

General Anesthetics: Inhaled and Intravenous Anesthetics

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Inhaled anesthetics are either volatile or gaseous anesthetics used to induce general anesthesia. Volatile anesthetics include halothane, enflurane, isoflurane, desflurane, and sevoflurane. These anesthetics are liquid at room temperature. Gaseous anesthetics include nitrous oxide and xenon both of which are gaseous at room temperature.



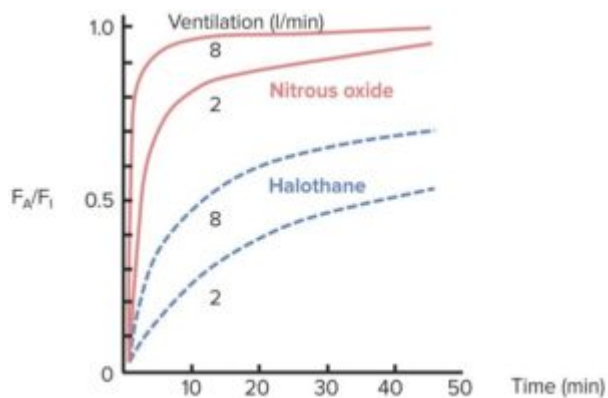
Pharmacokinetics of Inhaled Anesthetics

It is important for the anesthesiologist to understand the pharmacokinetic properties of the different types of inhaled anesthetics for safe and optimum use.

Inhaled anesthetics enter the central nervous system by gaseous diffusion through the alveoli. Therefore, the effects of these anesthetics are dependent on **alveolar concentration**. The **partial pressure of the inhaled anesthetic** and the **alveolar ventilation** are two important parameters that affect the alveolar concentration of a given anesthetic.

The **partial pressure** or intrinsic concentration is defined as the partial pressure of an

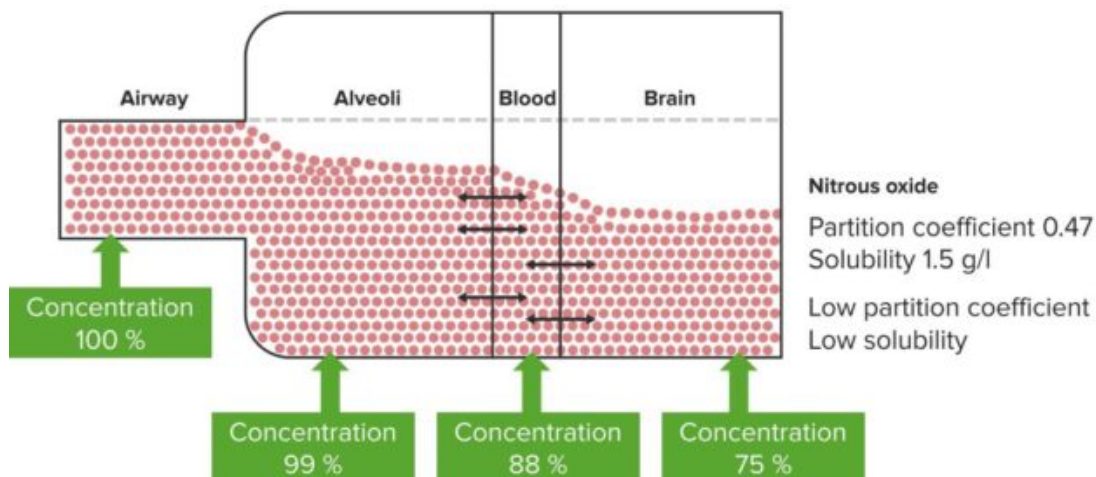
inhaled anesthetic compared to the other components of the ventilated air, i.e. oxygen, nitrogen, etc. Increasing the intrinsic concentration of the inhaled anesthetic is therefore directly related to an increase in the blood concentration of the anesthetic compound and also to the rate at which anesthetic induction can be achieved.



“Effect of ventilation on the ratio of alveolar drug concentration to inhaled concentration” Image created by Lecturio

Alveolar ventilation also contributes to the equation. The higher the tidal volume and the faster the ventilation rate, the more rapid the anesthetic concentration is going to rise in the blood.

In addition to these two parameters, the anesthetic effects of the different inhaled anesthetics also depend on their **solubility**. Anesthetics with low solubility such as **nitrous oxide** are going to have a rapid onset and rapid recovery of the effect while anesthetics with good blood solubility such as **halothane** are expected to have a slower rate for onset and recovery.



“The-Blood-Gas-Partition-Coefficient” Image created by Lecturio

Cardiac output is another important parameter that impacts anesthetic uptake but not induction. While increased cardiac output can allow for faster uptake of the inhaled anesthetic from the alveoli, the brain is well protected from rapid changes in blood concentrations of these compounds by a well-regulated **blood-brain barrier**. Therefore, a high cardiac output may result in a peripheral distribution of the anesthetic without increasing the brain concentrations.

Elimination of the inhaled anesthetic is also dependent on the solubility of the compound.

Similar to the induction rate, the higher the solubility of the inhaled anesthetic in the blood the slower it will be eliminated. Newer inhaled anesthetics such as **desflurane** or **sevoflurane** are mainly dependent on ventilation for elimination and do not need to be metabolized making them safer for patients with **liver or kidney disease**.

Treatment strategies

Inhaled anesthetics		Intravenous anesthetics	
Gases	Volatile Liquids	Barbiturates • Thiopental	Opioids • Fentanyl
Nitrous oxide	<ul style="list-style-type: none"> • Halothane • Enflurane • Desflurane • Isoflurane • Methoxyflurane • Sevoflurane 	Dissociative • Ketamine	Benzodiazepines • Midazolam • Lorazepam • Diazepam
		Miscellaneous • Etomidate • Propofol	

Pharmacodynamics of Inhaled Anesthetics

Inhaled anesthetics also affect the **cardiovascular system**, the **respiratory system**, the **renal system**, the **liver** and the **smooth muscle cells of the uterus**.

Inhaled anesthetics work through a **suppressive effect on brain metabolism and cerebral blood flow**. While they decrease cerebral blood flow similar to intravenous anesthetics, they can also cause **vasodilation** in the brain. The central nervous system effects can be divided into four stages.

First, **analgesia** is achieved, followed by **excitement**, **surgical anesthesia** and finally **medullary depression**. The anesthesiologist aims to achieve either stage III or IV depending on his or her goals and the type of procedure to be performed.

The surgical anesthesia stage can be achieved by the minimal alveolar concentration which is different for each inhaled anesthetic. At the medullary suppression stage, the patient would die if **respiratory and cardiac support** is not provided because the respiratory and cardiac control centers in the brain stem will be affected by the anesthetic.

The effects of the different inhaled anesthetics on the brain can also be appreciated by doing a simultaneous **electroencephalogram (EEG)** during induction.

While this procedure is usually done for research purposes it also gave us some insights about the epileptogenic effects of sevoflurane and enflurane. While sevoflurane can cause epileptic spikes and slow wave complexes on the EEG, only enflurane is associated with the induction of clinical seizures. Hence, the **use of enflurane for surgery on patients with the risk of epilepsy is not recommended**.

Inhaled anesthetics decrease cardiac contractility, **mean arterial blood pressure** and induce vasodilation. **Vasodilation** decreases peripheral vascular resistance which in turn

also contributes to the reduction in the mean arterial blood pressure.

Isoflurane, desflurane, and sevoflurane have a lower impact on the cardiac output compared to halothane or enflurane, hence they are recommended in patients with **heart failure**. Halothane can induce **arrhythmias** in these patients.

Inhaled anesthetics decrease ventilation, sensitivity to **hypoxia**, and might induce **bronchospasm**.

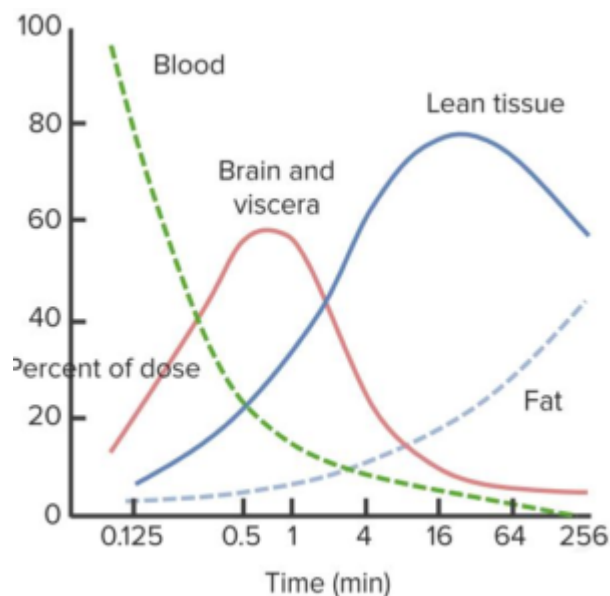
While newer inhaled anesthetics are not metabolized, they can still have an **impact on the liver**. Patients who are in **hypovolemic shock** are at an increased risk of inhaled anesthetic-induced hepatitis (from reduced blood flow to the liver causing ischemia). Patients on nitrous oxide for long periods of time may develop **megaloblastic anemia** due to methionine deficiency.

Malignant hyperthermia is currently believed to be a heritable condition. In addition to volatile anesthetics, **succinylcholine**, a depolarizing muscle relaxant, can also cause malignant hyperthermia. Patients develop **muscle rigidity, hyperthermia, tachycardia, hypercapnia, hyperkalemia, and metabolic acidosis**. Patients develop these symptoms due to a sudden increase in the free cytosolic calcium concentration in skeletal muscles after exposure to one of the triggering agents.

Management of malignant hyperthermia includes appropriate **fluid and electrolytes replacement therapy** and the administration of **dantrolene**. Dantrolene prevents calcium release from the sarcoplasmic reticulum. Patients who are known to be at risk, i.e. family history of malignant hyperthermia, should undergo the **caffeine-halothane contracture test**. A skeletal muscle biopsy is taken from the patient and caffeine-halothane mixture is injected. If the test is positive, then the patient should not be administered a volatile anesthetic.

Intravenous Anesthetics

Barbiturates



"Barbiturates" Image created by Lecturio

Barbiturates such as **thiopental** and **methohexital** induce anesthesia by acting on **GABA_A receptors**.

Thiopental is also recommended in traumatic brain injury patients to induce coma or for urgent surgical interventions such as epidural hematoma because it decreases the intracranial pressure by decreasing the cerebral blood flow without inducing vasodilation.

Benzodiazepines

Diazepam can be used rectally for **seizure abortion** but is unlikely to be of benefit in patients undergoing surgery because it does not have an anesthetic or an analgesic effect. It can, however, decrease **anxiety** before surgery.

Midazolam, on the other hand, is used to induce anesthesia. Benzodiazepines act on **GABA receptors**.

Ketamine

Ketamine is a **dissociate analgesic**. It does not induce loss of consciousness but causes analgesia and amnesia. The patients can undergo 'awake' procedures with ketamine. They will be awake during the procedure but the procedure will be painless and they will not remember the procedure afterward.

Ketamine acts by inhibiting the **NMDA glutamate receptors**. Ketamine should not be used in patients with brain tumors or traumatic brain injuries because it can increase intracranial pressure. Additionally, ketamine should be used with caution in patients with [cardiovascular disease](#) because it can elevate blood pressure.

Propofol

Propofol is one of the most commonly used induction anesthetics. It induces anesthesia very rapidly and the effects wear off very quickly. It is currently being used in the [intensive care unit](#), in **surgeries**, and during **laparoscopic surgeries**.

Additionally, Propofol has been previously used in patients undergoing **therapeutic endoscopy**. Propofol can cause hypotension which may complicate cases with increased risk of peripheral vascular injury, i.e. hypovolemic patients with GI bleeds.

References

Smyth EM, FitzGerald G a. Basic and clinical Pharmacology. 2012.

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