INHALED ANAESTHETICS

Introduction

- These are the most common drug used for G/A
- Popularity is based on their
  - Ease of administration
  - Ability to monitor their effects
  - Relatively inexpensive
  - Prevents recalls and provides MR also

History

- The discovery of anaesthetic properties of N_2O, diethyl ether and chloroform in 1840s
- Long duration of 80 years before other inhaled anaesthetic were introduced. In 1950, all were flammable toxic exception of N_2O
- Halothane was synthesized in 1951
- Introduced for clinical use in 1956
- Due to enhance dysarrhythmogenic effect of epenephrine led to search for new derivative

History (contd…)

- Enflurane
  - Introduced in clinical use in 1973
  - Nephrotoxicity seems less likely
  - Does not enhance dysarrhythmogenic effect of epinephrine
  - It has epileptogenic potential
- Isoflurane, isomer of enflurane, introduced in 1981. Resistant to metabolism making organ toxicity unlikely

History (contd…)

- Desflurane was introduced in 1993
- Sevoflurane was introduced in 1995
- Low blood gas solubility of these agents
  - Rapid induction and rapid recovery
  - Precise control of anaesthetic concentration

Inhalational agents

Classification

A. Volatile anaesthetics

1. Diethyl Ether (CH_3CH_2-OCH_2CH_3)
2. Divinyl Ether [$(C_2H_3)_2$ O]
3. Ethyl chloride (C_2H_5Cl)
4. Chloroform ($CHCl_3$)
5. Trichloroethylene (CCl_2CHCl)
6. **Halothane ($CF_3CHClBr$)**
7. **Methoxyflurane**
8. **Enflurane**
9. **Isoflurane**
10. **Desflurane**
11. **Sevoflurane**

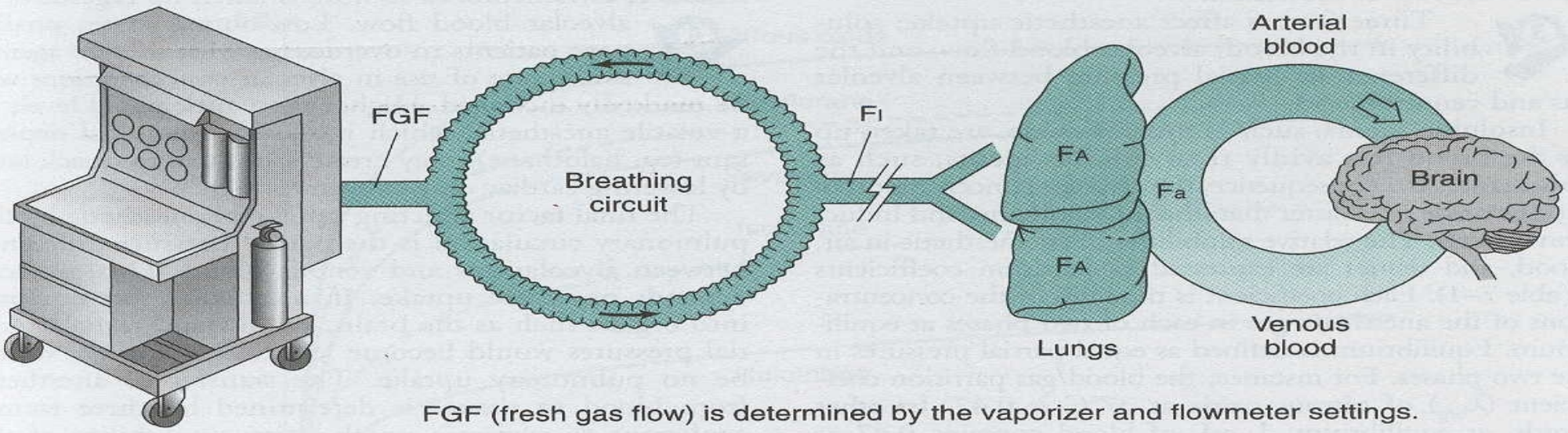
B. Anaesthetic gases

1. **Nitroux oxide**
2. Cyclopropane
3. Ethylene
4. Xenon, Argon
5. Sulphur hexafluoride

Uptake and Distribution

- Liquid anesthetic is vaporized and mixed with oxygen
- Mixture is delivered to the patient via a mask or endotracheal tube (ET tube)
- Mixture travels to lungs (alveoli) and diffuses into the bloodstream
- Diffusion rate is dependent on concentration gradient (alveoli/capillary) and lipid solubility of the anesthetic gas
  - Concentration gradient is greatest during initial induction

ANESTHETIC TRANSFER



FGF (fresh gas flow) is determined by the vaporizer and flowmeter settings.

F_I (inspired gas concentration) is determined by (1) FGF rate; (2) breathing-circuit volume; and (3) circuit absorption.

F_A (alveolar gas concentration) is determined by (1) uptake (uptake = $\lambda_{b/g}$ x C(A-V) x Q); (2) ventilation; and (3) the concentration effect and second gas effect:
a) concentrating effect
b) augmented inflow effect

F_a (arterial gas concentration) is affected by ventilation/perfusion mismatching.

Figure 7–1. Inhalation anesthetic agents must pass through many barriers between the anesthesia machine and the brain.

Physical and Chemical Properties of Inhalant Anesthetics

- Important properties to consider
  - Vapor pressure
  - Partition coefficient
  - Minimum alveolar concentration (MAC)
  - Rubber solubility

Vapor Pressure

- Is the amount of pressure exerted by the gaseous form of a substance when in equilibrium
  - i.e. – ***it's ability to evaporate***
- Determines how readily an inhalation anesthetic will evaporate in the anesthetic machine vaporizer
- Dependent upon temperature and anesthetic agent

Blood:Gas Partition Coefficient

- The measure of the solubility of an inhalation anesthetic in blood as compared to alveolar gas (air)
- Indication of the speed of induction and recovery for an inhalation anesthetic agent
- Low blood:gas partition coefficient
  - Agent is more soluble in alveolar gas than in blood at equilibrium
  - Agent is less soluble in blood
  - Faster expected induction and recovery

MINIMUM ALVEOLAR CONCENTRATION (MAC)

- It is the steady state expired gas concentration of an anesthetic
  - At 1 atm pressure
  - That prevents movement
  - In response to surgical stimulus
  - In 50% patients

Analogous to ED 50

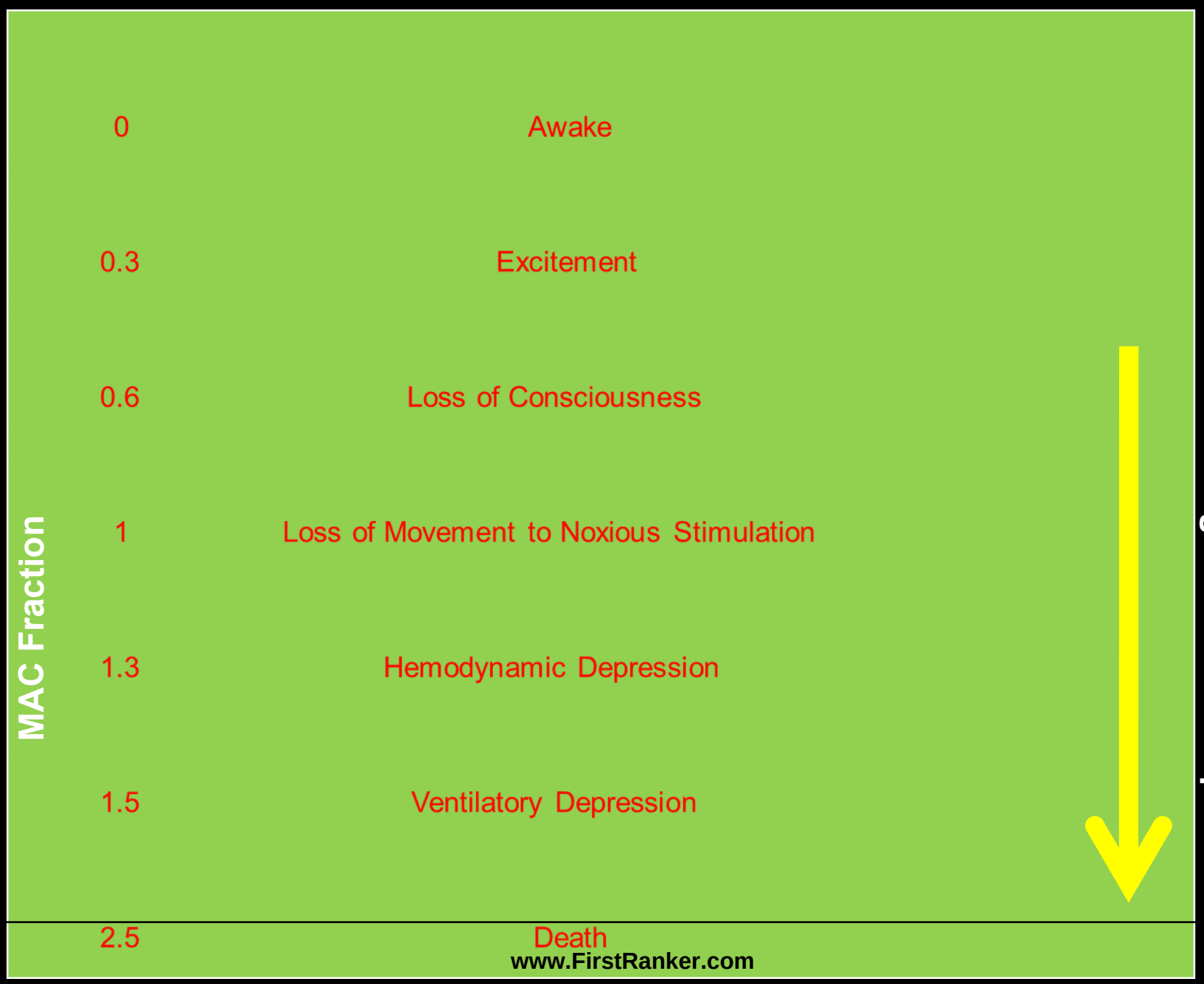
- Best measure of anesthetic potency as it mirrors the brain partial pressure.
- MAC values of different anesthetic are roughly additive.

MAC

MAC BAR- MAC that blunts adrenergic response to noxious stimulus (1.5MAC)

MAC UNCONSCIOUS- MAC at which pt loses consciousness (0.4-0.5MAC)

MAC AWAKE- MAC at which patient opens his or her eyes to command (0.15-0.5MAC)



MAC

- MAC of inhalational agents

N2O	104
Halothane	0.75
Isoflurane	1.17
Desflurane	6.6
Sevoflurane	1.8

- Roughly 1.3 MAC of any of the volatile anesthetic can prevent movement in 95% pts during surgical stimuli.

FACTORS AFFECTING MAC

INCREASING MAC

- ↑CNS metabolism
- ↑ CNS neurotransmission
- Hyperthermia
- Chronic alcohol abuse
- Hyponatremia
- Drugs - MAO I
  - Amphetamine
  - Cocaine
  - Ephedrine
  - L -DOPA

Decreasing MAC

- ↓CNS metabolism
- ↓ CNS neurotransmission
- ↑age
- Hypothermia
- Acute alcohol
- Hypotension(<50mmhg MAP)
- Hypoxemia(<38mmhg)
- Pregnancy
- Narcotics
- Ketamine
- Benzodiazepines

NO EFFECTS ON MAC

- Gender
- Duration of anesthesia
- Hypertension
- Anemia
- Thyroid status
- Hypo or hypercarbia
- Metabolic alkalosis
- Hyperkalemia
- Magnesium levels

Diethyl Ether (CH_3CH_2-O-CH_2CH_3)

History

- Prepared originally by Valerius Cordus- Sweet oil of vitriol
- Introduced in profession by W.T.G. Morton of Boston on Oct 16, 1846
- Classic stages and planes of anesthesia described using ether

Diethyl Ether (CH_3CH_2-O-CH_2CH_3) (contd..)

Manufacture

- By heating together conc H_2SO_4 and 95% ethyl alcohol at 130°C

Physical properties

- Colorless, pungent volatile liquid
- Blood / gas solubility 12, MAC 3.04
- Relatively inert
- Acetaldehyde and ether peroxide as impurities, greater the EP → Lesser potency
- Stored in dark cool place
- Unaltered in the body 85-90% - Lungs, 15% metabolized in liver
- inflammable in air and explosive in O_2

EFFECTS ON ORGAN SYSTEM

A. Circulatory system

- Heart rate → First increased → Unaltered

  Blood pressure
  - Decreased BP after 1st hour – below phase II
  - Vaso Motor Centre paralysis in deep plane
  - Functioning Sympathetic Nervous System → BP
  - Ether → increase in sympathetic adrenal activity
- Cardiac output
  - Lighter Plane of Anaesthesia → CO increases
  - Deep Plane of Anaesthesia → CO decreases
- Arrhythmia – rare, adrenaline safer with ether

B. Respiratory system

- RR increase Ist then → decrease in deeper plane
- Ether vapour – Irritant → Laryngospasm
- Ether dilates bronchial musculature
- Hence induction – Gradual

C. Nervous system

- Central nervous system
  - Induce analgesia → Excitement → Anaesthesia
  - Medullary depression → Late, precedes the serious cardiac depression
  - CBF increases → increases CSF pressure

- Sympathetic nervous system
  - Ether
    - Central stimulation → increase blood catecholamine level
    - Increase in HR
    - Increased production of glycogen → increased BS level
    - Centration of spleen
    - Dilatation – Gut and inhibition of movements
    - Dilatation of coronary arteries
    - Dilation of pupils
- Parasympathetic – NS central depression

D. Alimentary system

- PONV (>50% patients)
- Salivary gland stimulation – Induction and depressed later on
- Gastrointestinal atony
- Liver function decreased, decreased sec of bile and bile salts

E. Urinary system

- Urine flow – diminished
- Dec in plasma volume and renal Vaso-Constriction

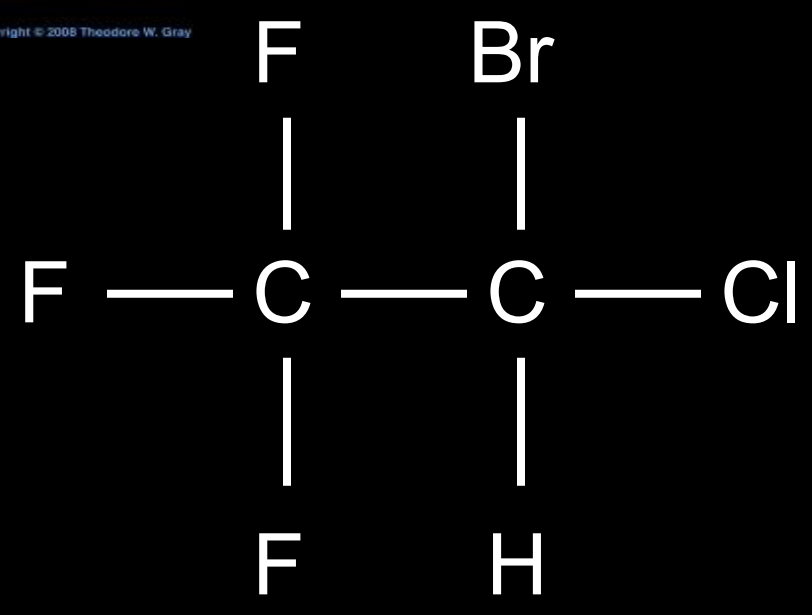
Advantages of Ether

- Relatively non-toxic, safe and potent
- Relatively cheap and can be used without sophisticated apparatus
- Excellent relaxation
- Respiratory depression not accompanied by serious cardiac damage in A/o hypoxia
- Maintained BP, no tendency to arrhythmias
- Thus ether – very safe, less experienced anaesthetist. Having wide safety margin

Disadvantages of Ether

- Induction and recovery slow
- Mucous secretion from upper airway
- Causes albumin urea
- Inflammable: Explodes, sparks flames
- Ether convulsion : Triad
  - Deeper ether anaesthesia
  - Hyperthermia
  - Hypocapnea

HALOTHANE



- It is halogenated alkene.
- Least expensive
- 2 bromo-2-chloro 1,1,1-trifluroethane
- Non-flammable and non explosive
- Non irritant vapors
- Decomposed by light (0.01%thymol,amber bottles)
- Absorbed by rubber
- Corrodes metals
- B:G -2.54
- 20-46% metabolized in the liver
- MAC- 0.87-1.19

EFFECTS ON ORGAN SYSTEM

1. CARDIOVASCULAR:

- Dose dependent reduction of arterial blood pressure by direct myocardial depression.
- It is a coronary artery vasodilator.
- It causes slowing of SA node conduction resulting in bradycardia.
- *Sensitizes heart to catecholamine and induces arrhythmias*

2. RESPIRATORY SYSTEM:

- Causes rapid ,shallow breathing.
- ~~Decrease in alveolar ventilation and Paco2 elevated.~~
- Potent bronchodilator.

3. CEREBRAL:

- Increased cerebral blood flow
- *Increased temperature- malignant hyperthermia-* Dantrolene is used for treatment

4. NEUROMUSCULAR:

- Relaxes skelatal muscle and potentiates non depolarizing neuro-muscular blocking agents.

5.RENAL:

- Reduces renal blood flow, glomerular filtration rate and urinary output.

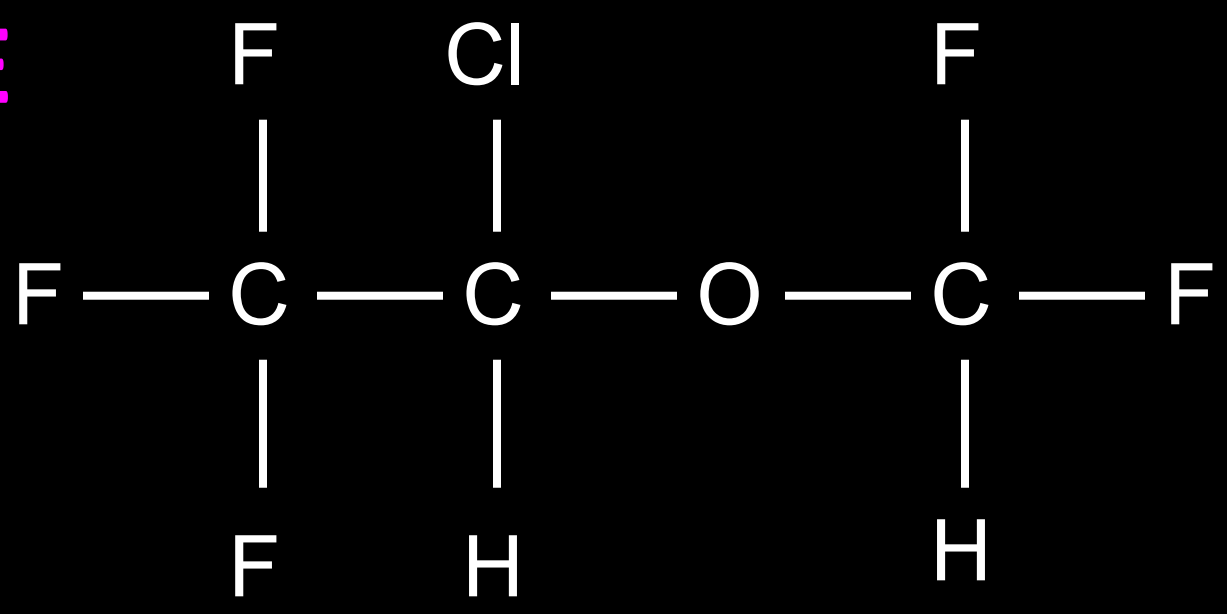
6. HEPATIC:

- Decreases hepatic blood flow.

CONTRAINDICATION

- Unexplained liver dysfunction.
- Intra-cranial mass lesions.
- Hypo-volemic patient with severe cardiac diseases.

ISOFLURANE



- 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether
- Colorless volatile liquid
- Pungent
- No preservative
- Does not react with metals

Isoflurane

- It is non flammable volatile with a pungent smell.
- Physical Properties
  - High vapor pressure: need a precision vaporizer
  - Low blood:gas partition coefficient (1.4): rapid induction and recovery
  - Good for induction with mask or chamber ???
  - MAC = 1.3% to 1.63%: helps determine initial vaporizer setting
  - Low rubber solubility
  - Stable at room temperature; no preservatives needed = no build up in the machine
  - Almost completely eliminated through the lungs- 0.2% metabolized by the liver

EFFECTS ON ORGAN SYSTEM

CARDIOVASCULAR:

- Causes minimal cardiac depression.
- Maintains cardiac output, heart rate, and rhythm
- Fewest adverse cardiovascular effects
- Rapid increase in MAC lead to increase in HR and BP.
- Dilates coronary arteries. (Coronary Steal)

2. RESPIRATORY SYSTEM:

- Respiratory depression .
- Irritant to upper airway

3. CEREBRAL:

Maintains cerebral blood flow

If conc > 1 MAC causes increase in CBF and Intracranial pressure.

4. NEUROMUSCULAR:

Induces adequate to good muscle relaxation

5. RENAL:

Decreases renal blood flow , glomerular filtration rate and urinary output.

6. HEAPTIC:

Reduces hepatic blood flow.

INDICATIONS

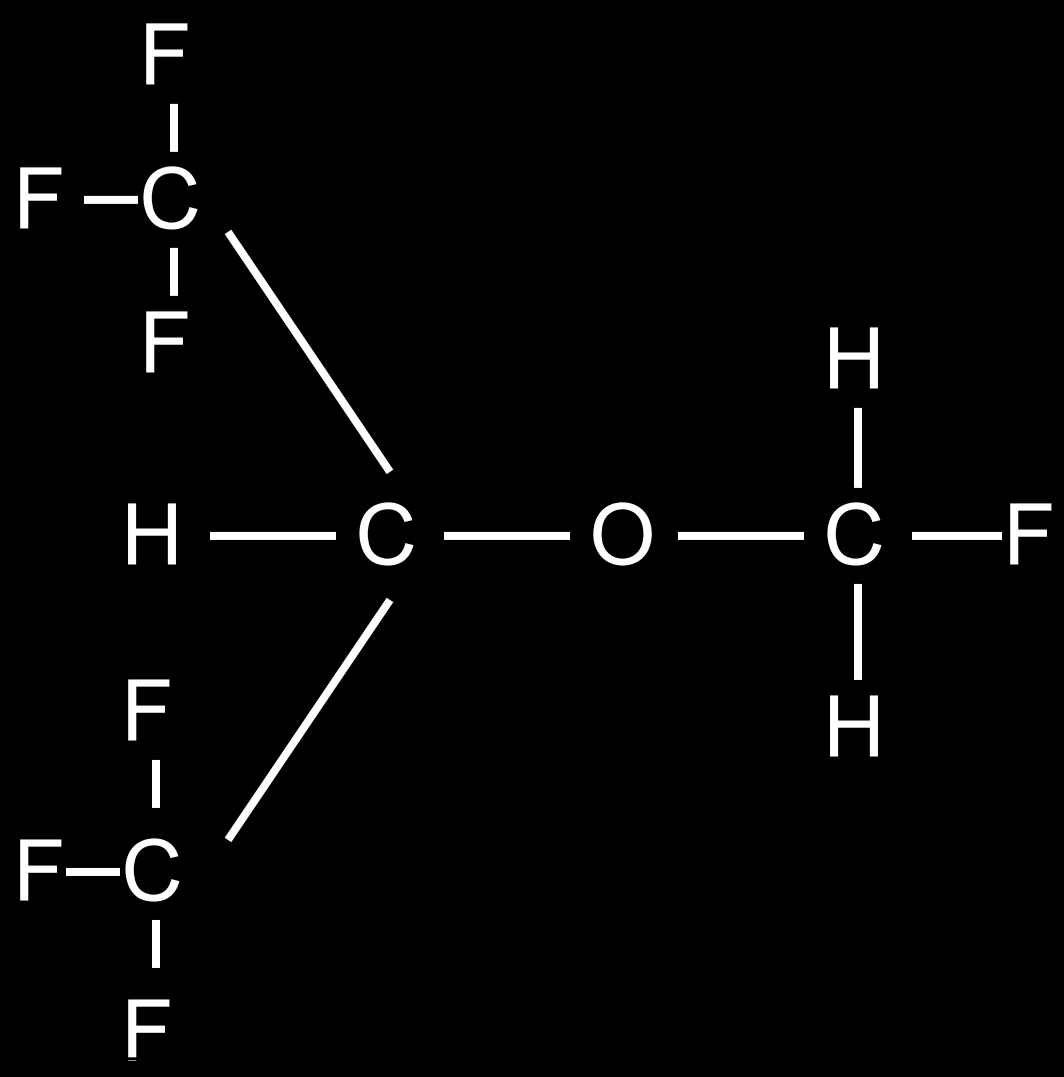
- For Cardiac and Neuro- Surgery
- In patients with hepatic or renal compromise

CONTRAINDICATION

- No such contraindication.
- Caution in asthmatics

SEVOFLURANE

- Methylpropylether
- Nonflammable pleasant smell
- MAC is higher in children (2.6%in O2 and 2.0%in N2O)and neonates (3.3%)
- Stable



Sevoflurane

- High vapor pressure: need a precision vaporizer
- Low Blood:gas partition coefficient (0.65)

= rapid induction and recovery

- Good for induction with a mask or chamber. Easier to mask a patient, more pleasant smelling
- High controllability of depth of anesthesia
- MAC = 2.34% to 2.58%
- Cost about 10x more than Isoflurane
- Eliminated by the lungs, minimal hepatic metabolism- 2-5%
- Can react with potassium hydroxide (KOH) or sodium hydroxide (NaOH) in desiccated CO_2 absorbent to produce a chemical (Compound A) that causes renal damage

EFFECTS ON ORGANS

1. CARDIOVASCULAR SYSTEM:
- Mildly depresses myocardial contractility.
- May prolong QT interval, but no significance.

2. RESPIRATORY SYSTEM:
- Depresses respiratory rate.
- It reverses broncho-spasm

3. CEREBRAL:
- Maintains cerebral blood flow
- Increases CBF and intra-cranial pressure.
- Some paddling and excitement during recovery
- No post-op analgesia

4. RENAL SYSTEM:

- Slightly decreases renal blood flow. Higher Conc Causes Nephro-toxicity

5. HEPATIC:

- Decreases portal vein blood flow but increases hepatic artery blood flow thus maintaining total hepatic blood flow.

6.NEUROMUSCULAR:

- Adequate muscle relaxation.

INDICATION

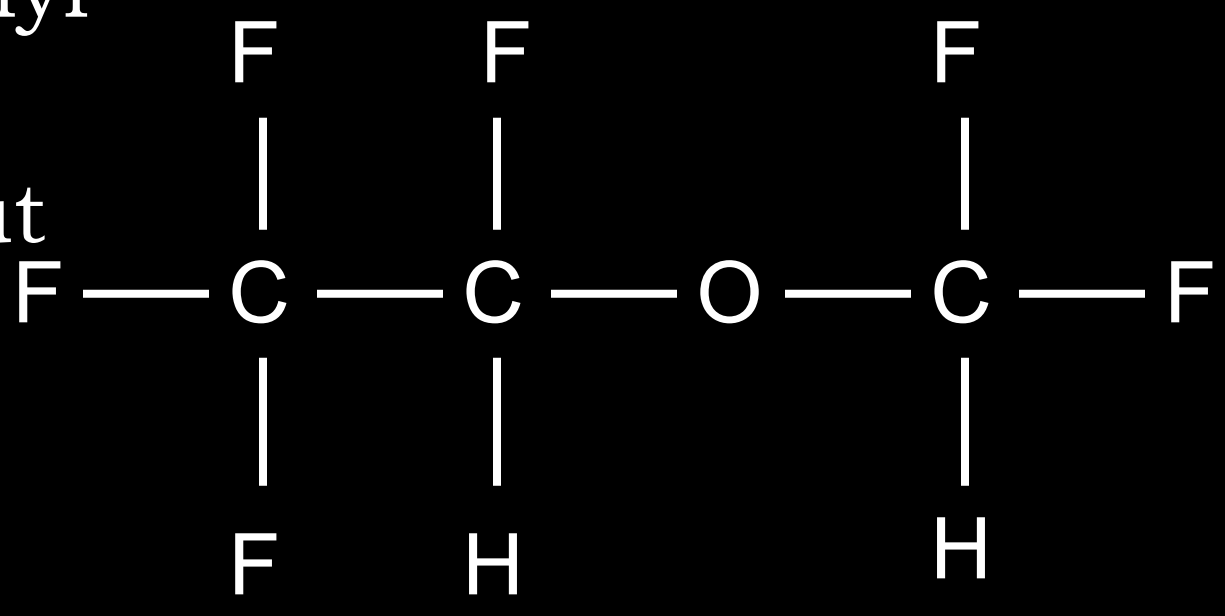
- For induction
- Especially useful in children
- In patients with reactive upper airway

CONTRAINDICATION

- No such contraindication
- Caution in severe hypo-volemia.

DESFLURANE

- Fluorinated methyl ethyl ether
- Colorless, without preservative
- Non flammable
- Special heated vaporizer



Desflurane

- Structure much similar to that of isoflurane.
- Recovery time are approximately 50 % less than those of Isoflurane.
- Pungent Smell
- Expensive
- Lowest blood:gas partition coefficient: very rapid induction and recovery
- Used with a special heated electronic precision vaporizer (TEC 6)
- MAC = 7.2% and 9.8%
  - Least potent inhalant agent
- Eliminated by the lungs- 0.02% metabolized in liver

EFFECTS ON ORGAN SYSTEM

1. CARDIOVASCULAR SYSTEM:

- Similar to Isoflurane (Increases HR and BP when increased MAC rapidly)
- Dilates coronary arteries.

2. RESPIRATORY SYSTEM:

- Causes decrease in tidal volume and increase in resp rate.
- Pungency and airway irritation so causes coughing and sometime bronchospasm.
- Strong vapors cause coughing and holding the breath= difficult to mask

2. 3. CEREBRAL:

- Increases CBF and Intracranial pressure.

4. NEUROMUSCULAR:

- Relaxes skeletal muscle.

5. RENAL AND HEPATIC SYSTEM:

- No any evidence has been documented.

INDICATION- For Hepatic and Renal Surgery

CONRAINDICATION – Same as isoflurane

NITROUS OXIDE

Physical properties:

- It is a laughing gas.
- It is only inorganic anesthetic gas in clinical use.
- Colorless and odorless
- Non Explosive and Non Infammable
- Gas at room temperature and can be kept as a liquid under pressure.
- It is relatively inexpensive.

Effects of Nitrous Oxide on Organ System

1. CARDIOVASCULAR SYSTEM
   - Stimulate sympathetic nervous system.
   - Directly depresses myocardial contractility.
   - Arterial blood pressure ,heart rate and cardiac output are slightly increased.
2. RESPIRATORY SYSTEM:
   - Increases respiratory rate with decreases tidal volume.
   - Minimal change in minute ventilation.

3. CEREBRAL:

- Increases CBF thus increasing intracranial pressure.

4. RENAL SYSTEM:

- It decreases renal blood flow thus leads to drop in glomerular filtration rate and urinary output.

5. HEPATIC SYSTEM:

- Decreases the Hepatic blood flow but to a lesser extent than other inhalation agents.

6. GASTROINTESTINAL:

- It causes post operative Nausea and Vomiting.

CONTRAINDICATION OF N2O

- Air embolism
- Pneumothorax
- Acute Intestinal Obstruction
- Tension Pneumocephalus
- Tympanic membrane grafting

Uses of N2O

- Mixed with oxygen at 40-67%, then delivered to patient

- Reduces MAC 20-30%
  - Used with Halothane and Methoxyflurane to reduce the adverse effects of these gases