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General Anaesthetics

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- **General Anesthesia**

"Global but reversible depression of CNS function resulting in the loss of response to and perception of all external stimuli"

- **Characteristics**
  - Analgesia
  - Amnesia
  - Attenuation of sensory & autonomic responses
  - Muscle relaxation - Immobility
  - Unconsciousness (no response to external stimuli)

- **History: ether/chloroform/N2O/cyclopropane/halothane**

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Pre-anaesthetic Medication

- **Aims**
  - Relief of anxiety and apprehension
  - Amnesia
  - Supplement analgesia
  - Decrease secretions and vagal stimulation
  - Anti-emetic effect (peri & postoperative)
  - Decrease acidity-avoid aspiration of gastric contents
  - Reduce dose of gen. anesthetics
- **Timing & Route of administration (30 m-1h prior, I/V)**

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Pre-anaesthetic Medication

- **Sedative / Hypnotic / Anxiolytics**
  - **Benzodiazepines (diff DOAs)**
    - **Diazepam (longest acting)**
    - **Lorazepam** (0.05mg/kg)
    - **Midazolam** (0.07mg/kg)
  - **Barbiturates** (100-200mg)
    - **Secobarbital**
    - **Pentobarbital**
- **Characteristics**
  1. **relieve anxiety / relax pt.**
  2. **sedate pt.**
  3. **provide amnesia**

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- **Opioid Analgesics** (10-20mg)
  - **Morphine (IV)**
  - **Pethidine (IV)**
  - **Fentanyl (transdermal patch) + congeners**
- **Characteristics (delayed awakening, constipation, asthma, urine retention, excessive hypotension—morphine)**
- **H2 Rec. blockers / PPIs (emergencies-dec. gastric secr.-dec. aspiration pneumonia)**
  - **Cimetidine & Ranitidine** (150 mg)
  - **Omeprazole**

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- **Antiemetics**
  - **Metoclopramide** (10-20mg IM)
  - **Antihistamines** (25-50mg)
  - **Phenothiazines (Promethazine)**
  - **$5HT_3$ Receptor Blockers**
    - **Ondansetron**
    - **Tropisetron**
    - **Granisetron**
- **Characteristics**
  - **Used in cancer chemotherapy pts**

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- **Anticholinergics:**
  1. decrease secretions
  2. inhibit vagal stimulation
  - Atropine (0.4-0.6mg IV)
  - Hyoscine (crosses BBB)
  - Glycopyrronium (doesn't cross BBB)

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- **Anti Histamines**
  - –Diphenhydramine
  - –Dimenhydrinate
- **Characteristics (anti-emetics, sedatives, anxiolytics & anti-cholinergics)**
- **Used in combinations according to:**
  1. **patient's requirement**
  2. **patient's clinical status**
  3. **type of operation**
  4. **duration of operation**

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Classification of General Anaesthetics

Inhalational Anaesthetics

- **Volatile Liquids**

  Halothane, Isoflurane, Sevoflurane, Methoxyflurane, Desflurane, Enflurane, Ethyl chloride, Trichloroethylene, Chloroform

- **Gases**

  Nitrous Oxide, Cyclopropane

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Intravenous Anaesthetics

- **Ultra Short Acting Barbiturates**
  - Thiopentone Sodium
  - Methohexital
- **Phencyclidine Derivatives**
  - Ketamine
- **Steroids**
  - Althesin
- **Eugenol Derivatives**
  - Propanidid
- **Alkyl Phenols**
  - Propofol
  - Etomidate

Neurolept anaesthesia (used in psychiatry)

Droperidol + Fentanyl + Nitrous oxide

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Stages of General Anesthesia

- Guedel's Signs – with Ether (not newer agents)
- Stage-I Stage Of Analgesia
  (no pain, drowsy, reflexes intact, no amnesia, HR/BP normal, pupil size normal)
- Stage-II Stage Of Excitement-most dangerous
  (excited, delirious, RR inc., jerky movements – injury, rapid eye movements, vagal stimulation - cardiac arrest, catecholamines - arrhythmias)
- Stage-III Stage Of Surgical Anesthesia
  - Plane-I : pupils constricted, inc. regular resp., muscles relax, corneal/conjunctival reflexes lost

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Stages of General Anesthesia

- Plane-II : pupils dilate, dec. regular resp., eye-balls fixed, dec. muscle tone, abdominothoracic resp., no light reflex
- Plane-III : thoracic resp. ceases, pupils dilated, muscles relaxed, laryngeal/pharyngeal reflexes dec. – surgery performed in this plane
- Plane-IV : abdominal resp. ceases, all reflexes lost – warning sign

- **Stage-IV** Stage Of Medullary Paralysis (CVS & resp. centers suppr – CVS collapse + Resp. failure)
- **Monitoring by anesthetist**

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Inhalational Anesthetics

- **Mode of Delivery**
  - Open Drop method - Ether
  - Anaesthetic machines assisted methods
    - Open System – accurate
    - Closed System – sodalime
      - Trichloroethylene
    - Semiclosed System

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Inhalational Anesthetics

- **Depth of anesthesia**
  - Potency
    - Dose-response characteristics
    - MAC – definition
      - example*
      - Partial Pressure (PP) in brain

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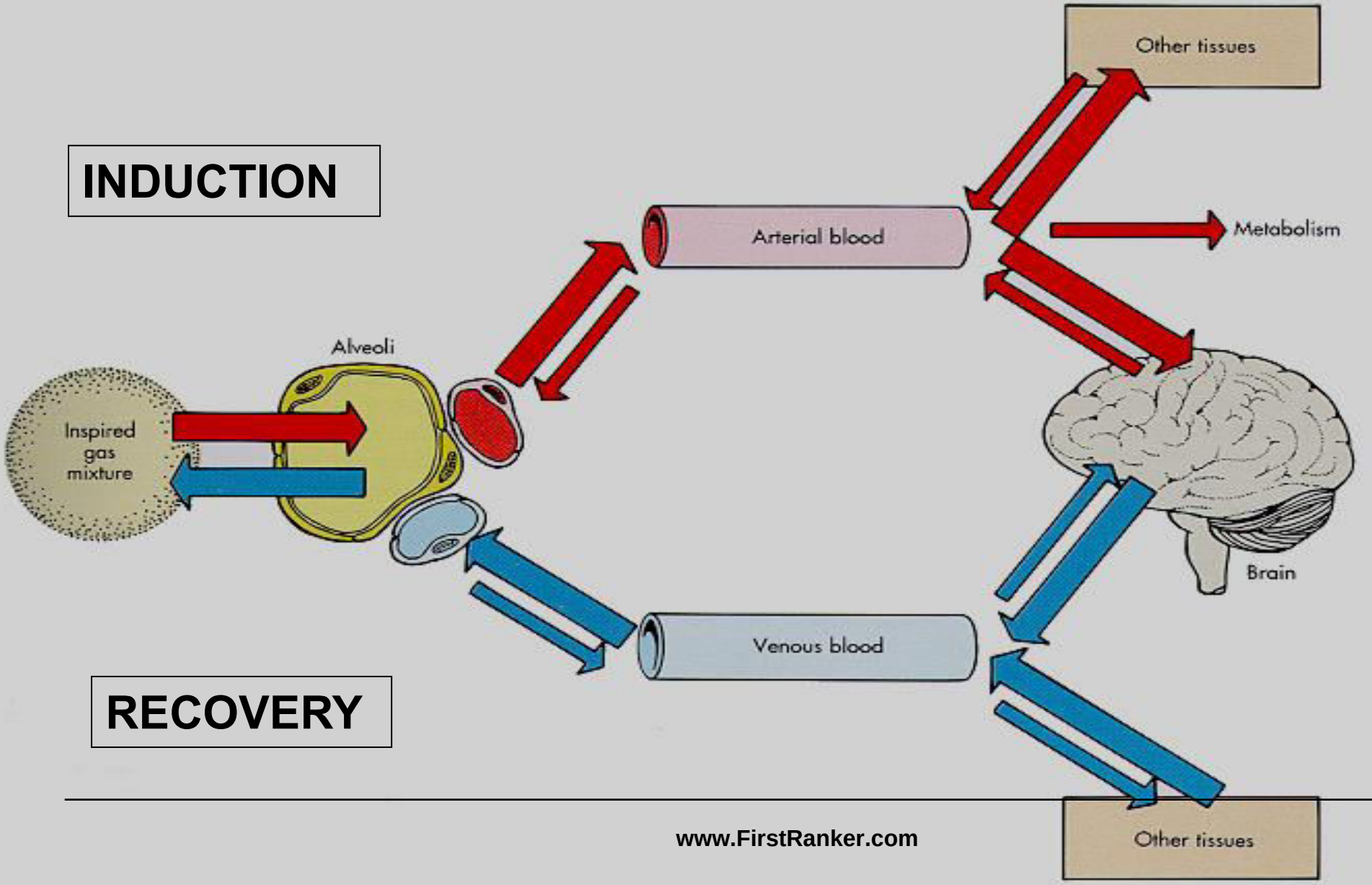
Pathway for General Anesthetics



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Pharmacokinetics

- Administration, Uptake, distribution & elimination
- Induction & Recovery***
  - Rate of change of PP
- FACTORS

  Related to drug
  - Concentration in inspired air
    - Fick's law
  - Solubility
    - In blood – Blood:gas partition coefficient**

      - Inverse relation with induction
    - In tissues – Tissue:blood partition coefficient*

      - Arteriovenous conc gradient

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Related to body

- Pulmonary ventilation
  - Rate & depth
  - Hyperventilation / Resp depession
- Pulmonary blood flow / perfusion
  - Shock
- Alveolar exchange
  - Pul vent / perfusion
  - Lung disease
- Cerebral blood flow
  - CO_2

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PROPERTIES OF INHALED ANESTHETICS

Anaesthetic	Blood: Gas Partition Coefficient	Minimal Alveolar Conc (MAC) %	Metaboli-sm	Comments
Nitrous Oxide	0.47	>100	None	Incomplete anesthetic rapid onset & recovery
Desflurane	0.42	6-7	<0.05%	Low volatility; poor induction agent; rapid recovery
Sevoflurane	0.69	2.0	2-5%	Rapid onset & recovery; unstable in soda-lime
Isoflurane	1.140	1.40	<2%	Medium rate of onset and recovery
Enflurane	1.80	0.75	>8%	Medium rate of onset & recovery
Halothane	2.30	0.75	>40%	Medium rate of onset and recovery
Methoxyflurane	12	0.16	>70 %	Slow onset & recovery

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PROPERTIES OF INHALED ANAESTHETICS

Anaesthetic	Blood: Gas Partition Coefficient	Brain: Blood Partition Coefficient	Metabol-ism	Comments
Nitrous Oxide	0.47	1.1	None	Rapid onset & recovery
Desflurane	0.42	1.3	<0.05%	Low volatility; poor induction agent; rapid recovery
Sevoflurane	0.69	1.7	2-5%	Rapid onset & recovery; unstable in soda-lime
Isoflurane	1.140	2.6	<2%	Medium rate of onset and recovery
Enflurane	1.80	1.4	>8%	Medium rate of onset & recovery
Halothane	2.30	2.9	>40%	Medium rate of onset and recovery
Methoxyflurane	12	2.0	>70 %	Slow onset & recovery

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Elimination

Recovery Depends on

- Routes
  - Lung
  - Hepatic Metabolism**
- Concentration in lungs
- Variable tissue concentration
- Duration of exposure

- Second gas effect : Nitrous oxide
- Diffusion hypoxia : Nitrous oxide
- Clearance & Metabolism

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Mechanism of Action of General Anesthetics

- **Old Theories**
  - Unitary Theory
  - Meyer-Overton Theory
  - Pauling's Theory
  - Ferguson's Theory
  - Mullen's Theory
- **Newer Concepts**
  - Specific Targets
  - Differential Sensitivity of Neurons- Stages

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- **Newer Mechanisms**
  - Molecular Actions
    - **Channels & Receptors**
      - **Different binding sites**
      - $GABA_A$ receptor-chloride channels

        Inhalational agents, barbiturates, propofol, etomidate
      - Glycine receptor-chloride channels

        Inhalational agents, barbiturates, propofol

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- Glutamate receptor-NMDA channels

  Ketamine, nitrous oxide, cyclopropane

- K^+ channels (TREK) – Hyperpolarization

  Inhalational agents, nitrous oxide, cyclopropane

- Nicotinic receptor-activated cation channels

  Inhalational agents

- Neurotransmitters
  - Acetylcholine
  - Endorphin

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Halothane

- **Chemical and Physical Properties**
  - 2-bromo-2-chloro-1,1,1-trifluoroethane
  - Volatile / odourless / colourless
  - Non-irritant / non-explosive / non-inflammable
  - Light-sensitive / corrosive / interaction - rubber
- **Pharmacokinetics**
  - MAC - 0.75
  - B:G part. coef. - 2.3
  - Medium rate of onset & recovery
  - Metabolism – trifluoroacetic acid
    - trifluoroacetylchloride
  - Clearance (hepatic)

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- **Pharmacological Effects**
  - **CVS**
    - ↓BP / HR
    - Myocardial sensitization to catecholamines
    - Atropine / beta-blockers
    - Redistribution of blood flow
  - **Respiratory system**
    - ↑ RR, ↓ Tidal vol., dec. ventilatory response to CO2
    - Inc. $PaCO_2$, raised apneic threshold
    - Bronchodilator – larnygeal/pharyngeal reflexes abolished
  - **CNS**
    - inc CBF & dec CMR
    - If CBF inc.—ICP inc.
    - EEG:initial activation-low dose, slowing-high dose

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- Kidneys (dec. GFR & RBF), -GIT
- Liver (dec. portal bl. flow, raised LFTs)
- Skeletal muscles (relaxation, inc. curare eff)
- Uterus (conc. dependant relaxation)

- **Use**
  - Maintenance anesthesia – 0.5-1%
  - Induction of anesthesia – 2-4%
  - Used in children
  - Low cost
- **Adverse effects**
  - Halothane shake/shivering during recovery
  - CVS / Resp. sys depression
  - Chronic toxicity - not carcinogenic/mutagenic

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- **Hepatitis**
  - Pathophysiology: immune response against triflouroacetylated proteins
  - Predisposing factors: elderly, obese, females, electrolyte imbalance, enzyme inducers, halothane exposure
  - Clinical S/S: nausea, vomiting, lethargy, fever, rash, gen. weakness (days later)
  - Biochemical tests: eosinophilia, LFTs deranged, autoantibodies, triflouroacetylated proteins
  - Treatment: liver transplant in severe cases
- **Malignant Hyperthermia (seen with halothane & succinylcholine)**

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- Pathophysiology:
  autosomal dominant genetic disease
  - Ryanodine Rec (RyR1) gene mutation
  - L-type Ca^{+2} channels gene mutation
- Clinical S/S: hyperthermia, hypertension, hypercapnia, hyperkalemia, inc. HR, metabolic acidosis, muscle rigidity
- Biochemical tests: acidosis, hyperkalemia, deranged electrolytes, inc. free cytosolic Ca conc. in skeletal muscle cells (in vitro caffeine - halothane contracture test)
- Treatment :
  Dantrolene (reduces Ca release from SR)
  Symptomatic Rx for fever
  Restoration of electrolyte & acid-base balance

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HALOTHANE

ADVANTAGES	DISADVANTAGES
POTENT	NOT AN ANALGESIC
LESS IRRITANT	VARIABLE MUSCLE RELAXATION
INDUCTION SMOOTH AND RAPID	SENSITIZES HEART TO CATECHOLAMINES
QUICK RECOVERY	HYPOTENSION
NON – INFLAMMABLE	BRADYCARDIA
COMPATIBLE WITH SODA LIME	HEPATITIS
BRONCHODILATOR	RESPIRATORY DEPRESSION
UTERINE RELAXANT	SHIVERING DURING RECOVERY

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ADVANTAGES	DISADVANTAGES
LESS INCIDENCE OF POST-OPERATIVE NAUSEA/VOMITING	MALIGNANT HYPERPYREXIA
DOES NOT CAUSE LARYNGOSPASM	ENZYME INDUCER
EASIER ENDOTRACHEAL INTUBATION DUE TO RELAXATION OF MASSETER MUSCLES	CORRODES METALS
COST-EFFECTIVE	REACTS WITH RUBBER EQUIPMENTS

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ENFLURANE

- Chemically it is halogenated ether
- Non inflammable
- Non irritant
- Clear, colorless liquid with sweet odor
- Blood : Gas coefficient 1.80
- MAC : 0.75
- Metabolism 8%
- Stable with soda lime
- Medium rate of onset & recovery

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ENFLURANE

Pharmacological actions:

CVS

Resp System

CNS

Renal System

Better Muscle Relaxant

- Produces convulsions and involuntary movements during induction or recovery
- Liver damage is rare
- Not recommended in children & epileptics
- USE:

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Maintenance of anesthesia. Not used in children

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ISOFLURANE

- Volatile liquid
- Non inflammable
- B:G partition coefficient; 1.4
- MAC : 1.4
- Metabolism: 2%
- Costly
- Medium rate of onset & recovery

Pharmacological Actions

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ISOFLURANE

Most widely used volatile anesthetic.

Resemble Halothane Except:

- Less incidence of hypotension
- Less sensitization of heart to Catecholamines
- Less toxic
- Powerful Coronary vasodilator, may cause coronary steal phenomenon
- No pro-convulsive properties
- Not cost effective
- Irritant, resp depression

USE:

Maintenance of anesthesia

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DESFLURANE

- Volatile halogenated compound
- TEC 6, an apparatus required for vapourization
- Non inflammable, Non explosive
- Pungent smell (not for induction, but maintenance)
- B:G partition coefficient: 0.42
- MAC: 6-7
- Metabolism: 0.05%
- Rapid induction & rapid recovery (low B:G coeff)

Pharmacological actions

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DESFLURANE

- Newer drug
- Chemically similar to Isoflurane
- Faster induction and recovery due to lower solubility in blood ,so preferred for use in day case surgery
- No significant metabolism
- Less potent due to high MAC about 6 %
- Concentration used for induction is 10 %.It can cause respiratory irritation leading to coughing, salivation and bronchospasm

USE:

Maintenance and ideal for outdoor procedures

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SEVOFLURANE

- Clear, colourless, volatile liquid
- Non inflammable, non irritant, pleasant smell
- B:G 0.69
- MAC: 2
- Metabolism: 2-5% (Nephrotoxic)
- Rapid induction & recovery (low B:G coeff)

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SEVOFLURANE

- CVS
- Resp System
- CNS
- Renal System

  Less toxic

  Can cause malignant hyperthermia

USE:

Outpatient anesthesia & induction

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METHOXYFLURANE

Properties Same as Halothane Except:

- Good muscle relaxation
- Good analgesic effect
- Slow induction & recovery
- Cause severe renal damage
- **Not used any more**

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- **Desflurane**
  - Rapid onset & recovery
  - Pungent / irritant
  - Low volatility

- **Sevoflurane**
  - Rapid onset & recovery
  - Nephrotoxic
    - Compound A - CO_2 absorbent (soda lime)
      - met. by beta-lyase (renal)
    - Hepatic – free inorganic F^- produced

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- **Enflurane**
  - Slow induction & recovery
  - Potential nephrotoxic – beta-lyase
  - Seizure-like activity (self limited)
- **Isoflurane**
  - Rapid onset & recovery
  - Coronary circulation (vasodilation)
  - Pungent (not used for induction, but maintenance)
- **Methoxyflurane**
  - Nephrotoxic – met. by beta-lyase

    - >30% hepatic met. - F^-
  - No longer used

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- **Ethyl chloride**
  - Explosive, kept under pressure (low boiling point)
  - Use – local anesthetic – cooling effect
    - cryosurgery
- **Trichloroethylene**
  - Analgesia > Anesthesia
  - Interacts with Soda lime – toxic metabolite
- **Chloroform (animal studies)**
  - Causes breath holding
  - Hepatotoxic
  - CVS depressant

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Cyclopropane

- Potent GA
- Non-irritant / explosive / flammable
  (cautery couldn't be used)
- Severe CV collapse - Cyclopropane shock
  Rx : small amount of CO2 administered

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Nitrous Oxide

- **Chemical and Physical Properties**
  - Inorganic gas (N_2O)
  - Odourless / colourless / heavier than air
  - Non-explosive / non-inflammable / supports combustion
  - Laughing gas: euphoria-small amounts, abused in past
- **Pharmacokinetics**
  - MAC - 105
  - B:G part. coef. – 0.47 at 37 C
  - Rapid induction & recovery
  - Not metabolized (99.9% exhaled unchanged)
  - Elimination (0.1% degraded by int. bacteria)

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- **Pharmacological Effects**
  - CVS / Respiratory system (depends on other agents)
  - CNS (inc. CBF – inc. ICP)
  - GIT / Muscles
- **Uses**
  - Analgesia (40%)
  - Sedation (30-80%)
  - Anesthesia – less potency
    - adjuvant
    - second gas effect
    - short surgical procedures

  (dental extraction, postoperative pain, painful dressings, fracture manipulation, child birth)

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Adverse effects

- Diffusional hypoxia / anoxia
- Vitamin B_{12} deficiency (inhibits methionine synthetase, req. for vitamin B12 synthesis)
  - Megaloblastic anemia
  - Peripheral neuropathy
- Replaces N2 in air-containing cavities (obstructed middle ear, air embolus, pneumothorax) enlarges it
- Effect of NO_2 & O_2 in same cylinder (1^{st} insufficient anesthesia – later-on hypoxia)

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ADVANTAGES

- Non-inflammable Non-irritating
- Very Potent Analgesic: 30 – 40 % Analgesia

  65 – 70 % Loss of consciousness

  80 % plane one of Surgical Anesthesia
- Non-explosive, however supports combustion.
- Rapid induction and recovery.
- Use in procedures of short durations (tooth extraction, obstetrical analgesia, cleaning and debridement of wounds).

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- **Induction and maintenance of anesthesia**

  I/V Thiopentone-Gas-Oxygen-Halothane technique

- **Safe, no organ toxicity (Resp, CVS, Renal or Hepatic)**
- **↓ the dose of GA when combined ➔**

  ↓ adverse effects, ↓ complications ↓ recovery period from anaesthesia

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DISADVANTAGES

- Not a potent anesthetic & muscle relaxant
- Violent excitement
- Carbon dioxide accumulation and hypoxia ➔ cardiac irregularities during anesthesia

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DISADVANTAGES

- Specialized apparatus to control its administration
- Adm for more than 7hrs ➔ Bone marrow depression (leucopenia, anemia)
- Prolonged adm ➔ Peripheral neuropathy & Megaloblastic anemia due to interference with B_{12} metabolism, Abortion, peripheral Neuropathy
- Second gas effect leading to transient hypoxia
- Diffusion hypoxia

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NITROUS OXIDE

ADVANTAGES	DISADVANTAGES
STRONG ANALGESIC	LESS POTENT
RAPID INDUCTION	TRANSPORTATION DIFFICULT
RECOVERY RARELY EXCEEDS 1-4 MIN	SPECIAL EQUIPMENT FOR ADMINISTRATION
NON IRRITANT	PENETERATES INTO CAVITIES
NAUSSEA / VOMITING UNCOMMON	CO_2 ACCUMULATION AND HYPOXIA ON PROLONGED ADMINISTRATION
LITTLE EFFECTS ON CIRCULATION, RESPIRATION, LIVER, KIDNEY	MEGALOBLASTIC ANEMIA ON PROLONGED ADMINISTRATION POOR MUSCLE RELAXANT
COST EFFECTIVE	DIFFUSIONAL ANOXIA

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Intravenous Anesthetics

- **Barbiturates**
  - Thiopental / Thiopentone Sodium
    - Induction / Onset

Narrow therapeutic index.

Ph is 7-10

Administered rapidly by I/V line

Onset of action	60sec
DOA	5-10min
α t1/2	3min (distr. t ½, resp. for DOA)
β t1/2	12hrs (elimination t ½, drowsiness)
PPB	85%

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- Pharmacological Effects
  - CNS (dec. CMRO2 & CBF)
  - CVS depressant (dec. CO & BP)
  - Resp. sys depressant
  - GIT
  - Poor analgesia / muscle relaxation
  - Renal system

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- **Uses**
  - Induction
  - Dental procedures
  - Endoscopy
  - Circumcision
  - Orthopedic procedures
  - Changing painful dressings
  - Head injuries
  - Psychoanalysis (truth drug)
- **Adverse effects**
  - laryngospasm, shivering & restlessness (recovery) injection site pain, Inadvertent injection
  - Acute porphyria, hypotension, apnea, resp depression, hyperalgesia, local necrosis, thrombophlebitis, gangrene

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THIOPENTONE

ADVANTAGES	DISADVANTAGES
RAPID AND PLEASANT INDUCTION	INSIGNIFICANT ANALGESIC ACTION
EASY ADMINISTRATION	VERY SHORT DURATION OF ACTION
NON EXPLOSIVE	REPEATED DOSES ACCUMULATE
LESS INCIDENCE OF NAUSEA / VOMITING	CAN NOT BE USED ALONE AS AN ANESTHETIC
NON IRRITANT	COUGHING, HICUP, LARYNGOSPASM, BRONCHOSPASM MAY DEVELOP DURING INDUCTION
QUIET RESPIRATION	MUSCLE RELAXATION IS NOT ADEQUATE

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ADVANTAGES	DISADVANTAGES
NO SENSITIZATION OF HEART TO CATECHOLAMINES	PHARYNGEAL/ LARYNGEAL REFLEXES ARE NOT ABLOLISHED
RAPID RECOVERY	IN OVER DOSAGE DEPRESSION OF VMC, MYOCARDIUM AND RESPIRATION
NO EXCITEMENT DURING INDUCTION	REGURGITATION DUE TO RELAXATION OF GASTROESOPHAGEAL SPHINCTER
	INJECTION MAY CAUSE NECROSIS, THROMBOPHLEBITIS, NERVE DAMAGE, VASOSPASM ON INTRA – ARTERIAL INJECTION

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Etomidate

- **Carboxylated imidazole**
- **Pharmacokinetics**
  - Rapid onset / recovery
  - $T_{1/2}$: distributive : 2-4 min
    eliminative : 2.9-5.3 h
  - Metabolism (Liver)
  - Excretion (78% renal, 22% biliary)
- **Pharmacological Effects**

-- little or no effects on CVS / Resp. sys

-- CNS (dec. CMRO2 & CBF)

-- no analgesia

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Etomidate

- **Use**
  - Poor cardiovascular reserve (old pts, IHD, cardiomyopathy)
- **Adverse effects**
  - Injection site pain (Rx : lignocaine)
  - Nausea, vomiting, restlessness, tremors
  - Steroidogenesis inhibition esp. cortisol,by inhibiting 11B hydroxylation. This effect is transient if given for short period but hypotension, electrolyte imbalance & oliguria can occur on long use

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Advantages

- Minimum CVS Depression
- Minimum Respiratory Depression
- Larger margin of safety
- Very rapid induction within seconds
- Rapid recovery within 3-5 minutes

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Disadvantages

- No analgesic effect
- Post operative Nausea & vomiting
- Pain during injection
- Myoclonus / involuntary movements during induction
- Adrenocortical Suppression (with prolonged use)

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Propofol

- Chemistry: 2,6 Diisopropylphenol
- **Formulations**
  - Conventional (oily)/ Ampofol / Fospropofol (water-soluble prodrug)
- **Pharmacokinetics**
  - Onset (10-15 s) / recovery /Dose 1.5 -2.5 mg/kg
  - T ½ : distributive : 2-4 min
    eliminative : 4-23 hrs
  - Metabolism / Excretion (Liver)

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Propofol

- **Pharmacological Effects**
  - CVS & Resp. sys depression
  - CNS (dec. CMRO2 & CBF)
  - Poor analgesia / muscle relaxation

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- **Uses**
  - Induction & maintenance
  - Ambulatory surgery (outpatient surgery)
  - Sedation (less dose, endoscopy, ventilator pts)
  - **Dexmedetomidine ***
- **Adverse effects**
  - CVS / resp. sys depression
  - Injection site pain (propofol + lignocaine)
  - Apnea, laryngospasm, myoclonus, tremors
    - Children with resp. inf.– acidosis (long use)

- neurological effects on withdrawal

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Advantages

- Rapid Induction
- Very rapid recovery as Compared to Thiopental, without any significant hangover effect
- Post operative nausea and vomiting is uncommon as has antiemetic actions.
- No cumulative effect.

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Disadvantages

- Very expensive
- Apnoea can occur
- CVS depression
- Pain at site of injection
- Clinical infections

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Ketamine

- **Phencyclidine congener (racemic mixture of S & R)**
- **Pharmacological Effects**
  - CNS
    - Blocks NMDA receptors (prevents glutamate binding)
    - Psychoactive drug—abused as hallucinogenic
    - Inc.CBF, CMRO2 & ICP (avoid in head injury)
  - Stimulates CVS – sympathetic stimulation + NE reuptake block (peak: 2-4 min, normal: 10-20 min)
  - Respiratory – doesn't abolish reflexes, bronchodilation– sympathetic stimulation + direct eff.

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Pharmacokinetics

Highly lipophilic , rapidly distributed in highly vascular organs, potent, crosses BBB rapidly

Route	I/V, I/M, Oral, Rectal
αt1/2	15 min
βt1/2	3 hrs
Onset of effect	2 – 5 min
DOA	5-10min
Metabolism	
Dose	0.5-1.5mg/kg

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- **Uses**

  Induction smooth but recovery unpleasant

  – Dissociative anesthesia: analgesia, catatonia, amnesia, hypnosis, unresponsive to painful stimuli, sometimes involuntary limb movements

  – Analgesia: short procedures

  – Old age (poor CV reserves) / children

  – Topical use (arthritic pains)

  – Hemodynamic stability (cardiogenic/septic shock)

  – Asthma / COPD (bronchdilation)

- **Adverse effects**

  – CVS: cardiostimulatory—avoid in IHD

  – Emergence delirium: hallucinations (Rx: BZs)

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KETAMINE

Advantages	Disadvantages
Effective by both I/V & I/M INJ	No Muscle Relaxation
Anesthesia is accompanied by profound analgesia	Tends to raise intraocular, Intracranial BP and heart rate
Does not produce Vomiting Hypotension, Bronchospasm	Cannot be used for surgery on Larynx, Pharynx & Bronchi
Less respiratory complications due to less impairment of Pharyngeal/ Laryngeal reflexes	Poor in relieving visceral pain
Useful for poor risk geriatric pts and in unstable pts	Emergence phenomena
Used in low doses as outpatient anesthesia	

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NEUROLEPT ANESTHESIA

- It is a method of IV anesthesia which combines the use of a neuroleptic drug with a narcotic analgesic drug.
- Administration of such a combination produces a state which differs from the classical general anesthesia in that the subject is conscious and is able to cooperate during the operative procedure.

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The most common combination is that of Droperidol (neuroleptic) and Fentanyl (opioid analgesic)

Fentanyl - 0.5-1 mg & Droperidol 2.5 -5mg/ml

Prep: INNOVAR Injection

NEUROLEPT ANALGESIA

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