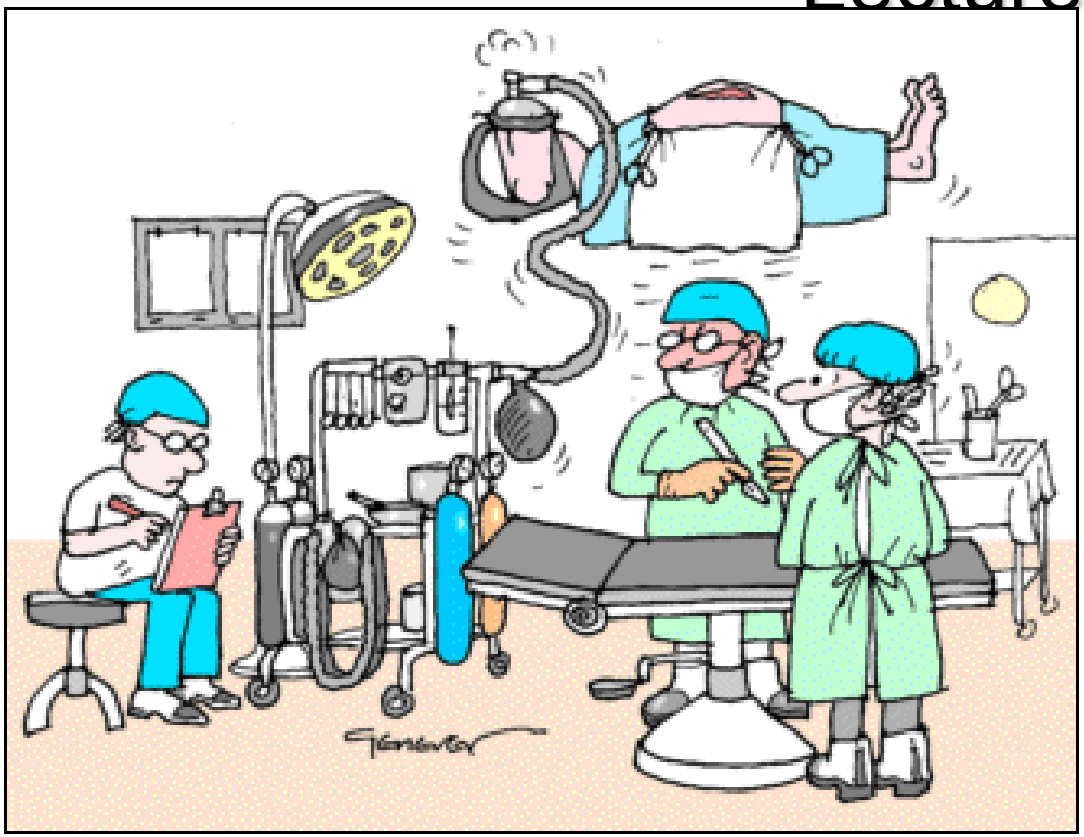
MINISTRY OF HEALTH OF UKRAINE
POLTAVA STATE MEDICAL UNIVERSITY
DEPARTMENT OF THE GENERAL SURGERY WITH PATIENT'S CARE

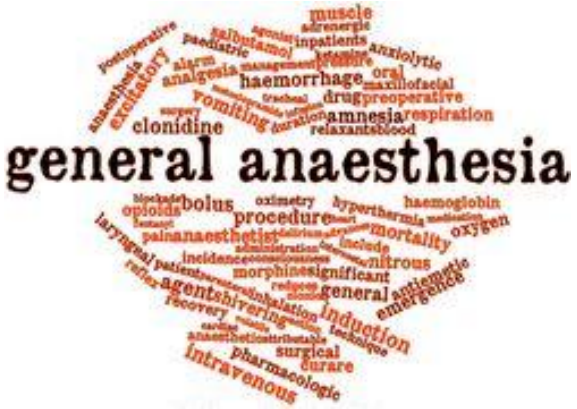
Narcosis - is Hours of boredom and instant of horror …

GENERAL ANAESTHESIA

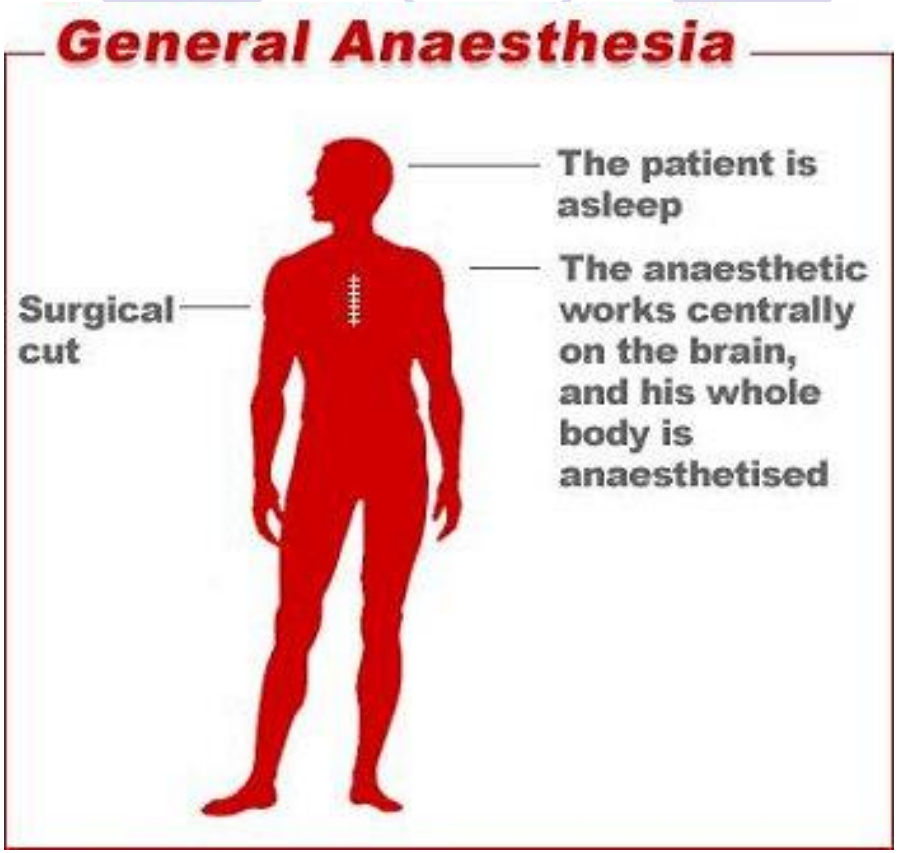
Lecture on general surgery

Chorna I.O.
Poltava





- 1. Definition
- 2. Terminology
- 3. History
- 4. Kind of narcosis
- 5. Drag 6. Stage
- 7. Equipment
- 8. Complication



Anesthesia?

The loss of feeling or sensation…

General Anesthesia

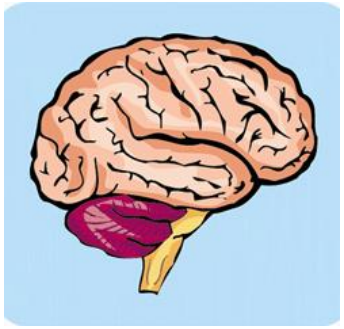
- A state of unconsciousness in which there is loss of sensation throughout the body.

Local Anesthesia

- Loss of sensation only in part of the body, the human remains conscious.

Four Major Objectives of Anesthesia

- **Hypnosis (amnesia)** -Loss of consciousness
- **Analgesia –** Loss of pain



- **Hyporeflexia –** Decreased spinal reflexes
- **Neuromuscular Blockade –** Adequate muscle relaxation

WHAT DOES ANESTHESIA MEAN?

The word **anaesthesia** is derived from the Greek: meaning insensible or without feeling.

The adjective will be ANAESTHETIC .

The means employed would properly be called the anti-aesthetic agent but it is allowable to say anaesthetic or in American anesthetic

Definition of Anaesthesia

Insensible does not necessary imply loss of consciousness.

So **General Anaesthesia** can be defined as :

Totally Reversible Induced Pharmacological type of Unconsciousness

so it can be differentiated from sleep, head injury, hypnosis, drug poisoning, coma or acupuncture.

Definition

General anesthesia is anesthetics-induced reversible suppression on CNS,

and has the following manifestations:

- producing unconsciousness
- pain relief (analgesia)
- blocking memory of the procedure (amnesia)
- inhibiting normal body reflexes to make surgery safe and easier to perform
- relaxing the muscles of the body

COMPONENTS OF ANAESTHESIA

The famous components of general anesthesia are

TRIAD

1. UNCOSCOUSNESS.

2. ANALGESIA

3. MUSCLE RELAXATION.

But those triad are under modifications

Unconsciousness replaced by amnesia or loss of awareness

Analgesia replaced by no stress autonomic response

Muscle relaxation replaced by no movement in response to surgical stimuli


Here our anesthesiologist is!

ROLE OF ANAESTHESIOLOGIST

So we can summarize the role of anaesthesiologist in:

1. Knowing physiology of body well.
2. Knowing the pathology of patient disease and co-existing disease
3. Study well the pharmacology of anaesthetic drugs and other drugs which may be used intra-operatively.
4. Use anaesthetics in the way and doses which is adequate to patient condition and not modified by patient pathology with no drug toxicity.
5. Lastly but most importantly administrate drug to manipulate major organ system, to maintain homeostasis and protect patient from injury by surgeon or theatre conditions.

Risk Assessment

Components for evaluating perioperative risk:

- patient's medical condition preoperatively
- extent of the surgical procedure
- risk from the anesthetic

"Most of the work, however, addresses the operative risk according to the patient's preoperative medical status"

ASA Physical Status Classification System

	medical status	mortality
ASA I	normal healthy patient without organic, biochemical, or psychiatric disease	0.06-0.08%
ASA II	mild systemic disease with no significant impact on daily activity e.g. mild diabetes, controlled hypertension, obesity .	Unlikely to have an impact 0.27-0.4%
ASA III	severe systemic disease that limits activity e.g. angina, COPD, prior myocardial infarction	Probable impact 1.8-4.3%
ASA IV	an incapacitating disease that is a constant threat to life e.g. CHF, unstable angina, renal failure ,acute MI, respiratory failure requiring mechanical ventilation	Major impact 7.8-23%
ASA V	moribund patient not expected to survive 24 hours e.g. ruptured aneurysm	9.4-51%
ASA VI	brain-dead patient whose organs are being harvested	

For emergent operations, you have to add the letter 'E' after the classification.

Kind of anestesia

I. Iinhalation:

- The mask
- intubation

II. Not inhalation:

- intravenous
- intramuscular
- Enteral
- Rectal
- Electroanaesthesia

III. Combined

1 . Not inhalation::

- TBA
- NLA
- Ataralgeziya
- With miorelaksant

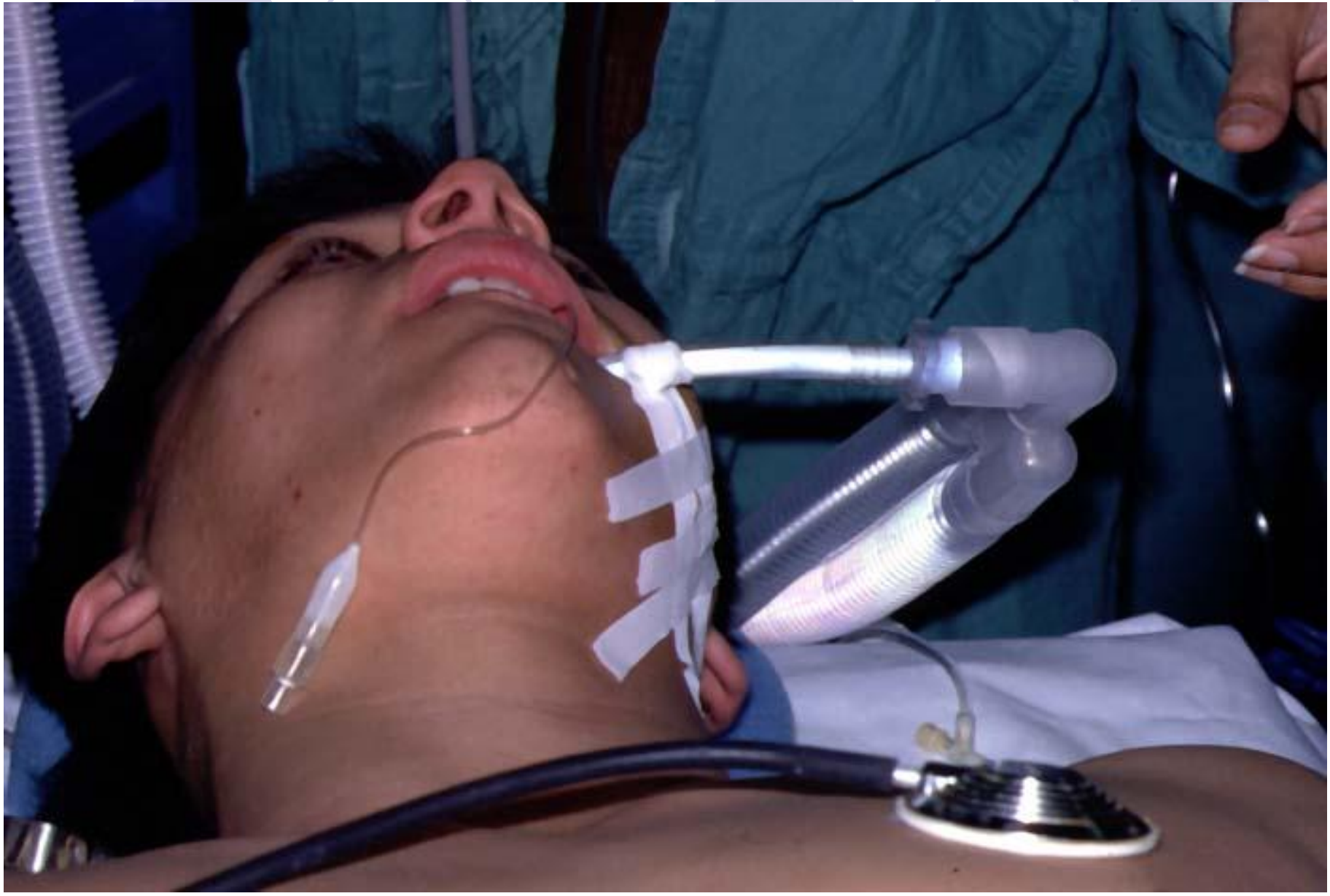
2 . Inhalation

- Azeotropny mix;
- Nitrogen-ftortan protoxide

3 . Inhalation and not inhalation:

- Nitrous oxide – кетамин
- GOMK-ftorotanovy

4 . With local anesthesia



APPROACH TO ANAESTHESIA

The empirical approach to anaesthetic drug administration consists of selecting an **initial** anaesthetic dose {or drug} and then titrating subsequent dose based on the clinical responses of patients, without reaching toxic doses.

The ability of anaesthesiologist to predict clinical response and hence to select optimal doses is the art of anaesthesia

TOOLS OF ANAESTHESIA

Knowing physiology, pathology ,and pharmacology is not enough to communicate safe anesthesia

But there is need for two important tools:

1. Anaesthetic machine.
2. Monitoring system.

ANAESTHETIC MACHINE

1. Oxygen gas supply.
2. Nitrous oxide gas supply.
3. Flow meter
4. Vaporizer (испаритель) specific for every agent
5. Mechanical ventilator
6. Tubes for connection.

MONITORING

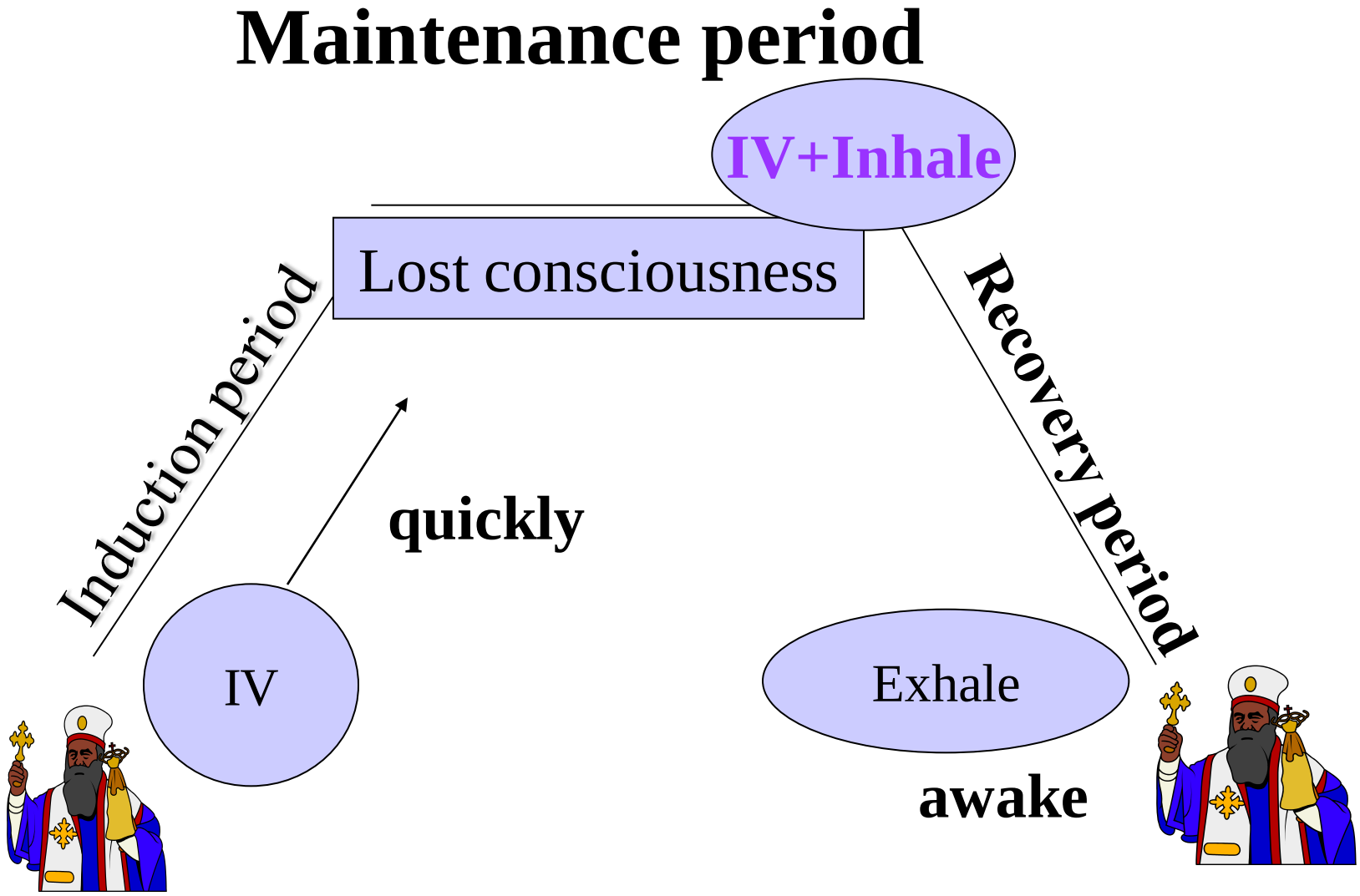
1. Pulse, ECG
2. Blood pressure
3. Oxygen saturation.
4. End tidal CO2
5. Temperature
6. Urine output, CVP, EEG, bispectral index, muscle tone, ECHO, drug concentration.

HOW CAN WE ACHIEVE ANAESTHESIA?

1. General anaesthesia
   a) Inhalational: by gas or vapor
   b) IV ,IM or P/R
2. Regional anaesthesia
3. Local anaesthesia

Or to combine between them

Course of General Anesthesia



Stages of Anesthesia

During induction of general anesthesia, animals pass through various stages indicative of the level of anesthesia.

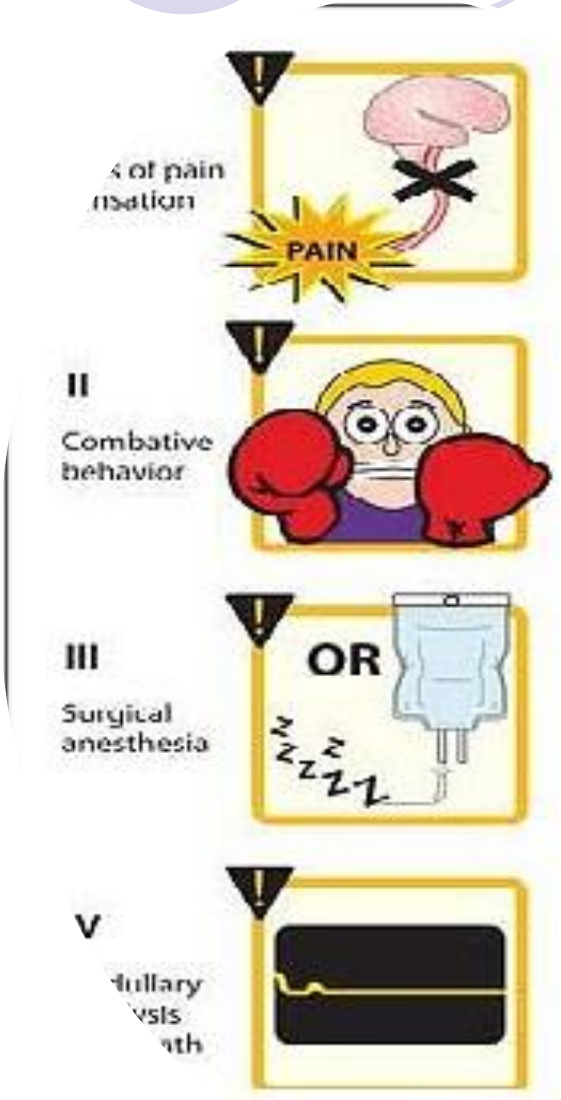
Stage 1: excitatory, disorientation, vocalization, urination, defecation.

Stage 2: loss of consciousness with or without struggling and whining, many reflexes are intact but righting reflex is lost, rapid irregular breathing and rigidity.

Stage 3: surgical stage of anesthesia, with loss of reflexes, muscle relaxation, deep and rhythmic breathing, planes 1-4 (light to deep).

Stage 4: medullary paralysis with respiratory arrest, hypotenstion and imminent death. Cardio-pulmonary resuscitation and drugs to reverse anesthesia must be given or anima will die.

Signs and stages of analgesia



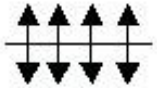
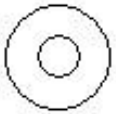
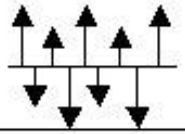
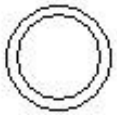
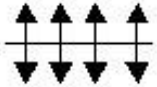
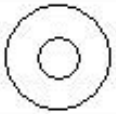
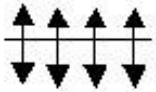
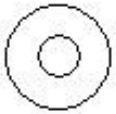
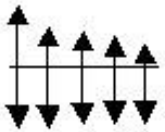
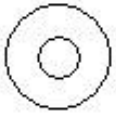
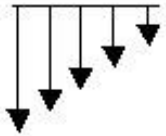
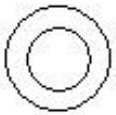
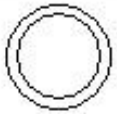
Stage of analgesia

Stage of Excitement

State of surgical anasthesia

Stage of Medullary depression

Guedel's Stages & Planes of Ether Anesthesia

Stage/Plane	Respiration	Pupils	Eyes	Reflexes
Stage I. Analgesia				
Stage II. Excitement			+++ +++ +++	Lid V
Stage III. Surgical Anesthesia Plane 1			+++ +++ ++ +	S Conjunctival P
Plane 2				L Corneal
Plane 3				
Plane 4				Light Carinal
Stage IV. Medullary Depression				

(Position of reflexes indicates at which depth of anesthesia reflexes are lost.)

↑=inspiration
↓=expiration

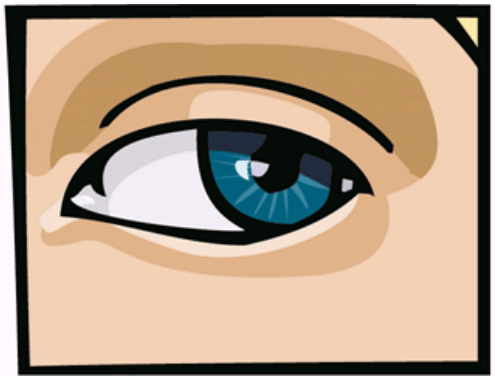
V=vomiting
S=swallowing
P=pharyngeal
L=laryngeal

Stage I: Analgesia

- Minimal CNS depression
- Some amnesia along with analgesia
- Respiration and pupils normal
- No eye movement or loss of reflexes
- Sensory transmission of nociceptive (painful) stimuli in spinothalamic tract are interrupted due to depression of substantia gelatinosa in dorsal horn of spinal cord

Stage II: Excitement (disinhibition)

- Due to inhibition of inhibitory neurons (e.g. Golgi type II cells) & release & paradoxical facilitation of catecholamines.
- Respiration – very irregular, coughing
- Pupils dilated
- Eye movements marked
- Loss of eyelid (blink) reflex



Stage III: Surgical Anesthesia

- Divided into 4 planes based on progressive depression of ARAS (ascending reticular activating system)
- **Plane 1**
  - Respiration normal and regular
  - Pupils normal
  - Diminishing eye movements to fixed stare
  - Loss of swallowing, conjunctival and pharyngeal reflexes
- **Plane 2**
  - Slight depression of respiratory movements
  - Loss of laryngeal & corneal reflexes
  - Adequate for tonsillectomy

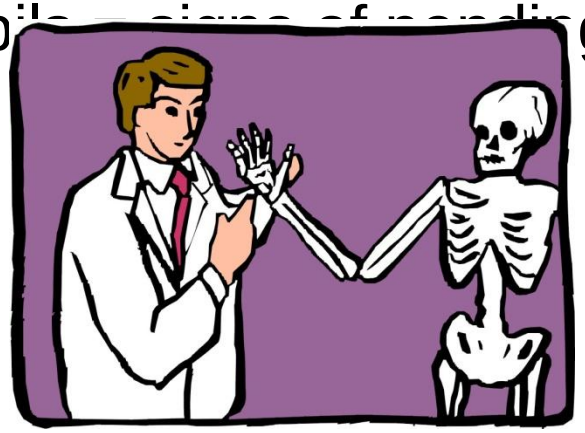
Stage III: Surgical (continued)

- **Plane 3**
  - **Marked decrease in depth of inspiration**
  - **Suppression of spinal reflexes contributes to muscle relaxation produced by some agents.**
  - **Patient needs to be on mechanical respirator or regularly respired by anesthetist.**
  - **<u>Preferred level for most surgeries</u>**

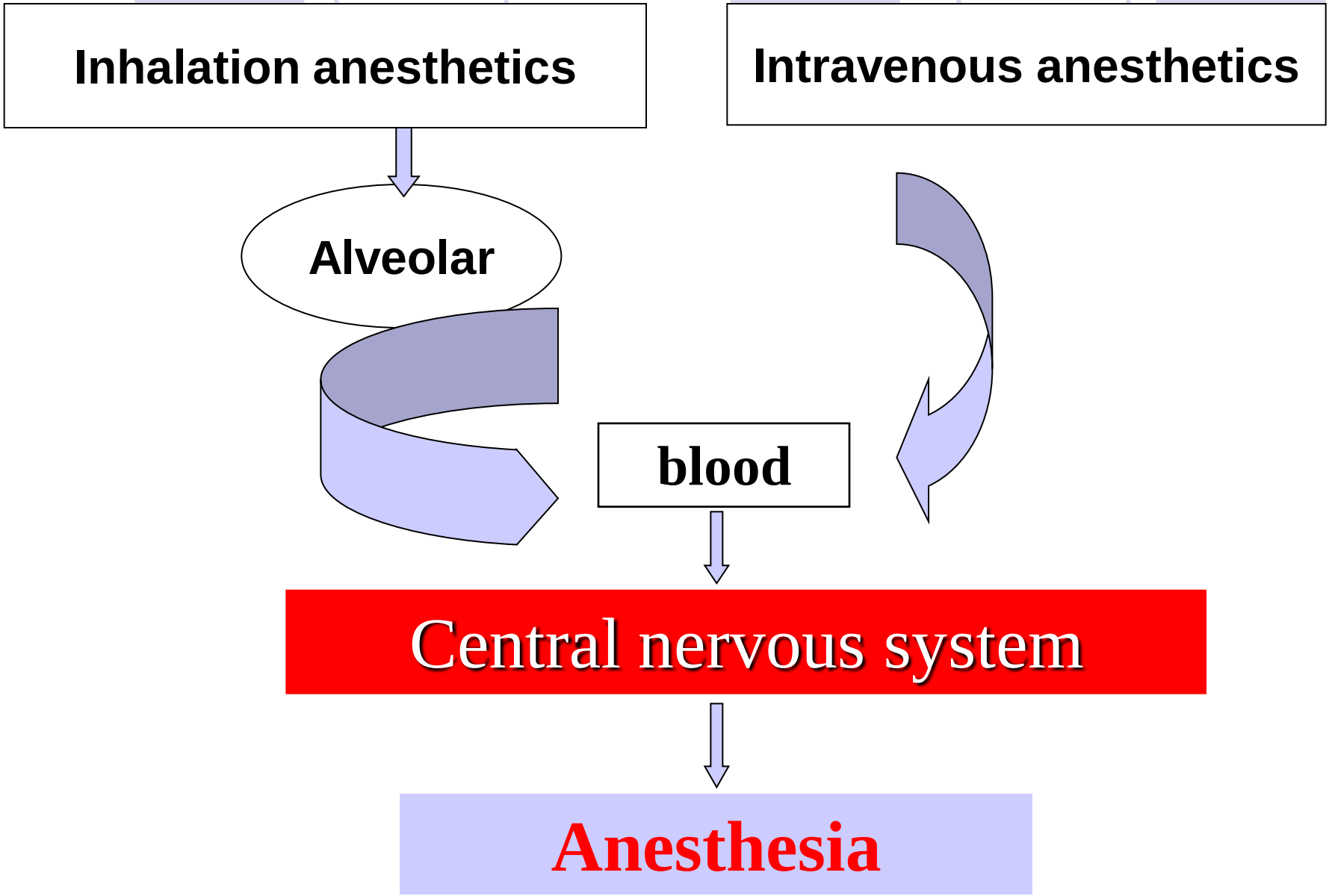
- **Plane 4**
  - **Depth of expiration decreases**
  - **Pupils dilate and won't respond to light**
  - **Loss of carinal reflex**
  - **Can rapidly progress to Stage IV unless action is taken to decrease depth of anesthesia & stress.**

Stage IV: Medullary Depression

- Cardio-respiratory collapse due to depression of respiratory and vasomotor centers of medulla. Fortunately, neurons are relatively insensitive to depressant effects of GA.
- Observed only at toxic doses
- Fixed, dilated pupils – signs of impending coma or death

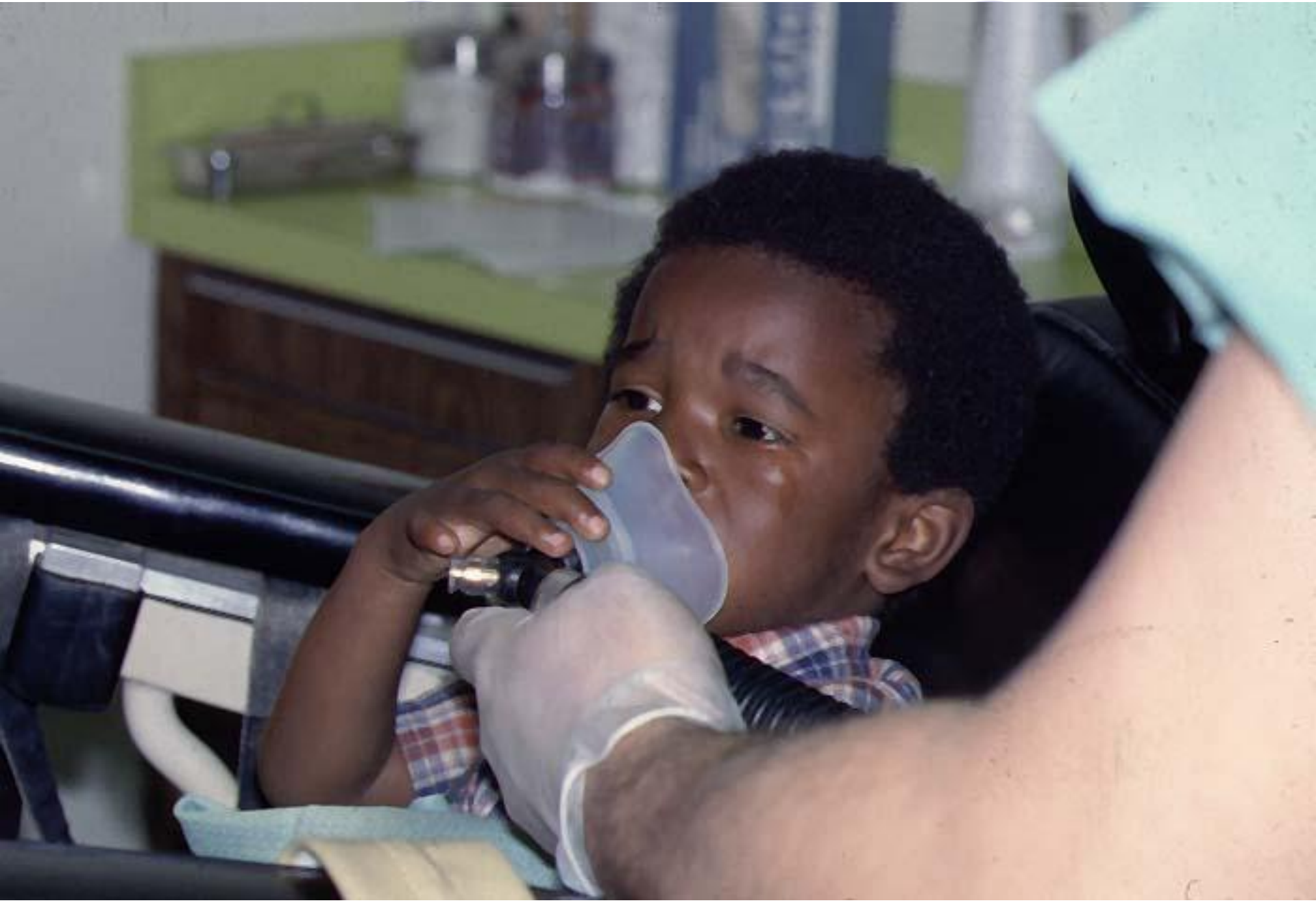


Route of Action



INHALATIONAL ANAESTHESIA

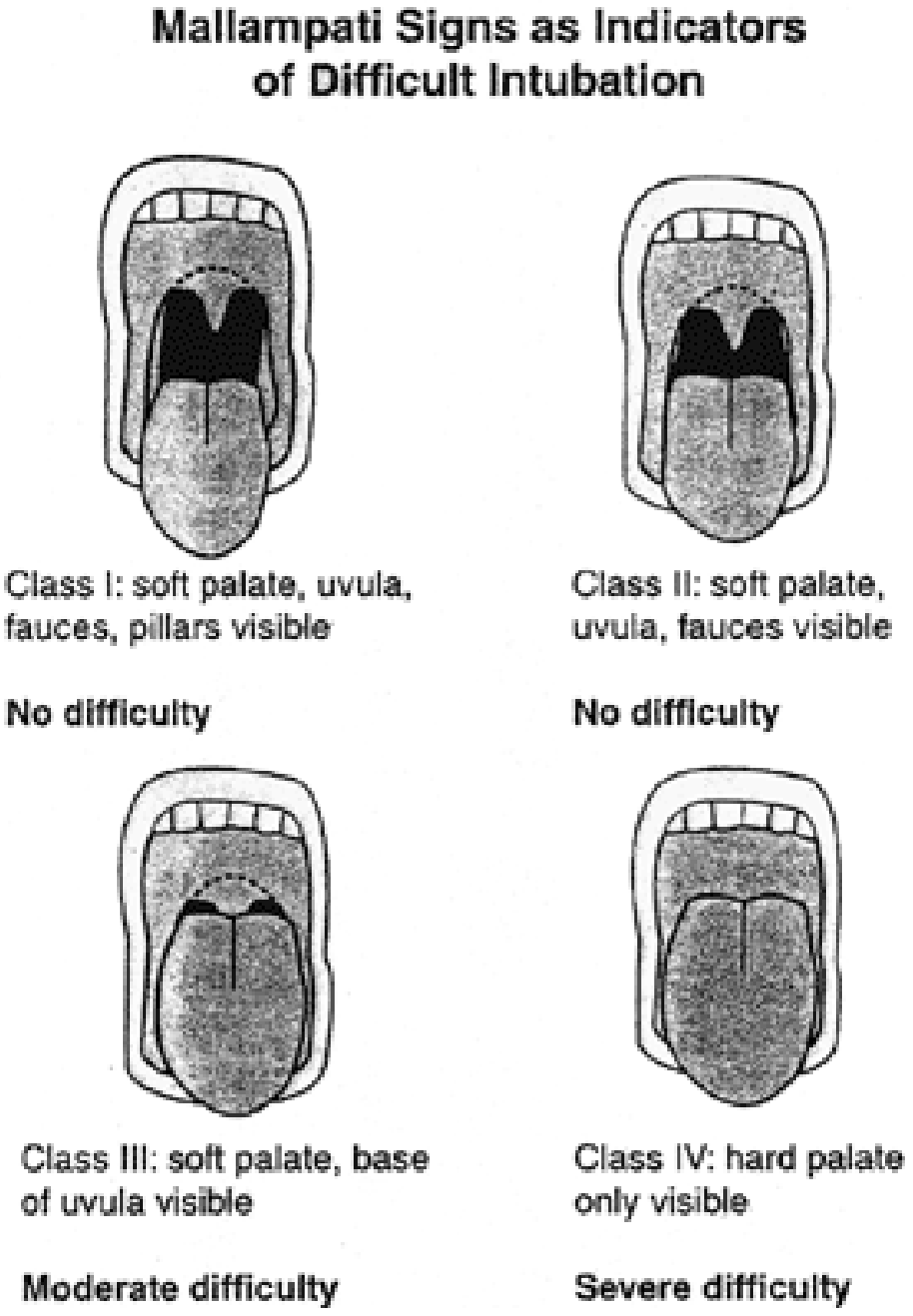
- Inhalational anaesthesia is achieved through airway tract by facemask, laryngeal mask or endotracheal tube.
- The agent used is a gas like nitrous oxide or volatile vapor like chloroform, ether, or flothane.
- Inhalational anaesthesia depresses the brain from up [cortex] to down [the medulla] by increasing dose.



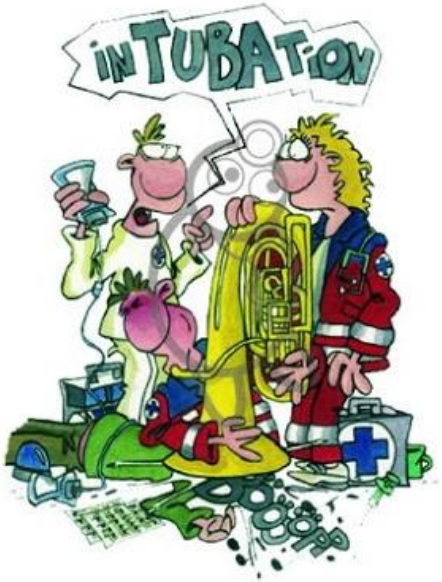
Anaesthesia Machine

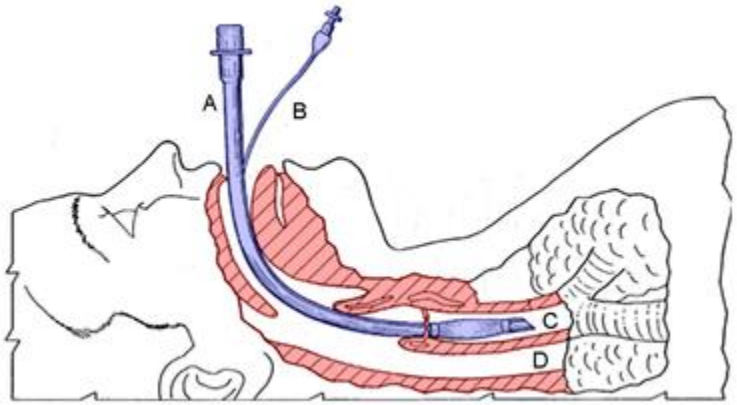
Airway Evalua

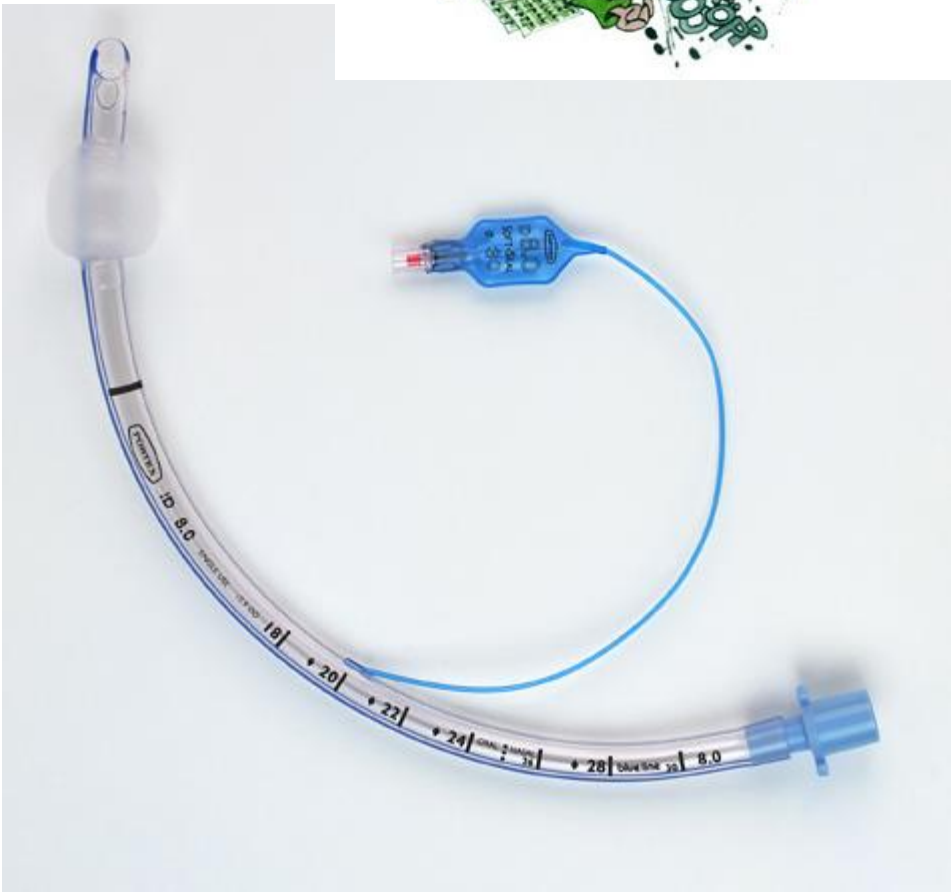
- Mallampati Classification
- Mouth Opening
- Thyromental Distance
- Neck ROM



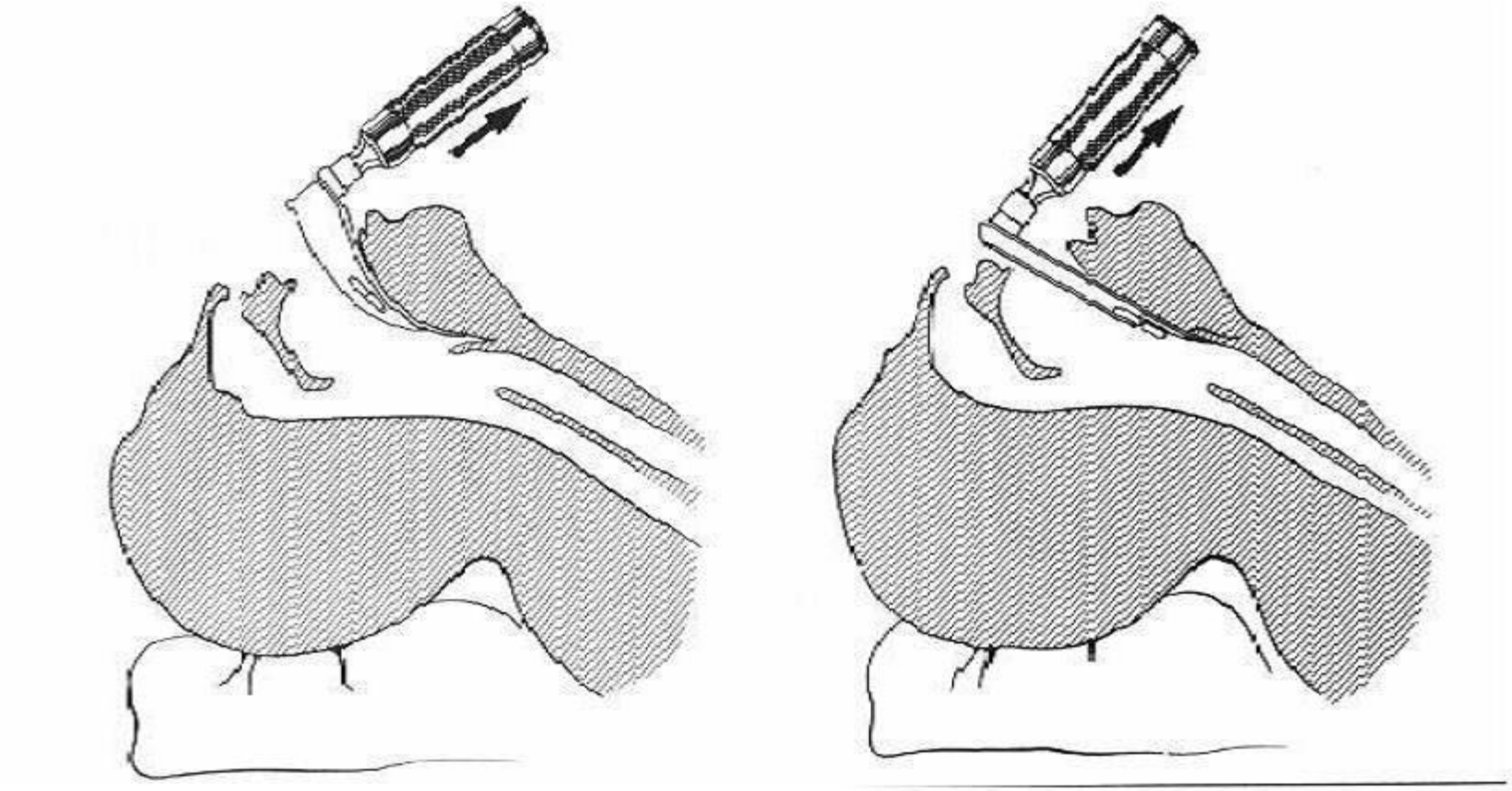
Endotracheal tubes







Laryngoscopy – Endotracheal Intubation



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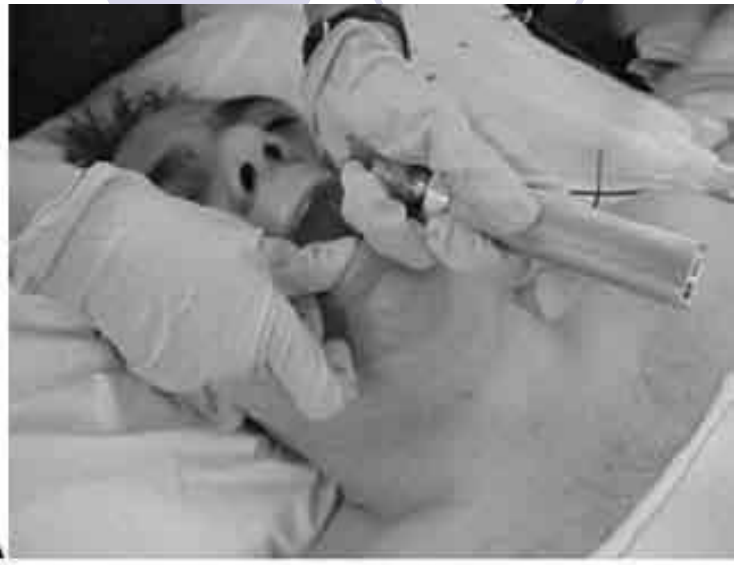

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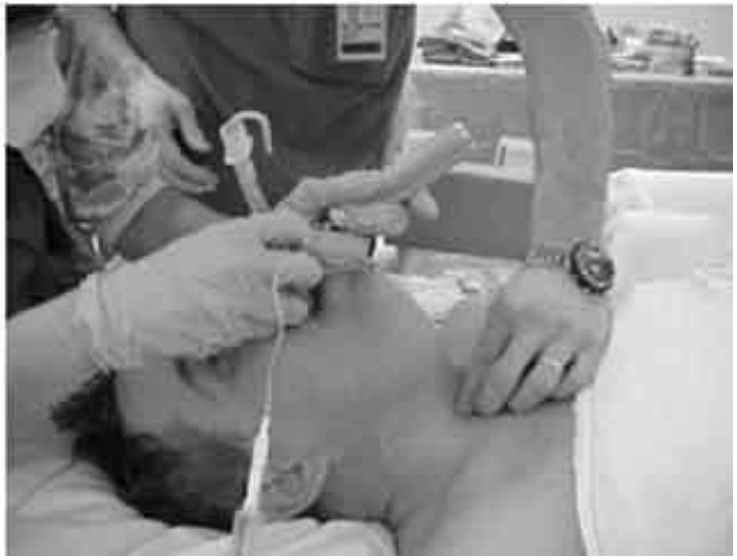

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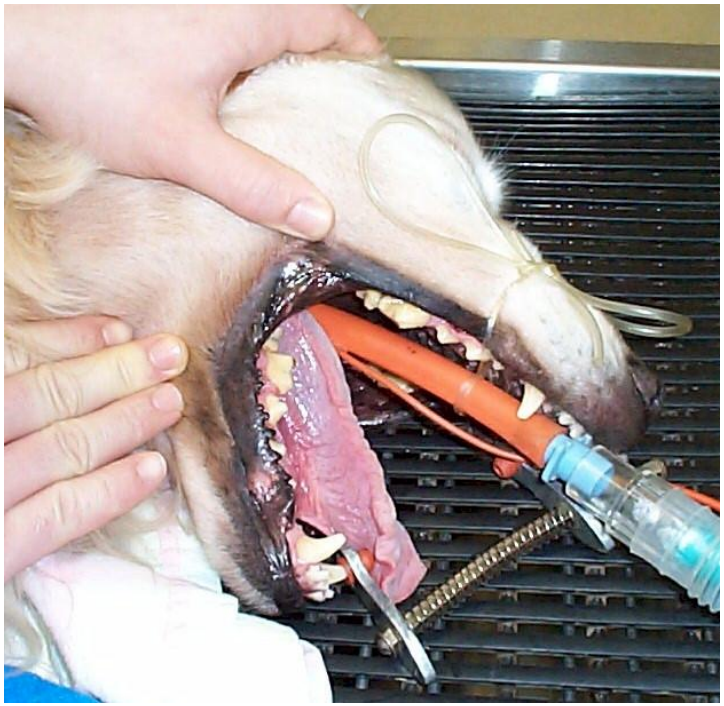
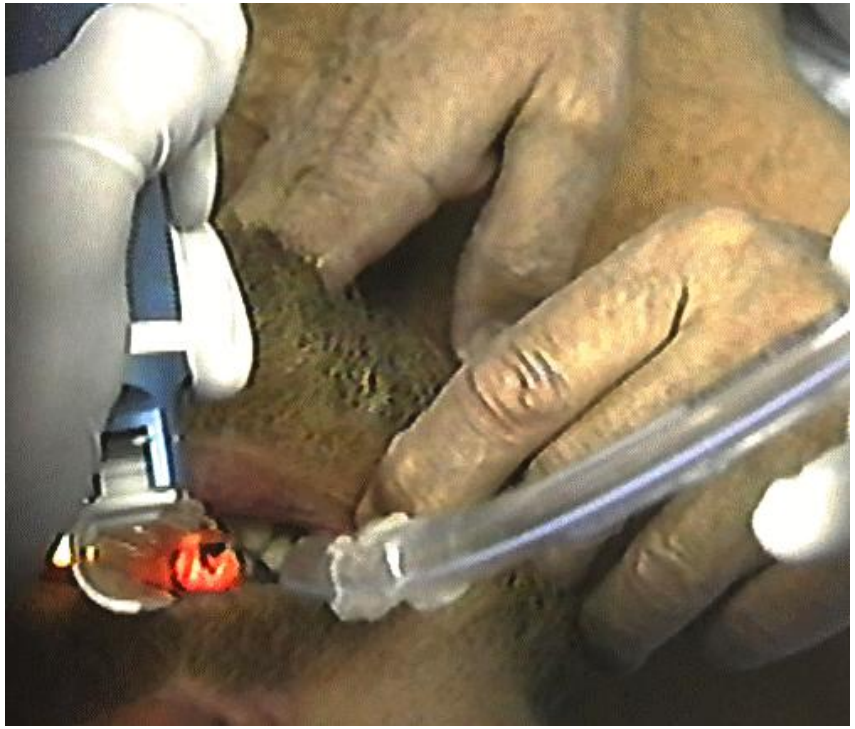
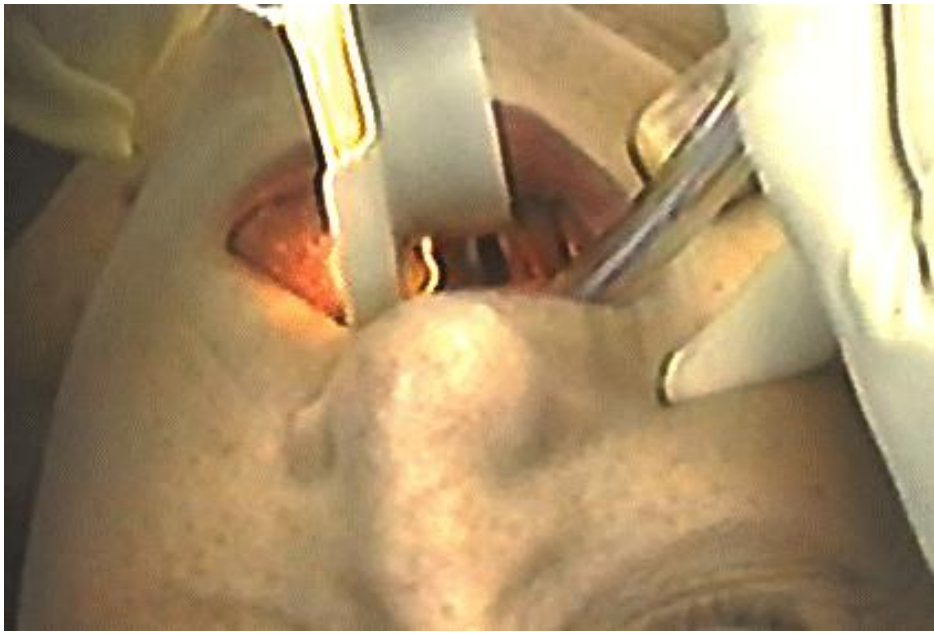


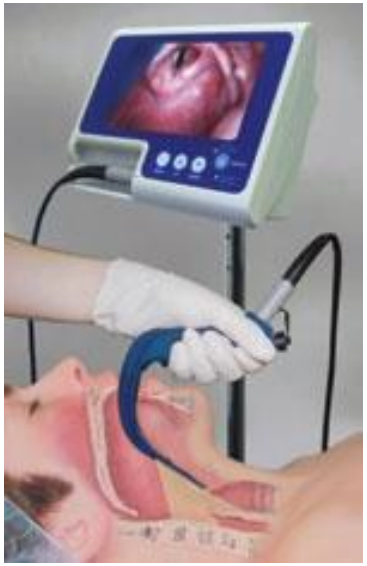
Laryngoscopy – Endotracheal Intubation

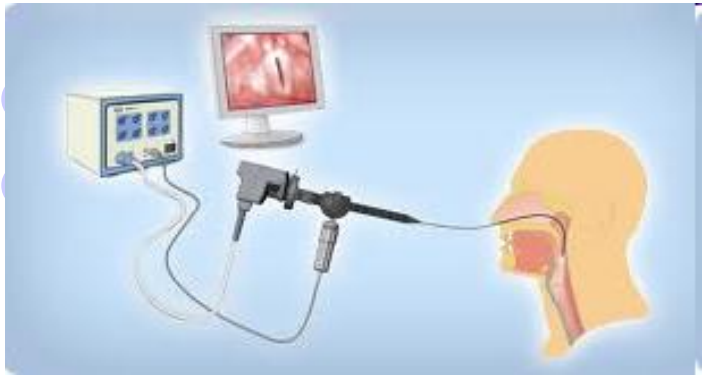




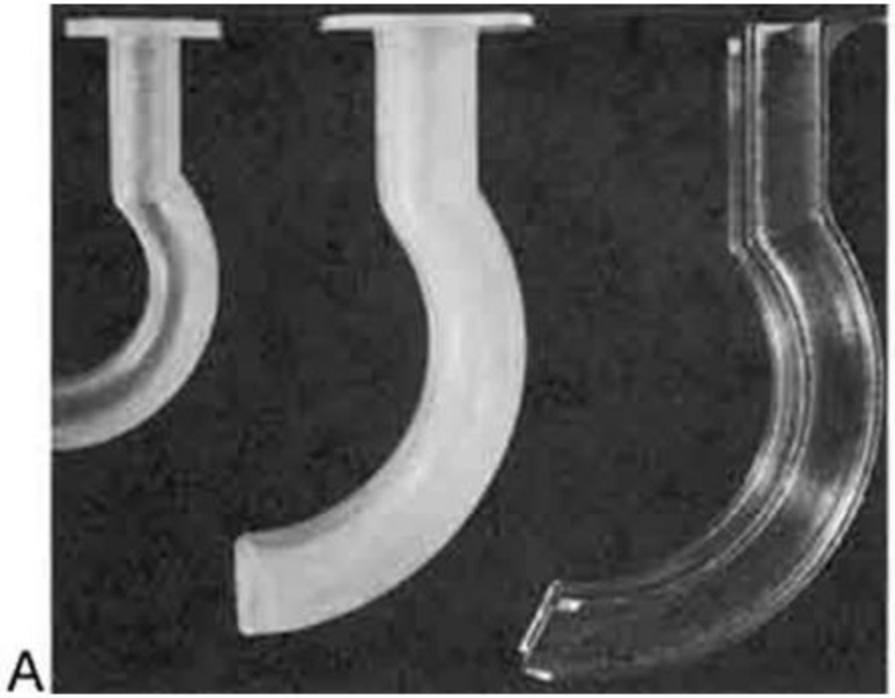
Airway Management - Equipment

- Oral and Nasal Airways
- Mask
- Laryngoscopes
  - Macintosh
  - Miller





Oropharyngeal and Nasopharyngeal Airways



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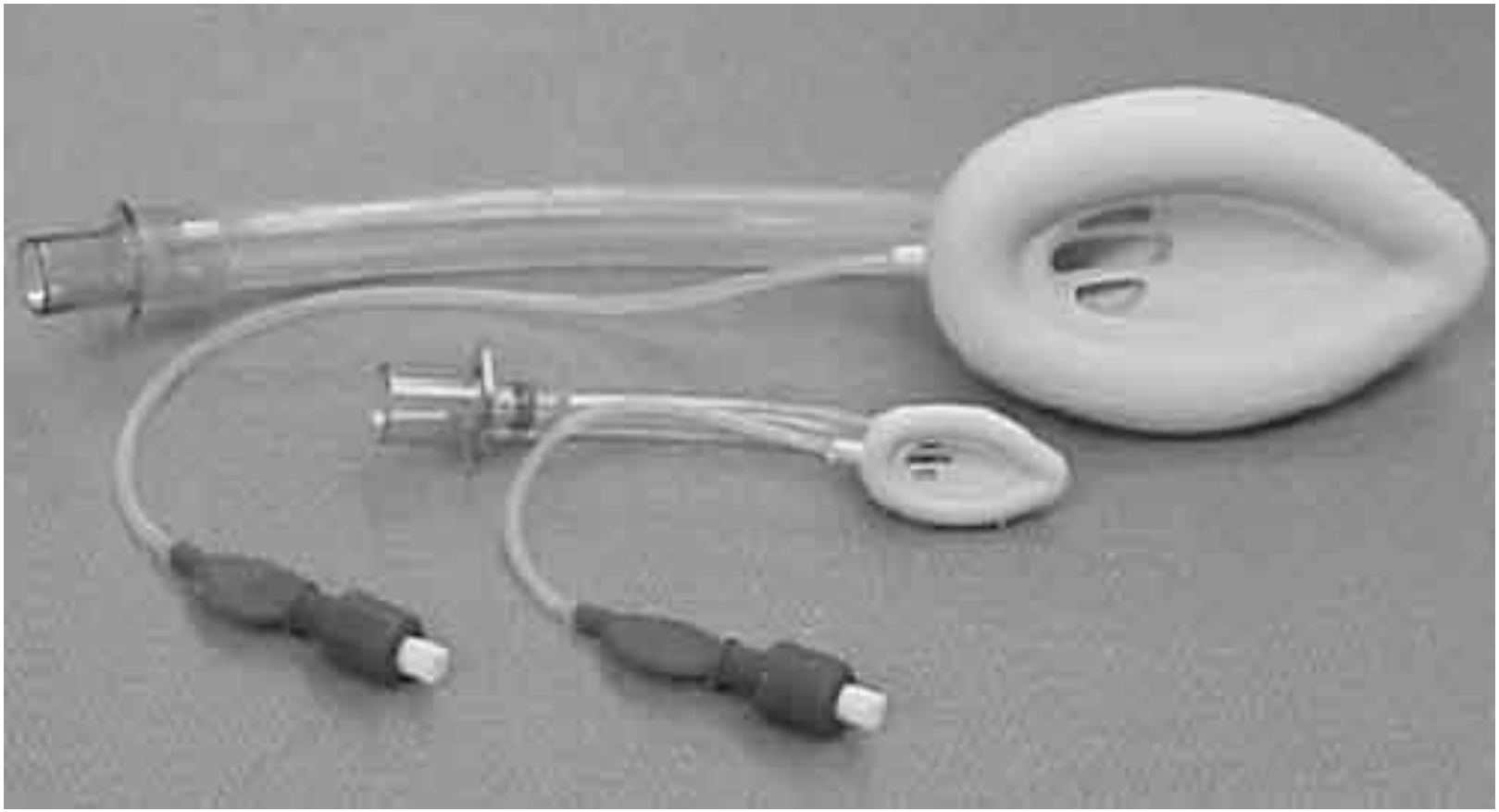
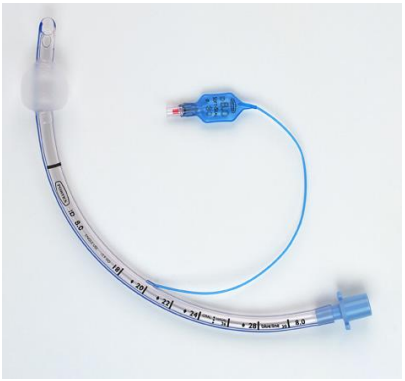
Laryngeal Mask Airway



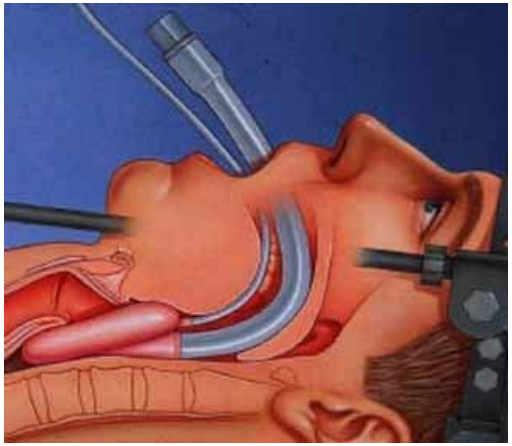
Airway Management

- Proper Positioning
  - “Sniff Position” – alignment of oropharynx, pharynx, and larynx

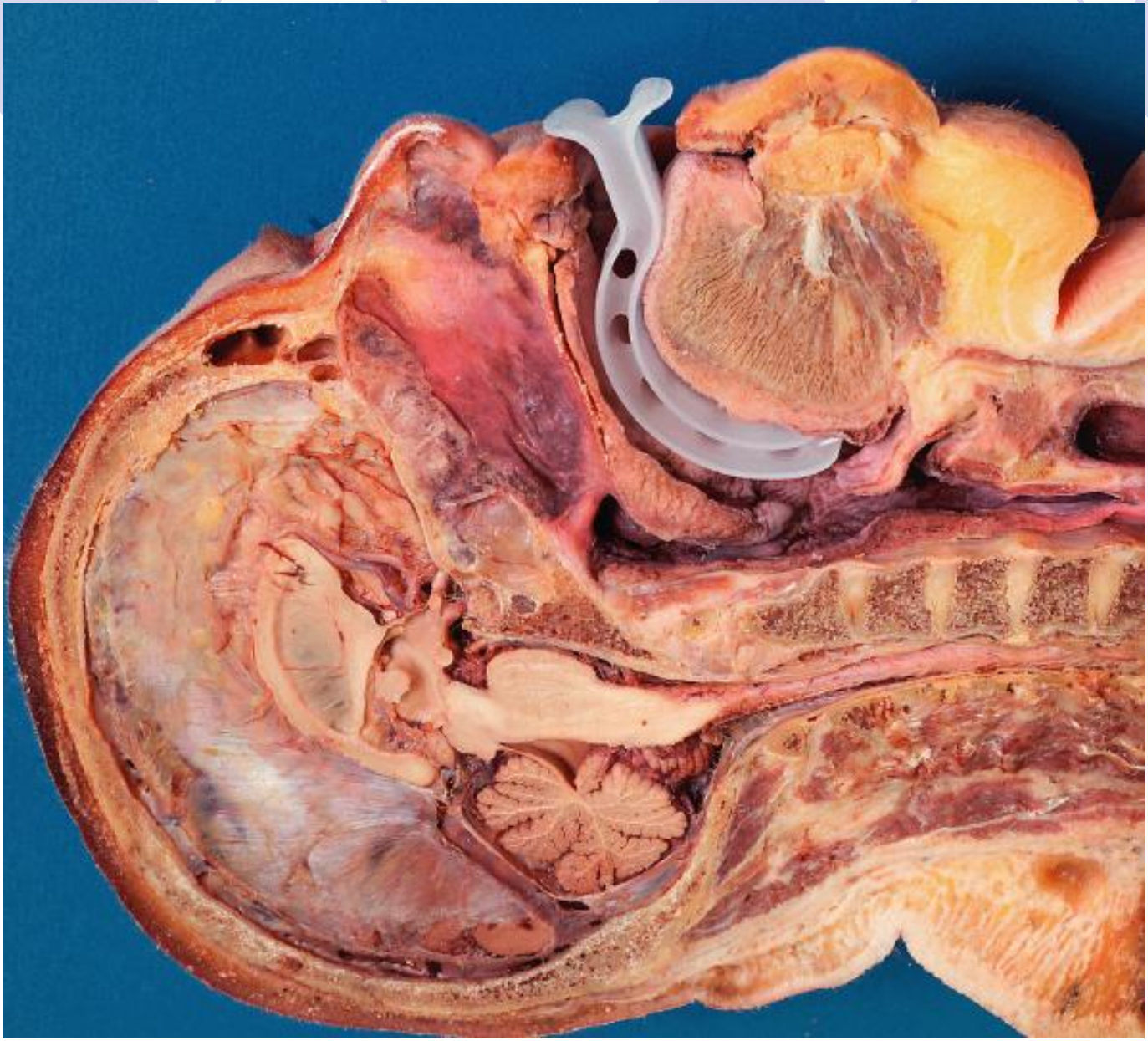
- Mask Ventilation



- Intubation



- LMA Insertion



General Anesthetics-Inhalational Agents

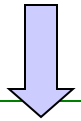
- Ether,
- Nitrous Oxide (N_2O)
- Sevoflurane
- Desflurane
- Isoflurane (Forane)
- Enflurane
- Halothane

Metabolism of inhalation anesthetics

Major: eliminated by lung

Minor: metabolized in liver

metabolic rate, media product and the final product



decide toxicity

ether	N_2O	halothane	enflurane	isoflurane	sevoflurane	desflurane
2.1-3.6	0.004	15-20	2-5	0.2	2-3	0.02

Diethyl ether (ether)

- Ether, a volatile liquid, was 1st demonstrated to be an effective anesthetic in 1846 by William Morton, a year 2 medical student at Mass. General Hospital.

Beneficial Effects

- Excellent analgesia and muscle relaxation
- Stimulates respiration down to plane 3 of stage 3 before depressing respiration at higher levels
- Maintains circulation
- Produces bronchodilation
- Large safety margin
- Still used in third world countries

Adverse Effects

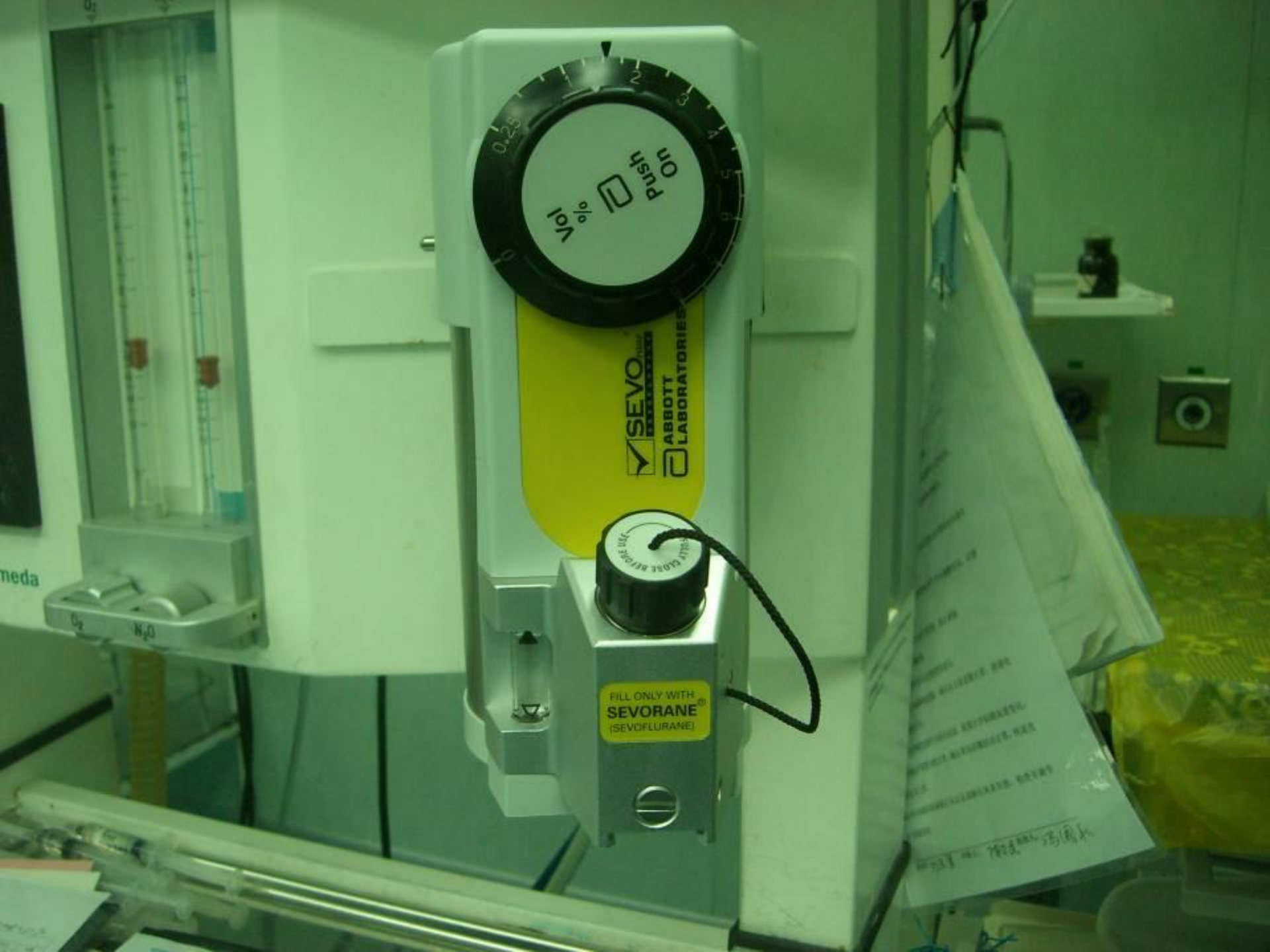
- No longer used for surgery in U.S. because it is explosive, flammable and irritating to mucous membranes
- Prolonged and stormy induction and recovery with coughing and breath holding
- Causes post-operative nausea and vomiting

Nitrous Oxide (N_2O)

- MAC: 105%, low anesthetic potency, inhalation conc.:50-70% (***F_iO_2>0.3***) , in combination with other agent
- B/G: 0.47, fast
- Respiratory system: non-irritant, no injury
- Cardiovascular system: almost no-depression
- ***Diffuse hypoxia***: inhale 100% O_2 5-10min
- Increase cavity pressure: forbidden in colon obstruction

inhalational induction agents

- The most commonly-used agent is **sevoflurane** because it causes less irritation than other inhaled gases.
- Sevoflurane
  - MAC 2.05%
  - Mild airway irritant
  - Suitable for mask induction
  - Rare hepatotoxicity
- Rapidly eliminated and allows rapid awakening.


Vol %
Push On
0.25
SEVO
ABBOTT LABORATORIES
FILL ONLY WITH
SEVORANE®
(SEVOFLURANE)

Inhalational Agents

- **Desflurane**
  - Blood gas partition coefficient 0.42
  - Irritating to airway
  - MAC 6%
  - Required heated vaporizer
  - Expensive compared to other anesthetic gases
  - Reduces SVR and MAP, but increase in heart rate causing stable CO
  - Low risk of hepatotoxicity
  - Rapid depth and recovery


Ohmeda
BOC Health Care
Use Only Isoflurane
Datex-Ohmeda
Tec 6
DESFLURANE
OPERATIONAL
NO OUTPUT
LOW AGENT
WARM-UP
ALARM
BATTERY LOW
Use only
Desflurane
Warning: Use vaporizers with interlocks. Use of vaporizers without interlocks
cause simultaneous delivery of anesthetic agents.
Danger: Possible explosion hazard. Do not
in the presence of flammable anesthetics.
Oxygen
Monitoring during each use of this machine.

Inhalational Agents

- **Isoflurane (Forane)**
  - Anesthesia of choice
  - Blood/gas partition coefficient 1.4 MAC 1.15%
  - “Pungent” odor
  - Can provide muscle relaxation (high concentrations)
  - Dose dependent depression of myocardial contractility
  - Coronary vasodilation
  - CO maintained
  - Can use catecholamines
  - Respiratory depression
  - Neither nephrotoxic or hepatotoxic

Enflurane

- Properties：clear colourless volatile anesthesia, pleasant smell
- MAC 1.7, B/G 1.9, Metabolism 2%
- Cardiovascular: Myocardial contractility reduced

  Systemic vascular resistance—BP ↓

  Sensitivity of myocardium to catecholamine ↑
- Respiratory: non-irritant; dose –dependent inhibition
- Muscle relaxation
- Induction and maintenance, unavailable in USA
- ***Patient with epilepsy history should be avoided (seizure activity on EEG)***

Inhalational Agents

- **Halothane**
  - Halogenated hydrocarbon
  - MAC is 0.75%
  - Blood/gas partition coefficient 2.3
  - Poor analgesic properties
  - Incomplete muscle relaxation
  - Decreased MAP
  - Depressant effect on myocardial contractility
  - Vasodilator
  - Depressant effect on respiration
  - Elimination-alveolar excretion and hepatic metabolism
  - Sensitizes heart to catecholamines
  - Associated with hepatoxicity
  - Malignant hyperthermia

Maintenance

- In order to prolong anaesthesia for the required duration (usually the duration of surgery), patient has to breathe a carefully controlled mixture of oxygen, nitrous oxide, and a volatile anaesthetic agent. This is transferred to the patient's brain via the lungs and the bloodstream, and the patient remains unconscious.

Maintenance

- Inhaled agents are supplemented by intravenous anaesthetics, such as **opioids** (usually **fentanyl** or morphine).
- At the end of surgery the volatile anaesthetic is discontinued.
- Recovery of consciousness occurs when the concentration of anaesthetic in the brain drops below a certain level (usually within 1 to 30 minutes depending upon the duration of surgery).

INTRVENOUS ANAESTHESIA

-Very rapid: 10 seconds, for 10 minutes

-Irreversible dose

-It is used in short operation or in induction of anaesthesia and anaesthesia maintained by inhalational route

-New agent now can be used in maintenance by infusion

Maintenance

- Total Intra-Venous Anaesthesia (TIVA): this involves using a computer controlled syringe driver (pump) to infuse Propofol throughout the duration of surgery, removing the need for a volatile anaesthetic.
- **Advantages:** faster recovery from anaesthesia, reduced incidence of post-operative nausea and vomiting, and absence of a trigger for malignant hyperthermia.

Ideal Intravenous anesthetic

- Water-soluble, no pain on injection
- Rapid onset, rapid recovery, little accumulation, little depression on respiratory-cardiovascular system. No nausea and vomiting, no interact with muscle relaxant, no release of histamine…….

Intravenous anesthetics

	Induction dose(mg/kg)	CVS	RS	CNS (CBF↓)	Side-effect	Other comments
propofol	1.5-2.5	hypotension	depression	yes	Pain on injection Movement	TIVA
etomidate	0.15-0.3	Less depression	depression	yes	Pain on injection movement	Suppress steroid synthesis
thiopentone	4-6	hypotension	depression	yes	rare	Delayed recovery after repeated use
ketamine	1-2 (iv) 6-10(im)	minimal	minimal	No	hallucination	Analgesia Dissociated anesthesia
midazolam	0.1-0.3	hypotension	depression	yes		amnesia

Intravenous Induction Agents

- Commonly used IV induction agents include **Propofol, Sodium Thiopental** and **Ketamine.**
- They modulate GABAergic neuronal transmission. (GABA is the most common inhibitory neurotransmitter in humans).
- The duration of action of IV induction agents is generally 5 to 10 minutes, after which time spontaneous recovery of consciousness will occur.

(1) **Propofol**

- Short-acting agent used for the induction, maintenance of GA and sedation in adult patients and pediatric patients older than 3 years of age.
- It is highly protein bound *in vivo* and is metabolised by conjugation in the liver.
- Side-effects is pain on injection hypotension and transient apnea following induction

(2) **Sodium thiopental**

- Rapid-onset ultra-short acting barbiturate, rapidly reaches the brain and causes unconsciousness within 30–45 seconds.
- The short duration of action is due to its redistribution away from central circulation towards muscle and fat
- The dose for induction is 3 to 7 mg/kg.
- Causes hypotension, apnea and airway obstruction

(3) **Ketamine**

- Ketamine is a general dissociative anaesthetic.
- Ketamine is classified as an NMDA Receptor Antagonist.
- The effect of Ketamine on the respiratory and circulatory systems is different . When used at anaesthetic doses, it will usually stimulate rather than depress the circulatory system.

Neuromuscular-blocking drugs

- Block neuromuscular transmission at the neuromuscular junction.
- Used as an adjunct to anesthesia to induce paralysis.
- Mechanical ventilation should be available to maintain adequate respiration.

Types of NMB

Non-depolarizing

competitive antagonists against ACh at the site of postsynaptic ACh receptors.

Examples:

Atracurium

Vecuronium

Rocuronium

Depolarizing

depolarizing the plasma membrane of the skeletal muscle fibre similar to acetylcholine

Examples:

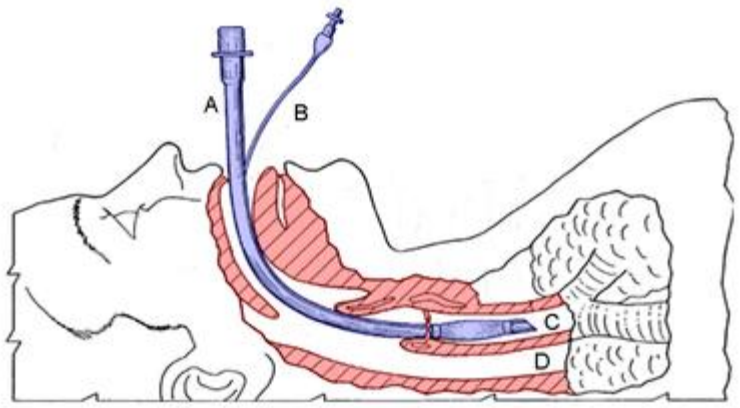
suxamethonium.

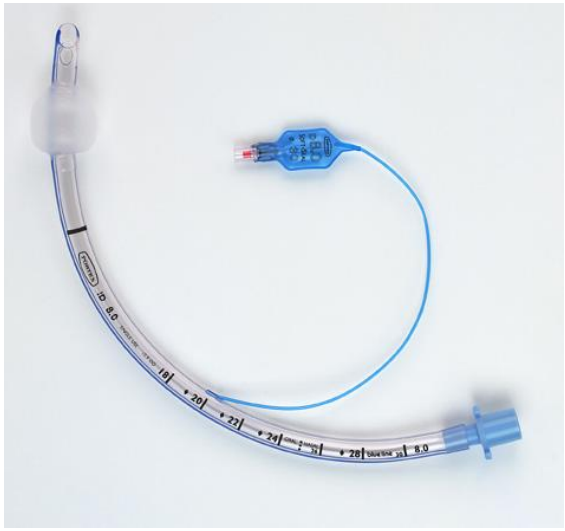
Osent: 30 seconds,

Duration: 5 minutes

Airway management

- To maintain an open airway and enable mechanical ventilation, an endotracheal tube or laryngeal mask airways are often used.





Monitoring

- ECG
- Pulse oximetry (SpO2)
- Blood Pressure Monitoring (NIBP or IBP)
- Agent concentration measurement
- Low oxygen alarm
- Carbon dioxide measurement (capnography)
- Temperature measurement
- Circuit disconnect alarm

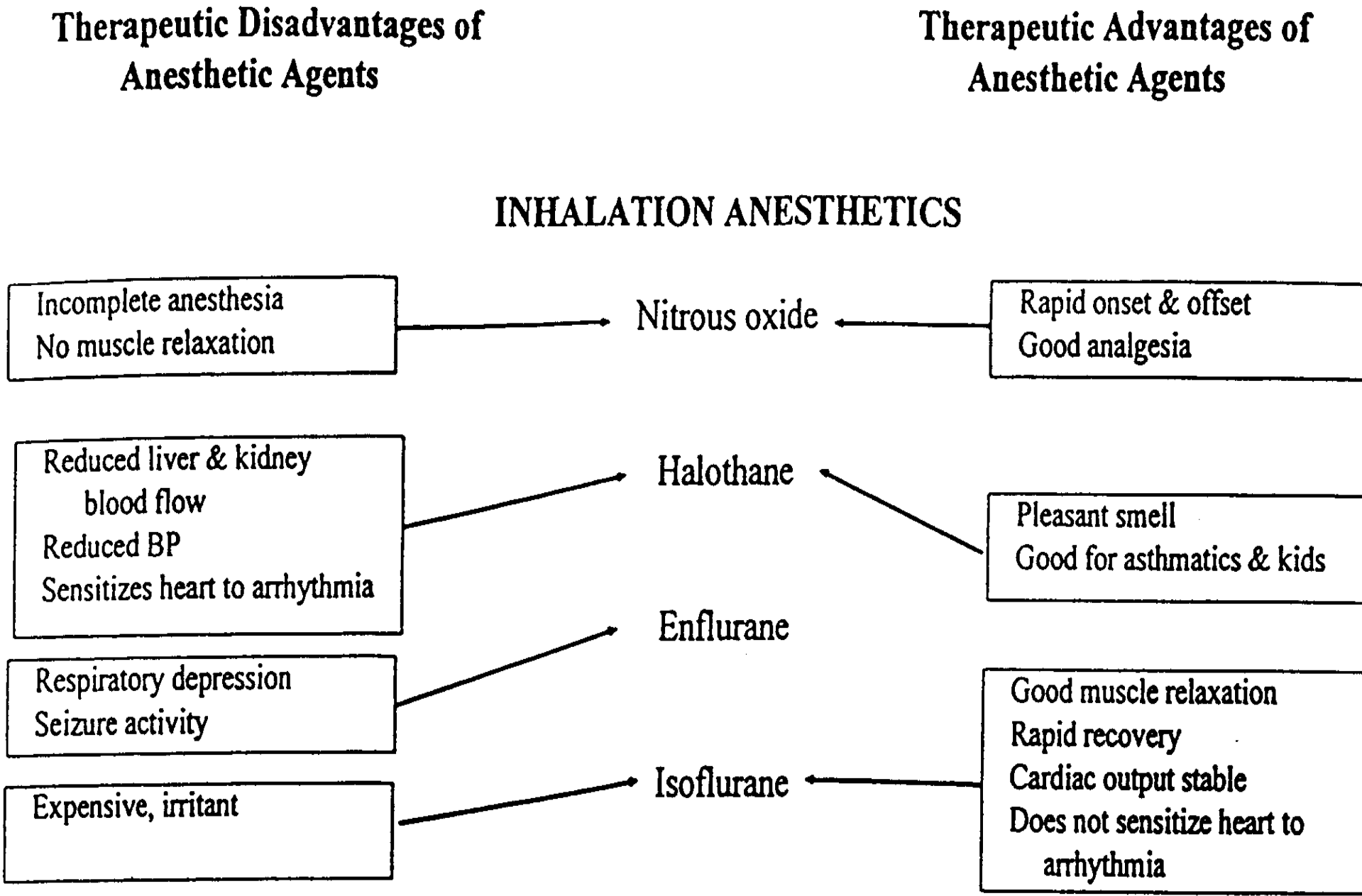
Modern General Anesthesia

- Extremely safe despite severe physiological trespasses made, due to:
  - Use of many drugs to tailor-make effect
  - Minimize individual toxicity
  - Improved monitoring of physiological parameters and presence of alarm systems

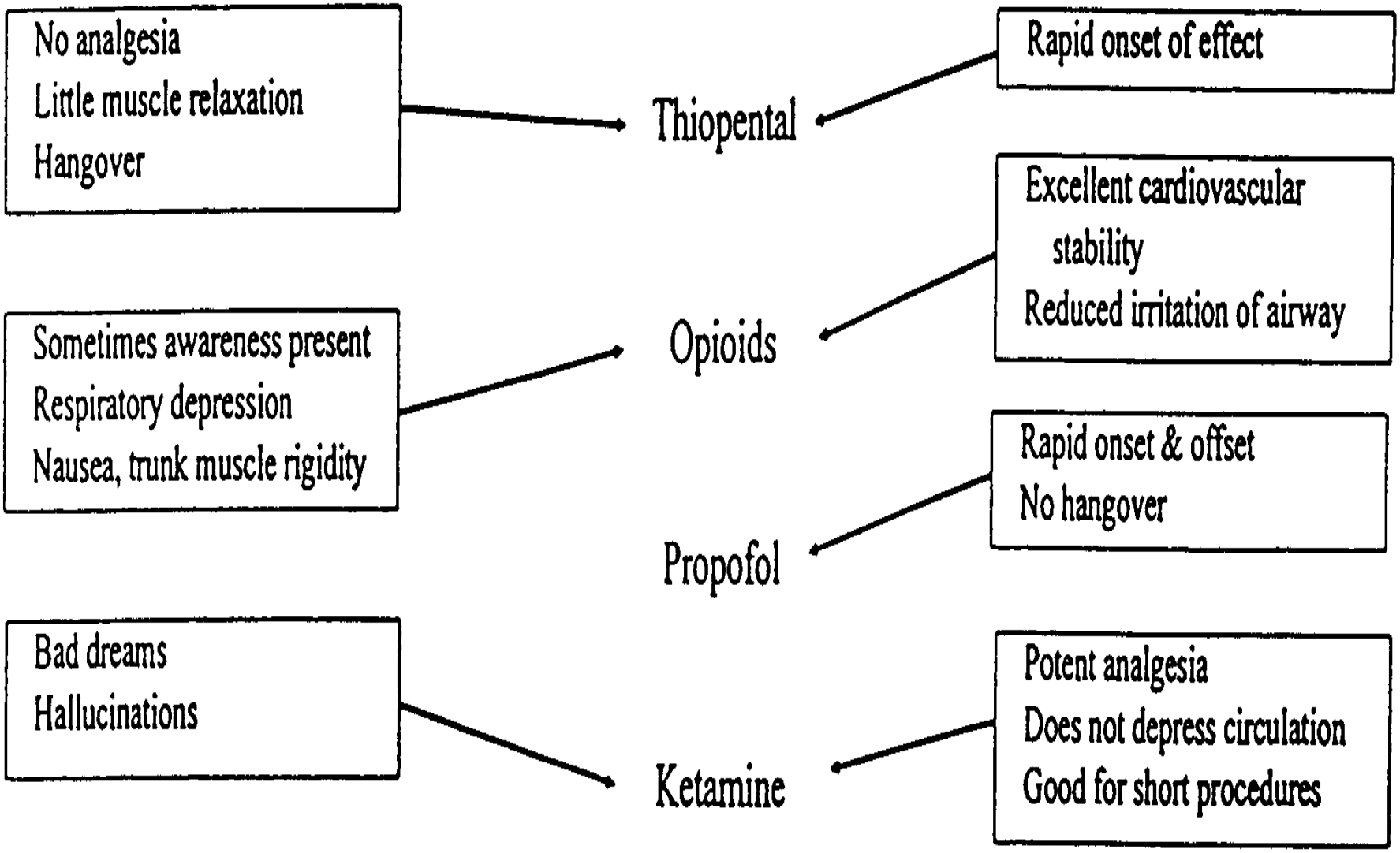
Suffice it to say that the life of an anesthetist consists of:

Hours of boredom and
moments of intense terror
thank goodness the patient is asleep

SUMMARY


Therapeutic Disadvantages of Anesthetic Agents
Therapeutic Advantages of Anesthetic Agents
INHALATION ANESTHETICS
Incomplete anesthesia
No muscle relaxation
Nitrous oxide
Rapid onset & offset
Good analgesia
Reduced liver & kidney blood flow
Reduced BP
Sensitizes heart to arrhythmia
Halothane
Pleasant smell
Good for asthmatics & kids
Enflurane
Respiratory depression
Seizure activity
Isoflurane
Good muscle relaxation
Rapid recovery
Cardiac output stable
Does not sensitize heart to arrhythmia
Expensive, irritant

INTRAVENOUS ANESTHETICS



Neuroleptanalgesia

- Causes patient to become indifferent to surrounding environment along with reduced motor activity
- Patient is sedated, sleepy, but remains responsive to voice instructions.
- Prototype = Innovar®

Fixed-dose combination of 2 drugs

Fentanyl - a short acting (30-60 min), potent opioid analgesic

Droperidol – a long acting (3-6 hours) psycho-sedative

Sufentanil is sometimes substituted for fentanyl. It is 10X more potent than fentanyl.

Both fentanyl and sufentanil have shorter time to peak analgesia & shorter recovery times than morphine.

Toxicity and Side Effects

- **Depression of respiratory drive**
  - Decreased CO2 drive (medullary chemoreceptors), Takes MORE CO2 to stimulate respiration
- **Depressed cardiovascular drive**
- **Gaseous space enlargement by NO**
- **Fluoride-ion toxicity from methoxyflurane**
  - Metabolized in liver = release of Fluoride ions
    - Decreased renal function allows fluoride to accumulate = nephrotoxicity
- **Malignant hyperthermia**
  - Rapidly cool the individual and administer Dantrolene to block S.R. release of Calcium

Mortality rates

- Overall, about five deaths per million.
- Most commonly related to surgical factors or pre-existing medical conditions (haemorrhage, sepsis).
- Common causes of death directly related to anaesthesia include:

1- aspiration of stomach contents

2- suffocation (due to inadequate airway management)

3- allergic reactions to anaesthesia

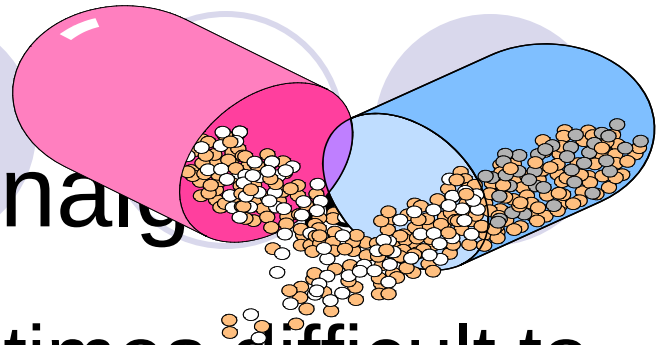
4- human error

5- equipment failure

Postoperative Analgesia

Minor surgical procedures	• oral pain relief medications • paracetamol and NSAIDS such as ibuprofen.
Moderate surgical procedures	• addition of mild opiates such as codeine
Major surgical procedures	• combination of modalities • Patient Controlled Analgesia System (PCA) involving morphine

Nonnarcotic & narcotic analg



- Pain = Very subjective - sometimes difficult to treat

  - Use of pain scales helpful

- Analgesics - nonnarcotic & narcotic - prescribed for relief of pain

  - Drug of choice depends on severity of pain

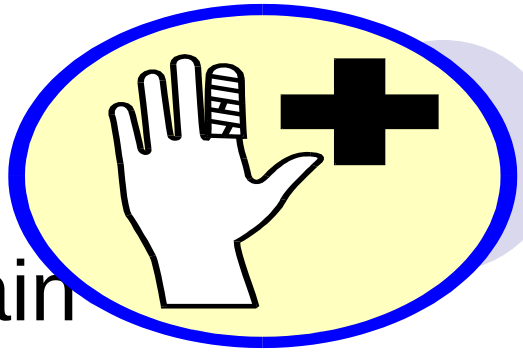
  - Mild to moderate of skeletal muscle & joints = nonnarc.

  - mod. to severe pain - in smooth muscle, organs & bones = narcotic

Analgesics

- The pain experience (unpleasant sensation) - composed of both physical & emotional components
- Perception = awareness of the sensation of pain
- Threshold = interprets sensation as painful
- Tolerance = ability to endure pain

Analgesics



- 5 Classifications & types of pain

1. Acute - mild, moderate, severe - occurs suddenly & responds to treatment
2. Chronic - Pain persists for > 6 mos. & is difficult to treat and control
3. Superficial - surface areas - skin & mucus membranes
4. Visceral (deep)- smooth muscle or organs - nonnarc.
5. Somatic (skeletal muscle, ligaments, joints) - nonnarc.

   - NSAIDS (antiinflammatory & muscle relaxants)

Analgesics
Nonnarcotics

- **Aspirin, Acetaminophen, Ibuprofen & Naproxen**

  - Not addictive & less potent than narcotics

  - For mild to severe pain - OTC

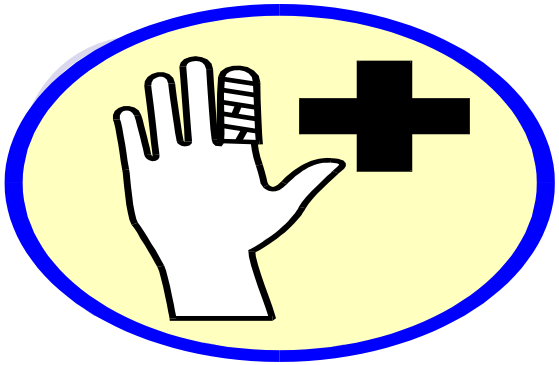
- Use - headaches, menstrual pain, muscular aches & pains, pain from inflammation

  - Most decrease elevated body temp. - antipyretic

  - Aspirin = antiinflammatroy & anticoagulant effects

- Action - Relive pain by inhibiting the enzyme cyclooxygenase needed for biosynthesis of prostaglandins

Analgesics
Nonnarcotics

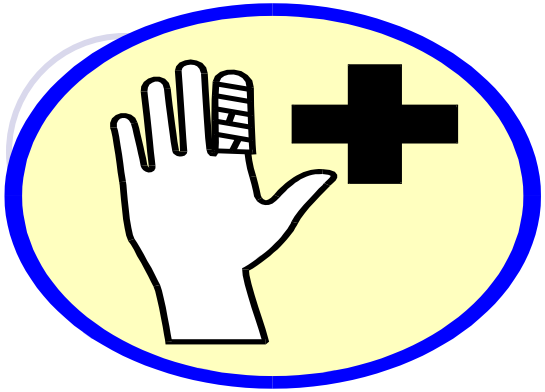


- Prostaglandins - Accumulate at injured tissue sites causing inflammation & pain (a group of fatty acids present in many tissues)
- 2 enzyme forms of cyclooxygenase - COX - 1 & COX - 2
  - COX - 1 - Protects stomach lining & regulates platelets
  - COX - 2 - Triggers pain & inflammation at injured site
- 2 groups of analgesics - salicylates (aspirin) & NSAIDS
  - Inhibit both COX - 1 & COX - 2
- People with arthritis would benefit from a drug that blocks COX - 2, but not COX - 1

Analgesics Nonnarcotics

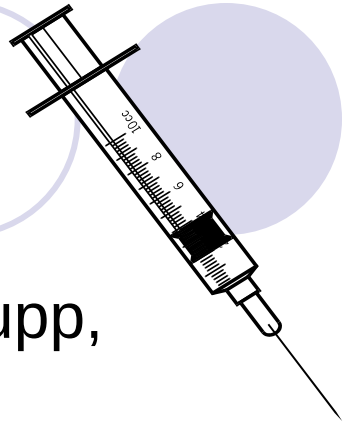
- 2 new products - COX 2 inhibitors = Celebrex & Voixx - Clients at risk for stroke or MI would not benefit
- SE - Gastric irritation (take w/ food), ASA taken 1st 2 days of menstration = excess bleeding, Hypersensitivity to ASA = tinnitis, vertigo, bronchospasm, uticaria
- Do NOT give ASA to children < 12 yrs. old - Reye's syndrome possible

Analgesics Nonnarcotics



- **Acetaminophen** - Tylenol, Panadol, Tempra
  - Safe for infants, children, adults & older adults
  - Use: analgesic & antipyretic = muscular aches & pains, fever
  - Little to no hastric distress, no link to Reye's syndrome, no increase in bleeding potential
  - No antiinflammatory properties
  - **OD = Toxic to hepatic cells = liver toxicity**

Analgesics
Narcotics



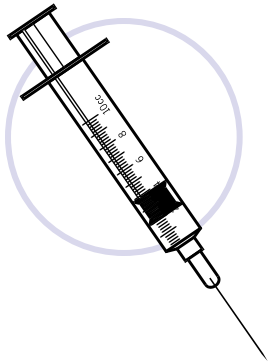
- Used for moderate to severe pain - IV, IM, PO, supp, epidural, patches
- 1803 - **Morphine** isolated form opium - obtained from the sap of seed pods of opium poppy plant. Drug used as early as 350 BC to relieve pain

  *** Codeine** = another drug from opium
- Action = Mostly on CNS (vs. nonnarc. that act on PNS) at pain receptor sites

  - Suppress resp. & cough centers as well as pain

  - many possess antitussive & antidiarrheal effects
- SE = N&V, constipation, BP, resp. depression, urinary retention, tolerance w/ chronic use withdrawl

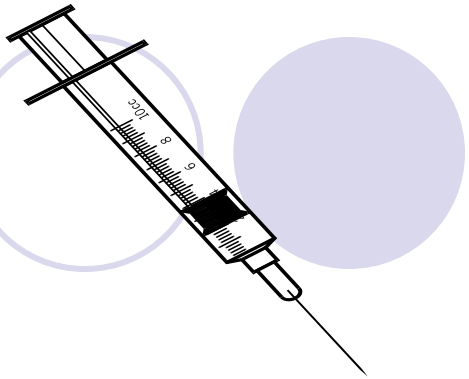
Analgesics
Narcotics



- **<u>Morphine</u>**

  * Potent narcotic analgesic
  * Use: Acute pain from - MI, CA, surgery
  * SE: Resp. depression, BP, constipation, cough suppression ⇩
  * Action: Depresses CNS, pain impulses - binds w/ opiate recepter in CNS
  * Crosses placenta & present in breast milk

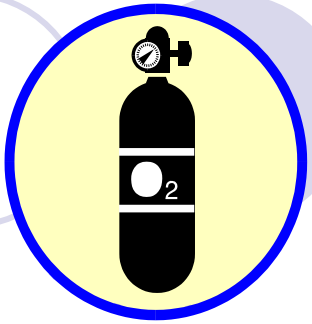
Analgesics
Narcotics



- **Meperidine (Demerol)**

* One of the first synthetic narcotics
* Use: Most commonly used narcotic for Post-op pain
* No antitussive properties
* safer for pregnancy - no decrease in uterine contractions
* SE: N & V, constipation, headache, dizziness, dec. BP
* Action: Depression of pain impulses by binding to the opiate receptor in the CNS

Analgesics Narcotics



- CI: For narcotic analgesics =

-Head injuries - Narcotics ↓ respirations = inc. carbon dioxide (CO2) levels & retention = blood vessels dialate (vasodilation), esp. cerebral vessels = ↑ intercranial pressure

- Respiratory disorders - narcs. intensify resp. distress

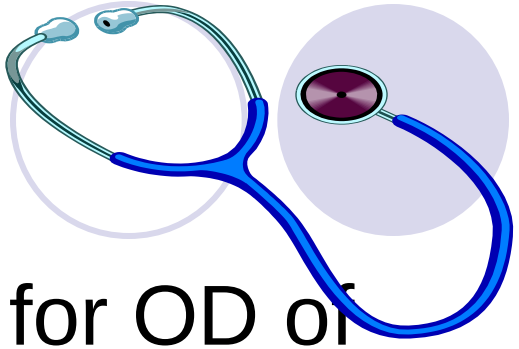
- Shock associated with low blood pressure

Analgesics
Narcotic Agonist-Antagonist

- Combo. of narcotic antagonist (Narcan) + Narcotic agonist developed in hopes of abuse

* Pentazocine (Talwin) - PO, IM, SC, IV schedule IV
* Butorphanol Tartrate (Stadol), buprenorphine (Buprenex), Nalbuphine HCL (Nubain)
* Use: Mod. to severe pain (short term use)
* Action: Binds w/ opiate receptors in CNS, altering both perception of & emotional response to pain - unknown
*SE: Similar to Narcs. - resp. depression, can cause HTN
* Caution - Pts. w/ a hx of abuse = poss. withdrawl

Analgesics
Narcotic Antagonist



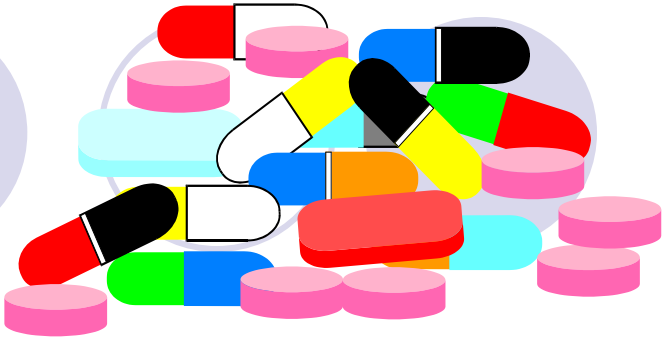
- **Naloxone (Narcan**) - Antidote for OD of narcotic analgesics - IM or IV

* Action - Higher affinity to opiate receptor site than the narcotic = blocks the receptor & displaces any narcotic at the receptor = inhibits narcotic action

* Use - Reverse resp. & CNS depression caused by narcotics

* SE - N&V, sweating, tachycardia, Inc. in BP

Antiinflammatory Drugs



- Inflammation - response to tissue injury & infection

  - A vascular action takes place - fluid, elements of blood, white blood cells (WBC's) leukocytes, & chemical mediators accumulate at site of injury or infection

  - A protective mechanism - body tries to neutralize and destroy harmful agents

- Infection - caused by microorganisms & results in inflammation, but not all inflammations are caused by infections

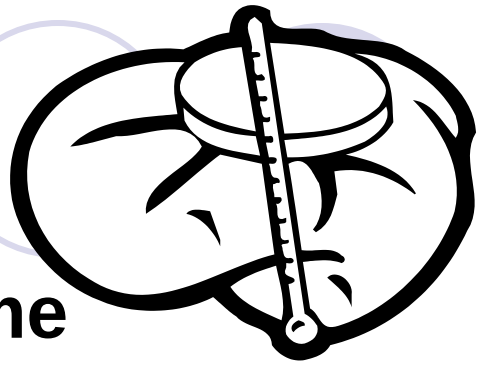
Antiinflammatory

- 5 cardinal signs of inflammation: redness, heat, swelling (edema), pain & loss of function
- 2 phases of inflammation: vascular & delayed

  - Vascular = 10 - 15 min. after injury - vasodilation & inc. capillary permeability (bld substances & fluid leave plasma to site of injury

  - Delayed = leukocytes infiltrate inflamed tissue
- Chemical mediators released during inflam. process
  - Prostaglandins = vasodilation, relaxation smooth muscle, inc. cap. permeability, sensitization of nerve cells to pain

Antiinflammatory NSAIDS



- ASA & “ASA-like” drugs **- inhibit exzyme cyclooxygenase** - needed for biosyn. of prostaglandins
- May be called prostaglandin inhibitors - primarily used for inflammation & pain

  Except for ASA & ibuprofen, NSAIDS have less antipyretic effect than antiinflammatory effect
- Dosage higher for pain relief than inflammation
- Used for reducing swelling, pain & stiffness in joints
- Cost more than ASA - Except for ibuprofen & naproxen (Aleve) - NSAIDS must be prescribed

Antiinflammatory

- Salicylate - ASA comes from this family derived from salicylic acid - ASA = **acetylsalicylic acid (aspirin)**

* ASA developed in 1899 by Dr. Bayer
* Most frequently used antiinflammatory before ibuprofen
* SE of ASA = gastric upset ⇨ stomach ulcers - there are enteric coated tablets available
* ASA + other NSAIDS = No - decrease bld level & effectiveness of the NSAID
* ASA also used for cardiac or cerebrovascular disorders - decreases platelet aggregation ⇨ a dec. in bld. clotting

Antiinflammatory NSAIDS

- Para-Chlorobenzoic Acid - i**ndomethacin** (Indocin)

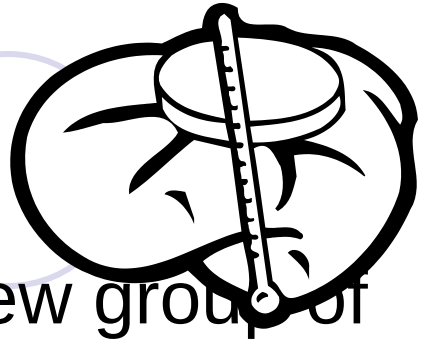
* Use: rheumatoid, gouty & osteoarthritis - potent prostaglandin inhibitor

  - Highly protein bound & displaces other drugs

  - Very irritating to stomach

* Other drugs in this classs = less adverse rxns, all may dec. BP & cause Na & H2O retention

Antiinflammatory



- Propionic Acid Derivatives - Relatively new group of NSAIDs - ASA like w/ stronger effects, but less GI upset

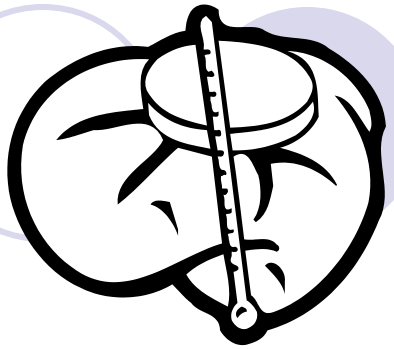
* Highly protein bound
* **Ibuprofen (Motrin)** - most widely used

  - Action: inhibits prostaglandin synthesis = relief

  - Use: reduce inflammation, relieve pain

  - DI: may increase effects of Coumadin, sulfonamides, cephalosporins, and phenytoin - Hypoglycemia may occur when taken w/ insulin or oral hypoglycemic agents

Antiinflammatory NSAIDS



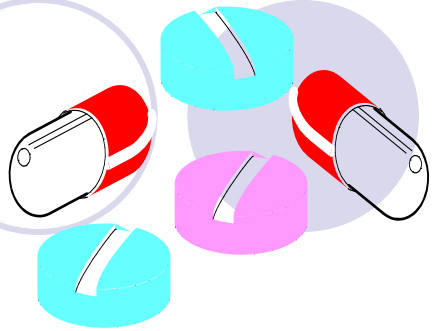
- Oxicams - **Piroxicam (Feldene)**

* Use: long term arthritic conditions
* Well tol. , long t1/2 = 1/day
* lower incidence of GI upset
* May take 1 to 2 weeks to work

- Phenylacetic Acid Derivatives - **Ketorolac** (Toradol) - First injectable NSAID

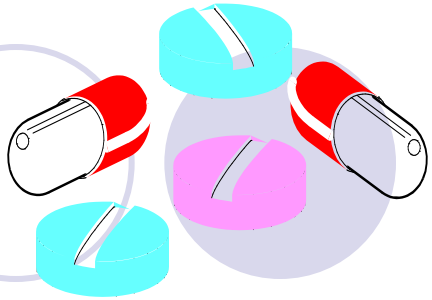
* Inhibits prostaglandin synthesis w/ greater analgesic properties
* Short term management of pain, including post-op (q6h)

Antiinflammatory
Corticosteroids



- **Prednisone, Prednisolone, dexamethasone**
- Controls inflammation by suppressing or preventing components of the inflammatory process at injured site
- Used for arthritic conditions
- Numerous side effects

Antiinflammatory



- Immunosuppressive Agents - Rheumatoid arthritis - arthritis nto responsive to antiinflammatory drugs

* azathioprine (Imuran), cyclophosphamide (Cytoxan) & methotrexate (Mexate) - primarily for cancer, but may suppress inflammatory process of rheumatoid arthritis - not first or second choice of drug

- Antimalarial drugs - rheumatoid arthritis when other drugs fail - action unclear

Antiinflammatory antigout drugs

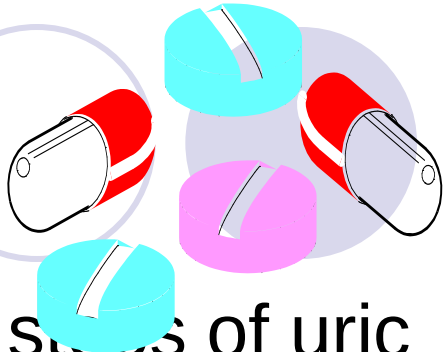
- Gout - an inflammatory condition that attacks joints, tendons & other tissues - most common site is the joint of the big toe

* Uric acid metabolism disorder = increase in urates (uric acid salts) & accumulation of uric acid or ineffective clearance by the kidneys

* Gout may appear as Bumps (tophi) in hands, & base of large toe

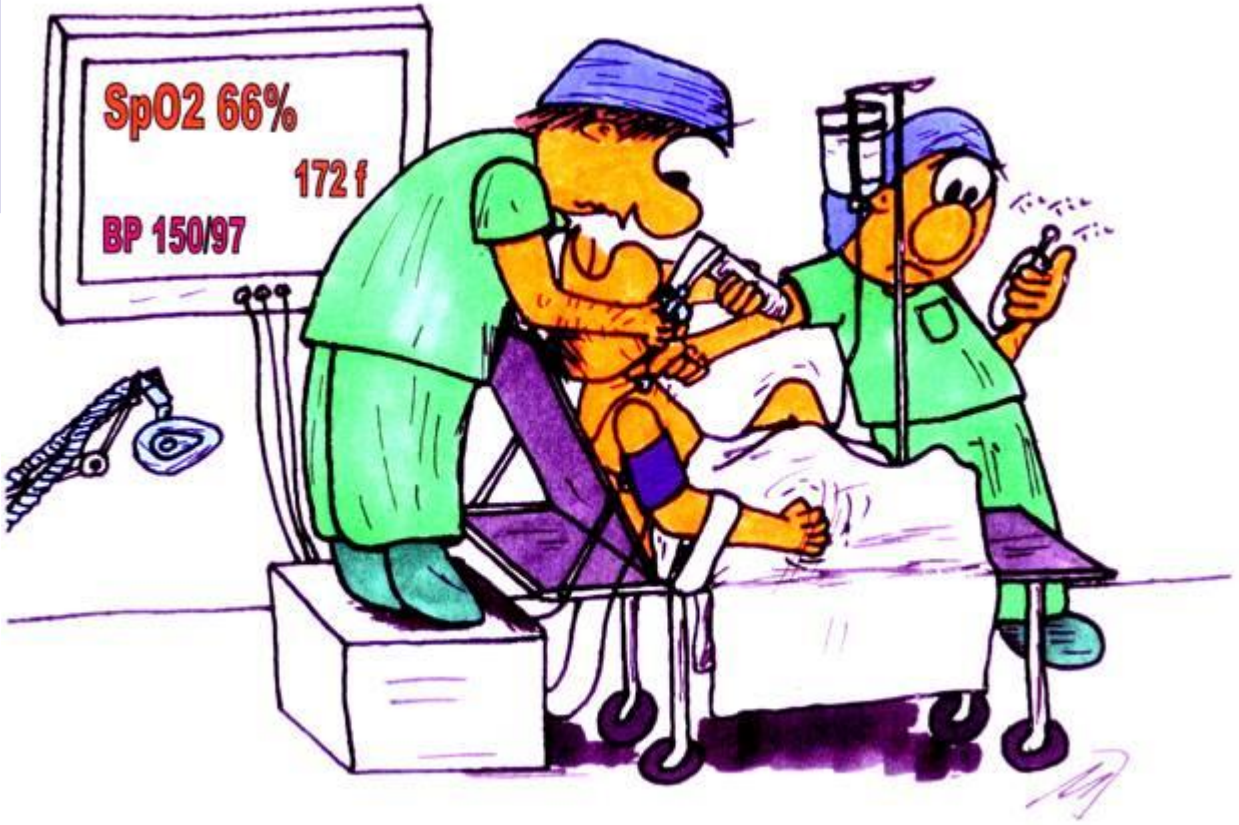
* Complications = gouty arthritis, urinary calculi, gouty nephropathy

Antiinflammatory
Antigout drugs



- **Allopurinol (Zyloprim)** - inhibits final steps of uric acid biosynthesis & lowers serum uric acid levels

* Use - chronic gout & prevention of gout, for clients w/ renal obstructions r/t uric acid stones
* Action - reduction of uric acid synthesis
* SE - N & V, diarrhea, rash, pruritus
* DI - can increase effect of coumadin & oral hypoglycemic drugs
* Avoid ETOH and caffeine, increase fluids, maintain an alkaline urine, acetaminophen for discomfort to acidity



thank you