

REVIEW DOCUMENT FOR DENTAL PHARMACOLOGY EXAM 4  
April 30, 2009

**LOCAL ANESTHETICS:**

Basic structural characteristics of local anesthetics.

Examples of ester- and amide-linked anesthetics.

Mechanism of nerve conduction.

Mechanisms of local anesthetic action.

Metabolism of ester- and amide-linked local anesthetics.

Why are vasoconstrictors often added to the local anesthetic preparations?

Toxicity and side effects of local anesthetics. Please pay attention to central nervous system toxicity and cardiovascular toxicity.

**Heavy Metal Toxicity**

1. Know specific chelating agents for each metal, and route of administration.

**Lead:** Calcium disodium EDTA (IV)

2, 3-dimercaptosuccinic acid (Succimer) (Oral)

2, 3-dimercaptoproponol (BAL, Dimercaprol) (IM)

Penicillamine (Oral)

**Cadmium:** Calcium disodium EDTA (IV)

Mercury: 2, 3-dimercaptosuccinic acid (Succimer) (Oral)

2, 3-dimercaptoproponol (BAL, Dimercaprol) (IM)

Penicillamine (Oral)

N-acetyl-penicillamine (Oral)

**Arsenic:** N-acetyl-penicillamine (Oral)

Penicillamine (Oral)

Arsine gas (AsH<sub>3</sub>) (hemolytic agent): transfusion

**Iron:** Deferoxamine (IM, slow IV, Oral-under rare circumstance)

2. Know the mechanism of absorption.

Skin, Inhalation, GI

3. Know the mechanisms of toxicity

**Lead:** Inhibits Heme Biosynthesis- d-aminolevulonic acid and Protoporphyrin IX increases in plasma and urine (Diagnosis); Children ingested large quantities of paint containing lead is called "**Pica**"

**Cadmium:** Inhibits  $\alpha$ 1-antitrypsin –(emphysema), nephrotoxicity

**Mercury:** Mercury salts precipitates proteins, necrosis, inhibits sulfhydryl (-SH) group containing enzymes; plastic industry-**Minamata disease**

**Arsenic:** Increases vascular permeability, Inhibits anaerobic and oxidative phosphorylation; (semiconductors, herbicides, pesticides, water contamination)

4. Know why EDTA given IV.

EDTA cannot cross the cell membrane.

5. Know why EDTA given as Calcium disodium salt.

To balance the calcium level

6. Know how to treat copper poison (Wilson's disease)

Penicillamine; N-acetyl-penicillamine

Allergic to penicilline – Trientine (triethylenetetramine Hcl)

## **GENERAL ANESTHETICS**

Definitions: partial pressure, MAC, blood/gas partition coefficient, oil/gas partition coefficient

What determines anesthetic potency?

What are the 4 potential targets for the action of general anesthetics?

How do blood/gas solubility, ventilation rate and cardiac output affect equilibration of anesthetics (rate of induction of anesthesia)?

What is the mechanism of the "concentration effect" and the related "second gas effect"?

What factors determine the rate of anesthetic equilibration into different tissues?

What is the route of elimination of general anesthetics and how is recovery from anesthesia affected by the blood/gas partition coefficient, ventilation rate and cardiac output?

What are the common pharmacological effects of inhalational anesthetics?

Know the major differences between the inhalational anesthetics (e.g., which is most/least potent, induction/recovery rate, etc.- see table p. 14 of handout; don't need to memorize numbers).

What are the major uses of the various intravenous anesthetic agents discussed and their major advantages and disadvantages?

### **OPIOID ANALGESIC DRUGS**

1. Know about mechanism of nociception (physiology)  
Dorsal horn of the spinal cord – gate control mechanism
2. Know about classification of opioid analgesic drugs  
**Strong agonists** – morphine, meperidine, methadone, heroin, fentanyl  
**Moderate agonists** – propoxyphene, codeine  
**Mixed agonists-antagonists** – pentazocine, nalbuphine, buprenorphine  
**Antagonist** – naloxone, naltrexone
3. Know about endogenous opioid peptides  
Enkepalins, endorphins, dynorphins, endomorphins
4. Know about opioid receptors and the mechanism of action  
Mu (m), Kappa (k), Delta (d). All G-protein coupled receptors. Increase K<sup>+</sup> efflux (hyperpolarization) and reduce voltage-gated Ca<sup>2+</sup> entry.
5. Know about the sites of opioid receptor expression  
m - periaqueductal gray, spinal trigeminal nucleus, cuneate and gracile nuclei, thalamus,  
nucleus of solittract, nucleus ambiguus, parabrachial nucleus, neurons of the postrema  
k - hyphothalamic region  
d - dorsal horn of the spinal cord
6. Know about the pharmacological actions of opioids  
CNS - analgesia, sedation, euphoria, mental clouding, **respiratory depression**,  
nausea and vomiting, cough reflex, pupillary constriction (miosis)  
GI – constipation, biliary tract spasm
7. Know about the contraindications of opioids  
Decreased respiratory reserve (emphysema, severe obesity, asthma), biliary colic,  
head injury, reduced blood volume, hepatic insufficiency, convulsant states
8. Know about tolerance and physical dependence  
Tolerance develops to – analgesia, euphoria, sedation, lethal dose, nausea  
Tolerance **does not** develop to - miosis, constipation, respiratory depression (partial)  
Physical dependence – treat with **methadone** (long acting opioid)

9. Know about antitussive and anesthetic usage of opioids

Antitussive – codeine, dextromethorphan

Anesthetic – fentanyl, sufentanil

10. Know about antagonists

Naloxone – readily reverses the coma and respiratory depression of opioid overdose

Naltrexone – longer duration of action (up to 48 hrs)

### **Antiseizure Drugs**

! Know what a seizure is, its potential causes and how it relates to epilepsy.

! Know how seizures are classified (i.e., simple partial vs. complex partial vs. tonic-clonic, etc. - see table in handout)

! Know the general principles of antiseizure drug therapy

! Know the identified mechanisms by which antiseizure drugs work.

! Know the drugs of choice for the various types of seizures, their mechanism of action and major side effects.

! What are the 4 major types of drug interactions seen with antiseizure drugs?

### **Psychopharmacotherapy**

Know mechanism of action for first generation (“traditional”) and second generation (“atypical”) antipsychotics, and the major classes of antidepressants and anxiolytics.

Know how first generation (“traditional”) and second generation (“atypical”) antipsychotics differ.

Understand what types of side effects are associated with blockade of  $\alpha_1$ -adrenergic, muscarinic, and histamine receptors.

Understand the principles of drug interactions such as CYP inhibitors and inducers, protein binding and protein saturation.

## **Antidepressants and mood stabilizers**

Identify various antidepressants classified by mechanism of action(s) (e.g., multiple receptor actions, SSRIs, MAO-Is).

Discuss the impact of agonism or antagonism at pre-synaptic autoreceptors (i.e., short-loop negative feedback system).

Recognize possible mechanisms by which mood stabilizers such as lithium may work (e.g., NE-ACh balance hypothesis; thyroid-catecholamine hypothesis).

Discuss possible drug interactions with antidepressants and mood stabilizers mediated by the P450 microenzyme system (e.g., inhibition may increase concentration of substrate agent and lead to toxicity).

## **Anxiolytic and sedative-hypnotic drugs**

- 1 Identify anxiolytic agents based on purported mechanism(s) of action (e.g., BZDs, azapirones, SSRIs).
- 2 Know the inter-relationship of the GABA receptor, the chloride ion channel and the BZD receptor.
- 3 Know the different types of ligands at the BZD receptor (e.g., full agonist, antagonist, full inverse agonist).
- 4 Know the impact of the pharmacokinetics of various anxiolytic-sedative hypnotics on their clinical effect (e.g., onset of action, duration of action, metabolism).
- 5 Know the most common adverse effects associated with the BZDs.

## **(Pharmacology of sleep)**

1. Know the sleep stages
2. Know the effects of acute and chronic alcohol use on sleep.
3. Know the role of GABA A receptor complex in the hypnotic action of barbiturates, benzodiazepines and non-benzodiazepines.
4. Know the effects on sleep of benzodiazepines, imidazopyridines, and cyclopyrrolones.

## **ORAL CONTRACEPTIVES AND PRO-FERTILITY DRUGS**

### **Oral Contraceptives:**

Describe the primary mechanism of action of combination oral contraceptive pills and of progesterone-only contraceptive pills.

Describe the two types of contraceptive pills (monophasic, multiphasic).

What are the 2 possible estrogenic components of combination oral contraceptive (OCP) pills?

Define how OCPs are divided into groups based on dose of estrogenic component.

Describe how progestins differ by progestational, androgenic, antiestrogenic and estrogenic activity.

Describe what factors are important in determining the final estrogenic and progestational activity of a combination oral contraceptive pill.

Describe factors that govern the initiation of oral contraceptive therapy. What are the criteria or important factors that influence choice of OCP?

Know the contraindications to OC therapy.

List the signs of excess estrogen or progesterone activity in an OCP.

Know an example of an estrogen antagonist (or partial agonist) and a progesterone antagonist, describe a therapeutic use for these drugs and give the mechanism of action.

### **SERMS**

Understand how a selective estrogen receptor modulator can act as an estrogen agonist in one tissue or cell type while acting as an antagonist in another.

Be familiar with effects of raloxifene and tamoxifen

### **Profertility Drugs**

Understand the basic pharmacological approaches to treating infertility

Understand the mechanisms of action of clomiphene, gonadorelin (short-acting GnRH), leuprolide (long-acting GnRH), menotropin (pergonal), and Human Chorionic Gonadotropin (pregnyl)

## **Histamine and Antihistamines**

Know the sources of Histamine in the body

Know the classification and general location of Histamine receptors (H1, H2, H3)

Know the physiological activity of Histamine in major organs and tissues

Know the general mechanism and consequences of Histamine release during the hypersensitivity response

Know the general differences among:

First generation H1 antagonists

Second generation H1 antagonists

Third generation H1 antagonists

H2 antagonists

## **Drugs for Gastrointestinal Disorders**

Learn the mechanisms of action and general uses of drugs that affect GI motility:

Pro-emetic agents

Anti-emetic agents

Prokinetic agents

Antidiarrheal agents

Laxatives and cathartics

Learn the mechanisms of action and uses of drugs that affect gastric acidity:

Antacids

H2 receptor antagonists

Proton pump inhibitors

Prostaglandins

Understand the general therapeutic strategies for Peptic Ulcer Disease, Gastro-esophageal Reflux Disease, and Inflammatory Bowel Disease

## **Insulin and oral hypoglycemic (antidiabetic) drugs**

1. Be able to describe the various types of Diabetes Mellitus, what is different about each type that affects therapeutic intervention?
2. Be able to define the normal profile of glucose and insulin levels in normal and diabetic patients.
3. Define the types of insulin therapies available to Type I diabetics. What is the rationale behind the choice of single or mixed insulin therapy and subcutaneous pumps. What formulations of insulin are used and why?
4. Define the mechanism of action of insulin.
5. Be able to define the major differences between hypoglycemic versus antihyperglycemic drugs. What are the major advantages/disadvantages of each class.
6. Be able to discuss the different types of hypoglycemic drugs and their mechanism of action.
7. Be able to discuss the different types of antihyperglycemic drugs and their mechanism of action.

## **Thyroid Disorders**

Know the steps in the pathway of Thyroid Hormone synthesis

Know the causes, symptoms, and treatment of Hyperthyroidism and Thyroid Storm

Know the causes, symptoms, and treatment of Hypothyroidism.