

1. Discontinue volatile anesthetic and succinylcholine. Notify the surgeon. Call for help.
2. Mix dantrolene sodium with sterile distilled water and administer 2.5 mg/kg intravenously as soon as possible.
3. Administer bicarbonate for metabolic acidosis
4. Institute cooling measures (lavage, cooling blanket, cold intravenous solutions).
5. Treat severe hyperkalemia with dextrose, 25–50 g intravenously, and regular insulin, 10–20 units intravenously (adult dose).
6. Administer antiarrhythmic agents if needed despite correction of hyperkalemia and acidosis
7. Monitor end-tidal CO_2 tension, electrolytes blood gases, creatine kinase, serum myoglobin, core temperature, urinary output, and color, coagulation status
8. If necessary, consult on-call physicians at the 24-hour MHAUS hotline, **1-800-644-9737**.

Data from the MHAUS protocol available at http://www.mhaus.org/nf/Shop/EmergencyTherapyMHPosterSample.gif.

a standard protocol for management of MH. First and most importantly, the triggering agent must be stopped and dantrolene must be given immediately.

A. Acute Treatment Measures

Volatile agents and succinylcholine must be discontinued immediately. Even trace amounts of anesthetics absorbed by soda lime, breathing tubes, and breathing bags may be detrimental. The patient should be hyperventilated with 100% oxygen to minimize the effects of uncontrolled CO_2 production and increased oxygen consumption.

B. Dantrolene Therapy

The mainstay of therapy for MH is immediate administration of intravenous dantrolene. Dantrolene, a hydantoin derivative, directly interferes with muscle contraction by binding the Ryr_1 receptor channel and inhibiting calcium ion release from the sarcoplasmic reticulum. The dose is 2.5 mg/kg intravenously every 5 min until the episode is terminated (upper limit, 10 mg/kg). Dantrolene is packaged as 20 mg of lyophilized powder to be dissolved in 60 mL of sterile water. Depending on the dose required and drug formulation used, reconstitution can be time consuming. **An assistant may be needed.** A new formulation is available that reconstitutes in about one third the time (20 versus 86 s) required for the older formulation. The effective half-life of dantrolene is about 6 h.

After initial control of symptoms, 1 mg/kg of dantrolene intravenously is recommended every 6 h for 24–48 h to prevent relapse (MH can recur within 24 h of an initial episode). Dantrolene is a relatively safe drug that is also used to decrease temperature in patients with thyroid "storm" and neuroleptic malignant syndrome. Although its use in chronic therapy for spastic disorders has been associated with hepatic dysfunction, the most serious complication following acute administration is generalized muscle weakness that may result in respiratory insufficiency or aspiration pneumonia. Dantrolene can cause phlebitis in small peripheral veins and should be given through a central venous line if one is available. The safety and efficacy of dantrolene therapy mandate its immediate use in this potentially life-threatening situation. Following administration of dantrolene, most patients revert to normal acid–base status promptly and no further pharmacological treatment is necessary.

C. Correction of Acid–Base/ Electrolyte Imbalances

Persisting metabolic acidosis should be treated with intravenous sodium bicarbonate, recognizing that this treatment will worsen the hypercarbia. Hyperkalemia should be treated with glucose, insulin, and diuresis. There is no useful role for intravenous calcium in this setting. Antiarrhythmic agents, vasopressors, and inotropes should be administered, if indicated. Calcium channel blockers should not be given to patients receiving dantrolene because this combination appears to promote hyperkalemia. Furosemide may be used to establish diuresis and prevent acute kidney failure, which may develop as a consequence of myoglobinuria. Dantrolene contains a considerable amount of mannitol (3 g per 20-mg bottle); thus furosemide or bumetanide should be used in preference to mannitol for diuresis.

D. Cooling the Patient

If fever is present, cooling measures should be instituted immediately. Surface cooling with ice packs over major arteries, cold air convection, and cooling blankets are used. Iced saline lavage of the stomach and any open body cavities (eg, in patients undergoing abdominal surgery) should also be instituted. Use of hypothermic cardiopulmonary bypass may be appropriate if other measures fail.

E. Management of the Patient with Isolated Masseter Muscle Spasm

MMR, or trismus, is a forceful contraction of the jaw musculature that prevents full mouth opening. This contrasts with incomplete jaw relaxation, which is a fairly common finding. Both myotonia and MH can cause masseter spasm. The two disorders can be differentiated by the medical history, neurological examination, and electromyography. The historical incidence of MMR following administration of succinylcholine with halothane in pediatric patients at some medical centers was higher than 1%. Isolated MMR occurs in only 15–30% of true MH episodes. Moreover, less than 50% of patients in whom MMR develops prove to be susceptible to MH by muscle testing. In the past, the

consensus of clinicians was to assume that any occurrence of MMR was diagnostic of MH and to postpone elective surgery. However, if there is no other sign of MH, and if monitoring and treatment capabilities are readily available, many anesthesiologists now advocate allowing surgery to continue using safe (nontriggering) anesthetic agents. Serum CK levels should be followed for 24 h after an episode of MMR, because an elevation of this enzyme may indicate an underlying myopathy.

Postoperative Considerations

A. Confirmation of the Diagnosis

Patients who have survived an unequivocal episode of MH are considered susceptible; in these patients a muscle biopsy need not be performed for diagnosis. If the diagnosis remains in doubt postoperatively, a fresh biopsy specimen of living skeletal muscle is obtained and exposed to a caffeine, halothane, or combination caffeine–halothane bath. The halothane–caffeine contracture test may have a 10–20% false-positive rate, but the false-negative rate is close to zero. Because of the relative complexity of this test, only a few centers worldwide perform it. If the halothane–caffeine contracture test is positive, genetic counseling and testing of family members are appropriate. Baseline CK may be elevated chronically in 50–70% of people at risk for MH, but the only reliable way to diagnose MH susceptibility is by muscle testing.

Both European and North American MH registries have been established to help physicians identify and treat patients with suspected MH, as well as provide standardization between testing centers. The Malignant Hyperthermia Association of the United States (MHAUS, telephone 1-800-986-4287) operates a 24-hour hotline (1-800-644-9737) and a web site (http://www.mhaus.org).

1. Differential diagnosis—Several disorders may superficially resemble MH (Table 52–5). However, MH is associated with greater degrees of metabolic acidosis and venous desaturation than any of these other conditions. In current practice, the most common condition confused with MH is hypercarbia from CO_2 insufflation for laparoscopy, with or without subcutaneous emphysema. This condition can result in an unexpected increase in end-tidal CO_2 with accompanying tachycardia. Surgery and anesthesia can precipitate thyroid storm in undiagnosed or poorly controlled hyperthyroid patients. The signs of thyroid storm include tachycardia, tachyarrhythmias (particularly atrial fibrillation), hyperthermia (often ≥40°C), hypotension, and in some cases congestive heart failure. In contrast to MH, hypokalemia is very common. Also unlike the typical intraoperative presentation of MH, thyroid storm generally develops postoperatively (see Chapter 34). Pheochromocytoma is associated with dramatic increases in heart rate and blood pressure but not with an increase in CO_2 production, end-tidal CO_2, or temperature (see Chapter 34). Cardiac arrhythmias or ischemia may also be prominent. Rarely such patients may have hyperthermia (>38°C), which is generally thought to be due to increased heat production from catecholamine-mediated increases in metabolic rate together with decreased heat elimination from intense vasoconstriction. Sepsis shares several characteristics with MH, including fever, tachypnea, tachycardia, and metabolic acidosis (see Chapter 57). Sepsis can be difficult to diagnose if there is no obvious primary site of infection.

Less commonly, drug-induced hyperthermia may be encountered in the perioperative period. In these cases, the drugs appear to markedly increase serotonin activity in the brain, causing hyperthermia, confusion, shivering, diaphoresis, hyperreflexia, and myoclonus. Drug combinations associated with this "serotonin syndrome" include monoamine oxidase inhibitors (MAOIs) and meperidine, and

TABLE 52–5 Differential diagnosis of hyperthermia in the intraoperative and immediate postoperative periods.

Malignant hyperthermia
Neuroleptic malignant syndrome
Thyroid storm
Pheochromocytoma
Drug-induced hyperthermia
Serotonin syndrome
Iatrogenic hyperthermia
Brainstem/hypothalamic injury
Sepsis
Transfusion reaction

MAOIs and selective serotonin reuptake inhibitors (SSRIs). Hyperthermia can also be caused by some illicit drugs, including 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy'), "crack" cocaine, amphetamines, phencyclidine (PCP), and lysergic acid diethylamine (LSD).

Iatrogenic hyperthermia is not uncommon, particularly in pediatric patients. Common sources of excessive heat in the operating room include humidifiers on ventilators, warming blankets, heat lamps, and increased ambient temperature. Injuries to the brainstem, hypothalamus, or nearby regions can be associated with marked hyperthermia.

2. Neuroleptic malignant syndrome (NMS)— This syndrome is characterized by hyperthermia, muscle rigidity with extrapyramidal signs (dyskinesia), altered consciousness, and autonomic lability in patients receiving antidopaminergic agents. The syndrome is caused by an imbalance of neurotransmitters in the central nervous system. It can occur either during drug therapy with antidopaminergic agents (eg, phenothiazines, butyrophenones, thioxanthenes, or metoclopramide) or less commonly following the withdrawal of dopaminergic agonists (levodopa or amantadine) in patients with Parkinson's disease. Thus, it appears to involve abnormal central dopaminergic activity, as opposed to the altered peripheral calcium release seen in MH. These differing mechanisms probably explain why nondepolarizing relaxants reverse the rigidity of NMS, but not the rigidity associated with MH.

NMS does not appear to be inherited and typically takes hours to weeks to develop; the majority of episodes develop within 2 weeks of a dose adjustment. Hyperthermia generally tends to be mild, and appears to be proportional to the amount of rigidity. Autonomic dysfunction results in tachycardia, labile blood pressure, diaphoresis, increased secretions, and urinary incontinence. Muscle rigidity can produce dyspnea and respiratory distress and, together with the increased secretions, can promote aspiration pneumonia. CK levels are typically elevated; some patients may develop rhabdomyolysis resulting in myoglobinemia, myoglobinuria, and kidney failure.

Mild forms of NMS promptly resolve after withdrawal of the causative drug (or reinstitution of antiparkinsonian therapy). Initial treatment of more severe forms of NMS should include oxygen therapy and endotracheal intubation for respiratory distress or altered consciousness. Marked muscle rigidity can be controlled with muscle paralysis, dantrolene, or a dopaminergic agonist (amantadine, bromocriptine, or levodopa), depending on the severity and acuity of the syndrome. Resolution of the muscle rigidity usually decreases body temperature.

This syndrome is considered a separate entity from MH; nevertheless some clinicians believe that NMS may predispose patients to MH and recommend that patients with NMS should not receive succinylcholine or a volatile anesthetic. In contrast to patients with NMS, patients susceptible to MH can safely receive phenothiazines.

B. Prophylaxis, Postanesthesia Care, and Discharge

10 Propofol, etomidate, benzodiazepines, ketamine, thiopental, methohexital, opiates, droperidol, nitrous oxide, nondepolarizing muscle relaxants, and all local anesthetics are nontriggering agents that are safe for use in MH-susceptible patients. An adequate supply of dantrolene should always be available wherever general anesthesia is provided. Prophylactic administration of intravenous dantrolene to susceptible patients is not necessary if a nontriggering anesthetic is administered.

For MH-susceptible patients, the consensus is that the vaporizers should be removed from the anesthesia workstation (or fixed in an "off" position) and the machine should be flushed with 10 L/min of fresh gas (air or oxygen) for at least 5 min. This step should reduce concentrations of volatile anesthetics to less than 1 part per million. Additionally, the CO_2 absorbent and circle system (or other anesthetic circuit), hoses should be changed.

MH-susceptible patients who have undergone an uneventful procedure with a nontriggering anesthetic can be discharged from the PACU or ambulatory surgery unit when they meet standard criteria. There are no reported cases of MH-susceptible patients experiencing MH after receiving a nontriggering anesthetic during uneventful surgery.

SUGGESTED READING

Benca J, Hogan K: Malignant hyperthermia, coexisting disorders, and enzymopathies: Risks and management options. Anesth Analg 2009;109:1049.

Kelly FE, Nolan JP: The effects of mild induced hypothermia on the myocardium: A systematic review. Anaesthesia 2010;65:505.

Kim TW, Nemergut ME: Preparation of modern anesthesia workstations for malignant hyperthermia-susceptible patients: A review of past and present practice. Anesthesiology 2011;114:205.

Klingler W, Rueffert H, Lehmann-Horn F, et al: Core myopathies and risk of malignant hyperthermia. Anesth Analg 2009;109:1167.

Mackensen GB, McDonagh DL, Warner DS: Perioperative hypothermia: Use and therapeutic implications. J Neurotrauma 2009;26:342.

Parness J, Bandschapp O, Girard T: The myotonias and susceptibility to malignant hyperthermia. Anesth Analg 2009;109:1054.

Sessler DI: Temperature monitoring and perioperative thermoregulation. Anesthesiology 2008;109:318.

WEB SITES

Association of Anaesthetists of Great Britain & Ireland http://www.aagbi.org/

Malignant Hyperthermia Association of the United States. http://www.mhaus.org/