

General Anesthetic Agents

- ANESTHESIA: loss of sensation
- General Anesthesia renders the patient:
 - amnesic
 - unconscious while causing muscle relaxation
 - suppression of undesirable reflexes

Theories of anesthesia

- Most anesthetics enhance the activity of inhibitory GABA A-receptors
- Many inhibit activation of excitatory receptors, such as glutamate and nicotinic acetylcholine receptors

Stages of Anesthetic Activity

- ***Stage I - Analgesia***
 - conscious but drowsy
 - responses to painful stimuli reduced
- ***Stage II - Excitement***
 - lose consciousness
 - no longer responds to non-painful stimuli
 - responds in a reflex fashion to painful stimuli
- ***Stage III - Surgical anesthesia***
 - movement ceases and respiration becomes regular
- ***Stage IV - Medullary paralysis***
 - respiration and vasomotor control cease
 - death occurs

Properties of Ideal Inhalational Anesthetics

- Rapid, pleasant anesthetic induction and recovery
- Rapid changes in anesthetic depth
- Adequate relaxation of skeletal muscles
- Wide margin of safety
- Absence of toxic effects or other adverse properties in normal doses

Anesthesiology

Inhalational anesthetics :

Non-halogenated gas:

- Nitrous oxide (NO)

Halogenated hydrocarbons:

- Halothane
- Enflurane
- Isoflurane
- Desflurane
- Sevoflurane
- Methoxyflurane – nephrotoxicity.

Anesthesiology

The important characteristics of Inhalational anesthetics which govern the anesthesia are :

- Solubility in the blood (blood : gas partition coefficient)
- Solubility in the fat (oil : gas partition coefficient)

Anesthesiology

Blood : gas partition co-efficient:

- It is a measure of solubility in the blood.
- It determines the rate of induction and recovery of Inhalational anesthetics.
- Lower the blood : gas co-efficient – faster the induction and recovery – Nitrous oxide.
- Higher the blood : gas co-efficient – slower induction and recovery – Halothane.

Solubility to blood

- Based on blood/gas partition coefficient
- Lowest to highest
- NO
- Isoflurane
- Enflurane
- halothane

POTENCY

- Clinical potency can't be predicted by chemical structure
- Potency correlates w/ lipid solubility
- Defined by MAC

- MAC: concentration of anesthetic gas needed to eliminate movement among 50% of patients challenged by standardized skin incision
- INVERSE of MAC is an index of potency: the more lipid soluble, the LOWER the concentration needed to produce anesthesia
- The lower the MAC, the more potent is the anesthetic

Highest to lowest MAC

- NO
- Ether
- Enflurane
- Isoflurane
- halothane

Individual Inhalation Anesthetics

Nitrous oxide:

- low potency, therefore must be combined with other agents
- rapid induction and recovery
- good analgesic, WEAK anesthetic properties
- can cause diffusion hypoxia
- Safest and least hepatotoxic
- risk of bone marrow depression with prolonged administration.
- laughing gas
- can retard O₂ uptake during recovery, thus 20% of O₂ is always needed

Inhalational anesthetics

Halothane:

- It is a potent anesthetic.
- Induction is pleasant.
- It sensitizes the heart to catecholamines.
- It dilates bronchus – preferred in asthmatics.
- It inhibits uterine contractions.
- Halothane hepatitis and malignant hyperthermia can occur.

HALOTHANE

- **Prototype**
- **Weak analgesic; POTENT anesthetic**
- **Usually co-administered w/ N₂O, opioids, or local anesthetics**
- **Metabolized to tissue-toxic hydrocarbons (trifluoroethanol) & bromide ion**

HALOTHANE

- **Disadvantages:**
- Reduced myocardial contractility & causes hypotension
- Arrhythmias
- Increase arterial pressure
- Atropine sensitive **bradycardia**

Inhalational anesthetics

Enflurane:

- Sweet and ethereal odor.
- Generally do not sensitizes the heart to catecholamines.
- **Seizures occurs at deeper levels – contraindicated in epileptics.**
- Caution in renal failure due to fluoride.

Inhalational anesthetics

Isoflurane:

- It is commonly used with oxygen or nitrous oxide.
- It do not sensitize the heart to catecholamines.
- Its pungency can **irritate the respiratory system.**

ISOFLURANE

- Disadvantages:
 - More pungent odor than halothane
 - Progressive respiratory depression & hypotension

Inhalational anesthetics

Desflurane:

- It is delivered through special vaporizer.
- It is a popular anesthetic for day care surgery.
- Induction and recovery is fast, cognitive and motor impairment are short lived
- **Malignant hyperthermia**
- It **irritates the air passages** producing cough and laryngospasm.

METHOXYFLURANE

- potent, high lipid solubility
- Used in child birth
- Disadvantages: Metabolized to flouride;
Respiratory and circulatory depression

IV Anesthetics

- **Thiopental**

- barbiturate with very high lipid solubility
- GABA- mimetic
- rapid action because of rapid transfer across blood-brain barrier
- Potent anesthetic, weak analgesic effect
- Little muscle relaxation
- **Laryngospasm, not for asthma pt, not w/ porphyria**

Anesthesiology

Thiopental

- It is an ultra short acting barbiturates.
- *Consciousness regained within 10-20 mins by redistribution to skeletal muscle.*
- It do not increase ICP.
- It is eliminated slowly from the body by metabolism and produce hang over.
- It can be used for rapid control of seizures.

IV anesthetics

Etomidate:

- It is a short acting anesthetic.
- **It suppress the production of steroids from the adrenal gland and no repeated injections.**
- It is a pro-convulsant and emetic.
- **Chorionic villus sampling (CVS) stability** is the main advantage over anesthetics.


IV Anesthetic Agents

Ketamine

- analogue of phencyclidine, w/ similar properties (psychotic reactions)
- effect on NMDA-type glutamate receptors
- onset of effect is relatively slow (2-5 minutes)
- produces “dissociative” anesthesia, in which patient may remain conscious and insensitive to pain
- can increase intracranial pressure
- Causes cardiovascular stimulation but not respiratory depression

IV anesthetics

Ketamine:

-  Emergence delirium, hallucinations and involuntary movements occurs in 50% cases during recovery.
- It is useful for burn dressing and trauma surgery
- Dangerous for hypertensive and IHD.

IV anesthetics

Propofol:

- Most commonly used IV anesthetic.
- Unconsciousness in ~ 45 seconds and lasts ~15 minutes.
- **Anti-emetic in action**
- Suited for day case surgery - residual impairment is less marked.
- **LOWERS ICP**

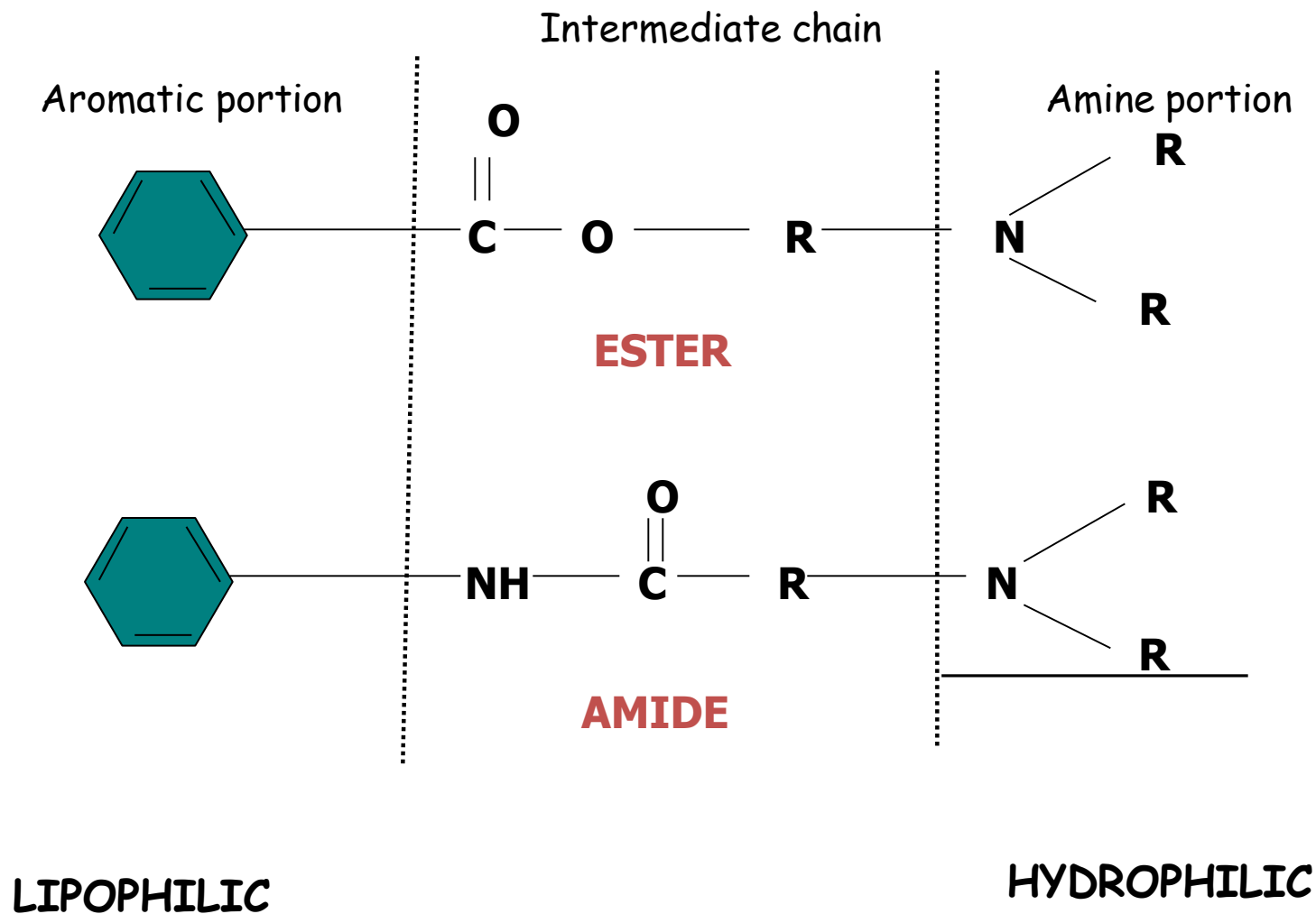
Local Anesthetics

DESIRABLE CHARACTERISTICS

- Rapid onset of action
- Brief, reversible block of nerve conduction
- Low degree of systemic toxicity***
- Soluble in water and stable in solution
- Effective on all parts of the nervous system, all types of nerve fibers and muscle fibers

- NONE totally meets these optimally yet!!

LAs are Weak Bases



Local Anesthetics

Clinical Significance of chemical classification

EPAL

- Biotransformation/duration of action
 - **ESTERS** are rapidly metabolized in the plasma by a cholinesterase
 - **AMIDES** are more slowly destroyed by liver microsomal P450 enzymes.

Local Anesthetics

MECHANISM OF ACTION

- LA have greatest affinity for sodium channel in **inactivated state** and slows its reversion to the **resting state**.
- Administration:
- Topical, injected into nerves, epidural or subarachnoid space (spinal)
- Notes:
- Reduced pH, as in inflamed tissues reduces effectiveness (cationic form predominates)
- Co-administered with vasoconstrictor epinephrine (1:100,000)

Local anesthetics (LAs)

The esters

The esters

- Benzoic acid derivatives
- P-aminobenzoic acid derivatives
- Acetanilide- lidocaine
- Toluidine - prilocaine
- thiophene - ultracaine

Benzoic Acid Derivatives

- **Cocaine**
- **Cyclomethicaine**
- **Hexylaine**
- **Isobuaine**
- **Meprylaine**
- **Piperocaine**

P-aminobenzoic acid Derivatives

- Benzocaine
- Butacaine
- Propoxyaine
- Proaine
- Proparaaine
- Chlorproaine
- Tetraaine

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME ESTER - type LA

Cocaine

- medical use limited to surface or topical anesthesia (corneal or nasopharyngeal)
- avoid epinephrine because cocaine already has **vasoconstrictor** properties (EXCEPTION!!!)
- A toxic action on heart may induce rapid and lethal **cardiac failure**
- A marked **pyrexia** is associated with cocaine overdose

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME ESTER - type LA

Benzocaine

- Used to produce anesthesia of mucous membranes and to **suppress gag** reflex during endoscopy
- methemoglobinemia

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME ESTER - type LA

Procaine

- Used for *infiltration* because of low potency and short duration but most commonly used for **spinal anesthesia**
- Short local duration -produces significant vasodilation. Epinephrine used to prolong effect
- **DOC** for patients with liver disease

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME ESTER - type LA

Tetracaine

- topical, infiltration and spinal anesthesia
- Frequently used **for topical ophthalmological anesthesia**
- slow onset and more prolonged effect than procaine (**longest duration of the esters**)

Local anesthetics (LAs)

The AMIDES

The amides

- Lidocaine
- Mepivacaine
- Bupivacaine
- Prilocaine
- Etidocaine
- Ropivacaine
- Levobupivacaine
- Articaine

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME AMIDE - type LA

LIDOCAINE:

- most widely used LA
- effective by **all routes**
- faster onset, more intense, longer lasting, than procaine
- good alternative for those allergic to ester type
- more potent than procaine but about equal toxicity
- **more sedative** than others

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME AMIDE - type LA

Mepivacaine:

- effective by **all routes except topical**
- similar onset and duration as lidocaine
- more toxic to neonates so not used in obstetrical anesthesia
- fetus poorly metabolizes mepivacaine

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME AMIDE - type LA

Bupivacaine:

- no topical effect
- slower onset and one of longer duration agents
- unique property of **sensory and motor dissociation**
- can provide sensory analgesia with minimal motor block
- has been popular drug for analgesia during labor

SELECTIVE PHARMACOLOGICAL PROPERTIES OF SOME AMIDE - type LA

Ropivacaine:

- enantiomer of bupivacaine (**S stereoisomer**)
- no topical effectiveness
- clinically ~ equivalent to bupivacaine
- similar sensory versus motor selectivity as bupivacaine
- significantly less cardiotoxicity than bupivacaine at equipotent doses.
- Long-acting LAs are very potent and may cause cardiac arrest with a misplaced injection or relative overdose

THANK YOU

s.hunaiti@ju.edu.jo