

Inhalational Anesthetics

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Inhalational anesthetics are commonly used in veterinary medicine to maintain general anesthesia. They are delivered to the patient via the anesthesia machine through the lungs and they do not require hepatic metabolism for their excretion. The amount of inhaled anesthetic can be easily monitored and controlled. The response to these agents is somehow predictable, since it is very similar among species. The main disadvantage is that an anesthesia machine is required to deliver inhalants, and these machines are bulky, expensive, and they need periodic maintenance.

Gas anesthesia is the most common technique used for general anesthesia in small animals, however the mechanism of action of these drugs is still unknown. There are several theories that try to explain how these gases produce anesthesia, but none of them fully explains their mechanism of action.

Vapor Pressure

All inhalants, except for nitrous oxide, are administered as vapor. A vapor is an agent in its gaseous phase that can be condensed to a liquid by increasing the pressure without reducing the temperature. This is possible because the room temperature is lower than the critical temperature of that specific vapor. The critical temperature is the temperature above which the gas cannot be liquified by pressure alone. The boiling point is the temperature at which the vapor pressure equals the barometric pressure. The vapor pressure is the pressure exerted by a vapor when it exists in equilibrium with its liquid state. We refer to partial pressure when the gas is mixed with other gases. In anesthesia, inhalants are measured in volume %, which represents the ratio between vapor pressure and barometric pressure ($\text{Vol}\% = \frac{\text{vapor pressure}}{\text{barometric pressure}} \times 100$). This means that 2% of isoflurane is equal to $0.02 \times 760 \text{ mmHg}$ (barometric pressure at sea level), which is 15.2 mmHg. The vapor pressure is temperature dependent and an increase in temperature will increase the vapor pressure of an inhalational anesthetic. According to Dalton's law the total partial pressure of a gas mixture is the sum of each gas partial pressure present in the mixture.

Inhalant	Boiling point (°C at 760 mmHg)	Vapor pressure (mmHg at 20°C)	Maximum concentration (Vol% at 20°C, 760 mmHg)
Isoflurane	48.5	238	31.3
Sevoflurane	58.6	157	20.7
Desflurane	22.8	669	88.0

Solubility

When we deal with injectable drugs, a solute is the substance dissolved in the solvent. When heat is applied to the solution, we can dissolve more solute in it. For gases dissolved in solvents, things are different. When we apply heat to a solution containing gas, more molecules of that gas escape from the solvent into the gaseous phase. When a gas is dissolved into a solute (i.e. liquid), there is a constant net movement of its molecules, until the equilibrium between the dissolved gas in the liquid and the undissolved gas above the liquid is reached. At this point the net movement stops. The amount of molecules dissolved into a solvent at equilibrium depends on the specific gas (and its partial pressure), the solvent, and the temperature. However, when equilibrium is reached, the partial pressure of the gas (but not the amount of molecules!) in the air above the liquid and the partial pressure of the gas dissolved in the liquid will be the same. The solubility of inhalational anesthetics in blood is measured using the blood/gas partition coefficient, which describes how the gas partitions itself between dissolved (in the blood) and the undissolved (in the alveoli) phases. The higher the blood/gas partition coefficient, the more soluble the anesthetic is in the blood. Inhalants with higher blood/gas partition coefficient will take longer to reach equilibrium. In general this means that if an anesthetic agent is more soluble in blood it takes longer to induce general anesthesia using this inhalant via facemask, longer to recover, and longer to make a change in the anesthetic depth. In other words solubility means *speed* and *control*. The

blood/gas partitional coefficient of isoflurane, sevoflurane, and desflurane at 37°C are 1.4, 0.6, and 0.4, respectively.

MAC

The minimum alveolar concentration (MAC) is the volume % at 1 atmosphere (760 mmHg) of an inhalation anesthetic required to prevent movement in 50% of subjects exposed to a supramaximal stimulus. MAC is the equivalent of the effective dose₅₀ (ED₅₀) and it is a measurement of potency. The lower the MAC the greater the potency. MAC can be used to compare different inhalants and to predict their pharmacodynamic effects, since they cause similar changes at equipotent MAC multiples. MAC is species specific and allows to predict what percentage we should use to prevent movement during surgery. Usually 1.3-1.5 x MAC prevents movement in 95% of subjects. MAC values are additive and 2 inhalants used in the same patient work synergistically. All anesthetic drugs that have anesthetic-sparing effects, decrease MAC, and that is why when we use some of these drugs for premedication or during surgery (i.e. opioids), so we can use less inhalant to achieve a surgical plane of anesthesia. Other factors that decrease MAC include: age (geriatric patients), severe hypotension, hypoxemia, and hypercarbia, hypothermia, hyponatremia, pregnancy, and metabolic acidosis.

Inhalant	MAC in the dog (%)	MAC in the cat (%)
Isoflurane	1.3-1.4	1.3-1.6
Sevoflurane	2.3	2.6-3.4
Desflurane	7.2-8.2	9.8-10.2

Delivery and uptake

Inhalational anesthetics move following a partial pressure gradient, from areas with high partial pressure to areas with low partial pressure until equilibrium is reached. At the beginning of the anesthetic event, the inhalant moves from the anesthesia machine to the patient's alveoli. The change in partial pressure of the anesthetic in the alveoli is influenced by the delivery and by the uptake. To increase the partial pressure in the alveoli:

- Increase delivery of inhalant to alveoli by
 - Increasing inhaled partial pressure
 - Turn up the vaporizer
 - Increase the fresh gas flow
 - Minimize the volume of the breathing circuit
 - Increasing alveolar ventilation
 - Increases delivery of the anesthetic to the alveoli
- Decrease the uptake factors
 - Solubility
 - Cardiac output
 - Alveolar-venous partial pressure difference

Elimination

This process is the opposite of the delivery and uptake, with some differences. During the first period of the anesthetic event, we can increase the delivery by using the overpressure techniques (high % of inhalant), however this is not possible during recovery (we cannot deliver less than 0%). The only thing we can do is flushing the breathing circuit with fresh O₂ during recovery to increase the partial pressure difference between alveoli and anesthesia machine and to facilitate the elimination of the inhalant. The duration of anesthesia is also important. The longer this period is, the more anesthetic is absorbed in the tissues and the longer the recovery is. This is more evident for inhalants with a higher blood/gas partition coefficient (higher solubility).