

# Anesthetics 2

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# INHALATION ANESTHETICS

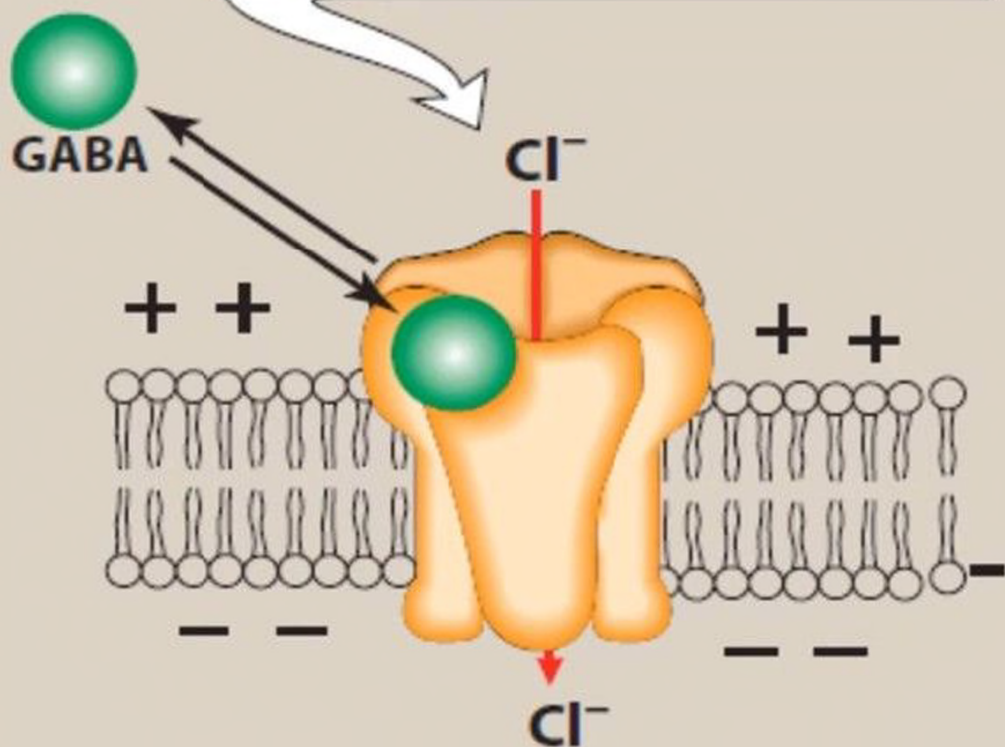
## Mechanism of action

No specific receptor has been identified as the locus to create a state of general anesthesia. The fact that chemically unrelated compounds produce unconsciousness argues against the existence of a single receptor, and it appears that a variety of molecular mechanisms may contribute to the activity of anesthetics. At clinically effective concentrations, general anesthetics increase the sensitivity of the  $\gamma$ -aminobutyric acid (GABAA) receptors to the inhibitory neurotransmitter GABA. This increases chloride ion influx and hyperpolarization of neurons. Postsynaptic neuronal excitability and, thus, CNS activity are diminished. Unlike other anesthetics, *nitrous oxide* and *ketamine* do not have actions on GABAA receptors. Their effects are mediated via inhibition of *N*-methyl-d-aspartate (NMDA) receptors.

[Note: The NMDA receptor is a glutamate receptor, which is the body's main excitatory neurotransmitter.] Receptors other than GABA that are affected by volatile anesthetics include the inhibitory glycine receptors found in the spinal motor neurons. Additionally, inhalation anesthetics block excitatory postsynaptic currents found on nicotinic receptors. However, the mechanisms by which anesthetics perform these modulatory roles are not fully understood.

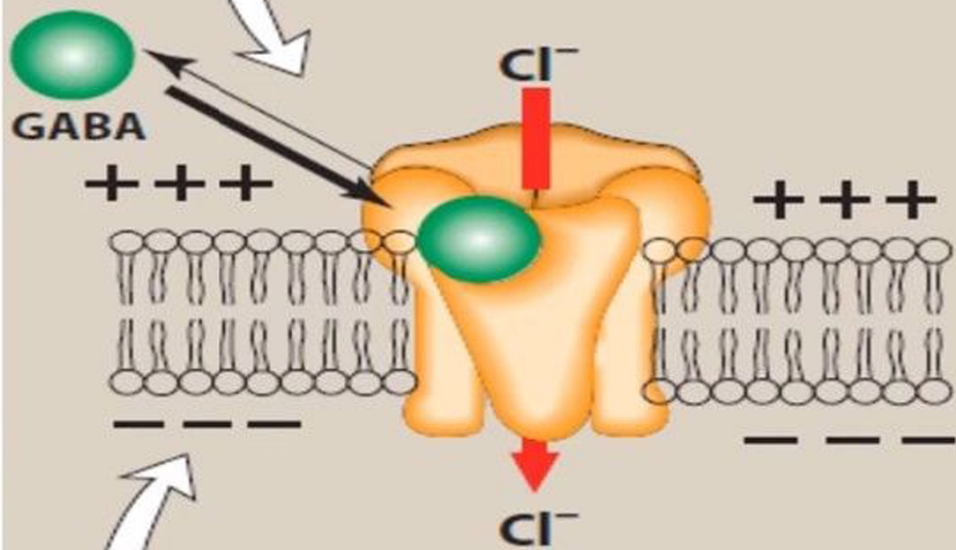
## **A** No anesthetic

Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.

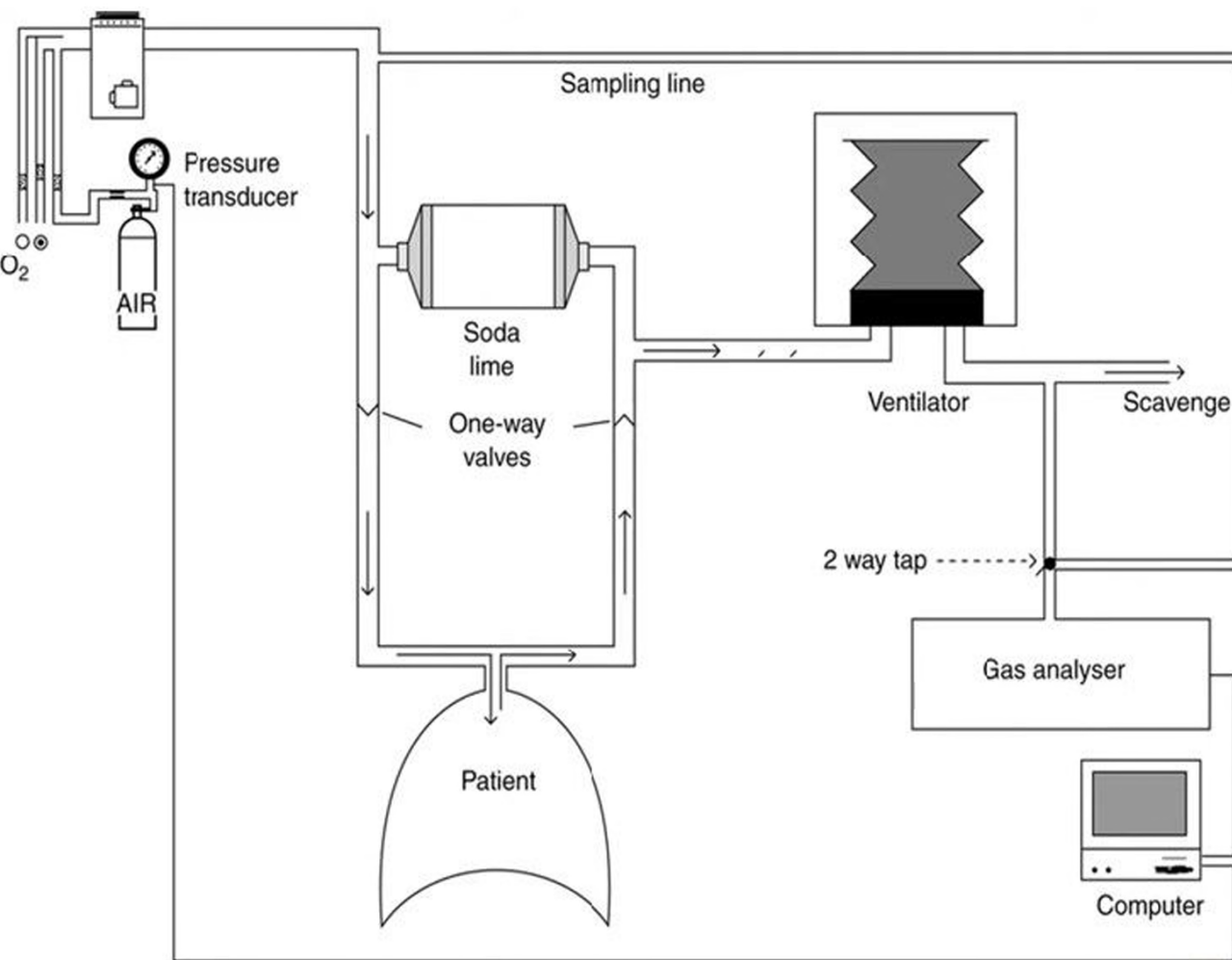


## **B** In presence of inhaled anesthetic

Binding of GABA is enhanced by inhaled anesthetics, resulting in a greater entry of chloride ion.



Entry of Cl<sup>-</sup> hyperpolarizes cell, making it more difficult to depolarize, and therefore reduces neural excitability.



## Soda Lime Reactions

1.  $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3$
2.  $\text{H}_2\text{CO}_3 + \text{NaOH} \rightarrow \text{NaHCO}_3$
3.  $\text{NaHCO}_3 + \text{Ca(OH)}_2 \rightarrow \text{CaCO}_3 + \text{H}_2\text{O} + \text{NaOH}$

- Soda Lime consist of 4% NaOH, 1% KOH, 76% TO 81% CaOH, 14% TO 19% H<sub>2</sub>O

4-8 Mesh size granules-higher the mesh number the smaller the granule

Large granules provide small surface area and decrease resistance to flow

Moisture is added to prevent drying out and silica is added for hardness

**CO<sub>2</sub> ABSORPTION**

## Isoflurane

*Isoflurane*, like other halogenated gases, produces dose-dependent hypotension predominantly from relaxation of systemic vasculature. Hypotension can be treated with a direct-acting vasoconstrictor, such as *phenylephrine*. Because it undergoes little metabolism, *isoflurane* is considered nontoxic to the liver and kidney. Its pungent odor stimulates respiratory reflexes (breath holding, salivation, coughing, laryngospasm), so it is not used for inhalation induction. With a higher blood solubility than *desflurane* and *sevoflurane*, *isoflurane* takes longer to reach equilibrium, making it less ideal for short procedures; however, its low cost makes it a good option for longer surgeries

## Desflurane

*Desflurane* provides very rapid onset and recovery due to low blood solubility. This makes it a popular anesthetic for short procedures. It has a low volatility, which requires administration via a special heated vaporizer. *Desflurane* has significant respiratory irritation like *isoflurane* so it should not be used for inhalation induction

## Sevoflurane

*Sevoflurane* has low pungency or respiratory irritation. This makes it useful for inhalation induction, especially with pediatric patients who do not tolerate IV placement. It has a rapid onset and recovery due to low blood solubility. *Sevoflurane* has low hepatotoxic potential, but compounds formed from reactions in the anesthesia circuit (soda lime) may be nephrotoxic with very low fresh gas flow that allows longer chemical reaction time.

## Halothane

*Halothane* is a noninflammable, nonirritant, photosensitive volatile agent with a sweet smell. It is a liquid at room temperature and it is administered with a special vaporizer. A precise control of the concentration of *halothane* is essential as it can cause direct effect on heart by interfering with calcium, thus causing depression of myocardial contractility. Dose-dependent fall in blood pressure is known during *halothane* anesthesia. It directly suppresses respiratory centers, thereby reducing ventilatory response to blood carbon dioxide levels. Decreased alveolar ventilation can cause increase in arterial CO<sub>2</sub> levels without compensatory increase in ventilation. Therefore, continuous arterial gas monitoring is essential during its usage.

*Halothane* dilates cerebral blood vessels and increases cerebral blood flow which in turn causes increased intracranial pressure, especially in patients with other susceptible comorbid conditions in the brain. It causes relaxation of skeletal muscle and potentiates the actions of competitive neuromuscular blockers. *Halothane* causes uterine smooth muscle relaxation. Although it is useful for the manipulation of fetus orientation, it is not used due to its action of inhibiting uterine contraction during parturition. Therefore, it is not used for vaginal delivery. More than 60% of the inhaled *halothane* is eliminated through lungs on recovery within 24 hours. The rest of *halothane* is metabolized by liver. Trifluoroacetic acid is a major metabolite which can cause hepatic injury (*halothane*-induced hepatic necrosis). This syndrome of hepatic necrosis is reported in 1 in 10,000 patients and it is referred to as “halothane hepatitis.”

## Nitrous oxide

*Nitrous oxide* (“laughing gas”) is a nonirritating potent sedative that is unable to create a state of general anesthesia. It is frequently used at concentrations of 30% to 50% in combination with oxygen to create moderate sedation, particularly in dentistry. *Nitrous oxide* does not depress respiration and maintains cardiovascular hemodynamics as well as muscular strength. *Nitrous oxide* can be combined with other inhalational agents to establish general anesthesia, which lowers the required concentration of the combined volatile agent. This gas admixture further reduces many unwanted side effects of the other volatile agent that impact cardiovascular output and cerebral blood flow. *Nitrous oxide* is poorly soluble in blood and other tissues, allowing it to move very rapidly in and out of the body. This can be problematic in closed body compartments because *nitrous oxide* can increase the volume (exacerbating a pneumothorax) or pressure (sinus or middle ear pressure); it replaces nitrogen in various air spaces faster than the nitrogen leaves. Its speed of movement allows *nitrous oxide* to retard oxygen uptake during recovery, thereby causing “diffusion hypoxia.” This can be overcome by delivering high concentrations of inspired oxygen during recovery.

## Malignant hyperthermia

In a very small percentage of susceptible patients, exposure to halogenated hydrocarbon anesthetics (or *succinylcholine*) may induce malignant hyperthermia (MH), a rare life-threatening condition. MH causes a drastic and uncontrolled increase in skeletal muscle oxidative metabolism, overwhelming the body's capacity to supply oxygen, remove carbon dioxide, and regulate temperature, eventually leading to circulatory collapse and death if not treated immediately. Strong evidence indicates that MH is due to an excitation–contraction coupling defect. Burn victims and individuals with muscular dystrophy, myopathy, myotonia, and osteogenesis imperfecta are susceptible to MH-like events and caution should be taken. Susceptibility to MH is often inherited as an autosomal dominant disorder. Should a patient exhibit symptoms of MH, *dantrolene* is given as the anesthetic mixture is withdrawn, and measures are taken to rapidly cool the patient. *Dantrolene* blocks release of  $\text{Ca}^{2+}$  from the sarcoplasmic reticulum of muscle cells, reducing heat production and relaxing muscle tone. It should be available whenever triggering agents are administered. In addition, the patient must be monitored and supported for respiratory, circulatory, and renal problems.