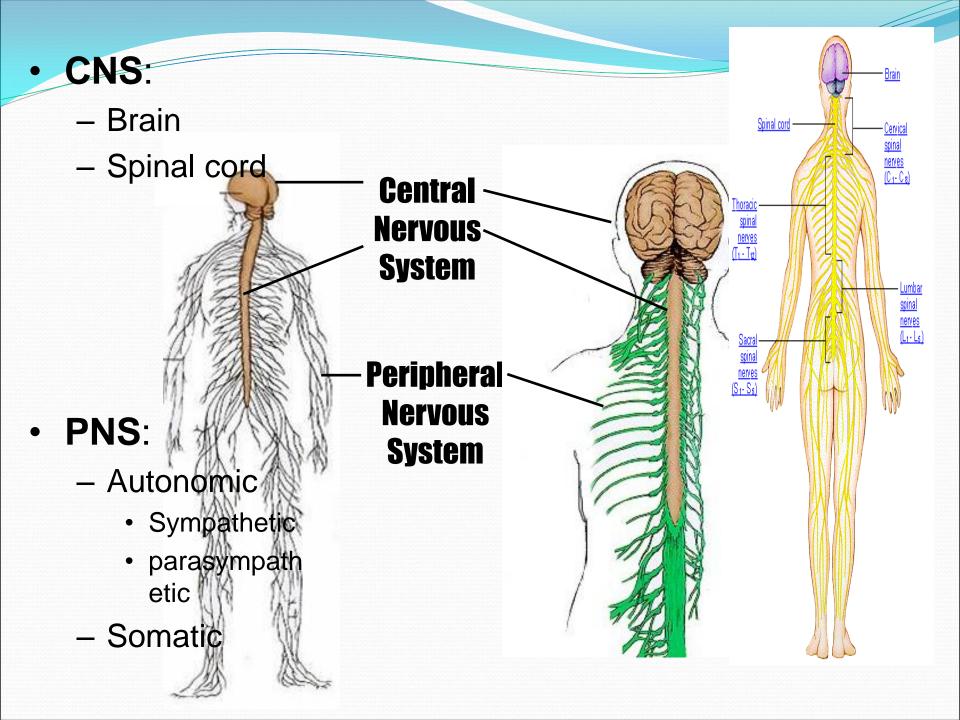
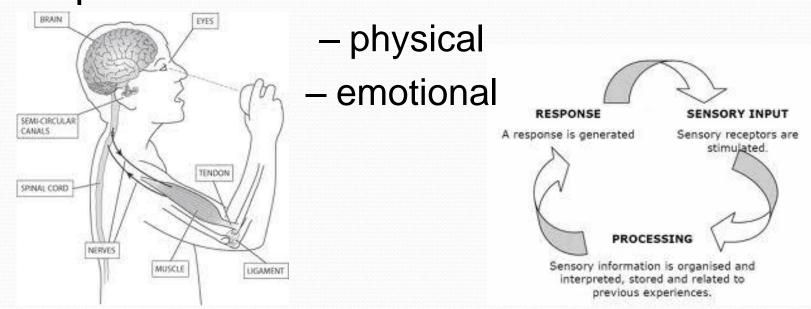


Introduction to **CNS** pharmacology Assoc. Prof. Bilgen Başgut 2014



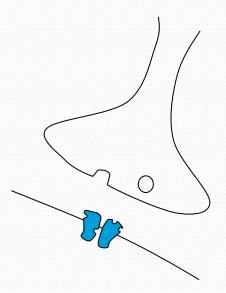
Function of the CNS

- Receive and process information (spinal cord is usually the conduit)
- Initiate and maintain appropriate response





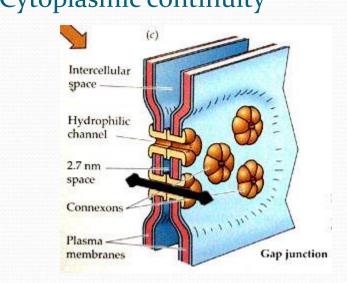
Transmission of information from one neurone to another



Chemical v/s Electrical Synapses

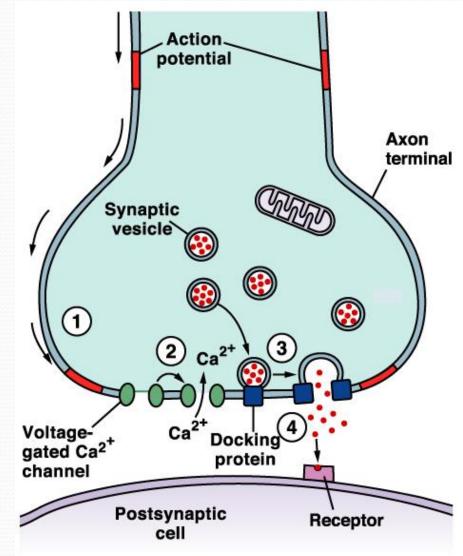
Electrical Synapses	Chemical Synapses
Rapid bidirectional transmission	Slow unidirectional transmission
Gap junctions	Presynaptic vesicles, active zones, postsynaptic receptors
Ion current	Chemical neurotransmitters
Electrotonic transmission	Complex amplifying excitatory/ inhibitory signals
Cytoplasmic continuity	Synaptic cleft

© 2004 Abcam Ltd. All rights reserved.



Synaptic Transmission

- An AP reaches the axon terminal of the presynaptic cell and causes V-gated Ca2+ channels to open.
- Ca2+ rushes in, binds to regulatory proteins & initiates NT exocytosis.
- NTs diffuse across the synaptic cleft and then bind to receptors on the postsynaptic membrane and initiate some sort of response on the postsynaptic cell.





Neurotransmitter (fast and slow synaptic transmission)

Neuromodulator (diffuse, slower action)

Types of neurotransmitter

Small molecules

- amino acids (glutamate, GABA)
- biogenic amines (ACh, NA, DA, 5-HT)

Neuropeptides

• (cholecystokinin, Substance P, enkephalins)

Diffusable gases

• nitric oxide

Lipid mediators

• (e.g. endocannabinoids)

Neurotrophins

- (e.g. nerve growth factor)
- Steroids

Seven Steps in Neurotransmitter Action

Neurotransmitter molecules are synthesized from precursors under the influence of enzymes.

Neurotransmitter molecules are stored in vesicles.

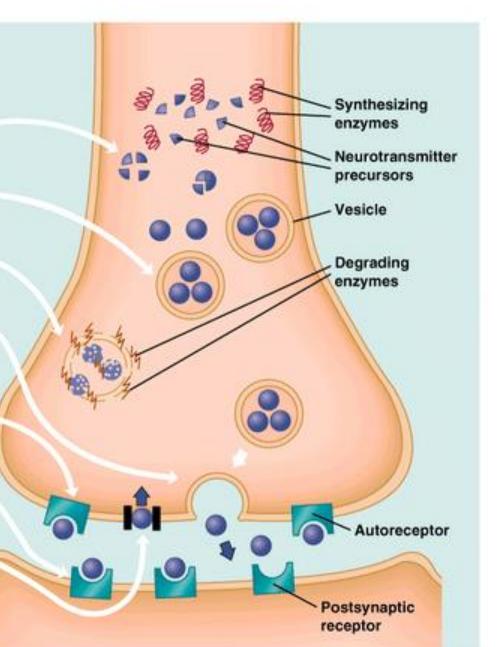
3 Neurotransmitter molecules that leak from their vesicles are destroyed by enzymes.

Action potentials cause vesicles to fuse with the presynaptic membrane and release their neurotransmitter molecules into the synapse.

Released neurotransmitter molecules bind with autoreceptors and inhibit subsequent neurotransmitter release.

Released neurotransmitter molecules bind to postsynaptic receptors.

Released neurotransmitter molecules are deactivated either by reuptake or enzymatic degradation.



Copyright © 2001 by Allyn & Bacon

CNS DRUGS CLASSIFICATION

- Chemical structure
 - Benzodiazepines, Butyrophenones
- Pharmacological
 - MAO inhibitors, SSRI,.....
- Clinical use
 - Antidepressants, Antipsychotic agents...

WHO Classification

- 1. Anxiolytic sedatives (hypnotics, sedatives, minor tranquillizers)
- "Drugs that cause sleep and reduce anxiety"

Examples

Barbiturates, benzodiazepines and ethanol



2. Antipsychotic drugs (neuroleptics, major tranquillizers, anti-schizophrenia
"Drugs that are effective in relieving symptoms of schizophrenic illness"
Examples
Phenothiazines and butyrophenones 3. Antidepressant drugs (thymoleptics)
" Drugs that alleviate the symptoms of depressive illness"
Examples
TCA, MAOI, SSRI



4. Psychomotor stimulants (Psychostimulants)
"Drugs that can cause wakefulness and euphoria"
Examples
Amphetamines, Cocaine, and caffeine

- 5. Hallucinogenic drugs (psychodysleptics, psychotomimetics)
- "Drugs that cause disturbance of perception and of behavior in ways that cannot be simply characterized as sedative or stimulant effects"

Examples

Lysergic acid diethylamide (LSD), mescaline and phencyclidine

Others

- Analgesics (opiate)
- Anesthetics (Ketamine)

GENERAL AND LOCAL ANESTHETICS

OVERVIEW

General anesthesia is a reversible state of central nervous system (CNS) depression.

For patients undergoing surgical and other medical procedures, anesthesia provides the following important benefits:

Sedation and reduction of anxiety

✓ Loss of consciousness

✓ Skeletal muscle relaxation

✓ Suppression of undesirable reflexes

✓ Analgesia

STAGES AND DEPTH OF ANESTHESIA

General anesthesia can be divided into three stages:

A. Induction,

It is defined as the period of time from the onset of administration of the potent anesthetic to the development of effective surgical anesthesia in the patient. Induction of anesthesia depends on how fast effective concentrations of the anesthetic drug reach the brain.

B. Maintenance; provides a sustained surgical anesthesia.

C. Recovery

is the time from discontinuation of administration of anesthesia until consciousness and protective physiologic reflexes are regained.

Recovery is essentially the reverse of induction and depends on how fast the anesthetic drug diffuses from the brain.

A.Induction

General anesthesia in adults is normally induced with an IV anesthetic like *propofol, which produces unconsciousness within 30–40 seconds* after injection. At that time, additional inhalation and/or IV drugs comprising the selected anesthetic combination may be given to produce the desired depth of surgical (Stage III) anesthesia.

For children without IV access, inhalation induction is used with nonpungent agents, such as *halothane* or *sevoflurane*, *to induce general anesthesia*.

B.Maintenance of anesthesia

Maintenance is the period during which the patient is surgically anesthetized.

Anesthesia is commonly maintained by the administration of volatile anesthetics, which offer good control over the depth of anesthesia.

C.Recovery

Postoperatively, the anesthetic admixture is withdrawn, and the patient is monitored for the return of 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.

Depth of Anesthesia

Depth of anesthesia is the degree to which the CNS is depressed and is a useful parameter for individualizing anesthesia.

It has traditionally been divided into four sequential stages. Each stage is characterized by increased CNS depression, which is caused by accumulation of the anesthetic drug in the brain.

With commonly used modern anesthetics, the stages are difficult to characterize clearly because of the rapid onset of surgical anesthesia.

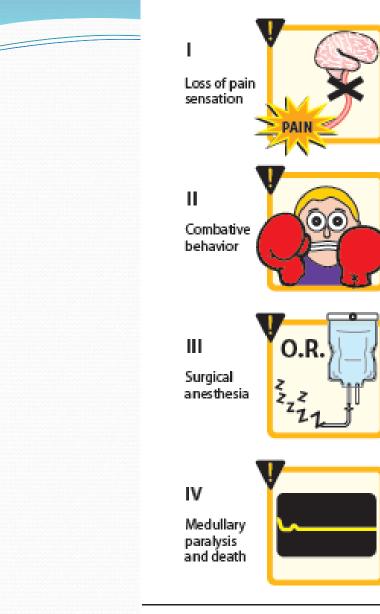


Figure 11.3 Stages of anesthesia. O.R. = operating room.

An ideal anesthetic drug must;

- provide a smooth and rapid loss of consciousness
- ✓ allow for a prompt recovery after its administration is discontinued
- ✓ possess a wide margin of safety and be devoid of adverse effects.

Because no single drug has all desirable properties mentioned, several groups of drugs are used in combination to produce optimal anesthesia.

PREANESTHETIC MEDICATIONS

Antacids Anticholinergics Antiemetics Antihistamines Benzodiazepines Opioids

Preanesthetic medications serve to calm the patient, relieve pain, and protect against undesirable effects of subsequently administered anesthetics or the surgical procedure itself.

Concomitant use of drugs;

- Commonly, surgical patients receive one or more of the following preanesthetic medications:
- H2 blockers to reduce gastric acidity (such as famotidine or ranitidine)
- Benzodiazepines to allay anxiety and facilitate amnesia (such as midazolam or diazepam)
- Opioids for analgesia (such as fentanyl)
- * Antihistamines for prevention of allergic reactions; (such as diphenhydramine)
- Antiemetics to prevent nausea and the possible aspiration of stomach contents (such as ondansetron)
- Anticholinergics to prevent bradycardia and secretion of fluids into the respiratory tract (such as glycopyrrolate).

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,*

Balanced anesthesia is a technique employed to compensate for the lack of an ideal anesthetic.

Drugs are combined to make sure that :

induction is smooth and rapid,

>analgesia and muscle relaxation are sufficient

The agent used most commonly for these purposes:

- 1. short- acting barbiturates (for induction of anesthesia)
- 2. neuromuscular blocking agents (for muscle relaxation)
- 3. opioids and nitrous oxide (for analgesia)

when administered concurrently, balanced anesthesia also lowers the dose of anesthetic required to maintain the desired level of surgical anesthesia.

However, such coadministration can also enhance undesirable anesthetic effects (for example, hypoventilation), and may produce negative effects that are not observed when each drug is given individually.

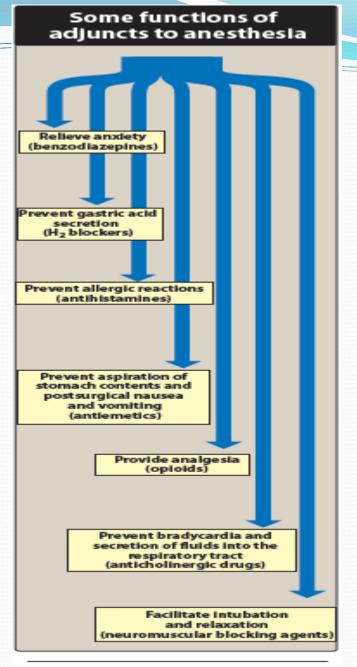


Figure 11.2 Components of balanced anesthesia.

Potent general anesthetics can be divided into two groups

GENERAL ANESTHETICS: INHALED

Desflurane SUPRANE Halothane FLUOTHANE Isoflurane FORANE Nitrous oxide NITROUS OXIDE Sevoflurane ULTANE

GENERAL ANESTHETICS: INTRAVENOUS

Barbiturates (eg. Thiopental, Methohexital) Benzodiazepines (eg. Midozolam, Diazepam) Propofol DIPRIVAN Ketamine KETALAR Opioid analgesics (eg. Morphine, Fentanyl, Sufentanil, Alfentanil, Remifentanil) Dexmedetomidine PRECEDEX Etomidate AMIDATE

INHALATION ANESTHETICS

Inhalation anesthetics are used primarily for the maintenance of anesthesia after administration of an IV agent.

One advantage of inhalation anesthetics is that the depth of anesthesia can be rapidly altered by changing the inhaled concentration of the drug.

Common features of inhalation anesthetics

Modern inhalation anesthetics include the gas nitrous oxide as well as a number of volatile, halogenated hydrocarbons.

✤ As a group, these agents decrease cerebrovascular resistance, resulting in increased perfusion of the brain.

✤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 minimum alveolar concentration (MAC).

✤ Put another way, MAC of drug in the alveolar air produces inmobility in 50% of patients exposed to a painful stimulus.

✤ MAC is usually expressed as the percentage of gas in a mixture required to achieve the effect.

MAC is small for potent anesthetics, such as *sevoflurane*, and large for less potent agents, such as *nitrous oxide (N2O)*. Note that *nitrous oxide alone cannot produce complete anesthesia*, because an admixture with sufficient oxygen cannot approach its MAC value.

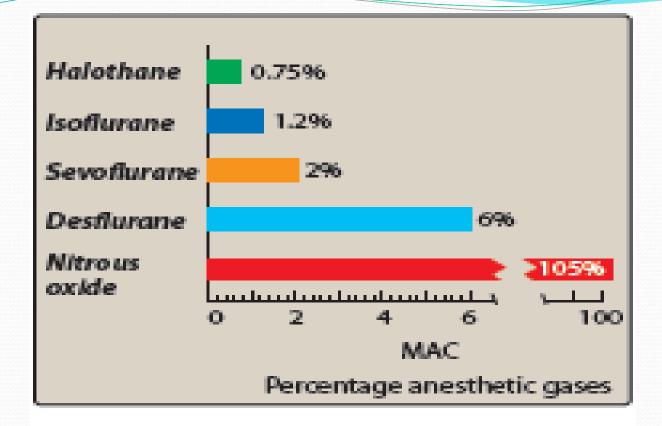


Figure 11.4 Minimal alveolar concentrations (MAC) for anesthetic gases.

Potency (Continue)

✤ 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.

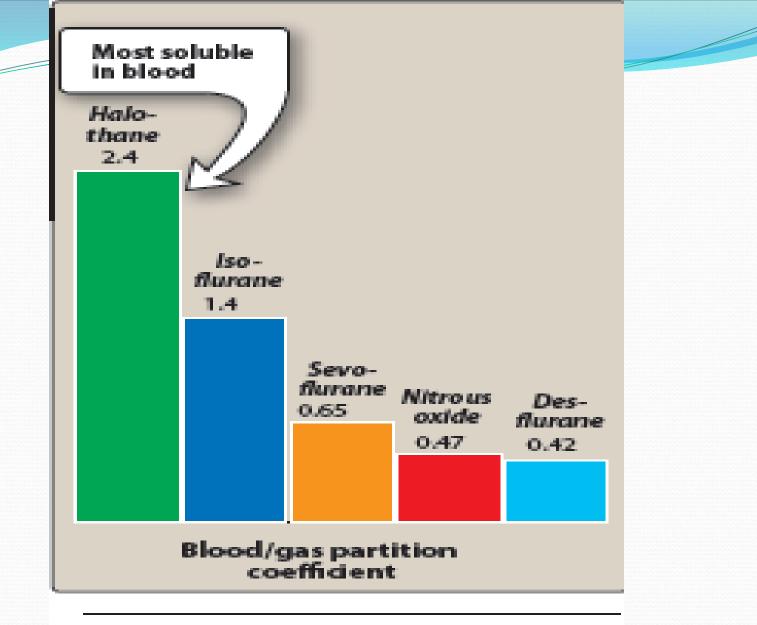


Figure 11.5 Blood/gas partition coefficients for some inhalation anesthetics.

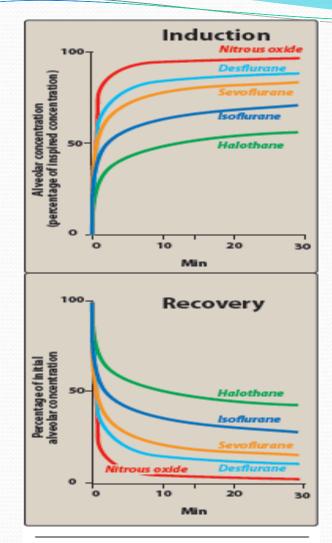


Figure 11.6

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

Mechanism of action

The general anesthetics increase the sensitivity of the γ -aminobutyric acid (GABAA) 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.

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 and the action of the excitatory neurotransmitter glutamic acid on N-methyl-D-apartate channel receptor. (Ketamine, nitrous oxide)

Halothane

 ✓ Halothane is a potent anesthetic but a relatively weak analgesic. Thus, halothane is usually coadministered with nitrous oxide, opioids, or local anesthetics.

✓ It is a potent bronchodilator and relaxes both skeletal and uterine muscle.

✓ *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 (anorexia, nausea, and vomiting, and hepatitis) developing in some patients (especially females) after *halothane* anesthesia.

✓ To avoid this condition, *halothane anesthesia is not* repeated at intervals of less than 2 to 3 weeks.

 ✓ Halothane is not hepatotoxic in pediatric patients. Therefore, it is suitable in children for inhalation induction (*sevoflurane* is now the agent of choice for this)

Halothane (continue)

✓ Like other halogenated hydrocarbons, *halothane* is vagomimetic and causes *atropine-sensitive bradycardia*.

 ✓ It has the undesirable property of causing cardiac arrhythmias. [Note: 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.]

 ✓ Halothane, like the other halogenated anesthetics, produces concentrationdependent hypotension. Should it is necessary, it is recommended that a direct-acting vasoconstrictor (such as phenylephrine) can be given.

✓ It has the potential to induce Malignant hyperthermia in combination with the neuromuscular blocking agent succinylcholine

Isoflurane

✤ It is a very stable molecule that undergoes little metabolism and is not, therefore, toxic to the liver or kidney.

✤ It does not induce cardiac arrhythmias and does not sensitize the heart to the action of catecholamines.

✤ Like the other halogenated gases, it produces dose-dependent hypotension due to peripheral vasodilation.

It has a pungent odor and stimulates respiratory reflexes (for example, breath-holding, salivation, coughing, and laryngospasm) and is, therefore, not used for inhalation induction.

With higher blood solubility than *desflurane and sevoflurane*, isoflurane is typically used now only when cost is a factor.

Desflurane

Desflurane provides very rapid onset and recovery due to its low blood solubility (the lowest of all the volatile anesthetics), causing it a popular anesthetic for outpatient surgery

Because it has a low volatility, must be delivered using a special heated vaporizer.

Like isoflurane, it decreases vascular resistance and perfuses all major tissues very well.

Because it is irritating to the airway and can cause laryngospasm, coughing, and excessive secretions, desflurane is not used for inhalation inductions.

Because it is relatively expensive, it is often not used for maintenance during extended anesthesia.

> Its degradation is minimal, and, therefore, tissue toxicity is rare.

Sevoflurane

✓ It has rapid onset and recovery due to low blood solubility.

✓ Sevoflurane has low pungency, allowing rapid induction without irritating the airway, thus making it suitable for inhalation induction in pediatric patients. It is replacing halothane for this purpose.

✓ Sevoflurane is metabolized by the liver, and compounds formed in the anesthesia circuit may be nephrotoxic if fresh gas flow is too low.

Nitrous oxide

Nitrous oxide ("laughing gas"), is non-irritating and a potent analgesic but a weak general anesthetic.

✤Nitrous oxide is frequently employed at concentrations of 30-50 percent in combination with oxygen for analgesia, particularly in dental surgery.

However, nitrous oxide at 80 percent (without adjunct agents) cannot produce surgical anesthesia. Therefore, it is commonly 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.

Nitrous oxide (continue)

This anesthetic does not depress respiration, and it does not produce muscle relaxation.

Under the usual circumstances of coadministration with other anesthetics, it also has moderate to no effect on the cardiovascular system or on increasing cerebral blood flow

✤ It is the least hepatotoxic of the inhalation anesthetics. Therefore, it is probably the safest of these anesthetics

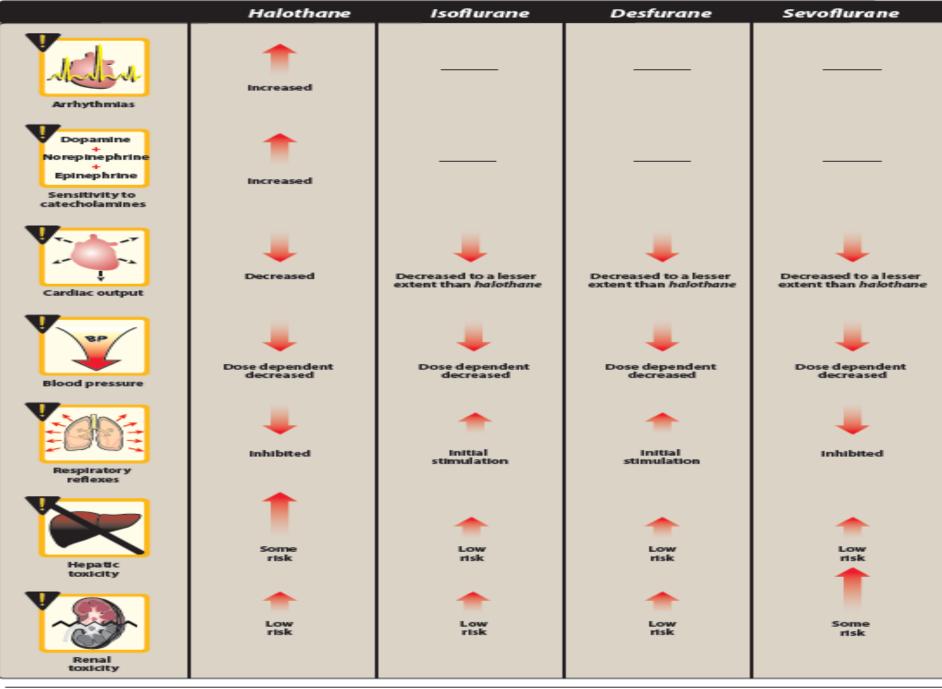


Figure 11.8

Characteristics of some inhalation anesthetics.

INTRAVENOUS ANESTHETICS

□ IV anesthetics cause the rapid induction of anesthesia. Anesthesia may then be maintained with an appropriate inhalation agent.

□IV anesthetics may be used as the sole agents for short procedures or administered as infusions to help maintain anesthesia during longer procedures.

□In lower doses, they may be used to provide sedation.

Induction

After entering the blood stream, they pass along a concentration gradient from the blood into the brain. The rate of this transfer is dependent on:

the arterial concentration of the unbound free drug,
the lipid solubility of the drug, and
the degree of ionization.

Unbound, lipid-soluble, non-ionized molecules cross the blood-brain barrier most quickly.

Once the drug has penetrated the CNS tissue, it exerts its effects. Like the inhalation anesthetics, the exact mode of action of the IV anesthetic drugs is unknown.

Propofol *Propofol is an IV sedative/hypnotic used in the induction* or maintenance of anesthesia.

□*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.

□The induction of anesthesia is smooth and occurs within about 30–40 seconds of administration.

□Plasma levels decline rapidly as a result of redistribution, followed by a more prolonged period of hepatic metabolism and renal clearance. The initial redistribution half-life is between 2 and 4 minutes.

The pharmacokinetics of propofol are not altered by moderate hepatic or renal failure.

Propofol (continue)

□ Supplementation with narcotics for analgesia is required.

□ *Propofol decreases blood* pressure without depressing the myocardium. It also reduces intracranial pressure, mainly due to systemic vasodilation.

□ *Propofol is commonly infused in lower doses to* provide sedation for outpatient procedures.

□ The incidence of postoperative nausea and vomiting is very low

Fospropofol D *Fospropofol is a new, water-soluble drug approved* only for sedation.

□ Fospropofol is metabolized to propofol in the body, and the pharmacological effects of fospropofol are attributed to propofol (thus, fospropofol is a "prodrug" of propofol).

□ Because *fospropofol is water soluble, the* problems associated with lipidformulated *propofol (such as pain at the* IV injection site and increased chance for bacterial contamination) are expected to be less frequent.

Barbiturates

□ Thiopental is a potent anesthetic but a weak analgesic.

□ It is an ultrashort-acting barbiturate with 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.

□ In contrast to the volatile anesthetics, thiopental is desirable drug for patient with head trauma and brain tumors

□ However, diffusion out of the brain can also occur very rapidly because of redistribution of the drug to other body tissues, including skeletal muscle and, ultimately, adipose tissue .

□ The short duration of anesthetic action is due to the decrease of barbiturate concentration in the brain to a level below that necessary to produce anesthesia.

□ 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.

□ *Thiopental has* minor effects on the cardiovascular system, but it may contribute to severe hypotension in patients with hypovolemia or shock.

□ All barbiturates can cause apnea, coughing, chest wall spasm, laryngospasm, and bronchospasm. [Note: The latter is of particular concern for asthmatic patients.]

□ Barbiturates are contraindicated in patients with acute intermittent porphyria.

Benzodiazepines

The benzodiazepines are used in conjunction with anesthetics to sedate the patient.

□The most commonly used is *midazolam*. *Diazepam and lorazepam are alternatives*.

□All three facilitate amnesia while causing sedation, enhancing the inhibitory effects of various neurotransmitters, particularly GABA.

□Minimal cardiovascular depressant effects are seen, but all are potential respiratory depressants (especially when administered intravenously).

They are metabolized by the liver with variable elimination half-lives, and *erythromycin may prolong their effects*.

□*Benzodiazepines can* induce a temporary form of anterograde amnesia in which the patient retains memory of past events, but new information is not transferred into long-term memory. Therefore, important treatment information should be repeated to the patient after the effects of the drug have worn off.

Opioids

□ Because of their analgesic property, opioids are commonly used with anesthetics, such as in combination with *nitrous oxide or volatile halogenated* anesthetics.

□ The most commonly used opioids are *fentanyl and its congeners*, *sufentanil* and *remifentanil*, *because they induce analgesia* more rapidly than *morphine does*.

□ *They may be administered either* intravenously, epidurally, or intrathecally (into the cerebrospinal fluid).

□Opioids are not good amnesics, and 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. Induction is* rapid, and the drug is short acting.

□*It is a hypnotic agent but lacks analgesic activity. Its water solubility is poor, so etomidate is formulated in a propylene glycol solution.*

□ It causes minimal cardiovascular and respriratory depression (major advantage compared with other IV anesthetics)

□It is usually only used for patients with coronary artery disease or cardiovascular dysfunction such as shock.

□ *Etomidate is hydrolyzed in the liver*. Its adverse effects include a decrease in plasma cortisol and aldosterone levels, which can persist for up to 8 hours. Therefore, *Etomidate should not be infused for an extended time, because prolonged* suppression of these hormones can be hazardous.

□Venous pain can occur on injection, and involuntary skeletal muscle movements are not uncommon. The latter are managed by administration of benzodiazepines and opioids.

Ketamine

□*Ketamine a short-acting, nonbarbiturate anesthetic,* 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.

□*Ketamine interacts* with the N-methyl-D-aspartate receptor.

□It also stimulates the central sympathetic outflow, which, in turn, causes stimulation of the heart with increased blood pressure and CO. This property is especially beneficial in patients with either hypovolemic or cardiogenic shock as well as in patients with asthma. Therefore, *ketamine is used when circulatory* depression is undesirable.

□*Ketamine is used* mainly in children and elderly adults for short procedures. However, it is not widely used, because it increases cerebral blood flow and induces postoperative hallucinations ("nightmares"), particularly in adults.

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 α_2 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.

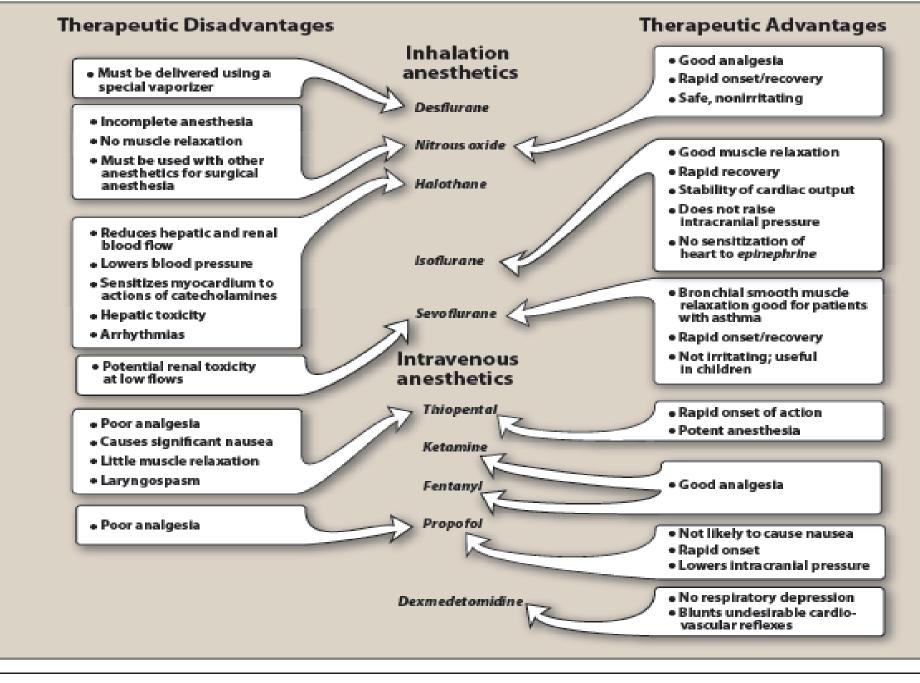


Figure 11.10

Therapeutic disadvantages and advantages of some anesthetic agents.

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, infi ltration, ring blocks, peripheral nerve blocks, and neuraxial (spinal, epidural, or caudal) blocks.

The small, unmyelinated nerve fi bers that conduct impulses for pain, temperature, and autonomic activity are most sensitive to the action of local anesthetics. The most widely used of the local anesthetic compounds are :

Amides

Lidocaine Bupivacaine Mepivacaine Ropivacaine Prilocain

Esters

Procaine Chloroprocaine Tetracaine .

Metabolisms of local anesthetics

Biotransformation of amides occurs primarily in the liver. Reduced hepatic function predisposes the patient to toxic effects.

Esters are biotransformed by plasma cholinesterase (pseudocholinesterase). Patients with pseudocholinesterase.

Actions

Local anesthetics cause vasodilation, when these drugs are administered alone.

Sy adding the vasoconstrictor *epinephrine to the local anesthetic, the rate of local anesthetic diffusion* and absorption is decreased.

Some of these local anesthetics agents confer additional benefits such as the antiarrhythmic effect of *lidocaine when administered intravenously*.

Clinical use of local anesthetics

They may be administered topically and injection

Topical anesthesia by applying directly to the skin or mucous membrane.

Administration by injection ✓ Infiltration anesthesia

- Nerve block anesthesia
- Epidural anesthesia
- Spinal anesthesia

CHARACTERISTIC		•Proc ESTERS •Chio		• Tetracaine • Cocaine	AMIDES	• Lidocaine • Mepivacaine • Bupivacaine, • Prilocaine • Ropivacaine
Metabolism		Rapid by plasma cholinesterase			Slow, hepatic	
Systemic toxicity		Less likely			More likely	
Allergic reaction		Possible- PABA derivatives form			Ver y rare	
Stability in solution		Breaks down in ampules (heat, sun)			Very stable chemically	
Onset of action		Slow as a general rule		Moderate to fast		
pK₂'s		Higher than physiologic		gic pH (8.5–8.9)	Close to physiologic pH (7.6–8.1)	
DRUG		POTENCY		ONSET		DURATION
Procaine	Low			Rapid		Short
Chloroprocalne	Low			Rapid		Short
Tetracaine	High			Slow		Long (spinal)
Lidocaine	Low			Rapid		Intermediate
Mepivacaine	Low			Moderate		Intermediate
Bupivacaine	High			Slow		Long
Ropivacaine	High			Moderate		Long

Figure 11.12

Summary of pharmacologic properties of some local anesthetics. PABA = para-aminobenzoic acid.