Pharmacology 4th year

Anesthetics:-

General anesthesia is essential to surgical practice, because it renders patients analgesic, amnesic, and unconscious, and provides muscle relaxation and suppression of undesirable reflexes. No single drug is capable of achieving these effects both rapidly and safely. Rather, several different categories of drugs are utilized to produce optimal anesthesia.

Benefits:- Preanesthetic medication serves to calm the patient, relieve pain, and protect against undesirable effects of the subsequently administered anesthetic or the surgical procedure. Skeletal muscle relaxants facilitate intubation and suppress muscle tone to the degree required for surgery.

Patient Factors in Selection of Anesthesia:-

During the preoperative phase, the anesthesiologist selects drugs that provide a safe and efficient anesthetic regimen based on the nature of the surgical or diagnostic procedure as well as on the patient's physiologic, pathologic, and pharmacologic state.

A. Status of organ systems

Liver and kidney: Because the liver and kidney not only influence the long-term distribution and clearance of anesthetic agents but can also be the target organs for toxic effects, the physiologic status of these organs must be considered. Of particular concern is that the release of fluoride, bromide, and other metabolic products of the halogenated hydrocarbons can affect these organs, especially if the metabolites accumulate with repeated anesthetic administration over a short period of time.

Respiratory system: The condition of the respiratory system must be considered if inhalation anesthetics are indicated. For example, asthma and ventilation or perfusion abnormalities complicate control of an inhalation anesthetic. All inhaled anesthetics depress the respiratory system. Additionally, they also are bronchodilators.

Cardiovascular system: Whereas the hypotensive effect of most anesthetics is sometimes desirable, ischemic injury of tissues could follow reduced perfusion pressure. If a hypotensive episode during a surgical procedure necessitates treatment, a vasoactive substance is administered. This is done after consideration of the possibility that some anesthetics, such as halothane, may sensitize the heart to the arrhythmogenic effects of sympathomimetic agents.

Nervous system: The existence of neurologic disorders (for example, epilepsy or myasthenia gravis) influences the selection of an anesthetic. So, too, would a patient history suggestive of a genetically determined sensitivity to halogenated hydrocarbonâ€“induced malignant hyperthermia.

Pregnancy: Some precautions should be kept in mind when anesthetics and adjunct drugs are administered to a pregnant woman. There has been at least one report that transient use of nitrous oxide can cause aplastic anemia in the unborn child. Oral clefts have occurred in the fetuses of women who have received benzodiazepines. Diazepam should not be used routinely during labor, because it results in temporary hypotonia and altered thermoregulation in the newborn.

Concomitant use of drugs

Multiple adjunct agents: Commonly, surgical patients receive one or more of the following preanesthetic medications: **benzodiazepines, such as midazolam or diazepam**, to allay anxiety and facilitate amnesia; **barbiturates, such as pentobarbital**, for sedation; **antihistamines, such as diphenhydramine**, for prevention of allergic reactions, or **ranitidine**, to reduce gastric acidity; **antiemetics, such as ondansetron**, to prevent the possible aspiration of stomach contents; **opioids, such as fentanyl**, for analgesia; and/or

anticholinergics, such as scopolamine, for their amnesic effect and to prevent bradycardia and secretion of fluids into the respiratory tract .These agents facilitate smooth induction of anesthesia, and when administered continuously, they also lower the dose of anesthetic required to maintain the desired level of surgical (Stage III) anesthesia. However, such coadministration can also enhance undesirable anesthetic effects (for example, hypoventilation), and it may produce negative effects that are not observed when each drug is given individually.

Concomitant use of additional nonanesthetic drugs: Surgical patients may be chronically exposed to agents for the treatment of the underlying disease as well as to drugs of abuse that alter the response to anesthetics. For example, alcoholics have elevated levels of hepatic microsomal enzymes involved in the metabolism of barbiturates, and drug abusers may be overly tolerant of opioids.

Induction, Maintenance, and Recovery from Anesthesia:-

Anesthesia can be divided into three stages: induction, maintenance, and recovery. Induction is defined as the period of time from the onset of administration of the anesthetic to the development of effective surgical anesthesia in the patient. Maintenance provides a sustained surgical anesthesia.Recovery is the time from discontinuation of administration of the anesthesia until consciousness and protective physiologic reflexes are regained. Induction of anesthesia depends on how fast effective concentrations of the anesthetic drug reach the brain; recovery is the reverse of induction and depends on how fast the anesthetic drug diffuses from the brain.

A. Induction:-

During induction, it is essential to avoid the dangerous excitatory phase (Stage II delirium) that was observed with the slow onset of action of some earlier anesthetics . Thus, general anesthesia is normally induced with an intravenous anesthetic like thiopental, which produces unconsciousness within 25 seconds after injection. At that time, additional inhalation or intravenous drugs comprising the selected anesthetic combination may be given to produce the desired depth of surgical (Stage III) anesthesia. [Note: This often includes coadministration of an intravenous skeletal muscle relaxant to facilitate intubation and relaxation. Currently used muscle relaxants include **pancuronium**, **doxacurium, rocuronium, vecuronium, cisatricurium, atracurium, mevacurium and succinylcholine**. For children, without intravenous access, nonpungent agents, such as **halothane** or **sevoflurane**, are used to induce general anesthesia. This is termed inhalation induction.

B. Maintenance of anesthesia

Maintenance is the period during which the patient is surgically anesthetized. After administering the selected anesthetic mixture, the anesthesiologist monitors the patient's vital signs and response to various stimuli throughout the surgical procedure to carefully balance the amount of drug inhaled and/or infused with the depth of anesthesia. Anesthesia is usually maintained by the administration of volatile anesthetics, because these agents offer good minute-to-minute control over the depth of anesthesia. Opioids, such as fentanyl, are often used for pain along with inhalation agents, because the latter are not good analgesics.

C. Recovery

Postoperatively, the anesthesiologist withdraws the anesthetic mixture and monitors the return of the patient to consciousness. For most anesthetic agents, recovery is the reverse of induction; that is, redistribution from the site of action (rather than metabolism of the anesthetic) underlies recovery. The anesthesiologist continues to monitor the patient to be sure that he or she is fully recovered with normal physiologic functions (for example, is able to breathe on his/her own). Patients are observed for delayed toxic reactions, such as hepatotoxicity caused by halogenated hydrocarbons.

D. Depth of anesthesia

The depth of anesthesia has been divided into four sequential stages. Each stage is characterized by increased central nervous system (CNS) depression, which is caused by accumulation of the anesthetic drug in the brain . These stages were discerned and defined with ether, which produces a slow onset of anesthesia. However, with halothane and other commonly used anesthetics, the stages are difficult to characterize clearly because of the rapid onset of anesthesia.

Stage I-Analgesia: Loss of pain sensation results from interference with sensory transmission in the spinothalamic tract. The patient is conscious and conversational. Amnesia and a reduced awareness of pain occur as Stage II is approached.

Stage II-Excitement: The patient experiences delirium and possibly violent, combative behavior. There is a rise and irregularity in blood pressure. The respiratory rate may increase. To avoid this stage of anesthesia, a short-acting barbiturate, such as thiopental, is given intravenously before inhalation anesthesia is administered.

Stage III-Surgical anesthesia: Regular respiration and relaxation of the skeletal muscles occur in this stage. Eye reflexes decrease progressively, until the eye movements cease and the pupil is fixed. Surgery may proceed during this stage.

Stage IV-Medullary paralysis: Severe depression of the respiratory and vasomotor centers occur during this stage. Death can rapidly ensue unless measures are taken to maintain circulation and respiration.

Inhalation Anesthetics

Inhaled gases are the mainstay of anesthesia and are used primarily for the maintenance of anesthesia after administration of an intravenous agent. No one anesthetic is superior to another under all circumstances.

Inhalation anesthetics have a benefit **(1)** that is not available with intravenous agents, because the depth of anesthesia can be rapidly altered by changing the concentration of the drug. **(2)** Inhalation anesthetics are also reversible, because most are rapidly eliminated from the body by exhalation.

A. Common features of inhalation anesthetics:-

Modern inhalation anesthetics are

1- nonflammable,
2- nonexplosive agents that include the gas nitrous oxide as well as a number of volatile, halogenated hydrocarbons.
3- As a group, these agents decrease cerebrovascular resistance, resulting in increased perfusion of the brain.
4- They also cause bronchodilation.
5- The movement of these agents from the lungs to the different body compartments depends upon their solubility in blood and tissues as well as on blood flow. These factors play a role not only in induction but also in recovery.

Potency:-

The potency of inhaled anesthetics is defined quantitatively as the median alveolar concentration (MAC). This is the end-tidal concentration of anesthetic gas needed to eliminate movement among 50 percent of patients challenged by a standardized skin incision. [Note: MAC is the median effective dose (ED_{50}) of the anesthetic.] MAC is usually expressed as the percentage of gas in a mixture required to achieve the effect. Numerically, MAC is small for potent anesthetics, such as halothane, and large for less potent agents, such as nitrous oxide. Therefore, the inverse of MAC is an index of the potency of the anesthetic. MAC values are useful in comparing pharmacologic effects of different anesthetics. The more lipid soluble an anesthetic, the lower the concentration of anesthetic needed to produce anesthesia and, thus, the higher the potency of the anesthetic.

Mechanism of action:-

No specific receptor has been identified as the locus of general anesthetic action. Indeed, the fact that chemically unrelated compounds produce the anesthetic state argues against the existence of such a receptor. The focus is now on interactions of the inhaled anesthetics with proteins comprising ion channels. For example, the general anesthetics increase the sensitivity of the γ -aminobutyric acid ($GABA_A$) receptors to the neurotransmitter, GABA, at clinically effective concentrations of the drug. This causes a prolongation of the inhibitory chloride ion current after a pulse of GABA release. Postsynaptic neuronal excitability is thus diminished . Other receptors are also affected by volatile anesthetics; for example, the activity of the inhibitory glycine receptors in the spinal motor neurons is increased. In addition, the inhalation anesthetics block the excitatory postsynaptic current of the nicotinic receptors.

Halothane:-

This agent is the prototype to which newer inhalation anesthetics have been compared. When halothane was introduced, its ability to induce the anesthetic state rapidly and to allow quick recovery and the fact that it was non explosive made it an anesthetic of choice.

Therapeutic uses: halothane is a potent anesthetic, it is a relatively weak analgesic. halothane is usually coadministered with nitrous oxide, opioids, or local anesthetics. Halothane relaxes both skeletal and uterine muscle, and it can be used in obstetrics when uterine relaxation is indicated. Halothane is not hepatotoxic in pediatric patients (unlike its potential effect on adults, and combined with its pleasant odor, this makes it suitable in children for inhalation induction.

Pharmacokinetics:

Halothane is oxidatively metabolized in the body to tissue-toxic hydrocarbons (for example, trifluoroethanol) and bromide ion. These substances may be responsible for the toxic reaction that some patients (especially females) develop after halothane anesthesia. This reaction begins as a fever, followed by anorexia, nausea, and vomiting, and patients may exhibit signs of hepatitis. Although the incidence of this reaction is low approximately 1 in 10,000 individuals 50 percent of affected patients will die of hepatic necrosis. To avoid this condition, halothane anesthesia is not repeated at intervals of less than 2 to 3 weeks.]

Adverse effects:

Cardiac effects: Like other halogenated hydrocarbons, halothane is vagomimetic and causes atropine-sensitive bradycardia. In addition, halothane has the undesirable property of causing cardiac arrhythmias. These are especially serious if hypercapnia (increased arterial carbon dioxide partial pressure) develops due to reduced alveolar ventilation or an increase in the plasma concentration of catecholamines.]

Enflurane:-

This gas is less potent than halothane, but it produces rapid induction and recovery. About 2 percent of the anesthetic is metabolized to fluoride ion, which is excreted by the kidney. Therefore, enflurane is contraindicated in patients with kidney failure.

Difference between halothane and enflurane:-

Enflurane anesthesia exhibits the following differences from halothane anesthesia: fewer arrhythmias, less sensitization of the heart to catecholamines, and greater potentiation of muscle relaxants due to a more potent curare-like effect.

A disadvantage of enflurane:- is that it causes CNS excitation at twice the MAC (median alveolar concentration) and also at lower doses if hyperventilation reduces the partial pressure of carbon dioxide. For this reason, it is not used in patients with seizure disorders.

Isoflurane:-
It is a very stable molecule that undergoes little metabolism; as a result, little fluoride is produced. Isoflurane is not tissue toxic. Unlike the other halogenated anesthetic gases, isoflurane does not induce cardiac arrhythmias and does not sensitize the heart to the action of catecholamines. It also dilates the coronary vasculature, increasing coronary blood flow and oxygen consumption by the myocardium. This property may make it beneficial in patients with ischemic heart disease.

Desflurane:-
The rapidity with which desflurane causes anesthesia and emergence has made it a popular anesthetic for outpatient surgery. However, desflurane has a low volatility and, thus, must be delivered using a special vaporizer. Like isoflurane, it decreases vascular resistance and perfuses all major tissues very well.

Side effects:- Because it is irritating to the airway and can cause laryngospasm, coughing, and excessive secretions, desflurane is not used to induce extended anesthesia. Its degradation is minimal; thus, tissue toxicity is rare.

Sevoflurane:-
Sevoflurane has low pungency, allowing rapid uptake without irritating the airway during induction, thus making it suitable for induction in children. It is replacing halothane for this purpose. The drug has low solubility in blood and is rapidly taken up and excreted. Recovery is faster than with other anesthetics. It is metabolized by the liver, releasing fluoride ions; thus, like enflurane, it may prove to be nephrotoxic.

Nitrous oxide:-
Nitrous oxide (laughing gas) is a potent analgesic but a weak general anesthetic. For example, nitrous oxide is frequently employed at concentrations of 30 percent in combination with oxygen for analgesia, particularly in dental surgery. However, nitrous oxide at 80 percent (without adjunct agents) cannot produce surgical anesthesia. It is therefore frequently combined with other, more potent agents to attain pain-free anesthesia. Nitrous oxide is poorly soluble in blood and other tissues, allowing it to move very rapidly in and out of the body.

Intravenous Anesthetics:-
Intravenous anesthetics are often used for the rapid induction of anesthesia, which is then maintained with an appropriate inhalation agent. They rapidly induce anesthesia and must therefore be injected slowly. Recovery from intravenous anesthetics is due to redistribution from sites in the CNS.

Barbiturates:-
Thiopental is a potent anesthetic but a weak analgesic. It is an ultrashort-acting barbiturate and has a high lipid solubility. When agents such **as thiopental** and **methohexital** are administered intravenously, they quickly enter the CNS and depress function, often in less than 1 minute. However, diffusion out of the brain can occur very rapidly as well because of redistribution of the drug to other body tissues, including skeletal muscle and, ultimately, adipose tissue.
These drugs may remain in the body for relatively long periods of time after their administration, because only about 15 percent of the dose of barbiturates entering the circulation is metabolized by the liver per hour. Thus, metabolism of thiopental is much slower than its tissue redistribution. The barbiturates are not significantly analgesic and, therefore, require some type of supplementary analgesic administration during anesthesia to

avoid objectionable changes in blood pressure and autonomic function. Barbiturates are contraindicated in patients with acute intermittent or variegate porphyria.

Benzodiazepines:-
The benzodiazepines are used in conjunction with anesthetics to sedate the patient. The most commonly employed is midazolam, which is available in many formulations, including oral. Diazepam and lorazepam are alternatives. All three facilitate amnesia while causing sedation.

Opioids:-
Because of their analgesic property, opioids are frequently used together with anesthetics; for example, the combination of morphine and nitrous oxide provides good anesthesia for cardiac surgery. The choice of opioid used perioperatively is based primarily on the duration of action needed. The most frequently employed opioids are fentanyl and its congeners, **sufentanil or remifentanil**, because they induce analgesia more rapidly than morphine does. They are administered either intravenously, epidurally, or intrathecally.

Side effects :-they can all cause hypotension, respiratory depression, and muscle rigidity as well as postanesthetic nausea and vomiting. Opioid effects can be antagonized by naloxone .

Etomidate:-
Etomidate is used to induce anesthesia. It is a hypnotic agent but lacks analgesic activity. Its water solubility is poor, so etomidate is formulated in a propylene glycol solution. Induction is rapid, and the drug is short-acting. It is only used for patients with coronary artery disease or cardiovascular dysfunction, such as shock. Etomidate is hydrolyzed in the liver. Among its benefits are little to no effect on the heart and circulation. Its adverse effects include a decrease in plasma cortisol and aldosterone levels, which can persist for up to 8 hours. This is apparently due to inhibition of 11-β-hydroxylase.

Ketamine:-
Ketamine a short-acting, nonbarbiturate anesthetic, induces a dissociated state in which the patient is unconscious but appears to be awake and does not feel pain. This dissociative anesthesia provides sedation, amnesia, and immobility.

Mode of action:- Ketamine interacts with the N-methyl-D-aspartate receptor. It also stimulates the central sympathetic outflow, which, in turn, causes stimulation of the heart and increased blood pressure and cardiac output. This property is especially beneficial in patients with either hypovolemic or cardiogenic shock as well as in patients with asthma. Ketamine is therefore used when circulatory depression is undesirable. On the other hand, these effects mitigate against the use of ketamine in hypertensive or stroke patients.

Pharmacokinetics:- The drug is lipophilic and enters the brain circulation very quickly, but like the barbiturates, it redistributes to other organs and tissues. It is metabolized in the liver, but small amounts can be excreted unchanged. Ketamine is employed mainly in children and young adults for short procedures.

Propofol:-
Propofol is an intravenous sedative/hypnotic used in the induction or maintenance of anesthesia. Onset is smooth and occurs within about 40 seconds of administration. Supplementation with narcotics for analgesia is required. Whereas propofol facilitates depression in the CNS, it is occasionally accompanied by excitatory phenomena, such as muscle twitching, spontaneous movement, or hiccups. Propofol is widely used and has replaced thiopental as the first choice for anesthesia induction and sedation, because it produces a euphoric feeling in the patient and does not cause postanesthetic nausea and vomiting.

Dexmedetomidine

Dexmedetomidine is a sedative medication used by intensive care units and anesthesiologists. It is relatively unique in its ability to provide sedation without causing respiratory depression. Like *clonidine*, its mechanism of action is agonism of α2 receptors in certain parts of the brain. *Dexmedetomidine* has sedative, analgesic, sympatholytic, and anxiolytic effects that blunt many of the cardiovascular responses in the perioperative period. It reduces the volatile anesthetic, sedative and analgesic requirements of the patient without causing significant respiratory depression

PARALYTICS / NEUROMUSCULAR BLOCKERS

Neuromuscular blockers are used to abolish reflexes to facilitate tracheal intubation, and to provide muscle relaxation as needed for certain types of surgery. Their mechanism of action is blockade of the nicotinic acetylcholine receptors in the neuromuscular junction. These agents, which include *cisatracurium, pancuronium, rocuronium, succinylcholine,* and *vecuronium*

LOCAL ANESTHETICS

- Local anesthetics abolish sensation and, in higher concentrations, motor activity in a limited area of the body.
- They are applied or injected to block nerve conduction of sensory impulses from the periphery to the CNS.
- Local anesthesia is induced when propagation of action potentials is prevented, so that sensation cannot be transmitted from the source of stimulation to the brain.
- Local anesthetics work by blocking sodium ion channels to prevent the transient increase in permeability of the nerve membrane to sodium that is required for an action potential to occur.
- Delivery techniques include topical administration, infiltration, ring blocks, peripheral nerve blocks, and neuraxial (spinal, epidural, or caudal) blocks.
- The small, unmyelinated nerve fibers that conduct impulses for pain, temperature, and autonomic activity are most sensitive to the action of local anesthetics.
- Structurally, local anesthetics have fundamental features in common.
- These include a lipophilic group, joined by an amide or ester linkage to a carbon chain, which, of the local anesthetic compounds are *bupivacaine* ,*lidocaine* , *mepivacaine* , *procaine* , *ropivacaine,* and *tetracaine* .
- Of these, *lidocaine* is probably the most commonly used.
- *Bupivacaine* is noted for its cardiotoxicity.
- *Mepivacaine* should not be used in obstetric anesthesia due to its increased toxicity to the neonate.

Metabolism

- Biotransformation of amides occurs primarily in the liver.
- *Prilocaine* is also metabolized in the plasma and kidney, and one of its metabolites may lead to methemoglobinemia.
- Esters are biotransformed by plasma cholinesterase (pseudocholinesterase).

- Patients with pseudocholinesterase deficiency may be expected to metabolize ester local anesthetics more slowly.
- However, at normal doses, this has little clinical effect.
- Reduced hepatic function predisposes the patient to toxic effects but should not significantly increase the duration of action of local anesthetics.

Onset and duration of action

- Onset and duration of action of local anesthetics are influenced by several factors.
- These include tissue pH, pKa of the drug, nerve morphology, concentration, and lipid solubility of the drug.
- Of these, the most important are pH of the tissue and pKa of the drug.
- At physiologic pH, these compounds are charged.
- The ionized form interacts with the protein receptor of the sodium channel to inhibit its function and, thereby, achieve local anesthesia.
- The pH may drop in sites of infection, which causes onset to be delayed or even prevented.
- Within limits, higher concentration and greater lipid solubility improve onset to some degree.
- Duration of action depends on the length of time the drug can stay in the nerve to block sodium channels.

Actions

- Local anesthetics cause vasodilation, which leads to rapid diffusion away from the site of action and results in a short duration of action when these drugs are administered alone.
- By adding the vasoconstrictor *epinephrine* to the local anesthetic, the rate of local anesthetic diffusion and absorption is decreased.
- This both minimizes systemic toxicity and increases the duration of action.
- Hepatic function does not affect the duration of action of local anesthesia, which is determined by redistribution and not biotransformation.
- Some of these local anesthetics agents confer additional benefits such as the antiarrhythmic effect of *lidocaine* when administered intravenously.

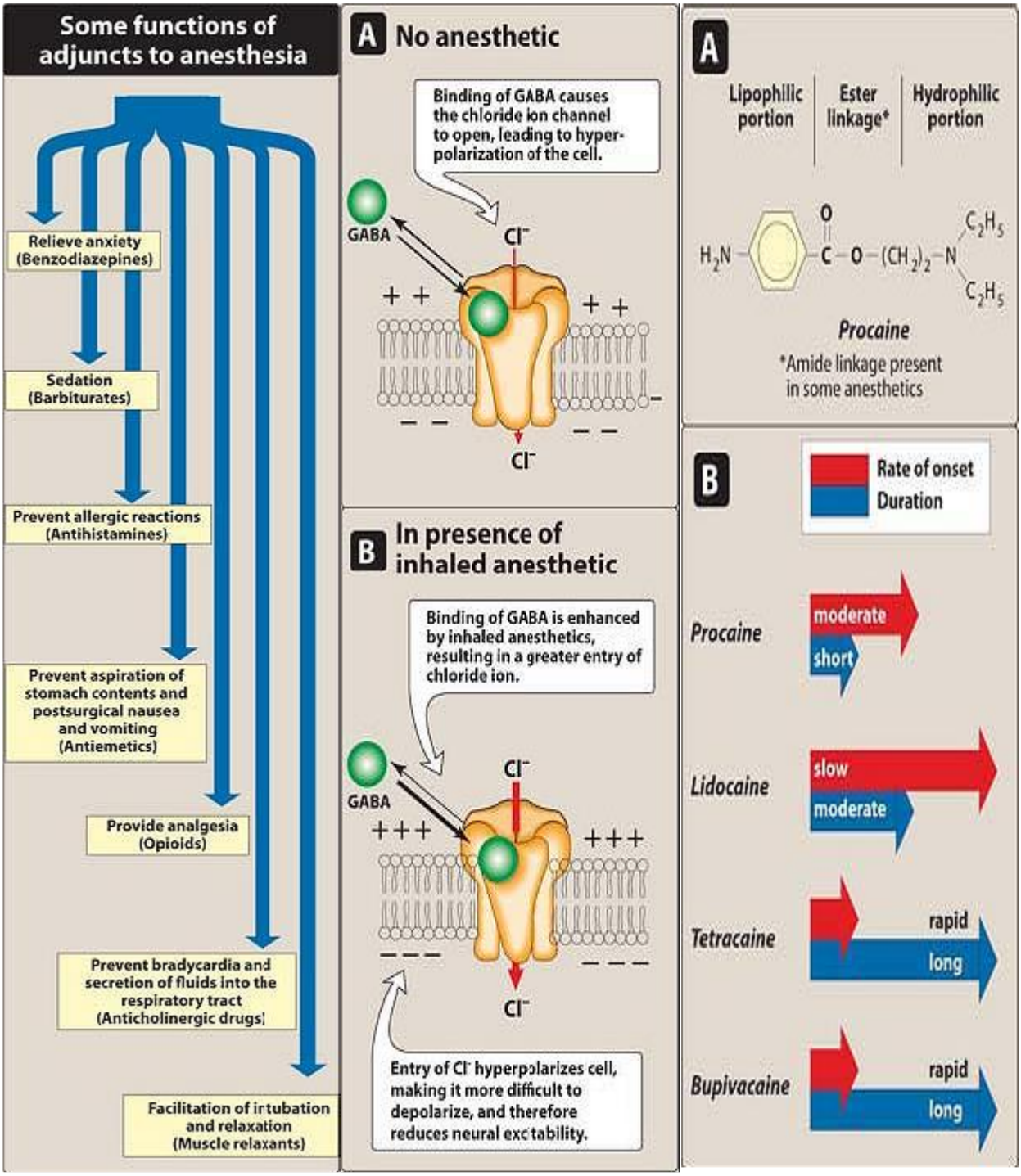
Administration to children and the elderly

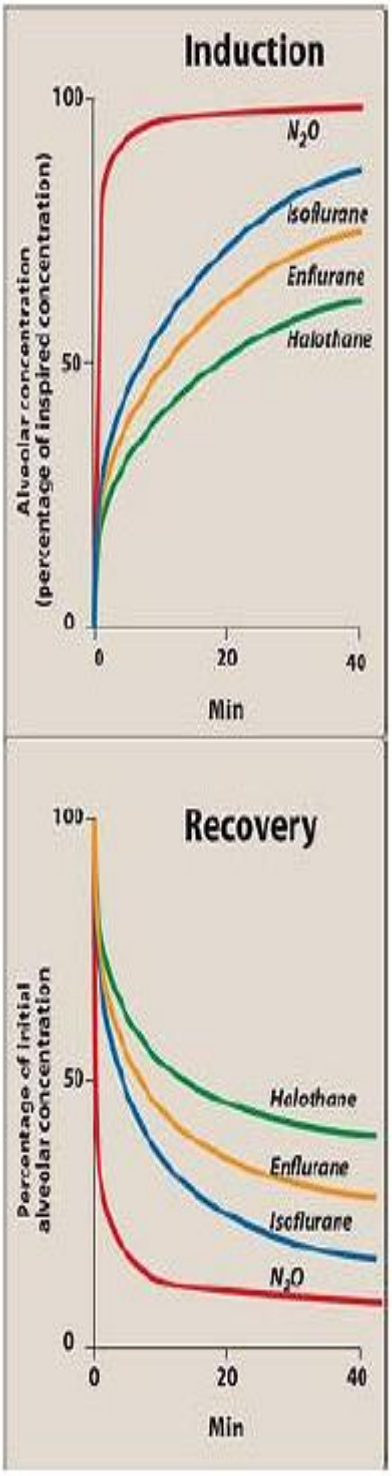
- Before administering local anesthetic to a child, the maximum dose based on the child's weight should be calculated to help prevent inadvertent overdose.
- There are no significant differences in the response to local anesthetics between younger and older adults, and the doses required for each block are the same regardless of patient age.
- However, it is prudent to stay well below the maximum recommended doses in elderly patients who often have some compromise in liver function.
- Because some degree of cardiovascular compromise may also be expected in elderly patients, reducing the dose of *epinephrine* may be prudent.

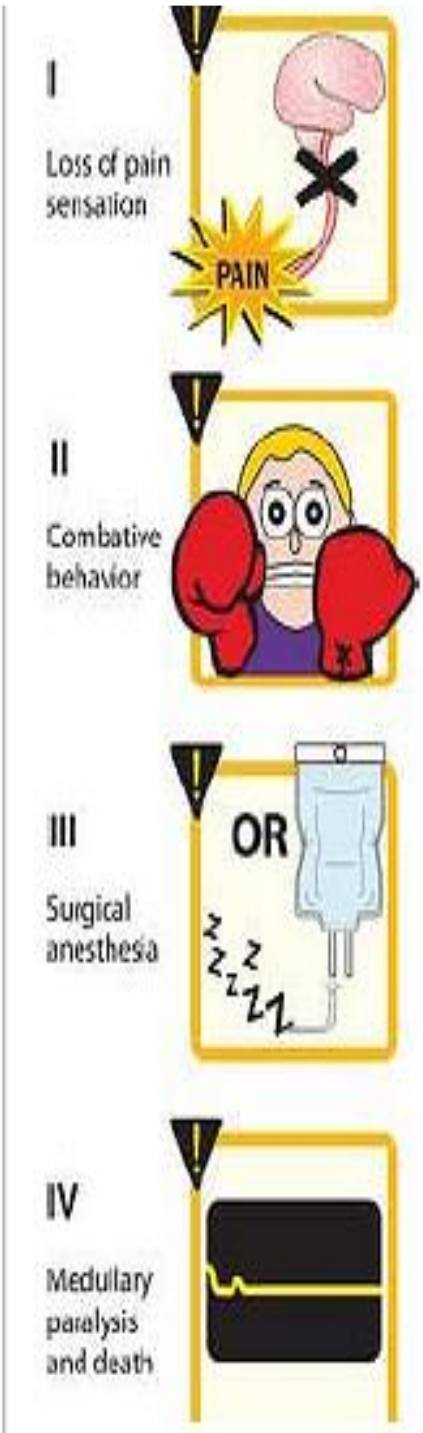
- Previous recommendations, now known to be wrong, precluded the use of specific local anesthetics in patients who are susceptible to MH(malignant hyperthermia). Today, it is well accepted that all local anesthetics are safe for these patients.

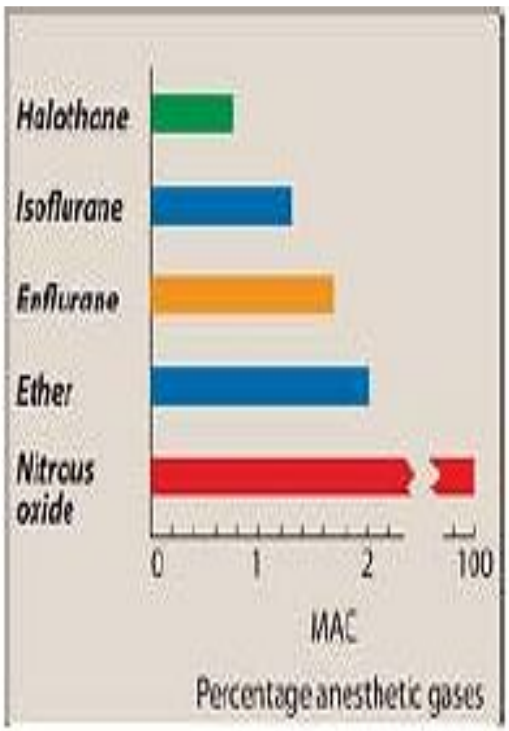
Systemic local anesthetic toxicity

- The most important step in treating local anesthetic toxicity is to consider the diagnosis in any patient with altered mental status or cardiovascular instability following injection of local anesthetic.
- CNS symptoms (either excitation or depression of the CNS) may be apparent but may also be subtle, nonspecific, or absent.
- Treatment for systemic local anesthetic toxicity includes airway management, support of breathing and circulation, seizure suppression, and, if needed, cardiopulmonary resuscitation.
- Administering a 20-percent lipid emulsion infusion (lipid rescue therapy) is a promising asset in treating local anesthetic toxicity.


Some functions of adjuncts to anesthesia
Relieve anxiety (Benzodiazepines)
Sedation (Barbiturates)
Prevent allergic reactions (Antihistamines)
Prevent aspiration of stomach contents and postsurgical nausea and vomiting (Antiemetics)
Provide analgesia (Opioids)
Prevent bradycardia and secretion of fluids into the respiratory tract (Anticholinergic drugs)
Facilitation of intubation and relaxation (Muscle relaxants)
A No anesthetic
Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.
GABA
Cl⁻
Cl⁻
B In presence of inhaled anesthetic
Binding of GABA is enhanced by inhaled anesthetics, resulting in a greater entry of chloride ion.
GABA
Cl⁻
Cl⁻
Entry of Cl⁻ hyperpolarizes cell, making it more difficult to depolarize, and therefore reduces neural excitability.
A
Lipophilic portion
Ester linkage*
Hydrophilic portion
Procaine
*Amide linkage present in some anesthetics
B
Rate of onset
Duration
Procaine
moderate
short
Lidocaine
slow
moderate
Tetracaine
rapid
long
Bupivacaine
rapid
long


Induction
100
50
0
Alveolar concentration (percentage of inspired concentration)
N_2O
Isoflurane
Enflurane
Halothane
0
20
40
Min
Recovery
100
50
0
Percentage of initial alveolar concentration
Halothane
Enflurane
Isoflurane
N_2O
0
20
40
Min


I
Loss of pain sensation
PAIN
II
Combative behavior
III
Surgical anesthesia
OR
IV
Medullary paralysis and death


Halothane
Isoflurane
Enflurane
Ether
Nitrous oxide
0
1
2
100
MAC
Percentage anesthetic gases