# INHALANT ANAESTHESIA

## INTRODUCTION

Inhalation anaesthetics are used widely for the anaesthetic management of animals. They are unique among the anaesthetic drugs because they are administered, and in large part removed from the body, via the lungs. A special apparatus is usually used to deliver the inhaled agents. This apparatus includes a source of oxygen ($O_2$) and a patient breathing circuit that in turn usually includes an endotracheal tube or face mask, a means of eliminating carbon dioxide ($CO_2$), and a compliant gas reservoir. These components help minimize patient morbidity or mortality because they facilitate lung ventilation and improved arterial oxygenation. In addition, inhalation anaesthetics in gas samples can now be readily and affordably measured almost instantaneously. Measurement of inhalation anaesthetic concentration enhances the precision and safety of anaesthetic management beyond the extent commonly possible with injectable anaesthetic agents.

All contemporary inhalation anaesthetics are organic compounds except $N_2O$, cyclopropane and xenon which are inorganic anaesthetics. To render these agents less reactive, more potent, nonflammable inhalation anesthetic, focus on halogenation (i.e., addition of fluorine, chlorine, or bromine; iodine is least useful) of these compounds has predominated. Chlorine and bromine especially convert many compounds of low anaesthetic potency into more potent drugs.

The inhalant anaesthetics are chloroform, ether, cyclopropane, enflurane, desflurane, halothane, isoflurane and sevoflurane. Their uptake and distribution determine the anaesthetic action of these inhalant agents. The uptake and distribution depend on-

- Solubility coefficient - At any given temperature the mass of a gas dissolved in a solution (i.e., its concentration in the solution) varies directly with its tension and is governed by the solubility of the gas in a particular solvent. For example, the blood gas partition coefficient of nitrous oxide is 0.47. This means that there will be 47 parts of nitrous oxide in blood for every 100 parts of nitrous oxide per unit volume (litre) of alveolar air. The solubility of most of the inhalant agents in brain and other tissues except fat are almost common as that of blood. That means the tissue – blood partition coefficient will be almost the same. Whereas halothane is almost 60 times more soluble in fat than other tissues; hence the blood partial coefficient will be lesser than the fat. Brain – lipid (fat) coefficient will be almost equal (2.6) because of the lipid nature of brain.
- Blood flow - The inhaled anaesthetic gas is diluted in the residual air when it enters pulmonary ventilation and then distributed to alveolar membrane. From alveolar membrane two types of diffusion take place. The major diffusion process takes place into the pulmonary blood (pulmonary circulation) and it reaches equilibrium with alveolar tension immediately. The second process occurs across the capillary membrane of the lung into the interstitial fluid, then to the cells through the cell membrane and finally into the venous blood leaving the lung (bronchial circulation). In this manner the arterial and venous tension of the anaesthetic slowly increases towards the neutral equilibrium with the inspired air.
- Solubility of inhalant anaesthetic is defined as a concentration distribution ratio between alveolar concentration and the tissue concentration. The solubility of inhalant anaesthetics influences the induction and recovery time. Methoxyflurane is highly soluble than isoflurane in the body tissues hence the induction and recovery will be slow.
- Minimum alveolar concentration (MAC) - It is the concentration of the inhalant anaesthetic in the alveoli to produce lack of response in 50% of the subjects to a standard stimulus. This term is used to mention the potency of the anaesthetic. The MAC of each inhalant anaesthetic varies in each species.

The other factors are- Physical and chemical properties of the agent, absorption, Pulmonary blood flow, cardia output perfusion, lipid content of tissues and final elimination

## NITROUS OXIDE

Nitrous oxide is the oldest anaesthetic gas available as liquid at room temperature in cylinders (See anaesthetic equipment).

- Its MAC is more than 100% in animals (Dogs 188%, Cats 255%).
- It has got good analgesic property and combining narcotics, which interact selectively with opiate receptor endorphin system, potentiates the analgesia.
- Nitrous oxide is used as the principal anaesthetic at a level of 80% in combination with 20% oxygen for dental extraction in human. In veterinary anaesthesia, it is combined with other injectable and inhalant agents.
- It is used as fresh gas source or carrier gas. It helps in additional uptake of the inhalant agent and potentiate the desirable effects at a minimal concentration of the inhalant agent (Second gas effect).
- It is eliminated rapidly from the body because of low partition coefficient and relatively insoluble nature.
- Nitrous oxide moves rapidly through tissues faster than carbon dioxide and diffuses into the closed cavities filled with gas such as pneumothorax and distended intestinal loops due to obstruction or strangulation and induces detrimental effects by inducing further distension.
- It is not used in ruminants, as it will diffuse into the rumen and results in distension and increase in transdiaphragmatic pressure. In horses prolonged administration induce distension of bowels and increase in transdiaphragmatic pressure.
- It induces tachypnoea at higher concentration due to direct central stimulation.
- During recovery it may induce diffusion hypoxia following prolonged administration. The outward movement of nitrous oxide from the alveoli reduce the alveolar partial pressure of oxygen. The expired air may contain more than 10% of nitrous oxide. In older animals and animals maintained for a longer duration with nitrous oxide must be supplemented with oxygen.
- Prolonged exposure to nitrous oxide causes bone marrow depression due to depletion of Vit.B12. Hence it can cause occupational hazards to humans. The theatre environment must have less than 25 ppm of nitrous oxide.
- Nitrous oxide is administered at 66 to 70% of the total inspired air. Oxygen is given at 30% concentration.

## DIETHYL ETHER

- It is a colourless, highly volatile and inflammable liquid with a boiling point 35°C.
- One pound of ether mixed in air can give 277 cubic feet of flammable mixture. The ignition temperature is 304 C.
- The MAC is 1.92%.
- It gives an irritating vapour and may cause salivation if not premedicated with anticholinergics.
- In low concentration the vagal activity is decreased and at higher concentration it induce arrhythmia.
- Catecholamine level increases following ether administration.
- The use of ether is decreased due to its explosive and inflammable nature.
- Health hazards are more in human exposed to ether for a prolonged period.

## METHOXYFLURANE

- Methoxyflurane is a halogen-substituted ethyl ether (O2,2-dichloro-1,1 difluoro ethyl methyl ether).

- Its boiling point is 104°C and is non-flammable and nonexplosive. Its molecular weight is 165.9 and the specific gravity is 1.41 at 25°C.
- It has fruity odour and an antioxidant butylated hydroxyflurane is added for stability.
- This antioxidant may accumulate in the vaporizer wick hence methoxyflurane vaporizer must be often clea2ned and rinsed with diethyl ether.
- The MAC is 0.23.
- It reacts with metal, rubber and soda lime, and decomposes if exposed to ultraviolet light.
- Methoxyflurane induce dose dependent central nervous system depression. Though it can be used to mask induction, it is better to induce with injectable anaesthetics.
- It does not alter the cardiac function much except slight hypotension, which is associated with reduction in cardiac contractility, and cardiac output.
- Concurrent use of epinephrine and adrenaline are contraindicated as methoxyflurane sensitizes the myocardium to the actions of catecholamines.
- Compared to halothane the sensitization and cardiac arrhythmia are less.
- Methoxyflurane reduce the minute volume and induces respiratory acidosis.
- It is highly soluble in fat hence recovery will be prolonged in obese patients.
- Biotransformation of methoxyflurane results in fluoride ions, which are potent toxic agents to kidneys and is further aggravated by the concurrent use of tetracycline. Methoxyflurane is contraindicated in patients with renal disease.
- In veterinary practice its use is restricted to small animals.
- It can be used in most of the breathing circuits with oxygen and nitrous oxide.

**HALOTHANE**

- Halothane is colourless volatile liquid with a boiling point of 50.2°C and the vapour pressure is 244.1 mmHg at 20°C.
- It is non-flammable and nonexplosive.
- Halothane is a potent anaesthetic with a molecular weight of 197.4 and specific gravity 1.86 at 25°C.
- Halothane reacts with metal and soda lime and decomposes if exposed to ultra violet light.
- It is marketed in amber-coloured bottles with thymol.
- The MAC varies in various species.
    - Dogs 0.87%,
    - Cats 0.75%,
    - Horses 0.9%
    - Pigs 1.25%
- The MAC is reduced when combined with agents like morphine (reduced 84%), alfentanil (48%), xylazine and nitrous oxide.
- Halothane reduces cerebrospinal fluid production and pressure hence can be used in patients undergoing brain and spinal cord surgeries and in patients with increased intracranial pressure.
- It suppresses adrenal cortical hormone release by 50% due to its action and inhibition on the carrier - mediated transport system of choline.
- Halothane depress cardiac output, mean arterial pressure and coronary blood flow.
- Halothane decreases arrhythmogenic thresholds and sensitizes the myocardium for the actions of catecholamines. Exogenous administration of epinephrine or adrenaline induces cardiac arrhythmia and ventricular stand still.
- It induces AV shunts (arterio-venous shunts) and is further aggravated by hypoxia. (21 to 22%) thus resulting in ventilation perfusion mismatch. Oxygen exchange is further reduced in patients with pulmonary diseases.

- The minute volume decreases during halothane anaesthesia due to the decreased contractility of inspiratory muscles.
- Halothane induces hepatic hypoxia.
- Halothane undergoes biotransformation in the liver. The metabolic products or the intermediary products induce allergic and toxic responses similar to autoimmune diseases. The metabolic intermediary products bind with the bivalent genes responsible for self-protein synthesis in the liver. Following binding the genes will alter the coding and non-self-protein will be synthesized which may result in allergy, anaphylaxis or autoimmune like diseases.
- Experimental studies revealed that halothane has got teratogenic and mutagenic properties. In human the rate of successful deliveries following embryo transfer or gamete intra fallopian transfer were less as compared with isoflurane. Initial conception rate was high followed by higher incidence of absorption.
- Halothane suppress the number and activity of natural killer cells (NK cells) and produce immune suppression, thus favouring higher incidences of post anaesthetic infection. This property is taken as an advantage in patients undergoing tissue transplantation. It's better to revaccinate horses with tetanus toxoid following halothane exposure.

**ISOFLURANE**

- Isoflurane is the new inhalant anaesthetic widely used in human anaesthesia.
- It is relatively insoluble hence induction and recovery are quick.
- It is non-inflammable and does not react with metal, rubber or soda lime.
- It does not decompose if exposed to ultra violet light.
- Its vapour pressure is almost equal to halothane hence halothane vaporizers can be used after cleaning thymol. It has got pungent odour.
- It provides cardiac stability. Reduction in blood pressure is noticed during isoflurane anaesthesia due to the reduction in peripheral vascular resistance, not due to myocardial depression as in halothane. It increases the myocardial perfusion by reducing the coronary vascular resistance. It has little or no action on sensitizing the myocardium for the actions of catecholamines. Hence it is recommended in patients with cardiac diseases.
- It does not interfere with of central autoregulation of blood pressure, hence indicated in patients with head injuries.
- It has better muscle relaxation property than halothane and does not promote convulsions.
- It induces more respiratory depression than halothane and results in hypoventilation.
- Only 2% are metabolized in the liver due to its relative insolubility, hence recommended in patients with liver diseases.

**SEVOFLURANE**

- It is the newest inhalant anaesthetic used in humans. Still trials are conducted in veterinary anaesthesia.

*MAC values of some inhalant agents*

| **Agent** | **Dog** | **Cat** | **Horse** |
|---|---|---|---|
| *Halothane* | 0.86 | 0.98 | 0.88 |
| *Enflurane* | 2.2 | 2.37 | 2.12 |
| *Isoflurane* | 1.28 | 1.63 | 1.31 |
| *Methoxyflurane* | 0.23 | 0.23 | Not available |
| *Desflurane* | 7.2 | NA | NA |
| *Nitrous oxide* | 188 | 255 | NA |