Inhalational Anesthesia

This week you will learn a new definition of MAC.

- As you already know, MAC is abbreviated for Monitored Anesthesia Care---a type of light Anesthesia to induce sedation in patients having surgery.
- MAC is also abbreviated for MAC Laryngoscope Blade or Macintosh Blade (a curved laryngoscope blade

In inhalational anesthesia, a method of General Anesthesia MAC is abbreviated for Minimal Alveolar Concentration.

Let me explain: When a patient goes off to sleep, the amount of inhaled anesthetic gas in the alveoli (the tiny air sacs) of the lungs is considered exactly the same as the amount of gas in the brain. The reason why the gas amount of the brain is compared to the gas amount in the alveoli is because of the gas exchange (CO2 and O2-ventilation and blood-perfusion) that takes place in the capillaries of the alveoli. The blood picks up oxygen and gas and carries both to the brain and the "used" anesthetic gas and CO2 gets carried back (via blood) to the alveoli and up the bronchioles and out---into the anesthesia machine waste system.

Minimal alveolar concentration is a concept used to compare the strengths, or potency, of anesthetic vapors or gases. In simple terms, it is defined as the concentration of the anesthetic vapor/gas in the lungs that is needed to prevent movement (motor response) in 50% of patients in response to surgical (pain) stimulus (ex. surgical skin incisions).

Note: The MAC of a volatile substance is inversely proportional to its lipid solubility (oil: gas coefficient), in most cases. Thus, a lower MAC value represents a more potent volatile anesthetic and a high MAC equals low potency (Meyer-Overton Hypothesis).
There are 2 types of MAC (minimal alveolar concentration) in Inhalational Anesthesia:

- MAC-BAR (=1.7-2.0 MAC) is the concentration required to block autonomic nervous system reflexes to nociceptive stimuli (painful stimulation of peripheral nerve fibers).

- MAC-aware (0.3-0.5 MAC), the concentration required to block voluntary reflexes and control perceptive patient awareness under anesthesia (memory loss).

### Altered MAC

Certain physiological and pathological states may alter MAC. MAC is higher in infants and lower in the elderly. Also, MAC increases with anxiety and thyrotoxicosis. Likewise, hypothermia, hypotension, hypothyroidism, and pregnancy seem to decrease MAC. Gender, height and weight seem to have little effect on MAC.

Opioid analgesics and sedative-hypnotics, often used as adjuvants to anesthesia, decrease MAC. It should also be noted that MAC values are additive. For instance, when applying 0.3 MAC of drug X and 1 MAC of drug Y the total MAC achieved is 1.3 MAC. In this way nitrous oxide is often used as a "carrier" gas to decrease the anesthetic requirement of other drugs.

### Inhalational Anesthetics

An inhalational anaesthetic is a chemical compound possessing general anaesthetic properties that can be delivered via inhalation. They are administered by anesthetists (a term which includes anesthesiologists, nurse anaesthetists, and anesthesiologist assistants) through an anesthesia mask, laryngeal mask airway or tracheal tube connected to some type of anaesthetic vaporizer and an anesthetic delivery system.

Agents of significant contemporary clinical interest include volatile anaesthetic agents such as: isoflurane, sevoflurane and desflurane, as well as certain anaesthetic gases such as nitrous oxide and xenon.

### List of Currently Used Inhalational Anesthetic Agents:

- Isoflurane
- Desflurane
- Nitrous oxide
- Sevoflurane
**List of Previously Used Agents:**

Although some of these are still used in clinical practice and in research, the following anaesthetic agents are primarily of historical interest in developed countries:

- Aliflurane
- Chloroform
- Cyclopropane
- Diethyl ether
- Enflurane
- Ethylene
- Halothane
- Methoxyflurane
- Methoxypropane
- Roflurane
- Teflurane
- Trichloroethylene
- Vinyl ether

**Future Agents**

Xenon

**Mechanism of Action of Inhaled Anesthetics**

"Inhaled anesthetics act in different ways at the level of the central nervous system. They may disrupt normal synaptic transmission by interfering with the release of neurotransmitters from presynaptic nerve terminal (enhance or depress excitatory or inhibitory transmission), by altering the re-uptake of neurotransmitters, by changing the binding of neurotransmitters to the post-synaptic receptor sites, or by influencing the ionic conductance change that follows activation of the post-synaptic receptor by neurotransmitters."
Sevoflurane, isoflurane, enflurane, and desflurane, are the common fluorinated ether anesthetics used in clinical practice. These agents are color-coded for safety purposes. A desflurane bottle has a special fitting and note that desflurane boils near ambient conditions.

Volatile anesthetic agents share the property of being liquid at room temperature, but evaporating easily for administration by inhalation. All of these agents share the property of being quite hydrophobic (i.e., as liquids, they are not freely miscible with water, and as gases they dissolve in oils better than in water).

The ideal volatile anesthetic agent offers smooth and reliable induction and maintenance of general anesthesia with minimal effects on other organ systems. In addition it is odorless or pleasant to inhale; safe for all ages and in pregnancy; not metabolized; rapid in onset and offset; potent; and safe for exposure to operating room staff. It is also cheap to manufacture; easy to transport and store, with a long shelf life; easy to administer and monitor with existing equipment; stable to light, plastics, metals, rubber and soda lime; non-flammable and environmentally safe.

None of the agents currently in use are ideal, although many have some of the desirable characteristics. For example, sevoflurane is pleasant to inhale and is rapid in onset and offset. It is also safe for all ages. However, it is expensive (approximately 3 to 5 times more expensive than isoflurane), and approximately half as potent as isoflurane.
Pharmacological Profile of Currently Used Inhaled Anesthetics
Mnemonic Hints: SHINE

Sevoflurane
Halothane
Isoflurane
Nitrous oxide
Enflurane

Halothane (Fluothane):

This volatile anesthetic is a nonflammable halogenated alkene. It has a vapor pressure of 244 mm Mercury at 20 degree Celsius and boils at 50.2 degree Celsius. Halothane is susceptible to decomposition. For this reason, it is stored in amber-colored bottles and thymol is added as preservative. It is known to sensitize the myocardium to the action of epinephrine and norepinephrine and to have the potential for serious cardiac dysrhythmias.

Halothane lowers airway resistance and might be used in the treatment of asthma if conventional therapy fails. It is not recommended for obstetric anesthesia except when uterine relaxation is required. It crosses the placental barrier and can cause fetal and neonatal depression resulting in hypotension, hypoxemia, and acidosis. Halothane does not cause coronary artery vasodilatation and therefore does not lead to coronary artery steal syndrome. Decrease in blood pressure is due to negative inotropic effects of halothane. Systemic vascular resistance does not change significantly. Increase in cerebral blood flow due to cerebral vasodilatation produced by halothane is greater than the one produced by isoflurane or enflurane.

Halothane is able to trigger malignant hyperthermia, a potential lethal complication of anesthesia. Fulminant hepatic necrosis and/or jaundice (halothane hepatitis) are other severe complications of halothane anesthesia. Halothane has excellent hypnotic but no analgesic properties. Induction of anesthesia can be achieved by using 1 to 3 percent halothane in air or in oxygen, or by using 0.8 percent halothane in 65 percent nitrous oxide. Induction occurs relatively quickly. This is one of the reasons why halothane was the drug of choice for mask induction of pediatric patients but its popularity changed in the recent years with the availability of sevoflurane. Maintenance of anesthesia can be achieved with 0.5 to 1.5 percent halothane. Emergence might be delayed in obese patients due to storage of the inhalation agent in fatty tissues.
**Isoflurane (Forane):**

This volatile anesthetic is a nonflammable halogenated methyl ethyl ether. It has a vapor pressure of 239 mm Mercury at 20 degree Celsius and boils at 48.5 degree Celsius.

Isoflurane is resistant to degradation by the absorber and can therefore be used during low flow or closed system anesthesia. Isoflurane produces a dose-dependent reduction in blood pressure due to peripheral vasodilatation. It does not sensitize the myocardium for arrhythmias. It can cause coronary artery vasodilatation that might lead to coronary artery steal syndrome. During such an event blood is diverted away from critically perfused areas because of vasodilatation in healthy parts of the heart. This might lead to myocardial ischemia or infarction. Emergence from anesthesia with isoflurane is faster than with halothane or enflurane.

However, most clinical studies failed to prove higher incident of myocardial ischemia due to isoflurane. Isoflurane should be avoided in patients with aortic valve stenosis since they poorly tolerate a decrease in systemic vascular resistance. Like halothane, isoflurane can trigger malignant hyperthermia.

**Enflurane (Ethrane):**

This volatile anesthetic is a nonflammable fluorinated ethyl methyl ether. It has a vapor pressure of 172 mm Mercury at 20 degree Celsius and boils at 56.5 degree Celsius.

Enflurane is resistant to degradation by soda lime and can be therefore used during low flow or closed system anesthesia. Its biotransformation releases fluoride ions but their concentration does not reach nephrotoxic levels. Enflurane produces a dose-dependent reduction in arterial blood pressure as consequence of negative inotropy. Like isoflurane, enflurane does not sensitize the heart for arrhythmias. In addition, it does not cause a coronary artery steal syndrome.

Enflurane has been found to increase intracranial pressure and, especially in combination with hyperventilation, to increase the risk of seizure activity. It is therefore contraindicated in patients with seizure disorders. As halothane and isoflurane, enflurane can trigger malignant hyperthermia. Enflurane enhances the action of paralyzing agents more than other inhalation anesthetics. Emergence from anesthesia with enflurane is a little slower than with isoflurane.
**Desflurane (Suprane):**

This volatile anesthetic is a nonflammable fluorinated methyl ethyl ether. It has a vapor pressure of 673 mm Mercury at 20 degree Celsius and boils at 23.5 degree Celsius. Unlike other inhalation anesthetics, desflurane cannot be delivered by standard vaporizers. It requires the use of electrically heated vaporizers. Desflurane is very resistant to degradation by soda lime and can therefore be used during low flow or closed system anesthesia. Desflurane produces a dose-dependent reduction in arterial blood pressure due to peripheral vasodilatation. It might as well cause an increase in heart rate. It should therefore not be used in patients with aortic valve stenosis. It does not sensitize the heart to arrhythmias or cause coronary artery steal syndrome.

Like other inhalation anesthetics, desflurane can trigger malignant hyperthermia. Desflurane may cause coughing and excitation during induction and should therefore rather not be used without intravenous anesthetics. The low tissue solubility of desflurane results in rapid elimination and awakening.

**Sevoflurane (Ultane):**

This volatile anesthetic is a nonflammable fluorinated isopropyl ether. It has a vapor pressure of 162 mm Mercury at 20 degree Celsius and boils at 58.5 degree Celsius.

Sevoflurane undergoes temperature dependent degradation by baralyme and soda lime. Therefore, it cannot be used in low flow or closed systems anesthesia. Sevoflurane reacts with CO2 absorbents to form a special haloalkene, the so-called Compound A. Compound A is metabolized to nephrotoxins and can lead to kidney damage. The minimum fresh gas flow has been recommended to be at least two liters per minute. Sevoflurane produces a dose-dependent decrease in arterial blood pressure due to peripheral vasodilatation. It should therefore not be used in patients with aortic valve stenosis. It does not sensitize the heart to arrhythmias or cause coronary artery steal syndrome.

Unlike desflurane, sevoflurane does not irritate the airway. Due to its low solubility in blood it can be used for rapid induction of anesthesia without intravenous anesthetics. This is one of the reasons why it is currently replacing halothane for mask induction in pediatric patients. Like all other inhalation anesthetics, sevoflurane can trigger malignant hyperthermia in susceptible patients. The low tissue solubility of sevoflurane results in rapid elimination and awakening.
Nitrous oxide (nitrous oxide):

This is an inorganic nonflammable gas that supports combustion. It has a vapor pressure of 39,000 mm Mercury at 20 degree Celsius and boils at minus 88 degree Celsius. The blood/gas coefficient is 0.47 and the MAC in 100 percent oxygen is 104. This means that one MAC nitrous oxide can only be reached in a hyperbaric chamber.

Nitrous oxide is stored in blue cylinders (This is the case in the USA. In some parts of Europe, blue is the color for oxygen and green the color for nitrous oxide). At room temperature, nitrous oxide in the cylinder is in equilibrium between liquid and gaseous form. The pressure within the cylinder is constant as long some of the gas is in liquid form. Therefore, there is only little nitrous oxide left when the pressure in the cylinder decreases.

Nitrous oxide is a weak anesthetic. It is used to supplement other inhalation agents. Its low solubility results in rapid induction or awakening.

Administration of high concentrations of nitrous oxide will facilitate the increase in alveolar concentration of a simultaneously administered second gas. This is called the second gas effect.

Nitrous oxide is resistant to degradation by soda lime and can therefore used in low flow or closed systems anesthesia. Unlike other inhalation anesthetics, nitrous oxide does not inhibit the hypoxic pulmonary vasoconstriction response in the lungs. It might produce an increase in pulmonary vascular resistance, especially in patients with pre-existing pulmonary hypertension. It is therefore contraindicated in patients with intra-cardiac right-to-left shunt.

Nitrous oxide is sympathomimetic and increases systemic vascular resistance. It does not cause a decrease in blood pressure. Unlike order inhalation anesthetics, nitrous oxide does not produce skeletal muscle relaxation. It does not have any significant effect on uterine contractility. Nitrous oxide is a weak trigger for malignant hyperthermia.

Nitrous oxide diffuses into air containing cavities 34 times faster than nitrogen can leave that space. This can cause dangerous accumulation of volume and increase in pressure in closed spaces such as bowel, middle year, pneumothorax, pneumocranium, pneumoperitoneum, or cuffs of endotracheal tubes. In patients with ileus, the volume of air in the bowel can double within 4 hours of nitrous oxide administration. The volume of air within a pneumothorax can double within 10 minutes if 70 percent nitrous oxide is
administered. This can lead to a life-threatening tension pneumothorax. Diffusion of nitrous oxide into air bubbles will increase their size. It has therefore to be stopped immediately when air embolism is suspected.

The main danger however is the occurrence of hypoxemia. The maximum dose of nitrous oxide should not exceed 70 percent. Hypoxic inspiratory gas mixtures due to high doses of nitrous oxide or failing admixture of oxygen have lead in the past to hypoxic brain damage. A fail-safe valve in the anesthesia machine should prevent such a complication. Nitrous oxide can be used in doses of 0 to 70 percent during induction or maintenance of anesthesia. Administration of 70 percent nitrous oxide should always be accompanied by 30 percent oxygen. The combination of 70 percent nitrous oxide with 30 percent regular air results in a hypoxic air mixture (Wenker, 1999).

"CLEAN-UP AND DISPOSAL OF LIQUID ANESTHETIC AGENT SPILLS"

Small volumes of liquid anesthetic agents such as halothane, enflurane, isoflurane, desflurane, and sevoflurane evaporate readily at normal room temperatures, and may dissipate before any attempts to clean up or collect the liquid are initiated. However, when large spills occur, such as when one or more bottles of a liquid agent break, specific cleaning and containment procedures are necessary and appropriate disposal is required (AANA 1992). The recommendations of the chemical manufacturer's material safety data sheet (MSDS) that identify exposure reduction techniques for spills and emergencies should be followed.

In addition, OSHA Standard for Hazardous Waste Operations and Emergency Response (29 CFR 1910.120) would apply if emergency response efforts are performed by employees. The employer must determine the potential for an emergency in a reasonably predictable worst-case scenario, and plan response procedures accordingly. Only adequately trained and equipped workers may respond to spills. When the situation is unclear or data are lacking on the exposure level, the response needs to be the same as for high levels of exposure. Responses to incidental releases of liquid anesthetic agents where the substance can be absorbed, neutralized, or otherwise controlled at the time of release by employees in the immediate release area, or by maintenance personnel do not fall within the scope of this standard.

Because of the volatility of liquid anesthetics, rapid removal by suctioning in the OR is the preferred method for cleaning up spills. Spills of large volumes in poorly ventilated areas or in storage areas should be absorbed using an absorbent material, sometimes called a sorbent, that is designed for clean-up of organic chemicals.

"Spill pillows" commonly used in hospital laboratories, vermiculite, and carbon-based sorbents are some of the materials commercially available and regularly used for this purpose. Caution should be exercised if broken glass bottles pose a hazard.
***Cat Litter can also be used to help absorb large spills of anesthetic gases. Use appropriate PPEs when cleaning up spills.

Both enflurane and desflurane are considered hazardous wastes under the EPA regulations because these chemicals contain trace amounts of chloroform (a hazardous substance), a by-product of the manufacturing process. Consequently, sorbents that have been saturated with enflurane or desflurane should be managed as an EPA hazardous waste material due to the trace concentrations of chloroform present. Isoflurane and halothane do not contain trace amounts of chloroform or any other regulated substance and are therefore not considered hazardous wastes by EPA.

To minimize exposure to all liquid anesthetic agents during clean-up and to limit exposure during disposal procedures, the following general guidelines are recommended. The waste material should be placed in a container, tightly sealed, properly labeled, and disposed of with other chemical wastes sent to a facility's incinerator or removed by a chemical waste contractor. After a large spill has occurred and the appropriate response action taken, airborne monitoring should be conducted to determine if the spill was effectively contained and cleaned up.

Determination of appropriate disposal procedures for each facility is the sole responsibility of that facility. Empty anesthetic bottles are not considered regulated waste and may be discarded with ordinary trash or recycled. Furthermore, the facility as well as the waste handling contractor must comply with all applicable federal, state, and local regulations.

To minimize exposure to waste liquid anesthetic agents during clean-up and disposal, the following general guidelines are recommended by the manufacturers of liquid anesthetic agents:

- Wear appropriate personal protective equipment.

- Where possible, ventilate area of spill or leak. Appropriate respirators should be worn.

- Restrict persons not wearing protective equipment from areas of spills or leaks until clean-up is complete.

- Collect the liquid spilled and the absorbent materials used to contain a spill in a glass or plastic container. Tightly cap and seal the container and remove it from the anesthetizing location. Label the container clearly to indicate its contents.
• Transfer the sealed containers to the waste disposal company that handles and hauls waste materials.

• Health-care facilities that own or operate medical waste incinerators may dispose of waste anesthetics by using an appropriate incineration method after verifying that individual incineration operating permits allow burning of anesthetic agents at each site.

AIR MONITORING

Air monitoring is one of the fundamental tools used to evaluate workplace exposures. Accordingly, this section presents some of the appropriate methods that can be used to detect and measure the concentration of anesthetic gases that may be present in the health-care environment. The data provided by monitoring are necessary to establish proper engineering, work practice, and administrative controls to ensure the lowest reasonably achievable gas levels in the operatory and PACU room air.

OSHA recommends that air sampling for anesthetic gases be conducted every 6 months to measure worker exposures and to check the effectiveness of control measures. Furthermore, OSHA recommends that only the agent(s) most frequently used needs to be monitored, since proper engineering controls, work practices and control procedures should reduce all agents proportionately. However, the decision to monitor only selected agents could depend not only on the frequency of their use, but on the availability of an appropriate analytical method and the cost of instrumentation. [ASA emphasizes regular maintenance of equipment and scavenging systems, daily check-out procedures for anesthesia equipment, and education to ensure use of appropriate work practices. It does not believe that a routine monitoring program is necessary when these actions are being carried out. ASA prefers to use monitoring when indicated such as in the event of known or suspected equipment malfunction (OSHA, 2000)."

Information Sources: