

Anesthetics

General anesthesia: a reversible state of central nervous system depression resulting in loss of response to and perception of external stimuli

For patients undergoing surgical and other medical procedures anesthesia provides these benefits:

- Sedation and reduction of anxiety
- Lack of awareness and amnesia
- Skeletal muscle relaxation
- Suppression of undesirable reflexes
- Analgesia

Because no single agent can provide all those benefits, several drugs are used in combination to produce optimal anesthesia

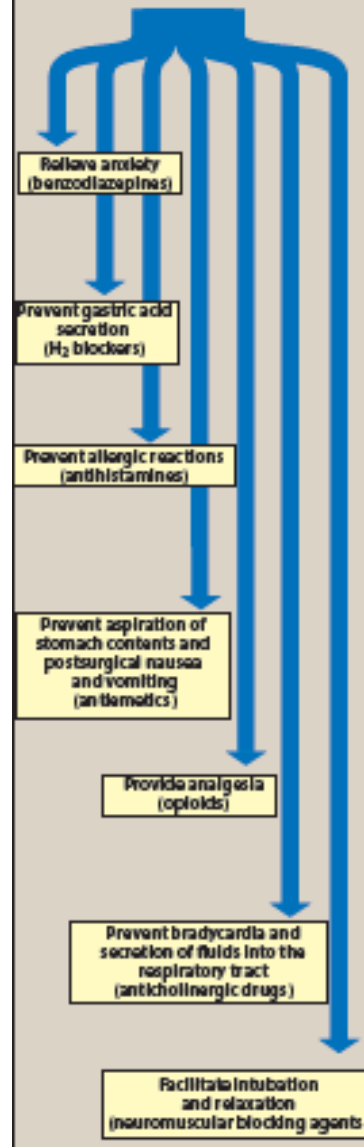
Preanesthetic medications

- Serve to calm the patient, relieve the pain and protect against undesirable effects of anesthetics or the surgical procedure
 - Antacids (neutralize stomach acidity)
 - H₂ blockers like famotidine (Reduce gastric acidity)- في المعدة وظيفته غير عن الحساسية كلياً
 - Anticholinergics like glycopyrrolate (Prevent bradycardia and secretion of fluids)
 - Antiemetics like ondansetron (Prevent aspiration of stomach contents and postsurgical nausea and vomiting)
 - Antihistamine like diphenhydramine (Prevent allergic reactions)
 - Benzodiazepines like diazepam (Relieve anxiety)
 - Opioids like fentanyl (Provide analgesia)
 - Neuromuscular blockers (Facilitate intubation and relaxation)

Skeletal muscle relaxants

- ▶ Facilitate intubation of the trachea and suppress muscle tone to the degree required for surgery
 - Neuromuscular blockers
 - Pancuronium-NonDepolarization
 - Succinylcholine- اشخاص يقتلوا ازواجهم بهذا
بتوقع وبكون صاحي
Depolarization agent

Some functions of adjuncts to anesthesia



Patient factors in selection of anesthesia

Choice of anesthetic drugs are made to provide safe and efficient anesthesia based on the **nature of the surgical or diagnostic procedures** and **patient's physiologic, pathologic and pharmacologic state**

التخدير بنزل من نبض القلب
إذا المريض بوخذ مميعات للدم لازم نوقفها قبل العملية بأيام
فبتم تأجيل العملية-ومستحيل يعملوا العملية

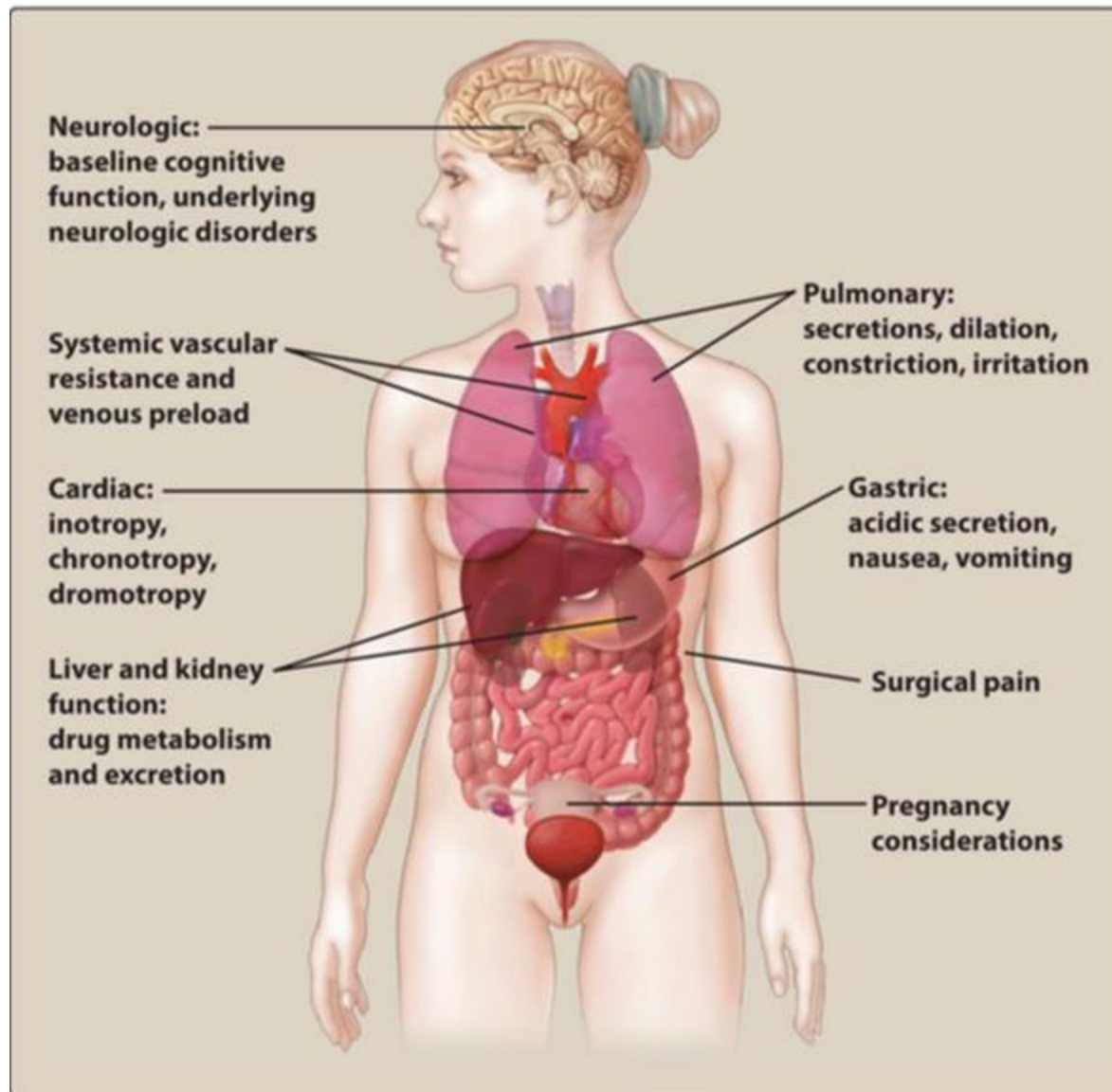


Figure 13.2 Overall considerations when delivering an anesthetic.

Patient factors in selection of anesthesia

- 2 factors are important
 1. Status of organ system
 - Cardiovascular system
 - Respiratory system
 - Liver and kidney
 - Nervous system
 - Pregnancy
 2. Concomitant use of drugs
 - Multiple adjunct agents
 - Nonanesthetic drugs

Status of organ systems

▀ Cardiovascular system:

- Anesthetic agents suppress cardiovascular functions.
- Ischemic injury to tissues may follow reduced perfusion pressure if a hypotensive episode occurs during anesthesia, treatment with vasoactive substances may be necessary
- Some anesthetics like **halothane**- الكتاب مش ذاكره لانه بأمریکا- sensitize the heart to arrhythmogenic effects of sympathomimetics
وقفوه ولكن عندنا اعتقد لساته موجود

Status of organ systems

▶ Respiratory system

- Asthma may **complicate** **تصعب وصول الدواء** control of inhalation anesthetic
- Inhaled anesthetics **depress the respiratory system**
- IV anesthetics and opioids suppress respiration
- These effects may influence the ability to provide adequate **ventilation** and **oxygenation** **لازم نراقب Vital Signs**

Status of organ systems

▮ Liver and kidneys

- Affect distribution and clearance of anesthetics, and might be affected by anesthetic toxic effects
- Their **physiologic** must be considered

▮ Nervous system

- Presence of neurologic disorders like epilepsy, myasthenia gravis, problems in cerebral circulation

▮ Pregnancy

- Effects of anesthetic agents on the fetus
 - Nitric oxide causes **aplastic anemia** in the unborn child
 - **Benzodiazepines might cause oral clefts- تشوهات بالفم** in the fetus

Concomitant use of drugs

Multiple adjunct agents

- Multiple agents are administered preanesthesia, these agents facilitate induction of anesthesia and lower the needed dose of anesthetics
- They may enhance adverse effects of anesthesia like **hypoventilation** مثل المورفين
في حد لازم يراقب المريض طول فترة العملية

Concomitant use of additional nonanesthetic drugs

- Example: Opioid abusers may be intolerant to opioids
المدخنين كذلك يحتاجوا جرعة أكبر

Stages of Anesthesia

- ▶ **Induction:** the period of time from the onset of administration of the potent anesthetic to the development of effective surgical anesthesia in the patient.
 - Depends on how fast effective concentration of the drug reaches the brain نحاول تقليل هذه الفترة قد ما منقدر
 - ▶ **Maintenance** of anesthesia: providing a sustained surgical anesthesia
 - ▶ **Recovery:** the time from discontinuation of administration of anesthesia until consciousness and protective physiologic reflexes are regained
 - Depends on how fast the drug leaves the brain
- Recovery Room

Induction

- General anesthesia in adults is normally induced with an IV anesthetic like **propofol**
 - At that time, additional inhalation and/or IV anesthetic drugs may be given to produce the desired depth of surgical anesthesia
 - Often includes coadministration of an IV skeletal muscle relaxant such as rocuronium, vecuronium, or succinylcholine to facilitate intubation and muscle relaxation
 - For children without IV access, inhalation induction is used such as halothane or sevoflurane, to induce general anesthesia
- صعب نلاقي الوريد

Maintenance of anesthesia

- Maintenance is the period during which the patient is surgically anesthetized
- Patient's vital signs and response to various stimuli are monitored continuously throughout the surgical procedure Opioids such as **fentanyl** هذه ابرة الظهر are often used for pain relief
- IV infusions of various drugs may also be used

Recovery

- Postoperatively, the anesthetic admixture is withdrawn, and the patient is monitored for the return of consciousness
- If skeletal muscle relaxants have not been fully metabolized, reversal agents may be used
- The **anesthesiologist** لازم يكون موجود continues to monitor the patient for full recovery, with normal physiologic functions

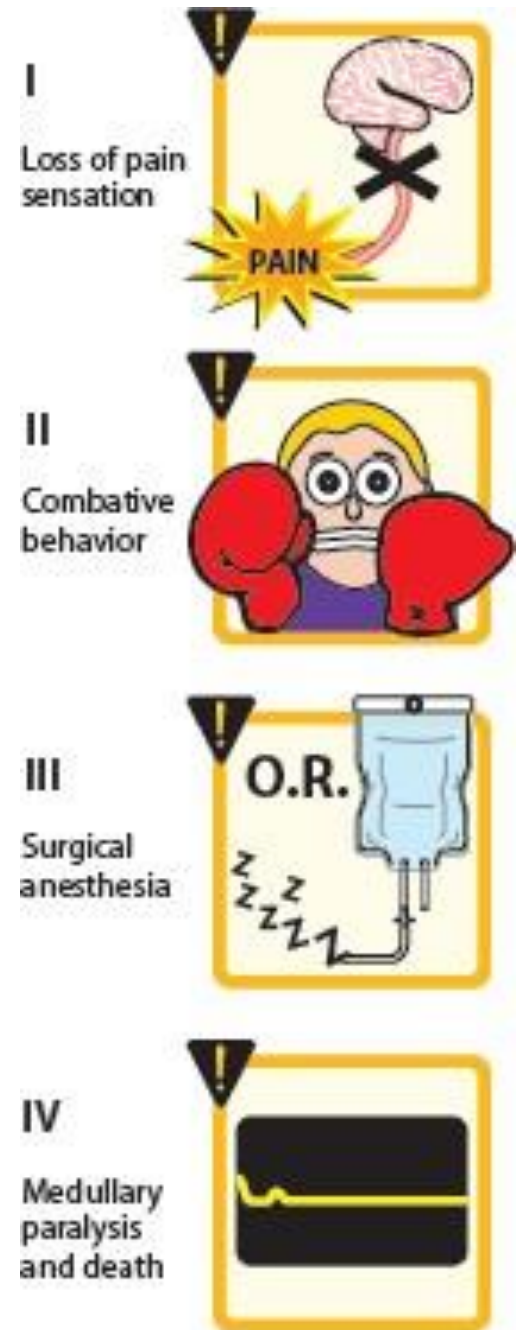
تخبيص كلام وغيره

	MINIMAL (ANXIOLYSIS)	MODERATE	DEEP	GENERAL
Mentation	Responds normally to verbal stimuli	Responds purposefully to verbal or tactile stimuli	Responds purposefully to repeated verbal or painful stimuli	Unarousable to painful stimuli
Airway competency	Unaffected	Adequate	Intervention may be required	Intervention usually required
Respiratory system	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular system	Unaffected	Usually maintained	Usually maintained	May be impaired

Figure 13.3 Anesthetic levels of sedation.

Depth of anesthesia

- Depth of anesthesia is the degree to which the CNS is depressed
- Useful parameter for individualizing anesthesia
 - Stage I **Analgesia**
 - Stage II **Excitement**
 - Stage III **Surgical anesthesia**
 - Stage IV **Medullary paralysis** ما بدنا نوصل لهذه المرحلة ونحاول ما نشوف هذه المراحل نقفز للمرحلة الثالثة فقط



Stages of anesthesia

□ Stage I

Analgesia
Loss of pain sensation

- Drowsiness
- Amnesia and reduced awareness of pain

□ Stage II Excitement

- Delirium انفعال، هذيان، اهتياج
- Rise and irregularity in blood pressure and respiration
- Risk of laryngospasm
- To shorten this period a rapid acting anesthetic like propofol is administered IV before inhaled anesthetic

Stages of anesthesia

- Stage III Surgical anesthesia نريد ان نبقي هنا
 - Loss of muscle tone and reflexes
 - Ideal stage for surgery
 - Requires careful monitoring

- Stage IV Medullary paralysis
 - Severe depression of the respiratory and vasomotor centers
 - Death can occur unless respiration and circulation are maintained

Anesthetics

- ▶ Potent general anesthetics are delivered via inhalation or IV injection
 - Inhaled general anesthetics
 - Intravenous general anesthetics
- ▶ Local anesthetics

Inhaled anesthetics

- Desflurane
- Halothane الكتاب حذفه
- Isoflurane
- Sevoflurane
- Nitrous oxide

Inhaled anesthetics

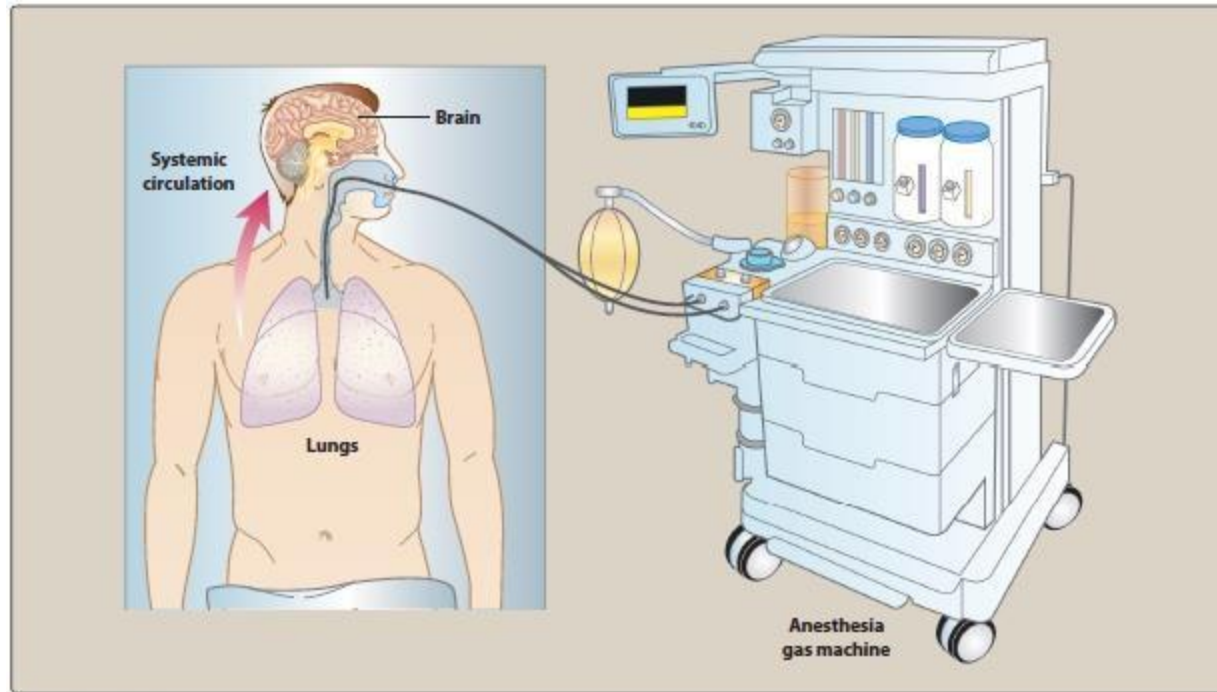


Figure 13.4

Volatile anesthetics delivered to the patient are absorbed via the lungs into the systemic circulation causing dose-dependent CNS depression.

Inhaled anesthesia

- ▶ Used for maintenance of anesthesia after administration of an IV agent
- ▶ The **depth** of anesthesia can be altered rapidly by changing inhaled **concentration** of the drug
- ▶ **Narrow therapeutic index** (from 2 -4)
- ▶ The difference between the dose causing no effect, surgical anesthesia and severe cardiac and respiratory depression is **small**
- ▶ No antagonists exist

Inhaled anesthetics

- ▶ **Potency** of inhaled anesthetic is defined as the **minimum alveolar concentration (MAC)**
- ▶ **MAC**: the concentration of anesthetic gas needed to eliminate movement among 50% of patients — مهم —
- ▶ Expressed as the percentage of gas in a mixture required to achieve the effect
- ▶ The smaller MAC is the more potent the drug
- ▶ Nitrous oxide alone cannot produce complete anesthesia أضعف شيء Inhale but not General Anesthesia.

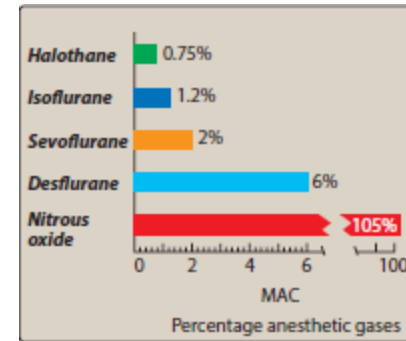


Figure 13.5
Minimal alveolar concentrations (MAC) for anesthetic gases.

اقوى شيء : Halothane

Inhaled anesthetics

- The more the **blood solubility** منيحة ليوصل للدماغ, ولكن بتخليه قاعد بالدم وبضل مبسوط, the more the anesthetic dissolves in the blood and the longer the induction and recovery time needed and slower changes in the depth of anesthesia occur as we change the concentration of inhaled drug
- Blood Solubility اذا كثيرة بتحدد قدش الدواء بده وقت ليبلش مفعوله بطول ل ينتقل لخلايا الدماغ وبطول الخروج من المخدر
- Halothane > isoflurane > sevoflurane > nitrous oxide > desflurane

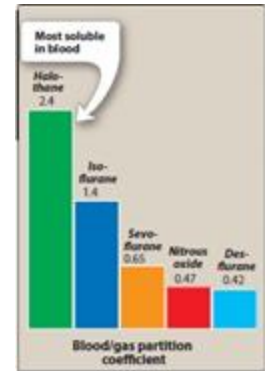


Figure 13.6
Blood/gas partition coefficients for some inhalation anesthetics.

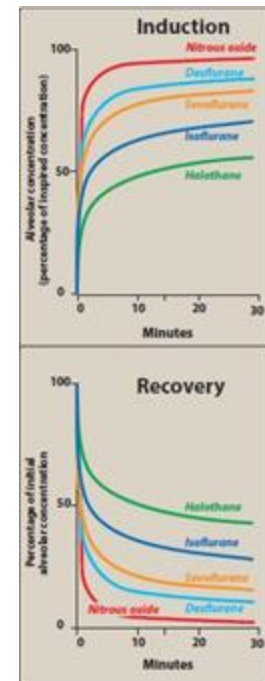


Figure 13.7
Changes in the alveolar blood concentrations of some inhalation anesthetics over time.

Inhaled anesthetics

- ▶ **Cardiac output** affects the removal of anesthetic to peripheral tissues (not the site of action)
- ▶ The higher the cardiac output, the more the anesthetic is removed, the slower the induction time الرياضيين
- ▶ أقل بحاجة لمخدر أقل CO إذا كان

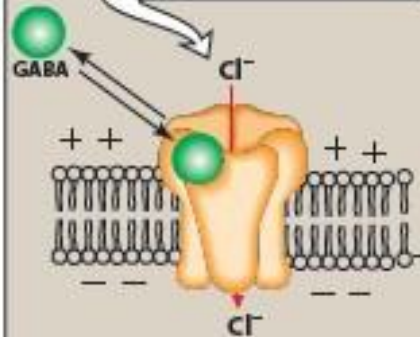
Inhaled anesthetic

► Mechanism of action

- No specific receptor has been identified as the locus of general anesthetic action
- Anesthetics increase the sensitivity of GABA receptors to the neurotransmitter GABA prolonging the inhibitory chloride ion current after GABA release, reducing the postsynaptic neurons excitability
- Anesthetics increase the activity of the inhibitory glycine receptors in the spinal motor neuron
- Anesthetics block excitatory postsynaptic nicotinic currents
- The mechanism by which the anesthetics perform these modulatory roles is not understood

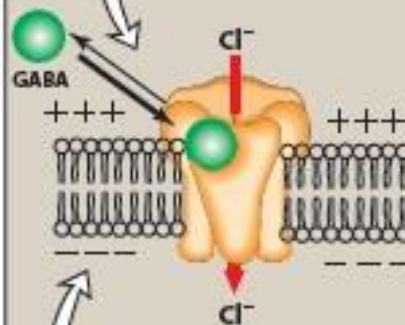
A No anesthetic

Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.



B In presence of inhaled anesthetic

Binding of GABA is enhanced by inhaled anesthetics, resulting in a greater entry of chloride ion.



Entry of Cl^- hyperpolarizes cell, making it more difficult to depolarize, and therefore reduces neural excitability.

Halothane

- ▶ Potent anesthetic, weak analgesic.
- ▶ Administered with nitrous oxide, opioids or local anesthetics
- ▶ Being replaced by other agents due to its adverse effects كثير له آثار جانبية
- ▶ Halogenated Gases

Halothane

Adverse effects

- Cardiac effects: Vagomimetic effects, bradycardia, can cause cardiac arrhythmias
- Malignant hyperthermia**: لذلك هكذا اسمه
 - UnRare and life threatening condition
 - controlled increase in skeletal muscle oxidative Metabolism العضلات بتصير تشتغل بشكل كبير وتخرج طاقة ولكن الجسم the body's capacity to supply oxygen, remove carbon dioxide, and regulate body temperature
 - If untreated would cause circulatory collapse and death
 - Treatment: **Dantrolene** administration Muscle Relaxant بقلل تحرير الكالسيوم بالعضلات

Isoflurane

- Undergoes little metabolism, **not toxic** to the liver or kidney
- Does not induce cardiac arrhythmias
- Produces dose-dependent hypotension due to peripheral vasodilation

أرخص من يلي بعده

Malignant hyperthermia ممكن يسبب

Desflurane

- Provides very **rapid onset and recovery** due to its **low blood solubility**, the lowest of all the volatile anesthetics
- Popular anesthetic for **outpatient** surgery
- Irritating to the airway and can cause laryngospasm, coughing, and excessive secretions,
- Degradation is minimal, **tissue toxicity is rare**

ممكن يسبب Malignant hyperthermia

Sevoflurane

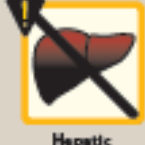
- ▶ Low pungency لاذع, allowing rapid induction without irritating the airway, making it suitable for inhalation induction in pediatric patients
- ▶ Replacing halothane for this purpose
- ▶ Metabolized by the liver, and compounds formed in the anesthesia circuit may be nephrotoxic

ممكن يسبب Malignant hyperthermia

Nitrous oxide

- Non-irritating and a potent analgesic but a weak general anesthetic
- Nitrous oxide is frequently employed at concentrations of 30–50% in combination with oxygen for analgesia, particularly in **dental surgery**.
- Nitrous oxide at **80 percent** (without adjunct agents) **cannot produce surgical anesthesia** بموت المريض فعشان هيك ما منستخدمة او منخلطه مع غيره 100% اذا
- Combined with other, more potent agents to attain pain-free anesthesia
- Mechanism of action is unresolved, might involve activity on GABA_A and NMDA receptors
- **Least hepatotoxic** of all inhaled anesthetics

هالوثين اكثر واحد هيپاتوتوكيس
اذا صار مشكلة بالتنفس نعطي اكسجين

	<i>Halothane</i>	<i>Isoflurane</i>	<i>Desflurane</i>	<i>Sevoflurane</i>
 Arrhythmias	 Increased	—	—	—
 Sensitivity to catecholamines	 Increased	—	—	—
 Cardiac output	 Decreased	 Decreased to a lesser extent than halothane	 Decreased to a lesser extent than halothane	 Decreased to a lesser extent than halothane
 Blood pressure	 Dose dependent decreased	 Dose dependent decreased	 Dose dependent decreased	 Dose dependent decreased
 Respiratory reflexes	 Inhibited	 Initial stimulation	 Initial stimulation	 Inhibited
 Hepatic toxicity	 Some risk	 Low risk	 Low risk	 Low risk
 Renal toxicity	 Low risk	 Low risk	 Low risk	 Some risk

Intravenous Anesthetics

- ▶ Used in situations that require **short duration anesthesia** (outpatient surgery)
- ▶ Primarily used as **adjuncts**- **مساعد او ثانوي** to inhalationals
- ▶ Administered first
- ▶ Rapidly induce unconsciousness
- ▶ In lower doses, they may be used to provide sedation

IV Anesthetics

Induction

- ▶ After entering the blood stream, a percentage of the drug binds to the plasma proteins بضل يلف بالدم, and the **rest remains unbound (free)** وهذا يلي بروح على القلب والدماغ
- ▶ The drug is carried by venous blood to the heart
- ▶ The majority of the CO (70%) flows to the brain, liver, and kidney
- ▶ Once the drug has penetrated the CNS tissue, it exerts its effects
- ▶ The exact mechanism of action of IV anesthetics is unknown

Recovery

- ▶ Recovery from IV anesthetics is due **to redistribution from sites in the CNS** -يخرج من الدماغ والحبل الشوكي لأجل الحركة

IV Anesthetics

- Propofol
- Fospropofol
- Barbiturates
- Benzodiazepines
- Opioids هي أكثر مسكنات
- Ketamine

Propofol

- IV sedative/hypnotic used in the **induction** **بداية** or **maintenance** **خلال التخدير** of anesthesia
- Widely used and has replaced **thiopental-ultra rapid acting-** as first choice for anesthesia induction and sedation, because it does not cause postanesthetic nausea and vomiting PONV
- The induction of anesthesia occurs within 30–40 seconds of administration
- Supplementation with **narcotics-** **أدوية تؤثر على الدماغ** for analgesia is required
- Propofol decreases blood pressure without depressing the myocardium
- It also reduces intracranial **الجمجمة** **داخل** pressure due to systemic vasodilation

Fospropofol

- Approved only for sedation
- Prodrug of propofol

Barbiturates

- ▶ The barbiturates are not significantly analgesic, require some type of supplementary analgesic administration during anesthesia to avoid objectionable changes in blood pressure and autonomic function
 - ▶ Can cause apnea-توقف التنفس, coughing, chest wall spasm, laryngospasm, and bronchospasm
 - ▶ **Thiopental** الوحيد المستخدم
 - Potent anesthetic but a weak analgesic
 - Ultrashort-acting barbiturate
 - Has minor effects on the cardiovascular system, but it may contribute to severe **hypotension** in patients with hypovolemia or shock. All barbiturates
 - Duration little
- ION Entrapping because they are weak acids we give bicarbonate لإخراجهم نعمل ما في الها ترياق

Benzodiazepines

- Used in conjunction with anesthetics to **sedate** كمهدئات the patient
- Midazolam مثل المنظار Endoscope
- Diazepam
- Lorazepam
- Facilitate amnesia while causing sedation
- Enhance the inhibitory effects of various neurotransmitters, particularly GABA –Activate GABA A receptor-
- Minimal cardiovascular depressant effect
- Potential respiratory depressants
- Can induce a temporary form of **anterograde amnesia** لا نتذكر اي شيء صار خلال العملية رغم انه يكون صاحي بعض الشيء لحدما يروح مفعول الدواء، مهم نكتب التعليمات بكل الأحوال in which the patient **لا نتذكر اي شيء صار خلال العملية** للمريض لانه يمكن حتى لما يخلص العملية ينسى يلي حكيئاله اياه عن الدواء retains memory of past events, but new information is not transferred into long-term memory
 - Important treatment information should be repeated to the patient after the effects of the drug have worn off

Opioids

- Commonly used with anesthetics due to their **analgesic** property ليست ادوية تخدير
- The choice of opioid used perioperatively is based primarily on the duration of action needed
كلهم يعملوا على المُستَقْبَل نيو
- Fentanyl, remifentanyl**
 - Induce analgesia more rapidly than morphine تسكين الألم
 - Administered intravenously, (labour)epidurally, intrathecally -عمليات الولادة بدون ألم
- Not good amnesics
- Can cause hypotension, respiratory depression, muscle rigidity and postanesthetic nausea and vomiting, CNS depression
- Opioid effects can be antagonized by **naloxone** ميزة

Ketamine

- ▶ A short-acting nonbarbiturate anesthetic
- ▶ Used for short procedures
- ▶ Induces a dissociated state in which the patient is unconscious (but may appear to be awake) and does not feel pain
- ▶ This dissociative anesthesia provides sedation, amnesia, and immobility
- ▶ Interacts with the N-methyl-D-aspartate receptor
- ▶ Stimulates the central sympathetic outflow, which, in turn, causes stimulation of the heart with increased blood pressure and CO
 - Beneficial in patients with hypovolemic or cardiogenic shock and in patients with asthma)
 - Not used in hypertensive or stroke patients

Causes post-operative hallucinations تقریباً مثل Pregabalin

Paralytics / Neuromuscular blockers

- ▶ Used to stop reflexes to facilitate tracheal intubation, and to provide muscle relaxation as needed for certain types of surgery
- ▶ Mechanism of action is blockade of the nicotinic acetylcholine receptors in the neuromuscular junction
- ▶ Include pancuronium, rocuronium, succinylcholine, and vecuronium

Local anesthetics

- ▶ **Amides** (lidocaine) and **esters** (procaine) Na channel blocker, for arrhythmia
- ▶ Cause loss of sensation and, in higher concentrations, motor activity in a limited area of the body
- ▶ Applied or injected to block nerve conduction of sensory impulses from the periphery to the CNS

Local anesthetics

► Mechanism:

- 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
- 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

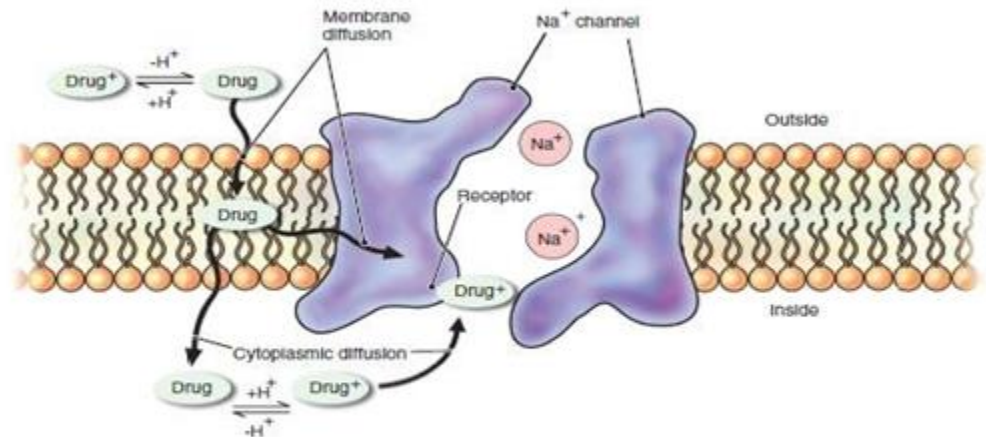


Figure 13.12
Mechanism of local anesthetic action.

Local anesthetics

- Lidocaine
- Bupivacaine
- Procaine
- Ropivacaine
- Tetracaine
- Mepivacaine
 - Not used in obstetric ولادة anesthesia due to its increased toxicity to the neonate

كلهم جايين من الكوكايين

Local Anesthetics

- Local anesthetics cause **vasodilation**, which leads to rapid diffusion away from the site of action and results in a short duration of action
- 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

Topical Anesthetics

- They are applied directly to the skin or mucous membranes
- Benzocaine is the major drug in this group
- Lidocaine and tetracaine can be used topically
- They are used to relieve or prevent pain from minor burns, irritation, itching
- They are also used to numb an area before an injection is given.
- Expected adverse effects involve skin irritation and hypersensitivity reactions

بعملوا نممة

مش مع استخدامه لانه ممكن يوصل انسجة ما بدنا اياه يوصل الها Baby gel
بالكبار مش مشكلة يعني ، اللي ولادهم عم بسننوا