Chapter 25

General Anesthetics

1. Introduction

- **General anesthetics:**

1. Analgesia
2. Amnesia
3. Loss of consciousness
4. Inhibition of sensory and autonomic reflexes
5. Skeletal muscle relaxation

- **An ideal anesthetic:**

1. A smooth and rapid loss of consciousness
2. A prompt recovery after its administration is discontinued
3. A wide margin of safety and be devoid of adverse effects

2. Type of General Anesthesia

- Intravenous Anesthetics
- The Inhaled Anesthetics
- Balanced Anesthesia

2. Type of General Anesthesia

- **Intravenous Anesthetics**

(1) barbiturates (eg, thiopental, methohexital)

(2) benzodiazepines (eg, midazolam, diazepam)

(3) propofol

(4) ketamine

(5) opioid analgesics (morphine, fentanyl, sufentanil, alfentanil, remifentanil)

(6) miscellaneous sedative-hypnotics (eg, etomidate, dexmedetomidine)

2. Type of General Anesthesia

- **The Inhaled Anesthetics**

  The most commonly used inhaled anesthetics are isoflurane, desflurane, and sevoflurane, as well as nitrous oxide.

  These compounds are volatile liquids that are aerosolized in specialized vaporizer delivery systems.

2. Type of General Anesthesia

- **Balanced Anesthesia**

  Although general anesthesia can be produced using only intravenous or only inhaled anesthetic drugs, modern anesthesia typically involves a combination of intravenous (eg, for induction of anesthesia) and inhaled (eg, for maintenance of anesthesia) drugs. However, volatile anesthetics (eg, sevoflurane) can also be used for induction of anesthesia, and intravenous anesthetics (eg, propofol) can be infused for maintenance of anesthesia.

3. Stages of Anesthesia

From observations of the effects of inhaled diethyl ether, anesthetic effects on the brain can be divided into four stages:

- **I. Stage of analgesia:** The patient initially experiences analgesia without amnesia. Later in stage I, both analgesia and amnesia are produced.
- **II. Stage of excitement:** The patient often appears to be delirious and may vocalize but is definitely amnesic. Respiration is irregular both in volume and rate, and retching and vomiting may occur.
- **III. Stage of surgical anesthesia:** This stage begins with the recurrence of regular respiration and extends to complete cessation of spontaneous respiration (apnea). Four planes of stage III have been described in terms of changes in ocular movements, eye reflexes, and pupil size, which may represent signs of increasing depth of anesthesia.
- **IV. Stage of medullary depression:** This deep stage of anesthesia includes severe depression of the CNS, including the vasomotor center in the medulla, as well as the respiratory center in the brain stem. Without circulatory and respiratory support, death rapidly happens.

4. Inhaled Anesthesia

brain uptake
tissue distribution

Table 25–2 Pharmacologic Properties of Inhaled Anesthetics.

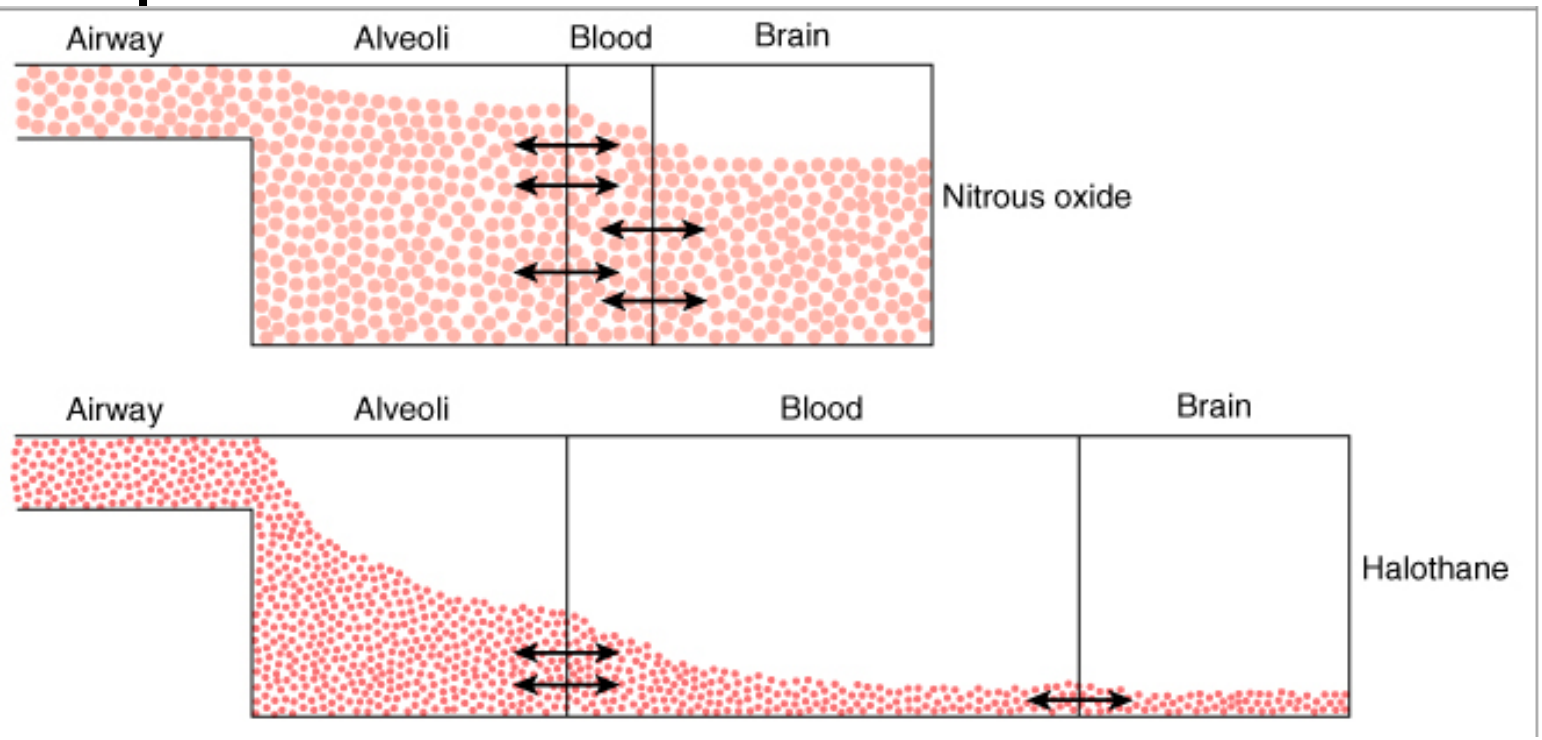
Anesthetic	Blood:Gas Partition Coefficient[1]	Brain:Blood Partition Coefficient[1]	Minimal Alveolar Concentration (MAC) (%)[2]	Metabolism	Comments
Nitrous oxide	0.47	1.1	> 100	None	Incomplete anesthetic; rapid onset and recovery
Desflurane	0.42	1.3	6–7	< 0.05%	Low volatility; poor induction agent (pungent); rapid recovery
Sevoflurane	0.69	1.7	2.0	2–5% (fluoride)	Rapid onset and recovery; unstable in soda-lime
Isoflurane	1.40	2.6	1.40	< 2%	Medium rate of onset and recovery
Enflurane	1.80	1.4	1.7	8%	Medium rate of onset and recovery
Halothane	2.30	2.9	0.75	> 40%	Medium rate of onset and recovery
Methoxyflurane	12	2.0	0.16	> 70% (fluoride)	Very slow onset and recovery

4. Inhaled Anesthesia

SOLUBILITY

One of the most important factors influencing the transfer of an anesthetic from the lungs to the arterial blood is its solubility. The blood:gas partition coefficient is a useful index of solubility and defines the relative affinity of an anesthetic for the blood compared with that of inspired gas. The partition coefficients for desflurane and nitrous oxide, which are relatively insoluble in blood, are extremely low. When an anesthetic with low blood solubility diffuses from the lung into the arterial blood, relatively few molecules are required to raise its partial pressure, and therefore the arterial tension rises rapidly. Conversely, for anesthetics with moderate-to-high solubility (eg, halothane, isoflurane), more molecules dissolve before partial pressure changes significantly, and arterial tension of the gas increases less rapidly.

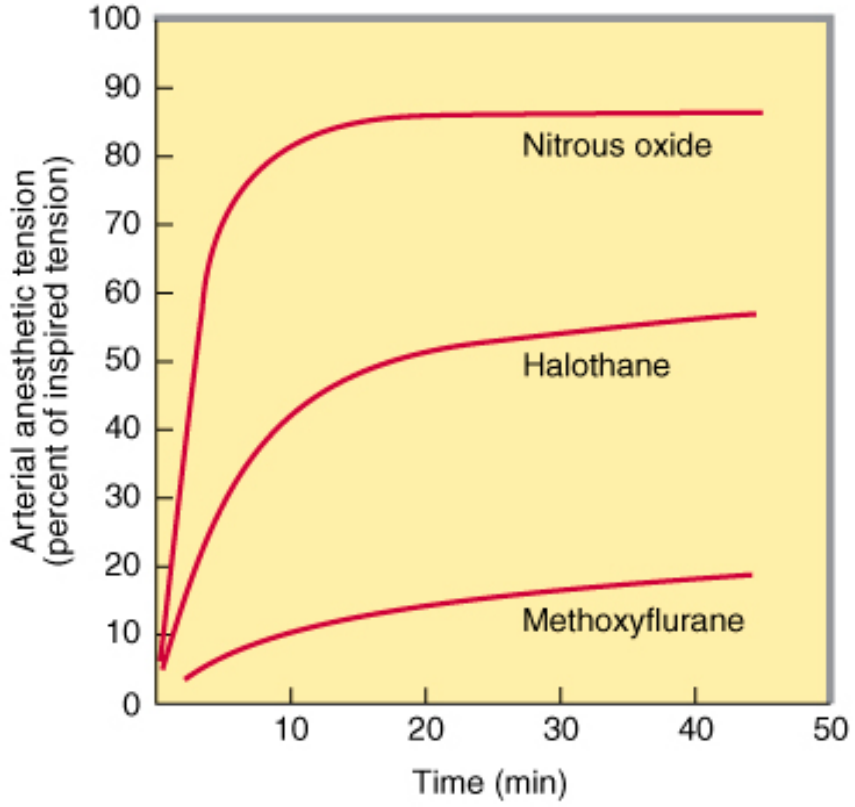
4. Inhaled Anesthesia



Why induction of anesthesia is slower with more soluble anesthetic gases. In this schematic diagram, solubility in blood is represented by the relative size of the blood compartment (the more soluble, the larger the compartment). Relative partial pressures of the agents in the compartments are indicated by the degree of filling of each compartment. For a given concentration or partial pressure of the two anesthetic gases in the inspired air, it will take much longer for the blood partial pressure of the more soluble gas (halothane) to rise to the same partial pressure as in the alveoli. Since the concentration of the anesthetic agent in the brain can rise no faster than the concentration in the blood, the onset of anesthesia will be slower with halothane than with nitrous oxide.

4. Inhaled Anesthesia

Figure 25–4



Tensions of three anesthetic gases in arterial blood as a function of time after beginning inhalation. Nitrous oxide is relatively insoluble (blood:gas partition coefficient = 0.47); methoxyflurane is much more soluble (coefficient = 12); and halothane is intermediate (2.3).

4. Inhaled Anesthesia

Elimination

1. Redistribution from brain to blood to air
2. Anesthetics that are relatively insoluble in blood and brain are eliminated faster

4. Inhaled Anesthesia

Mechanism of Action

1. To activate GABA A receptor-chloride channel
2. To activate glycine receptor
3. To inhibit NMDA channel receptor
4. To inhibit nicotinic acetylcholine receptor isoforms

4. Inhaled Anesthesia

The minimal alveolar anesthetic concentration (MAC)

The volatile anesthetic concentration is the percentage of the alveolar gas mixture, or partial pressure of the anesthetic as a percentage of 760 mm Hg (atmospheric pressure at sea level).

The minimum alveolar anesthetic concentration (MAC) is defined as the *median concentration that results in immobility in 50% of patients when exposed to a noxious stimulus* (eg, surgical incision).

4. Inhaled Anesthesia

MAC value greater than 100% for nitrous oxide demonstrates that it is the least potent inhaled anesthetic. At normal barometric pressure, even 760 mm Hg partial pressure of nitrous oxide (100% of the inspired gas) is still less than 1 MAC; therefore, it must be supplemented with other agents to achieve full surgical anesthesia

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4. Inhaled Anesthesia

Toxicity

- **HEPATOTOXICITY (HALOTHANE)**

Postoperative hepatic dysfunction is typically associated with factors such as blood transfusions, hypovolemic shock, and other surgical stresses rather than volatile anesthetic toxicity.

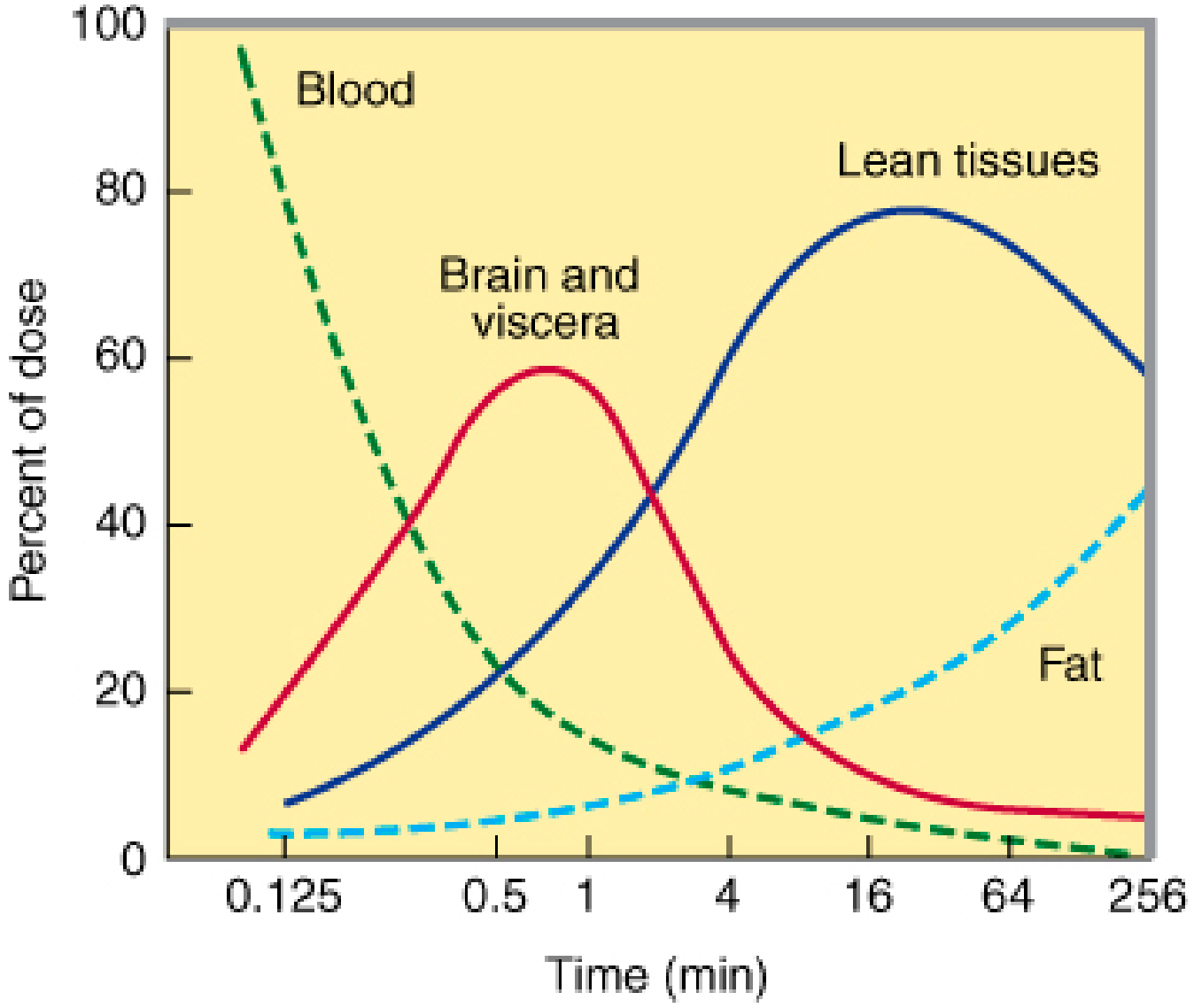
- **NEPHROTOXICITY**

Interference of chloride ion channel

- **MALIGNANT HYPERTHERMIA**

Malignant hyperthermia is an autosomal dominant genetic disorder of skeletal muscle that occurs in susceptible individuals undergoing general anesthesia with volatile agents and muscle relaxants (eg, succinylcholine).

5. Intravenous Anesthesia



Redistribution of thiopental after an intravenous bolus administration

5. Intravenous Anesthesia

Propofol (Diprivan)

- Mechanism similar to ethanol
- Rapid onset and recovery
- Mild hypotension
- Antiemetic activity

Short-acting barbiturates

- Thiopental (Pentothal)

Benzodiazepines

- Midazolam (Versed)

5. Intravenous Anesthesia

Ketamine

- Block glutamate receptors
- Dissociative anesthesia:

  Catatonia, analgesia, and amnesia without loss of consciousness
- Cardiac stimulant

5. Intravenous Anesthesia

Etomidate

- Non-barbiturate
- Rapid onset
- Minimal cardiovascular and respiratory toxicities
- High incidence of nausea and vomiting