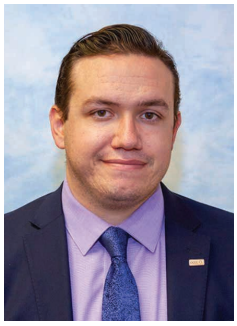
Inhalation Anesthetics & Vaporizers

The development and functionality of the anesthetic vaporizer and how Sevoflurane relates to its specific vaporizer model, physiological indication, and molecular structure.



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Historical Significance

The origins of the anesthesia vaporizer are quite muddled; However, that is beyond this paper's purpose. It would appear from historical accounts that the first public demonstration of a physician utilizing a vaporizing apparatus to anesthetize a patient for the purposes of a surgical procedure occurred on October 16, 1846 (WLM, 2019). This monumental moment in the history of anesthesia took place at the Ether Dome, a surgical operating amphitheater located in the Bulfinch Building at Massachusetts General Hospital in Boston. The patient, Edward Gilbert Abbott, was undergoing a

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tumor mass resection procedure (WLM, 2019). The surgical team accomplished this feat with the use of Ether and a Morton inhaler [fig.1]. The Morton inhaler, designed by William T.G. Morton that same year, is considered the first vaporizer but was simply a container to hold the volatile anesthetic. Despite this momentous period in history, the science of anesthesia would have to advance beyond a glass container and the highly flammable and explosive Ether (Pharmacopoeia, 2016).

Since 1846, there have been many scientific advances in volatile anesthetics. A primary advancement in general anesthetics revolves around the introduction of halogenated anesthetics. Halogenated anesthetics (HA) are currently the most widely used inhalation anesthetics in surgery today (NIH, 2019). The reason halogenated anesthetics hold a point of primacy is due in part to the nature of their chemical and molecular makeup. They are generally more chemically stable than their predecessors. Additionally, these HA's offer more diversity in attaining tailored potency, duration, and physiological modification as opposed to earlier volatile anesthetics. According to a study done in the American Journal of Health-System Pharmacy (AJHP, 2006), they said,

"Inhaled anesthetics have been shown to be both safe and effective in inducing and maintaining anesthesia. These agents differ in potency, adverse-effect profile, and cost. Newer anesthetic gases, such as Sevoflurane and desflurane, appear to have more favorable physiological/chemical properties. These factors, as well as patient characteristics, duration and type of procedure, must be considered when selecting an inhaled anesthetic."

~ American Journal of Health-System Pharmacy ~

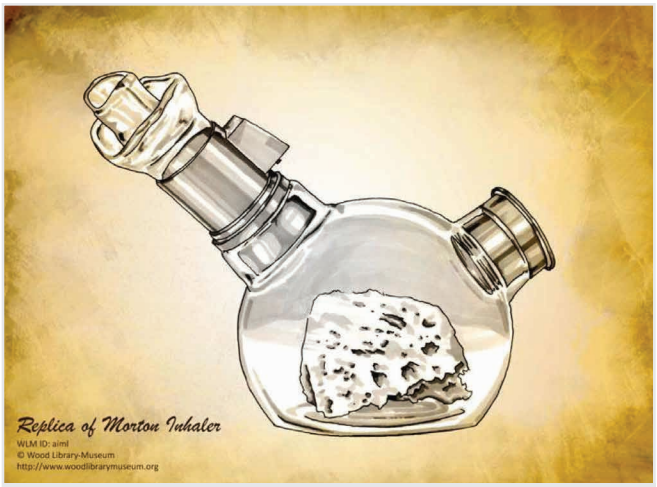

Figure 1: Morton Inhaler

What Are Halogenated Hydrocarbons?

What is a halogenated hydrocarbon (ie. halogenated anesthetic), also call halogenated ethers or Haloalkanes? A halogenated hydrocarbon is an organic compound consisting of only Carbon and Hydrogen, which contains one or more halogen atoms (Helmenstine, 2019). Just to re-establish base knowledge: a halogen is an element located in Group VII [fig. 2] of the periodic table. Halogens are reactive nonmetals having seven valence electrons. Specific molecules that fit within this designation are Fluorine, Chlorine, Bromine, and Iodine. Of the four listed, Fluorine is the most commonly used in the manufacturing of anesthetics. There are currently five halogenated anesthetics in use today by anesthetists in the United States. They are halothane, Isoflurane, Enflurane, Desflurane, and Sevoflurane (NIH, 2019). Concerning their makeup, Isoflurane is a chlorinated hydrocarbon base, whereas Sevoflurane and Desflurane are fluorinated anesthetics, the three of which are the most widely used anesthetics today. Halothane, a brominated hydrocarbon, is rarely used today, primarily being used on pediatric populations. Halothane is avoided in adults due to a linkage the gas has to a severe distinctive liver injury. Since liver injury is rare amongst the pediatric population, some facilities will still use halothane on children. Although rare, it is important to note that liver injury has been reported with all halogenated inhalations agents (NIH, 2019). Though relatively safe, Sevoflurane literature reveals a single case report of severe acute liver injury similar to Halothane Hepatitis being induced by Sevoflurane (LiverTox, 2018).

Sevoflurane (i.e. Ultane; Abbott Laboratories, Inc.) in particular is one of the most commonly used volatile anesthetic agents, particularly for outpatient anesthesia (LiverTox, 2018). 1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy) propane, as it's known by its IUPAC name, has a molecular

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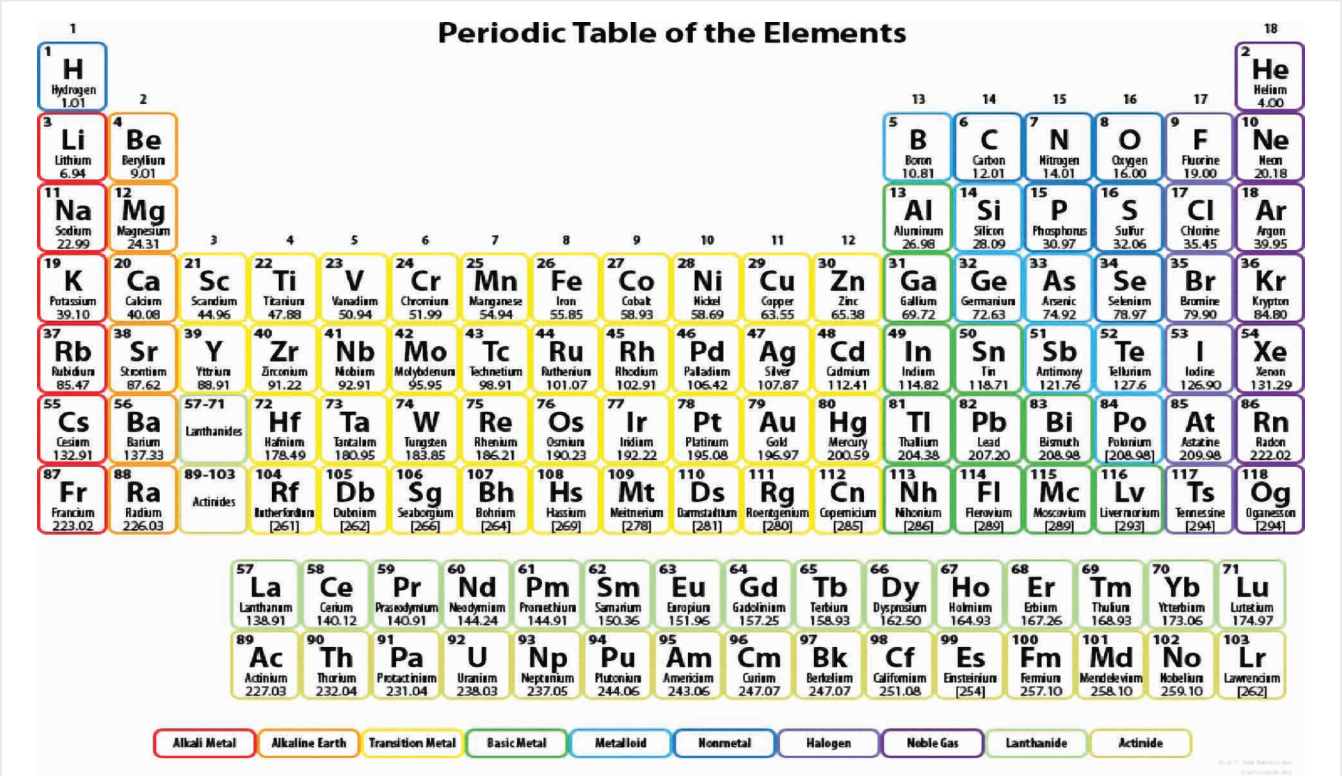

Figure 2: The Halogen group are colored in light purple.

formula of C4H3F7O with a molecular weight of 200.05 g/mol (PubChem, 2005) [refer to fig. 3]. Sevoflurane is a liquid at room temperature with a vapor pressure of 160 mmHg at 20°C (Butterworth, 2018). Due to this modest vapor pressure, the use of a conventional variable bypass vaporizer is permitted (this will be discussed in subsequent pages). Under unrestricted conditions, Sevoflurane has a volume percent of 21%. Regarding potency, the MAC (minimum alveolar concentration) or the alveolar concentration required to prevent movement in 50% of patients in response to a standardized stimulus with Sevoflurane is 2.0% (Butterworth, 2018). It is important to note that while Sevoflurane has a standard value of 2.0% ±0.1%, the relative MAC value will decrease with age (FDA, 2019).

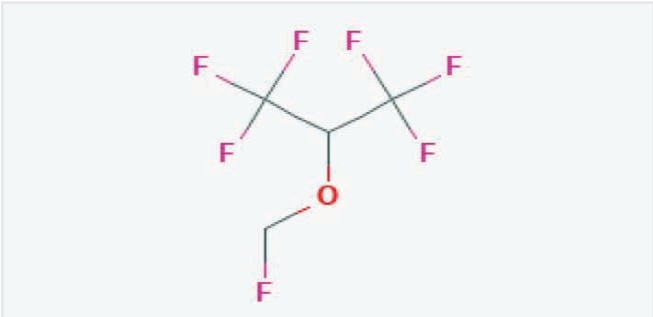

Figure 3: Sevoflurane Atomic Structure

Physiological Properties

Sevoflurane is quite common in outpatient surgery settings; this may be partly because its solubility in the blood is low. The benefit of this low solubility is that it yields a rapid fall in alveolar concentration upon discontinuation of administration (Butterworth, 2018). This low blood serum level and precipitous drop in concentration after discontinuation results in a reduced emergence from anesthesia. This rapid emergence from anesthesia allows for more efficient flow through the surgical schedule, hence why Sevoflurane is relied on heavily for outpatient surgery centers.

In the body, Sevoflurane exerts multiple effects on the various systems (i.e. cardiac, respiratory, cerebral, neuromuscular, renal, and hepatic). In the cardiovascular system, Sevoflurane mildly depresses myocardial contractility as compared to Isoflurane and Desflurane. Although the reasonings are still unknown, Sevoflurane is also seen to prolong the QT interval. In most cases, QT prolongation presents approximately 60-minutes following anesthetic emergence in an analysis performed on infants. Sevoflurane also has shown depression in the respiratory system, which can reverse a bronchospasm event similar to that of Isoflurane (Butterworth, 2018).

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In regards to the cerebrum, Sevoflurane is generally regarded as an anesthetic that causes a slight increase in CBF (Cerebral Blood Flow), and ICP (Intracranial Pressure) with maintenance of normal CO2 levels (normocarbia/capnia). However, some studies have linked decreases in is CBF to the use of Sevoflurane (Butterworth, 2018). In high-concentrations, those greater than 1.5 MAC, Sevoflurane may impair the auto-regulation of CBF. In cases of hemorrhagic hypotension, Sevoflurane furthers a drop in CBF (Butterworth, 2018). The literature indicates that the impairment of CBF autoregulation seems to be less pronounced in Isoflurane. It is recommended that an isoflurane vaporizer be attached to the interlock in designated trauma rooms for the above-mentioned reasons.

Sevoflurane produces sufficient muscle relaxation following an inhalation induction (Butterworth, 2018). Sevoflurane's muscle relaxation advantage can be utilized in conjunction with a multi-modal approach to induction by the use of propofol, lidocaine, and/or opioids. It has been shown that Sevoflurane slightly decreases renal blood flow and renal tubule function. Despite the reduced blood flow, the research has not suggested any post-operative renal toxicity or renal insufficiency (Butterworth, 2018). Hepatically, a decrease in portal vein flow has been reported, but there the research also shows an increase in hepatic artery blood flow, thus negating the decrease in the venous flow. In Butterworth's Mogan and Mikhail's Clinical Anesthesia, the text indicated that hepatic blood flow and oxygenation is sufficiently maintained through the use of Sevoflurane (Butterworth, 2018).

Contraindications for using Sevoflurane in certain patient populations include severe hypovolemia, family history of or confirmed malignant hyperthermia events and intracranial hypertension (Butterworth, 2018). As mentioned earlier, Sevoflurane should be avoided in hemorrhagic events as it can potentiate a drop in CBF beyond physiological autoregulation. Additionally, rooms designated for neurosurgery should have Isoflurane available since incidents of intracranial hypertension are more expected.

Drug interactions are not common; however, as stated previously, like other volatile anesthetics Sevoflurane can potentiate Neuromuscular blocking agents (NMBAs) (Butterworth, 2018).

Scientific Advancement:

With the development of the new inhalation anesthetics, technology had to be developed to make them even safer concerning dose, concentration, regularity, maintenance, and predictability. The vaporizers in use today are far more advanced than those of the 1800s [fig. 1]. The key attribute to an anesthetic vaporizer is dilution. Volatile anesthetics are liquid at room temperature, for the most part. The vaporizer must have the capacity to change the volatile liquid anesthetic into a non-hypoxic, breathable gas. The solute in this situation would be a fresh gas such as oxygen (Dorsch, 2008). Vaporizers in use today are concentration calibrated. Within the context of concentration calibration, vaporizers rely on variable bypass or injection to control concentration levels. Sevoflurane, due to its stable saturated vapor pressure, can accomplish safe vaporization through a variable bypass vaporizer. By variable bypass, we refer to splitting the fresh gas flow in a provider-determined ratio, referred to as the splitting ratio. Practically speaking, this is seen as a percentage of gas delivery. For context, a majority of the gas is diverted to the patient without ever interacting with the vaporizer; the remaining volume of gas is diverted through a sump line into the vaporizer unit where it flows over the gas vapor and binds to the oxygen. It later works its way to the bypass line where the volatile anesthetic can enter the breathing system and patient (Chakravarti, 2013).

Baffles are used to increase the surface area for the gas flow and anesthetic to bind, whereas wicks function in the same capacity of a candle in bringing the liquid agent closer to the fresh gas.

Today, the Tec 7 vaporizers (GE), Vapor 2000 Series (Drager), and the Sigma Delta (Penlon) are all variable bypass design vaporizers. The working principle of all these vaporizers is similar (Chakravarti, 2013). Some key features these vaporizers use to enhance vaporizing capabilities are baffles and wicks. Baffles are used to increase the surface area for the gas flow and anesthetic to bind, whereas wicks function in the same capacity of a candle in bringing the liquid agent

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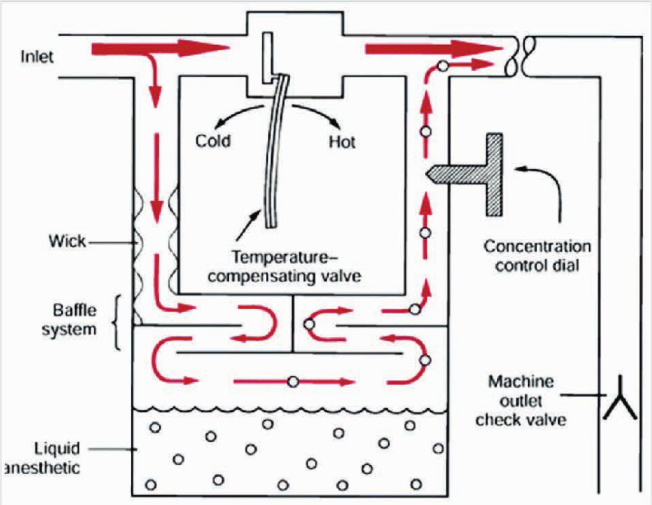

Figure 4: Principle of variable bypass vapouriser-plenum vapouriser

Modern Anaesthesia Vapourisers - Scientific Figure on ResearchGate. Available from: **https://www.researchgate.net/figure/Principle-of-variable-bypass-vapouriser-plenum-vapouriser_fig7_258703085** [accessed 18 Oct, 2020]

closer to the fresh gas. Both designs again help enhance vaporization and help ensure the proper concentration is delivered to the patient (Chakravarti, 2013) [refer to Fig. 4].

ASTM Regulations

To ensure regularity the American Society for Testing and Materials International (ASTM) sets multiple standards that all anesthetic vaporizers must have in order to be compliant to ensure the safe delivery of anesthetic. The ASTM International requires that manufacturers provide information regarding "...variations in ambient temperature and pressure, tilting, back pressure, and input flow rate and gas mixture composition on vaporizer performance must be stated in the accompanying documents (ASTM, 2000)." Since ambient temperature and pressure can vary from city to city, manufactures must inform health systems of their particular parameters. Additionally, since titling and back pressure are events that can result in unmetered anesthetic flow to reach the patient, the manufactures are required to provide the steps necessary to troubleshoot and correct back-pressure and tilting events. In most cases, the procedure is to engage the vaporizer in a minimal setting and turn on the oxygen flowmeter to a flow rate above 5L/min. This procedure will evaporate the resting liquid from the system and purge it from the breathing system.

The ASTM International also set standards for volume of delivery requiring a "...delivered concentration from the vaporizer shall not devi- ate from the set value by more than ±20% or ±5% of the maximum setting, whichever is greater, without back pressure (ASTM, 2000). Practically speaking, if the concentration calibrated dial is set to deliver 2% of Sevoflurane, the vaporizer is within regulation if it's actually delivering between 1.6% and 2.4%. Secondarily the regulations allow for a maximum delivery capacity variability of ±5%. Meaning that is the max percent of delivery is 8%, that the actual regulatory delivery can range from 7.6% to 8.4%. For the technologist, this is an important parameter to understand. Suppose the gas analysis is indicating an Inspiratory concentration greater than 20% to set delivery, then the vaporizer is not within regulatory bounds and needs to be exchanged. Clinically speaking, this excessive amount of gas delivery beyond the patient's MAC level could result in complications like a drop in CBP or acute liver injury.

The ASTM also mandates that the delivery of the anesthetic in the OFF position must be less than 0.05%, a parameter that accounts for minor clinically irrelevant leaks (ASTM, 2000). Furthermore, it dictates that regardless of brand, the vaporizer's control knobs must rotate in a counterclockwise fashion (ASTM, 2000). Regarding refilling the vaporizer unit, the ASTM mandates that the volume level must be displayed. The ASTM mandates that the vaporizer must have systems in place to prevent overfilling. The primary reason is that overfilling can result in a pumping effect which ejects liquid agent beyond the bypass into the breathing system. This excess liquid would result in an unmetered delivery of volatile anesthetic to the patient. The technologist needs to ensure proper refilling of the vaporizer and ensure the anesthesia provider follows proper protocols when refilling to limit damage to the unit and potential harm to the patient. The ASTM details other parameters for the anesthetic vaporizer unit; however, the above-mentioned items are of particular importance to the technologist.

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In Conclusion

Delivery of vaporized anesthetic agents has come a long way since their beginnings in the 1800s; from the small glass container containing highly volatile ether compound to today's use of halogenated hydrocarbons. Anesthesia delivery is far safer and far more practical in regards to predictability and efficacy. The advent of these newer volatile anesthetics and delivery devices has also allowed surgical suites to perform a wider array of surgical procedures once thought impossible. For the technologist, they must have a working understanding of the vaporizer units and the chemistry and physical properties behind the anesthetics themselves. When appropriately utilized by the anesthesia care team, halogenated anesthetic gases' delivery can yield a safe anesthetic with a smooth induction and emergence process.

Take the QUIZ On The Next Page

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Continuing Education Quiz

To test your knowledge on this issue's article, provide correct answers to the following questions on the form below. Follow the instructions carefully.

1. According to Butterworth what is the partial pressure of Sevoflurane?
a) 160mmHg
b) 669mmHg
c) 140mmHg
d) 559mmHg

2. What is the volume percent of Sevoflurane?
a) 21%
b) 31%
c) 41%
d) 11%

3. Why should Sevoflurane be avoided in Hemorrhagic events?
a) Potentiate an increase in CBF
b) Potentiate a decrease in CBF
c) Potentiate an increase in PVR
d) Potentiate a decrease in PVR

4. What does the inclusion of baffles do to the vaporizer?
a) Increases surface area
b) Decreases surface area
c) No change to surface area
d) Lowers Saturated vapor pressure

5. What BEST describes the TEC-7 vaporizer?
a) Variable bypass
b) Injection
c) Chiari proficiency vaporizer
d) Divisible bypass

6. Sevoflurane is seen to decrease _____.
a) Renal blood flow
b) Pulmonary blood flow
c) Hepatic blood flow
d) Pancreatic blood flow

7. What patient population may experience QT-prolongation 60-minumutes after sevoflurane administration?
a) Adult
b) Geriatrics
c) Pediatrics 6-12yo
d) Infants

8. What halogen is used to produce Isoflurane?
a) Fluorinated
b) Brominated
c) Chlorinated
d) Iodinated

9. Why is halothane not used in adult populations
a) It is linked to barotrauma
b) Its is linked to liver injury
c) It is linked to acute COPD
d) It is linked to the inducement of torsade de pointes

10. Sevoflurane has high blood solubility.
a) True
b) False

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2: A B C D	**7:** A B C D
3: A B C D	**8:** A B C D
4: A B C D	**9:** A B C D
5: A B C D	**10:** A B

Quiz 1 of 2

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