

Pharmacology of anesthetic and ICU drugs

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توصيف مقرر دراسي

1- بيانات المقرر		
الرمز الكودي :	اسم المقرر :	الفرقة /المستوى :
	Pharmacology of anaesthetic and ICU drugs	Grade 2
التخصص :	عدد الوحدات الدراسية :	نظري 2 عملي
Anesthesia and Intensive care		

2- هدف المقرر:	The aim of this course is to provide students with an understanding of the pharmacology of drugs frequently used by anesthesiologists including action, adverse effects, drug interactions and dosing.
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3- المستهدف من تدريس المقرر :	Students of technical health institute-anesthesia technician
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<u>Intended learning outcomes (ILOs):</u>	
Knowledge&Understanding	
At the end of the course the student should be able to understand his role in the operating theater and ICU as follow:	
<ul style="list-style-type: none"> Understanding the action of anesthetic drugs. Preparing <u>intravenous</u> drugs, dosing and vial content. Preparing <u>intravenous therapy</u> administration equipment Establish peripheral intravenous access. Assist in inducing and maintaining adequate anesthesia. Making sure that patients are positioned in such a way NOT to cause discomfort or injury during their procedure. Acquiring and administering transfusion fluids and equipment. Drugs for waking the patient. 	ا. المعلومات والمفاهيم :

<p>By the end of this course students should be able to :</p> <ul style="list-style-type: none"> • Identify how to deal with different anesthetic drugs, its dosing, concentration, the predicted action, side effects and its way of preparation. • Communicate with the patients. • Call for help when needed. • Communicate with operating room and critical care unit staff. 	<p>ب- المهارات الذهنية :</p>
<p>By the end of this course students should be able to :</p> <p>Prior to anesthesia</p> <ul style="list-style-type: none"> • Checking and setting up the Anesthesia machine for IV drug infusion. • Preparing intravenous drugs. • Preparing intravenous therapy administration equipment • Establish peripheral intravenous access. <p>During anesthesia</p> <ul style="list-style-type: none"> • Inducing and maintaining adequate anesthesia. • Making sure that patients are positioned in such a way NOT to cause discomfort or injury during their procedure. • Monitoring and maintaining patient's vital signs and anesthesia depth. • Temperature monitoring and regulation. • Collection and analysis of patient's (blood) samples. • Acquiring and administering transfusion fluids and equipment. <p>After anesthesia</p> <ul style="list-style-type: none"> • Assist in waking the patient. • Assist in removing airway devices. • Care of the patient safety during transferring patients to post-operative care units 	<p>ج- المهارات المهنية الخاصة بالمقرر:</p>
<p>By the end of this course students should be able to :</p> <p>Prepare equipment needed for the patient to safely undergo anesthesia.</p> <p>This involves:</p> <ul style="list-style-type: none"> • Identify normal electrocardiography (ECG), blood pressure, temperature, oxygen saturation and anesthesia depth monitors (EEG, bispectral index etc.) that may also be necessary to be aware about any 	<p>د- المهارات العامة :</p>

<p>deviation from these normal parameters during anesthesia or in the ICU.</p> <ul style="list-style-type: none"> • Know hazards of different patient positions. • Differentiate between anesthetized and fully conscious patient 	
<p>A-Anesthesia Drugs</p> <ol style="list-style-type: none"> 1. IV GA Drugs 2. Inhalational Anesthesia drugs 3. Local Anesthetics 4. Muscle relaxants 5. Carrier Gas(O₂) <p>B-Anesthesia Adjuvant drugs</p> <ol style="list-style-type: none"> 1. Vasopressors 2. Inotropes 3. Vasodilators 4. Bronchodilators 5. Antiarrhythmic drugs 6. Antihistaminics 7. Corticosteroids 8. Antidotes <p>C-ICU Related drugs :</p> <ol style="list-style-type: none"> 1. IV. Antibiotics 2. IV. Antifungal 3. IV. Antiemetic's 4. IV. Fluids 5. Anticoagulants& Thrombolytic Drugs 6. Potassium 7. Calcium 8. Magnesium 9. Hemostatic 10. Blood & blood Components 11. Antiepileptic's 12. NSAIDs 	<p>4- محتوى المقرر:</p>  
<ol style="list-style-type: none"> 1. Lectures 2. Active learning-discussion 3. Pair work 4. Group work-team workshops 	<p>5- أساليب التعليم والتعلم</p>
<p>(Premedical examination:should be fit for admission)</p> <p>In case of accidental disability after admission :</p> <p>Intervention of a Specialist according to the situation</p>	<p>6- أساليب التعليم والتعلم للطلاب ذوي القدرات المحدودة</p>

7- تقويم الطلاب :

Assignments Periodic quizzes Midterm Final exam	أ- الأساليب المستخدمة
Assignments and oral presentation Periodic quizzes Midterm Final exam (at the end of the year)	ب- التوقيت
Year work (20 pts) includes Assignments 30% Periodic quizzes 30% Midterm 40% Final exams (80%pts)	ج- توزيع الدرجات

8- قائمة الكتب الدراسية والمراجع :

	أ- مذكرات
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	Pharmacology of Anesthetic and ICU drugs	ب- كتب ملزمة
	1. Clinical Anesthesiology-Morgan 2. ICU Book-Pul marinu 3. Hand book of clinical anesthesia 4. Lippincott pharmacology text book	ج- كتب مقترحة
		د- دوريات علمية أو نشرات الخ

Course Description

The aim of this course is to provide students with an understanding of the pharmacology of drugs frequently used by anesthesiologists including action, adverse effects, drug interactions and dosing. The students will also gain practical experience by applying the knowledge gained during the first academic year to better understand their audience and create more effective health messages and programming.

Core Knowledge

By the end of this course, students should be able to:

- Understand the action and adverse effects of different anesthetic drugs.
- Identify how to induce and maintain adequate anesthesia.
- Describe the role of different antidote of anesthetic agents
- Discuss the action and precautions during administration of skeletal muscle relaxant and their antidote.
- Identify the precautions needed during local anesthetic administration.
- Describe the action, adverse effects, precautions and contraindications of the most common drugs used in intensive care unit.

Core Skills

By the end of this course, students should be able to:

- Induction and maintenance of general anesthesia
- Monitoring and maintaining patient's vital signs and anesthesia depth.
- Preparing intravenous drugs.
- Establish peripheral intravenous access.
- Collection and analysis of patient's (blood) samples.
- Acquiring and administering transfusion fluids
- Report the different drug adverse reactions and toxicities.
- Avoid drug interactions and adverse effects in ICU
- Assist in waking the patient and Assist in removing airway devices.
- Care of the patient safety during transferring patients to post-operative care units

Course Overview

ID	Topics	Methods of Teaching/Training with Number of Total Hours per Topic				
		Interactive Lecture	Field Work	Class Assignment	Research	Lab
1	Vasopressors - Inotropes	2				
2	Vasodilators - Antiarrhythmic drugs	2				
3	Antibiotics -IV. Antifungal	2				
4	Anticoagulant	2				
5	Hemostatic& Thrombolytic Drugs	2				
6	Potassium- Calcium- Magnesium	2				
7	Antiemetic - Acid suppressant	2				
8	Antiepileptic drugs	2				
9	bronchodilators	2				
10	Potassium - Calcium - Magnesium	2				
11	Non-steroidal anti-inflammatory drugs (NSAIDs)	2				
12	Opioid analgesics	2				
13	General anesthesia Drugs	2				
14	Local Anesthetics - Muscle relaxants	2				
15	Acid base disorders pharmacotherapy	2				
TOTAL HOURS (30)		30				

Chapter 1

Anesthesia Drugs

IV General Anesthesia Drugs

Inhalational Anesthesia drugs

Classification of General AnestheticsI. Inhalation Anesthetics (Mainly for Maintenance)

Slow: provide minute to minute control over depth of anesthesia

Halogenated agents:

- ✓ Halothane - Isoflurane.
- ✓ Desflurane- Sevoflurane.

II. IV Anesthetics (Mainly for Induction)

Rapid induction of anesthesia

A. Barbiturates

- Thiopental sodium

B. Non-barbiturates

- Propofol - Ketamine.
- Opioids- Benzodiazepines

Mechanism of Action of General Anesthetics

- ✓ General anesthetics inhibit neuronal activity in many brain regions, specially the midbrain reticular activating system & thalamus.

I. Inhalation anesthetics

MAC (Minimum alveolar concentration):

- ❖ MAC is the alveolar concentration of anesthetic gas resulting in immobility in 50 % of patients when exposed to a painful stimulus: e.g. a surgical skin incision.
- ❖ It measures potency
- ❖ MAC is ↓ by anesthetic adjuvants as opioids, sedatives hypnotics, clonidine, and in elderly patients. It is ↑ by drugs increasing catecholamines & by alcohol abuse.

Halogenated agents

A- Halothane

- ✓ Inhalation anesthetic for maintenance anesthesia.
- ✓ May also be used for induction (nonirritant; smooth & pleasant).
- ✓ Medium rate of induction & recovery.

Adverse Effects of halothane

- ✓ Hypotension: due to myocardial depression or VD.
- ✓ Heart: bradycardia - arrhythmia (sensitize myocardium to catecholamines).
- ✓ Hepatotoxic.
- ✓ Malignant Hyperthermia.

B- Newer halogenated agents

- ❖ Due to hepatotoxicity, halothane is replaced by newer agents, which may also induce CVS & respiratory depression & malignant hyperthermia but less than halothane:

1-Isoflurane

- No risk of convulsions.
- May precipitate ischemia in patient with coronary disease.
- Respiratory irritant: cough & laryngospasm.

2-Desflurane

- Similar to isoflurane with faster onset & recovery → suitable for day surgery.
- Respiratory irritant: cough & laryngospasm.

3-Sevoflurane

- Similar to desflurane with no respiratory irritation → preferred inhalation agent for induction of anesthesia especially in children.

li. Intravenous anesthetics

A. Ultra Short-Acting Barbiturates:

Thiopental

Kinetics

- Rapid onset due to rapid crossing of BBB (highly lipid soluble).
- Short acting; redistributes from brain to fat & skeletal muscle.
- Slowly metabolized & liable to accumulate in body fat, thus may cause prolonged effect if given repeatedly → toxicity.

Clinical Uses

1. Most widely used IV anesthetic for induction followed by maintenance with inhalation agents for major operations (the principal use).
2. Given alone in anesthesia for short procedures.

Adverse Effects (narrow safety margin)

1. Respiratory & cardiovascular depression (toxic doses).
2. Severe vasospasm if accidentally injected intra-arterially → gangrene.
3. Can precipitate porphyria.

B. Nonbarbiturate IV Anesthetics

Propofol

- Widely used IV anesthetic for induction & maintenance of anesthesia.
- Rapid induction & recovery (rapid metabolism) → given as IV bolus or infusion without maintenance by inhalation agent → useful in one day surgery.
- Used in conscious & deep sedation (in intensive care).
- ✓ Advantage: antiemetic (↓ risk of postoperative vomiting).
- ✓ Disadvantage: respiratory & CVS depression - pain at injection site.

Ketamine

- ✓ Short-acting IV anesthetic → dissociative anesthesia (hypnotic state with dissociation, amnesia & analgesia; patients are unresponsive to commands).
- ✓ Induces profound analgesia → used for dressings of burns & minor orthopedic procedures in children.
- ✓ CV stimulant (↑HR & BP) → used in poor risk patients (shock states).
- ✓ Potent bronchodilator: suitable for patients with ↑ risk for bronchospasm.

Disadvantages

- ↑ Cerebral blood flow & intracranial tension → avoid in head injuries.
- Hallucination & disorientation (emergence phenomenon) occur on recovery (avoided by pretreatment with diazepam).

Benzodiazepines (midazolam - diazepam - lorazepam)

- ✓ Midazolam is preferred due to its rapid & short action & its less irritant

effect.

- ✓ Commonly used for sedation rather than anesthesia because prolonged amnesia & sedation may result from anesthetic doses.

Used in:

- Conscious sedation (for minor procedures e.g. endoscopy)
- Pre-anesthesia.
- Balanced anesthesia, anesthetic adjuncts.
- ✓ Availability of the antidote, flumazenil, is an advantage in case of toxicity (respiratory depression).

Opioid Analgesics

- Fentanyl, sufentanyl, alfentanyl, remifentanyl & morphine.

N.B.: Total intravenous anesthesia may be produced by combining opioids with propofol rather than an inhalation agent.



Chapter 2

Local Anesthetics - Muscle relaxants

Local Anesthetics

Definition

- ❖ A local anesthetic (LA) is a drug that induces a reversible loss of sensation in a localized area of the body without inducing loss of consciousness or sleep.

Chemical Nature and Members

All LAs consist of:

1. Hydrophilic amine group
2. Lipophilic aromatic group
3. Connecting group: (Links both groups together).

Classification of LA

I. Esters (Connecting group is an "ester) Rapidly hydrolyzed by plasma pseudocholine esterases:

1. Short duration of action.
2. Less liable to systemic toxicity, more liable to allergy (PABA derivatives).
3. Duration of action is prolonged in genetic enzyme deficiency.

II. Amides (Connecting group is an "amide) Redistributed & metabolized by liver:

1. Long duration of action.
2. More liable to induce systemic toxicity.
3. Duration of action prolonged in liver disease & reduced hepatic blood flow (e.g. heart failure).

Members of LA

I. Esters

Procaine

- Short acting (30- 60 minutes).
- Slow tissue penetration→ not used for surface anesthesia.

Benzocaine

- Low solubility →cannot be prepared in injection form →used as a surface anesthetic only.

Cocaine

- Used only in surface anesthesia (limited use due to abuse potential).

II. Amides

Lidocaine

- Intermediate acting (2 h).
- Rapid penetration: 1st choice for surface anesthesia.

Bupivacaine

- Long duration (3 h); due to high binding to plasma protein.
- Moderate tissue penetration.

Ropivacaine

- Long duration. More selective on sensory than on motor nerves.

Mechanism of Action of LA

- ❖ LA bind to receptors on inner surface of Na channel in nerve membranes resulting in their blockade →inhibition of generation & propagation of action potential.

pH and LA Activity

- ❖ The local anesthetic exists in 2 forms in equilibrium according to its pKa &

to the extracellular pH: 1. Ionized form 2. Unionized form

- ❖ Only the unionized form can cross the nerve membrane.
- ❖ Once inside nerve cell, the amount that crossed will again re-equilibrate into unionized & ionized forms according to the intracellular pH.
- ❖ The intracellular ionized form is the active form that blocks Na⁺ channel.

Factors affecting activity of local anesthetics

1- Extracellular & intracellular pH

Extracellular pH

- Infections or repeated injections of lidocaine HCl → ↑extracellular acidity → ↑extracellular ionized form of LA → ↓ LA crossing → ↓ activity.
- Adding NaHCO₃ to LA solution → ↓extracellular acidity → ↑extracellular unionized form → ↑LA crossing → ↑activity (rapid onset).

Intracellular pH

- Carbonated solutions of LA have a rapid onset since they are saturated with CO₂ which readily enters nerve cells → ↑ intracellular acidity → ↑ intracellular ionized (active) form available to block Na⁺ channel.

2- Addition of vasoconstrictors: prolongs duration of action.

- LAs (except cocaine) induce VD → ↑absorption → termination of effect & ↑ risk of systemic toxicity.
- Vasoconstrictors are added to LA (except cocaine) to ↓ absorption → ↑ duration & ↓ systemic toxicity.

Precautions

- Vasoconstrictors are CI in anesthesia of fingers, toes & nose → gangrene.
- Felypressin is preferred in cardiac patients (no effect on HR & BP).

- Local anesthesia is also not preferred in infections to avoid spread of infection.

Adverse Effects & Toxicity (□ systemic absorption or accidental IV injection)

1. CNS:

- Low concentration:
 - Sleepiness- restlessness- numbness - metallic taste.
- High concentration (stimulation followed by depression)
 - Tremors - convulsions⁶⁷ - respiratory depression - coma - death.

3. Neurotoxicity: due to the direct local effect of high concentration of LA injected close to nerve trunks or spinal cord.

4. CVS: hypotension (due to vasodilation) & bradycardia.

- Bupivacaine is extremely cardiotoxic in high doses.

5. Allergy: with esters that are derivatives of PABA e.g. procaine.

6. Side effects of vasoconstrictor added to LA (↑ BP & arrhythmia).

Uses & Administration

1. Surface anesthesia (for minor surgeries):

- Applied to skin & mucous membranes of nose, mouth & cornea as a solution, jelly or cream.

2. Infiltration (for minor surgery):

- Injected sc & in submucosal tissues to reach nerve branches & terminals.

3. Nerve block (for dentistry & surgery):

- Injected close to nerve trunks (e.g. dental nerves - brachial plexus).

4. IV regional anesthesia

5. Spinal anesthesia:

- Injected in subarachnoid space below L2, acts on spinal roots & spinal cord.
- Used for surgery of abdomen, pelvis & legs when general anesthesia is contraindicated.

Side effects:

- Headache (due to CSF leakage & traction on sensitive structures, avoided by use of pencil point needles).
- Hypotension (sympathetic nerve block).
- Spinal root injury.
- Infection.

6. Epidural anesthesia:

- Injected outside the dura, blocks spinal roots.
- Same indications as spinal anesthesia with ↓ risk of side effects.
- Commonly used in obstetrics for painless labor.

Skeletal muscle relaxants

Drugs affecting skeletal muscle tone could be classified into 2 major divisions:

1. Neuromuscular blockers (mainly used as adjuncts to anesthetics).
2. Spasmolytic drugs (mainly used in spastic disorders of skeletal muscles).

Neuromuscular blockers (NMBs)

They are classified into 2 groups:

1. Nondepolarizing NMBs → prototype: d-tubocurarine.
2. Depolarizing NMBs → prototype: succinylcholine.

Therapeutic Uses of NMBs

1. Adjuncts to general anesthesia: induce muscle relaxation → facilitating incision, decreasing cough & laryngospasm & allowing reduction of the dose of the general anesthetic (nondepolarizing NMBs).
2. To assist mechanical ventilation (nondepolarizing NMBs)
3. Facilitation of endotracheal intubation (succinylcholine is 1st choice).
4. Electroconvulsive therapy: Control convulsions → ↓ pain & injury (succinylcholine is 1st choice).

Nondepolarizing (Competitive) Neuromuscular Blockers

D-Tubocurarine (prototype)

- ✓ Produces flaccid paralysis lasting more than 35 min (long-acting).
- ✓ Small muscles of face, eye and neck are affected first and diaphragm last.
- ✓ Recovery occurs in the reverse order (diaphragm first).
- ✓ Effects are antagonized by: Neostigmine
- ✓ Effects are potentiated by: Anesthetics e.g. halothane, ether and Antibiotics e.g. aminoglycosides.

Adverse Effects and Precautions

1. Histamine release:
 - Bronchoconstriction (CI: bronchial asthma).
 - Allergy (CI: allergic patients).
 - Hypotension
2. Ganglion blockade → hypotension.
3. CI in renal disease (clearance depends on renal excretion).

Toxicity of Competitive Neuromuscular Blockers

Respiratory muscle paralysis and hypoxia; treated by:

1. Artificial respiration.

2. Neostigmine, preceded by atropine to prevent bradycardia & cardiac arrest.

Newer NMBs:

- ❖ More potent than curare (except rocuronium) with no ganglion blockade & less (atracurium) or no histamine (HI) release.

1. Pancuronium (long acting)

- Avoid in renal & CV diseases (excreted renally; vagolytic effect → ↑HR).

2. Atracurium (intermediate duration; used for short procedures)

- May be given in renal or liver disease

Cisatracurium: less histamine release than atracurium → fewer side effects.

3. Vecuronium (intermediate duration; used for short procedures)

- May be given in renal but not in liver diseases (clearance is mainly hepatic), preferred in CV diseases.

4. Rocuronium (intermediate duration; 20-35 min)

- Similar to vecuronium.
- Rapid onset of action → alternative to succinylcholine for endotracheal intubation.

5. Mivacurium (short acting; 10- 20 min)

- Hydrolyzed by pseudo ChE (↓enzyme in renal disease → prolongs effect).
- Slower onset than succinylcholine; if dose is increased to speed onset → ↑ histamine release.

6. Gantacurium (rapid onset, very short duration of action)

- Profile similar to succinylcholine → used for endotracheal intubation & mechanical ventilation, its action can be reversed with cysteine.

Reversal of effects of neuromuscular blockers post operatively

1. Neostigmine: preceded by atropine or glycopyrrolate.
2. Sugammadex:
 - Advantages over neostigmine: faster reversal with fewer side effects (not preceded by anti-muscarinics, avoiding their troublesome side effects).
3. Cysteine: reverses the action of gantacurium

Depolarizing Neuromuscular Blockers

Succinylcholine

Mechanism of Action: Initial fasciculations (transient twitches)

- Phase I: Depolarization block
- Phase II: Desensitization block (antagonized by neostigmine)

Adverse Effects and Contraindications (CI)

1. Succinylcholine apnea

- ❖ Genetic abnormality of pseudo ChE (or ↓ pseudo ChE due to liver disease or malnutrition) → failure of succinylcholine breakdown → prolonged respiratory muscle paralysis → apnea.
- ❖ Management: Support ventilation
 - Phase I block → blood transfusion (to supply enzyme).
 - Phase II block → neostigmine preceded by atropine.

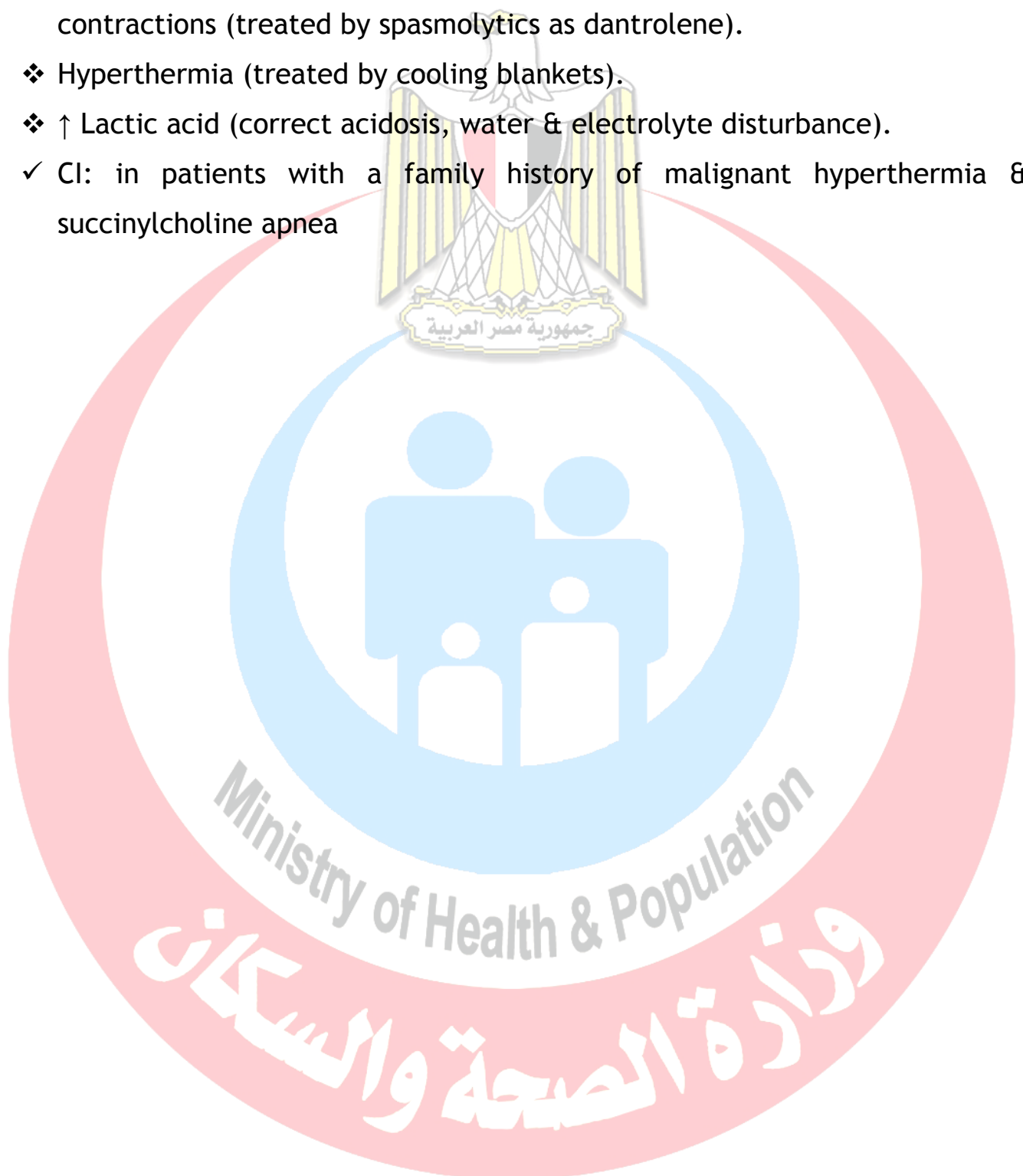
2. Fasciculations →

- a. Postoperative muscle pain (muscle damage due to unsynchronized contractions → CI: extensive muscle trauma).
- b. ↑ IOP → CI: narrow-angle glaucoma and penetrating eye injuries.
- c. ↑ Intra-gastric pressure → vomiting with aspiration of gastric contents.
- d. Hyperkalemia → cardiac arrest → CI: burns & trauma (↑ K⁺ outflux).

3. Bradycardia.

4. Malignant hyperthermia (genetic defect)

- ❖ -Skeletal muscles fail to sequester Ca^{2+} in sarcoplasmic reticulum following administration of succinylcholine & halothane \rightarrow \uparrow Muscle contractions (treated by spasmolytics as dantrolene).
- ❖ Hyperthermia (treated by cooling blankets).
- ❖ \uparrow Lactic acid (correct acidosis, water & electrolyte disturbance).
- ✓ CI: in patients with a family history of malignant hyperthermia & succinylcholine apnea



Chapter 3

Opioid analgesics

Opioid Analgesics

Morphine

Narcotic Analgesics:

- It include opium such as morphine, pethidine and fentanyl .
- These substances have similar pharmacological properties.

Dependence & Tolerance:

- Remember that all drugs of this group may lead to addiction.
- Psychological & physical dependence & tolerance develop even when using clinical doses.
- Tolerance usually develops because the patient requires shorter periods of time between doses or larger doses for relief of pain.

Effects of narcotic analgesics:

1- On CNS:

- Alteration of pain perception (analgesia)
- Euphoria
- Drowsiness - Change in mood
- Deep sleep

2- Depress respiration: over dose leads to respiratory arrest death.

3- Depress cough reflex: codeine in small doses is used as antitussive.

4- Nauseant & emetic effect stimulate the chemoreceptor trigger zone (CTZ).

5- Morphine induce vasodilation and hypotension.

6- Pupillary constriction (the most obvious sign of dependence).

7- Decreases the peristaltic motility constipation (some types used in Treatment of diarrhea)

Uses:

- Intrathecally, epidurally, orally or I.V. infusion for acute or chronic pain.
- Preoperative medication.
- To facilitate induction of anesthesia or to decrease the dose of anesthesia.
- Diarrhea
- Antitussive.

Contraindications:

- It is given epidural or intrathecal, if infection is present at injection site.
- In patients on anticoagulant therapy
- Bleeding disorders.
- If patients have received parenteral corticosteroids within the past 2 weeks.
- Asthmatic conditions
- Hepatic cirrhosis
- Children less than age of 6 months.

Side effects:

- Respiratory depression , apnea, dizziness
- Euphoria headache
- Insomnia
- Nausea, vomiting, constipation, dry mouth
- Skin rashes,
- Urinary retention
- Decreased libido.

Nursing considerations:

- ✓ Use supportive nursing measures as relaxation techniques to relieve pain before using narcotics.
- ✓ Explore the source of pain, use non-narcotic analgesia if possible.

- ✓ Administer the medication when needed, prolonging the medication administration will decrease the effect of the medication.
- ✓ Monitor vital signs & mental status.
- ✓ Monitor Respiratory rate (drug may lead to respiratory depression).
- ✓ Monitor blood pressure (hypotension may occur)
- ✓ Monitor pulse rate (if 60\m withhold the drug).
- ✓ Watch for constricted pupils. Document it and notify the physician.
- ✓ Monitor bowel function, since drug may cause constipation .
- ✓ Encourage patient to empty bladder every 3-4 hrs (since drug may cause urinary retention).
- ✓ Inform the family that the drug may become habit forming and leading to addiction.
- ✓ Document any history of asthma or other contraindications.
- ✓ Have emergency equipment and narcotic antagonist available.

Pethedine Hydrochloride

- It has no antitussive effect.
- The duration of action is less than that of morphine
- It can be given as I.V. continuous infusion on a concentration of 1 mg\ml.
- It also can be given IV slowly, and should be diluted in a concentration of 10mg/ml.

Uses:

Like morphine but added to it:

- ✓ Used in Obstetric preanesthetic medication.
- ✓ Treatment of biliary colic

Add. Contraindications:

- ✓ Induce Convulsive states.
- ✓ Transient hallucinations

Tramadol hydrochloride

Action:

- A centrally acting synthetic analgesic compound not chemically related to opiates. Thought to bind to opioid receptors and inhibit reuptake of norepinephrine and serotonin.

Indications & dosages

- Moderate to moderately severe pain

Adverse reactions

- CNS: dizziness, vertigo, headache, CNS stimulation, anxiety, confusion, euphoria, nervousness, sleep disorder, seizures, malaise, visual disturbances.
- CVS: vasodilation.
- GIT: nausea, vomiting, constipation, dyspepsia, dry mouth, diarrhea, abdominal pain, anorexia, flatulence.
- Renal: urine retention, urinary frequency, menopausal symptoms, proteinuria.
- Respiratory: respiratory depression.
- Skin: pruritus, diaphoresis, rash.

Contraindications & cautions

- ✓ Contraindicated in patients hypersensitive to drug or other opioids
- ✓ Breast-feeding women
- ✓ Patient on alcohol, hypnotics, centrally acting analgesics, opioids, or psychotropic drugs.
- ✓ Use cautiously in patients at risk for seizures or respiratory depression

- ✓ In patients with increased intracranial pressure or head injury, acute abdominal conditions, or renal or hepatic impairment; or in patients with physical dependence on opioids.

Nursing considerations

- ✓ Reassess patient's level of pain at least 30 minutes after administration.
- ✓ Monitor CV and respiratory status. Withhold dose and notify doctor if respirations decrease or rate is below 12 breaths/minute.
- ✓ Monitor bowel and bladder function. Anticipate need for laxative.
- ✓ For better analgesic effect, give drug before onset of intense pain.
- ✓ Monitor patients at risk for seizures.
- ✓ In the case of an overdose, naloxone may also increase risk of seizures.
- ✓ Monitor patient for drug dependence.
- ✓ Withdrawal symptoms may occur if drug is stopped abruptly. Reduce dosage gradually.
- ✓ Caution ambulatory patient to be careful when rising and walking.
- ✓ Warn outpatient to avoid driving and other potentially hazardous activities that require mental alertness until drug's CNS effects are known.

Naloxone Hydrochloride

Uses:

- ✓ Respiratory depression induced by morphine and other narcotics
- ✓ Drug of choice when the depressant drug is unknown.
- ✓ Diagnosis of acute opiate overdose

Side effects:

- ✓ Nausea, vomiting, sweating, hypertension, tremors.
- ✓ If used postoperatively: tachycardia, pulmonary edema, hypo or hypertension.

Chapter 4

Vasopressors – Inotropes

Objectives

- Identify the different groups of vasopressor and inotropic drugs
- Understand the mechanism of actions, indications, side effects, drug interactions and possible precautions of different groups of vasopressor and inotropic drugs

Common Vasopressors and inotropes:

- ✓ Adrenergic drugs
 - Norepinephrine (nor adrenaline)
 - Epinephrine (adrenaline)
 - Phenylephrine
- ✓ Dopamine
- ✓ Dobutamine
- ✓ Digoxin

Adrenergic drugsEffects of adrenergic drugs:

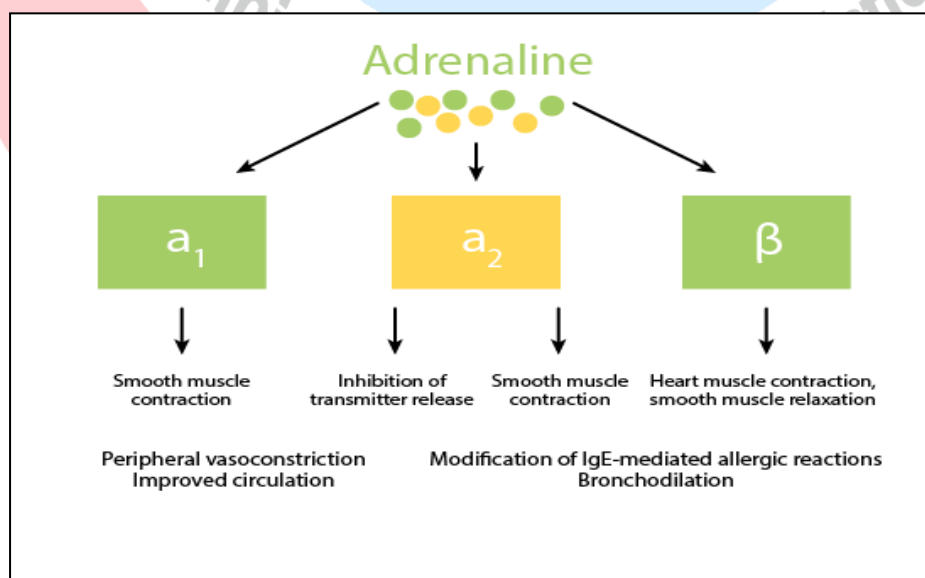
1. **Heart:** increase Heart rate, increase force of contraction, increase cardiac output.
 - **Uses:** cardiogenic shock, bradycardia, resuscitation, heart block.

2. **Blood vessels:** - Systemic vasoconstriction increase blood pressure and decrease blood supply to abdominal viscera & skin.
 - **Uses:** Hypotension, nasal decongestion, nose bleeds, migraine, headache, allergic reactions.
3. **GIT:** constriction of sphincters, decrease motility of GIT & urinary bladder
4. **Lungs:** Relaxation of muscles of bronchial tree.
 - **Uses:** Bronchial asthma
5. **Eyes:** mydriasis and decrease intraocular pressure
6. **CNS:** Respiratory stimulation, wakefulness.
7. **Metabolism:** increase in glycogenesis (sugar metabolism). Increase in lypolysis (release of fatty acids)

Epinephrine (adrenaline)

Mechanism of action

- Agonist on alpha 1 and 2 receptors induces vasoconstriction and elevation of blood pressure
- Agonist on beta 1 and 2 induced increase in heart contraction and rate and bronchodilation



Indications:

1. Local Anesthesia
2. Anaphylactic shock
3. Cardiac Arrest
4. Asthma
5. Arrests bleeding
6. Open Angle glaucoma



Side effects:

- Fatal ventricular fibrillation.
- Cerebral hemorrhage
- Urinary retention
- Headache
- Necrosis at injection side,
- Blurring of vision, photophobia.



Nursing considerations:

- Closely monitor patients receiving I.V. epinephrine infusion.
- Note the patient for signs of shock "loss of consciousness, clammy, cold skin, cyanosis.... etc.).
- Briskly massage site of S.C. or I.M. injection to hasten the action of the drug.
- Do not inject epinephrine into the buttocks or any other part of your body.
- Never administer 1: 100 solution IV. Use 1: 1000 mg sol. For I.V. use.

Norepinephrine

Mechanism of action:

Acts on alpha 1&2 ($\alpha 1$ &2) - beta 1 ($\beta 1$) receptors:

- α effect → marked vasoconstriction → marked increase in blood pressure or gangrene.
- $\beta 1$ effect → positive inotropic (increase heart contraction) & chronotropic effect (increase heart rate) but ,
- Marked increase BP → reflex vagal bradycardia masks its direct effect.

Clinical uses: Septic shock, carcinogenic shock (BP < 70 mmHg)

Phenylephrine

Action: It's an alpha 1 ($\alpha 1$) agonist induces vasoconstriction of blood vessels.

Uses:

- Hypotensive states to increase low blood pressure.
- Phenylephrine is also a nasal decongestant that provides relief from nasal discomfort caused by colds, allergies.

Precaution: should not be given in hypertensive patient as an OTC drug

Dopamine

Mechanism of action

- Low dose → stimulate dopamine 1 receptors → increase renal blood flow
- Intermediate dose → $\beta 1$ receptors stimulation → resulting in increasing myocardial contraction, cardiac output.
- High dose → alpha ($\alpha 1$) receptors stimulation → vasoconstriction of blood

vessels up to necrosis

Indications:

- Acute heart failure with renal impairment
- Iv infusion 2ug-20ug/kg/min gradually

Side effects:

- Hypertension
- Arrhythmia
- Necrosis at site of injection in case of extravasation



Nursing considerations:

- Drug must be diluted before use and administer through a central line or a big vein.
- Do not add dopamine to NaHCO₃ or other alkaline I.V. solutions since the drug is inactivated in alkaline solution.
- Administer only by IV infusion neither (Not IV bolus nor IM)
- Check I.V. site for extravasation. Available for hospital use only



Dobutamine



Mechanism of action

- It's a selective beta 1 receptor agonist
- Increase cardiac contractility and heart rate

Uses:

- In treatment of acute heart failure with normal kidney function
- Cardiogenic shock

Monitoring:

- Breathing, blood pressure, oxygen levels, and other vital signs should be watched closely while you are receiving dobutamine.

Adverse effect:

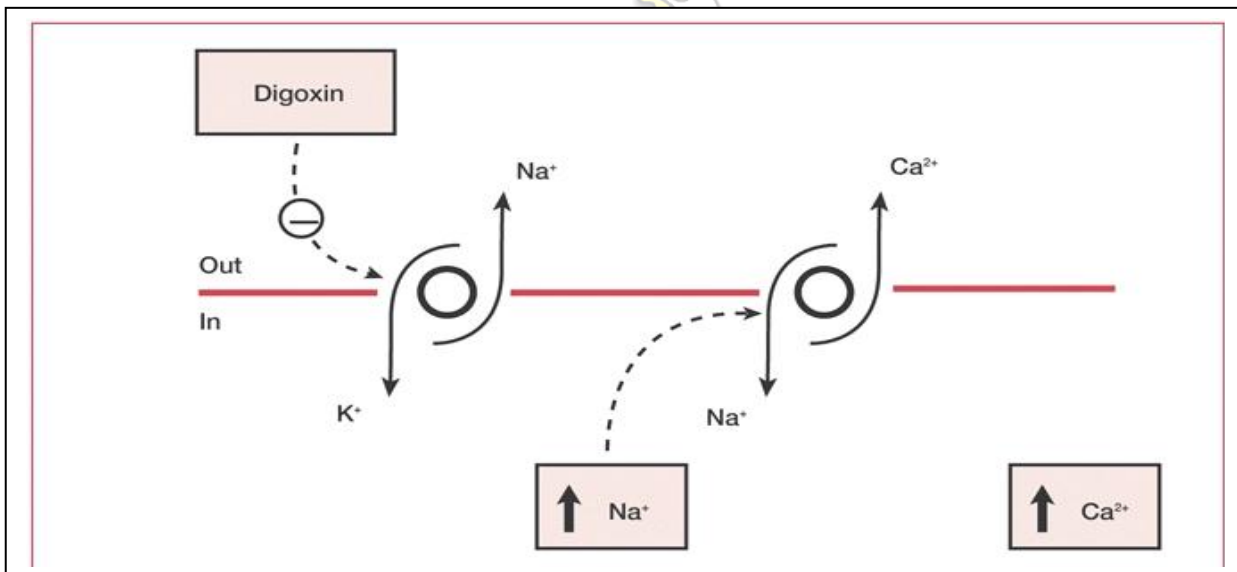
- Tachycardia & arrhythmia & angina pain

Digoxin

Mechanism of Action:

- They increase the force of myocardial contractions (positive inotropic).
- It increases the contractility of the heart muscle by minimizing the movement of Na⁺ and K⁺ ions and increasing the release of Ca⁺⁺ ions in the myocardial cells.
- It decreases the heart rate
- They are primarily excreted through the kidneys.

- The initial dose is the larger dose (the loading dose)
- The subsequent doses are referred to as (Maintenance doses).



Results:

- Decrease in venous pressure.
- Reduce heart size.
- Marked diuresis and decreasing edema.

Indications:

- Congestive heart failure (C.H.F).
- Cardiac arrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia).

Contraindication:

1. myocardial infarction
2. rheumatic heart disease
3. partial heart block
4. Given with caution for elderly and people who have kidney failure

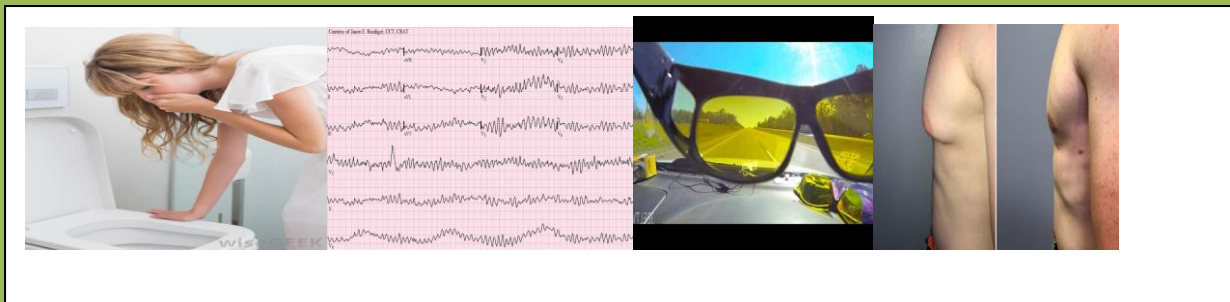
Drug interaction with digoxin

- ❖ Furosemide (Lasix): it increase K⁺ loss and increase the chance for digoxin toxicity.

Digoxin toxicity

Symptoms:

1. GIT: Anorexia ,Nausea, Vomiting ,Diarrhea (early)
2. CVS: cardiac arrhythmias (tachy or bradyarrhythmias)
3. CNS: hallucination ,confusion- yellow & green vision
4. Gynecomastia



Treatment of digitalis toxicity:

1. Stop digitalis and K losing diuretics
2. KCL if serum K is low (<3.5 mmol/L)
3. Lidocaine or phenytoin for ventricular arrhythmias
4. Atropine : in bradycardia and heart block
5. Digibind (fab fragment):help its excretion through kidney (in fatal toxicity)
6. Plasmapheresis: in renal dysfunction when Digibind are contraindicated

Predisposing factors for digitalis toxicity:

1. K loss (hypokalemia) which results from: diuretics and poor K⁺ intake.
2. Pathological conditions:
 - ✓ Liver disease: they decrease metabolism and therefore increase digitalis level.
 - ✓ Kidney disease: they decrease the excretion of drug and therefore increase digoxin levels.

Nursing considerations:

- ✓ Check doctor's order, medication record and bottle label accurately.
- ✓ Observe & monitor for evidence of bradycardia or arrhythmia.
- ✓ Measure intake and output accurately.
- ✓ Weigh the patient in daily basis.
- ✓ Pulse should be checked by 2 nurses.
- ✓ Provide the patient with food high in potassium as banana, orange.
- ✓ Monitor serum digoxin level.
- ✓ Elderly people should be assessed for early signs of toxicity.
- ✓ Teach patients that bradycardia, nausea, vomiting, diarrhea, appetite loss, and visual disturbances could be early signs of toxicity.
- ✓ Teach patient if heart rate is less than 60/minute to hold the medication and see the doctor.

Chapter 5

Vasodilators – anti arrhythmic drugs

Objectives

Identify the different groups of vasodilators drugs. Understand the mechanism of actions, indications, side effects, drug interactions and possible precautions of different groups of vasodilators drugs and anti-arrhythmic drugs.

Vasodilators

Common Vasodilators

The following are commonly prescribed vasodilators:

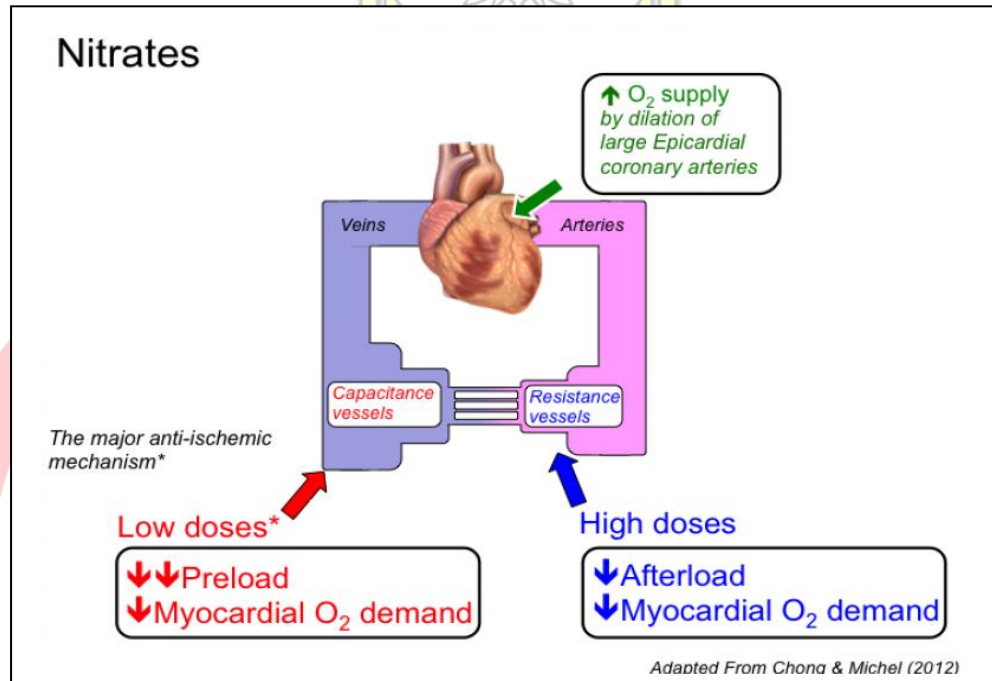
- Nitrates
- Calcium channel blockers
- ACEIs (angiotensin converting enzyme inhibitors)
- Na Nitroprusside

Nitrates

Mechanism of Action:

- direct relaxation of blood vessels and smooth muscles
 - ✓ Vasodilatation lead to increase O₂ requirements.

- Relaxation of smooth muscles of coronary arteries
- Relaxation of arteries and veins BP workload in the heart.



Uses:

- ✓ Prophylaxis and treatment of acute angina pectoris.
- ✓ Treatment of chronic angina pectoris.
- ✓ Treatment of hypertension associated with myocardial infarction or Congestive heart failure.

Contraindications:

- ✓ with sildenafil leads to sever hypotension
- ✓ Severe anemia.
- ✓ Hypotension.
- ✓ Cerebral hemorrhage.

Side effects:

- ✓ Headache, syncope, dizziness.
- ✓ Postural hypotension, transient flushing, and palpitation
- ✓ Topical application may lead to dermatitis.

Precautions:

1. Drug stored in tightly closed container
2. Patient should sit while taking drug and to lie down if syncope occur
3. Remove sl tablet on relief
4. Allow nitrate free interval 8hours/day to avoid tolerance
5. Avoid sudden stoppage to avoid rebound angina
6. Take sublingual tablets 5-15 minutes prior to any situation likely to cause anginal pain
7. If anginal pain is not relieved on 3 consecutive tablet on 5min interval consider myocardial infarction

Calcium channel blockers

Mechanism of action

These agents inhibit the influx of calcium through the cell membrane resulting in a depression of automatically and conduction velocity in both smooth and cardiac muscles leading to:

- ✓ Decrease myocardial contractility.

- ✓ Inhibit spasm of coronary arteries leading to dilatation.
- ✓ Peripheral vasodilatation leading to peripheral resistance.
- ✓ Decrease SAN automatically and conduction leading to heart rate.

Preparations:

- ✓ Amlodipine & Nifedipine
 - **Side effects:** pulmonary and peripheral edema, myocardial infarction, hypotension, dizziness, palpitation, headache, muscle cramps
- ✓ Verapamil & diltiazem
 - **Side effects:** AV block, bradycardia, headache, dizziness, abdominal cramps, blurring of vision, and edema.

Contraindications & cautions

- ✓ Contraindicated in patients hypersensitive to drug.
- ✓ Use cautiously in patients receiving other peripheral vasodilators, especially those with severe aortic stenosis, and in those with heart failure.
- ✓ Because drug is metabolized by the liver, use cautiously and in reduced dosage in patients with severe hepatic disease.

Nursing considerations

- ✓ Monitor blood pressure frequently during initiation of therapy. Because drug-induced vasodilation has a gradual onset, acute hypotension is rare.
- ✓ Notify doctor if signs of heart failure occur, such as swelling of hands and feet or shortness of breath.

- ✓ Teach patient to continue taking drug, even when feeling better.
- ✓ Grapefruit juice may increase drug level and adverse reactions.
Discourage use together.

Sodium nitroprusside

Mechanism of action:

- Arteriolar and venular VD

Uses:

- hypertensive emergency
- Sever acute heart failure with high blood pressure

Side effects:

- Sever hypotension
- Cyanide toxicity in liver dysfunction
- Thiocyanate toxicity in renal dysfunction

Precautions:

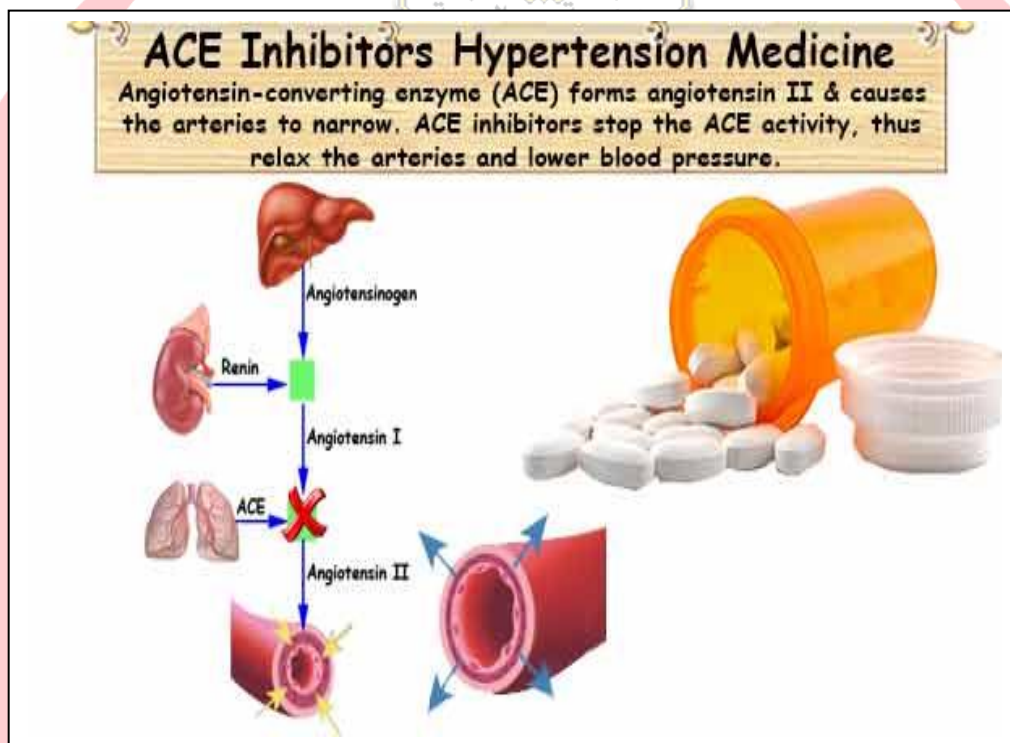
- Given slowly IV infusion
- Should be freshly prepared and covered with opaque foil
- Monitor BP (avoid drop in BP <95/70)
- avoid prolonged administration in liver & kidney dysfunction



Angiotensin converting enzyme inhibitors (captopril)

Mechanism of Action:

- ✓ Captopril is a highly specific competitive inhibitor of angiotensin I converting enzyme.
- ✓ The enzyme is responsible for the conversion of angiotensin I to angiotensin II which decrease BP.
- ✓ Reduce peripheral arterial resistance.
- ✓ Decrease aldosterone secretion which works to increase level of serum potassium



Uses:

- ✓ Hypertension.
- ✓ In combination with diuretics and digitalis in the treatment of CHF.

Contraindication:

- ✓ Hypersensitivity

- ✓ Renovascular disease
- ✓ Pregnancy.

Side effects:

- ✓ Skin rash
- ✓ Loss of taste
- ✓ Neutropnea
- ✓ Teratogenicity

- ✓ Nausea, vomiting,
- ✓ Hypotension
- ✓ Proteinuria
- ✓ Hyperkalemia.

Nursing considerations:

- ✓ In case of overdose, give normal saline to restore BP.
- ✓ Should not be discontinued without Dr. Order.
- ✓ Obtain baseline hematological studies, liver & renal functions tests prior to beginning the treatment.
- ✓ Observe patient closely for hypotension 3 hours after the initial dose.
- ✓ In case of hypotension, place client in supine position and give IV saline infusion.
- ✓ Withhold potassium sparing diuretics and consult with physician (Hyperkalemia may occur).
- ✓ Take captopril 1 hour before meal or on an empty stomach.
- ✓ Report skin rash, heartburn, and chest pain to physician.
- ✓ Explain to patient that he may develop loss of taste for 2-3 months, if it persist, notify the physician.

Antiarrhythmic drugs

Lidocaine

Indication:

- ✓ Acute ventricular arrhythmias as which follow myocardial infarction or cardiac surgeries
- ✓ Digoxin induced arrhythmia

Contraindications:

- ✓ Hypersensitivity
- ✓ Heart block.

Side effects:

- ✓ Cardiac: may precipitate cardiac arrest
- ✓ CNS: dizziness & convulsion

Dosage:

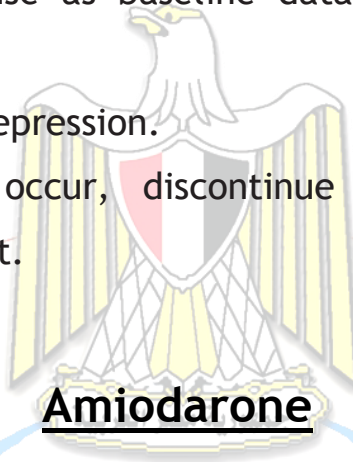
- ✓ Iv bolus → then maintenance dose by iv infusion (has very short half-life)
- ✓ Not effective orally due to extensive 1st pass metabolism

Nursing considerations:

- 2. Make certain that vials state “for cardiac arrhythmias”.
- 3. Use 5% dextrose solution to prepare drug (stable for 24 hours).
- Assess for history of hypersensitivity.



- Use electronic infusion device to regulate the infusion of the drug.
- Obtain vital data to use as baseline data to evaluate response to treatment.
- Assess for respiratory depression.
- If adverse reactions occur, discontinue infusion & prepare for emergency management.



Indications:

- Life-threatening arrhythmias resistant to other antiarrhythmic

Kinetics:

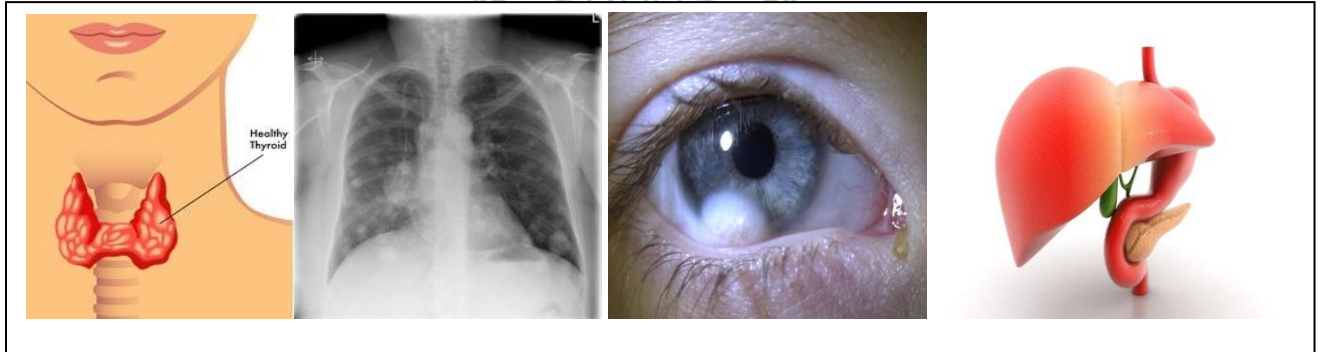
- long half-life 35-103 day
- start with loading dose followed by maintenance dose oral or IV
- delayed onset: 1-3 weeks
- displace digoxin from binding sites → increase its toxicity



Side effects:

1. Cardiac : bradycardia & heart block
2. Thyroid dysfunction
3. Pulmonary fibrosis
4. Eye: corneal opacities

5. Increase liver enzymes
6. Photosensitivity



Precautions:

- Amiodarone increases the risk of digoxin toxicity in patients also taking digoxin.
- Monitor blood pressure, heart rate, and rhythm for changes.
- Monitor for signs of pulmonary toxicity (dyspnea, nonproductive cough, and pleuritic chest pain).

Beta blockers

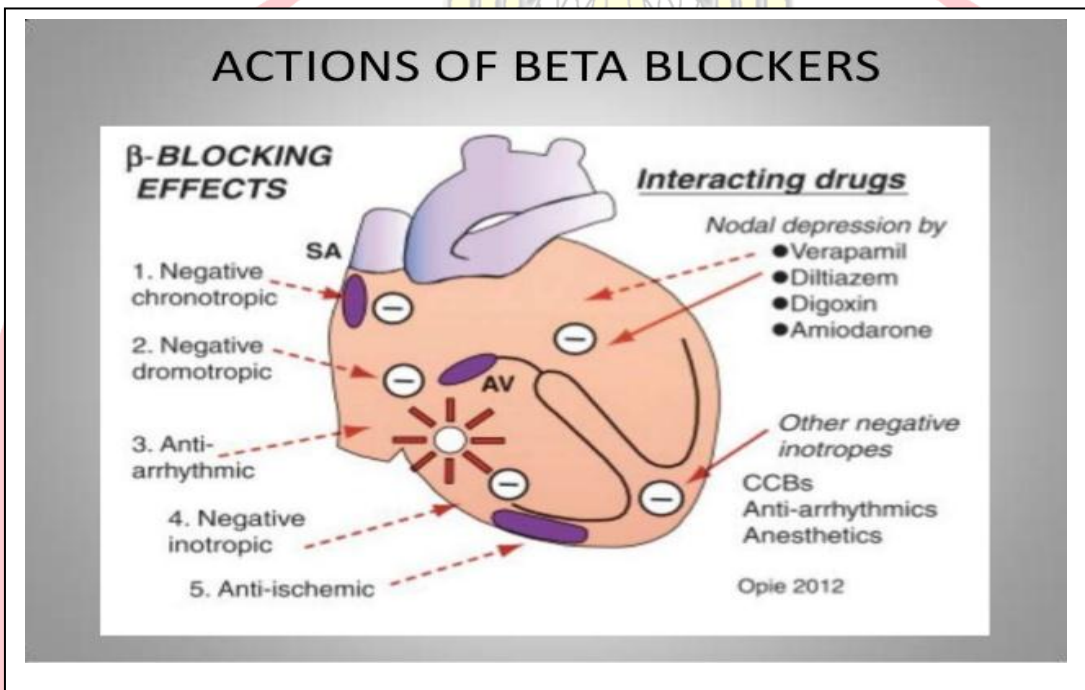
Preparations

Propranolol: Inderal

Others, Esmolol- carvidolol- bisoprolol -nebivolol -metoprolol

Action:

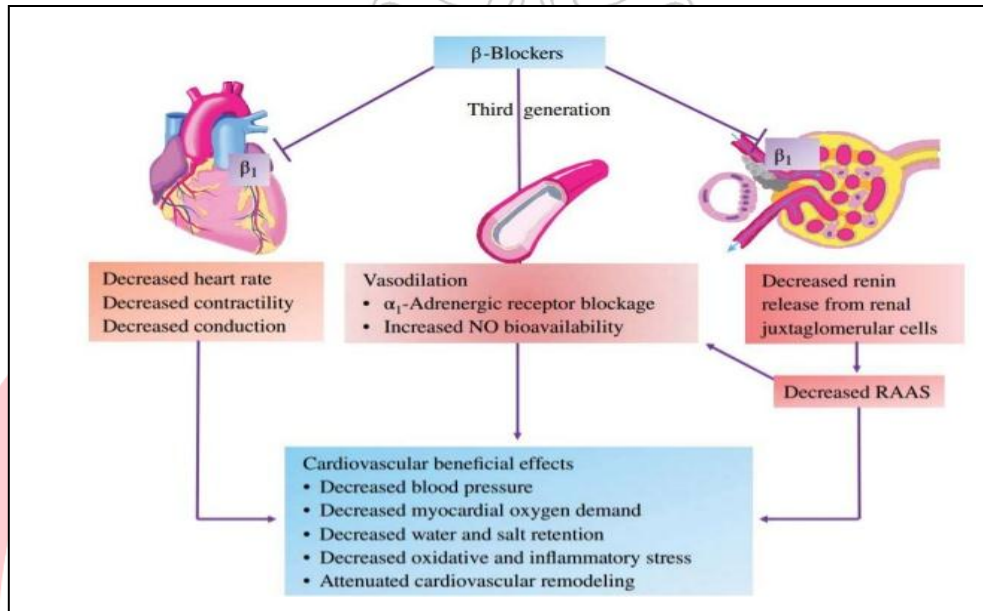
- Blocking of Beta 1 receptors → decrease heart rate, myocardial contractility and cardiac output, blood pressure.
- Blocking of Beta 2 receptors → bronchospasm and vasoconstriction.
- These drugs could be selective (working on one receptor such as β_1 selective drugs (Atenolol) or it could be nonselective (such as Propranolol)



Uses:

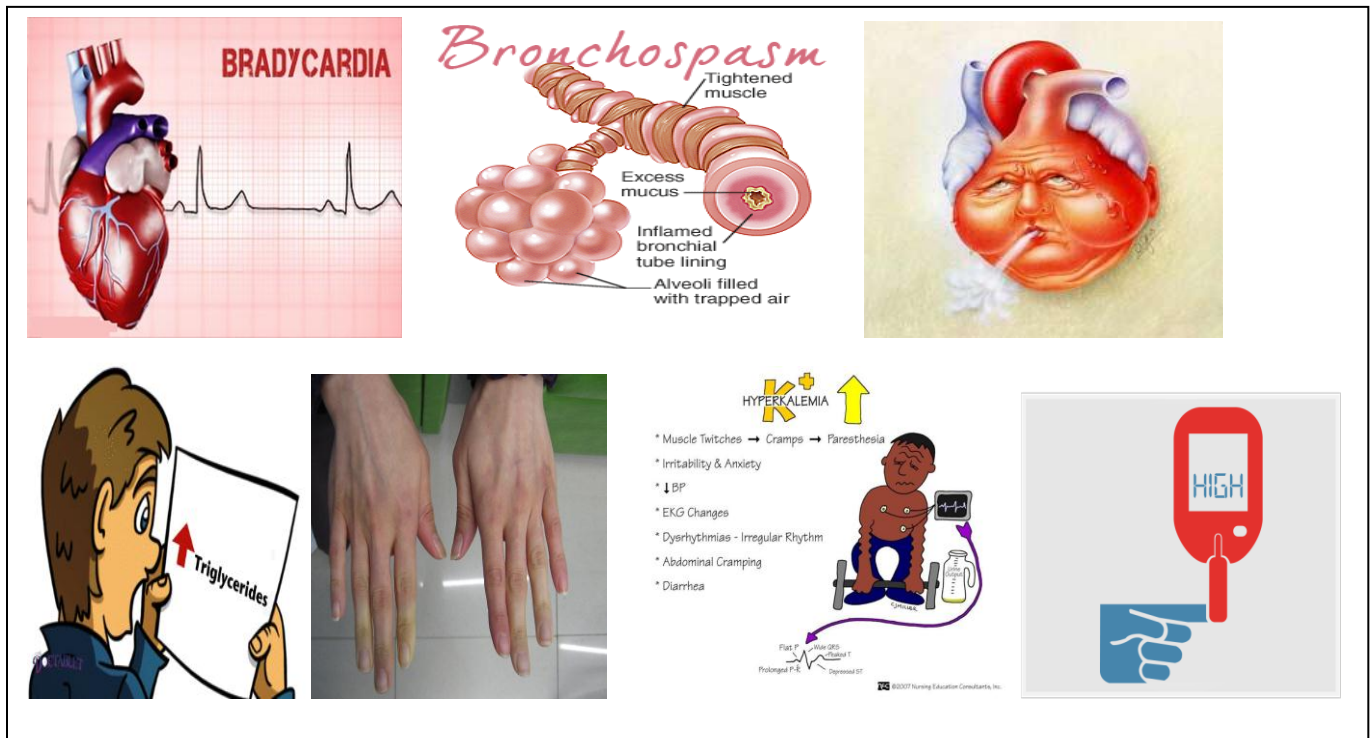
- Hypertension
- Angina pectoris.
- Heart failure.
- Cardiac arrhythmias.
- Myocardial infarction.
- Prophylaxis of migraine & esophageal varices
- Thyrotoxic crisis.

- Glaucoma.
- Tremors



Side effects and Contraindications:

- Bradycardia, heart block
- Heart failure & hypotension
- Bronchospasm (contraindicated in bronchial asthma)
- Hyperglycemia & increase triglycerides
- Cold extremities (contraindicated in peripheral vascular disease, vasospastic angina)
- Hyperkalemia (take care in renal impairment and diabetes mellitus)
- Sudden withdrawal → angina
- Prolong insulin induced hypoglycemia
- Sexual dysfunction



Treating overdose:

- Inducing vomiting, gastric lavage- Artificial respiration.
- Give atropine sulfate 0.6 mg (up to 3 mg)
- Intravenous fluids
- Adrenaline or dopamine to increase blood pressure.



Chapter 6

Antibiotics – Intravenous Antifungal

Objectives

- ❖ Identify and understand the pharmacological actions, indications, route of administration, common adverse effects, drug interactions, precautions during administration, common contraindications and specific antidote of commonly used antibiotics and antifungal drugs.

Antibiotics

- ❖ Antibacterial drugs, also known as antibiotics (drugs that inhibit the growth of bacteria), are used mainly to treat systemic (involving the whole body rather than a localized area) bacterial infections.

The antibacterial include:

- Aminoglycosides
- Penicillins
- Cephalosporins
- Vancomycin
- Carbapenems & Monobactams
- Fluoroquinolones

Aminoglycosides

Preparations:

Amikacin sulfate - gentamicin sulfate - neomycin sulfate - tobramycin sulfate.

Pharmacokinetics

- Aminoglycosides are absorbed poorly from the GI tract.
- They are usually given parenterally.

Distribution

- Aminoglycosides are distributed widely in extracellular fluid.
- They readily cross the placental barrier, but don't cross the blood brain barrier.

Metabolism and excretion

- Aminoglycosides aren't metabolized. They're excreted primarily unchanged by the kidneys.

Pharmacodynamics

- Aminoglycosides act as bactericidal drugs

Pharmacotherapeutics

- Infections caused by gram-negative bacilli
- Serious nosocomial (hospital-acquired) infections, such as gram-negative bacteremia, peritonitis and pneumonia in critically ill patients.
- Urinary tract infections (UTIs)
- Infections of the central nervous system (CNS) and the eye (treated

with local instillation).

N.B.

- ✓ Aminoglycosides are used in combination with penicillins to treat gram-positive organisms, such as staphylococcal or enterococcal
- ✓ Aminoglycosides are inactive against anaerobic bacteria.

Adverse Effects

1. Nephrotoxicity
2. Ototoxicity
3. Neuromuscular paralysis (inhibits Acetylcholine release)
4. Allergy

Penicillin

- ❖ Penicillin remain one of the most important and useful antibacterial, despite the availability of numerous others.

Pharmacokinetics

- After oral administration, penicillins are absorbed mainly in the duodenum and the upper jejunum of the small intestine.
- Most penicillins should be given on an empty stomach (1 hour before or 2 hours after a meal) to enhance absorption.
- Penicillins that can be given without regard to meals include amoxicillin, and amoxicillin/clavulanate potassium.

Distribution

- Penicillins are distributed widely to most areas of the body, including the lungs, liver, kidneys, muscle, bone, and placenta.
- High concentrations also appear in urine, making penicillins useful in treating UTIs.

Metabolism and excretion

- Penicillins are metabolized to a limited extent in the liver to inactive metabolites and are excreted 60% unchanged by the kidneys.

Pharmacodynamics

- Penicillins are usually bactericidal in action.

Pharmacotherapeutics

- Cover gram-positive, gram-negative, and anaerobic organisms.
- Penicillin is given by I.M. injection when oral administration is inconvenient
- Long acting penicillin are relatively insoluble, they must be administered by the I.M. route.

Adverse Effects (one of the safest antibiotics)

1. Hypersensitivity (most important): Cross-allergy may occur between beta lactam antibiotics.
2. Diarrhea: ampicillin.
3. Neurotoxicity: seizures if injected intrathecally or with high blood level.

Cephalosporins

- ✓ First-generation: cefadroxil and cephalexin monohydrate.
- ✓ Second-generation: cefoxitin and cefuroxime
- ✓ Third-generation: cefotaxime and ceftriaxone sodium.
- ✓ Fourth-generation: cefepime hydrochloride.

N.B.

- Because penicillins and cephalosporins are chemically similar cross sensitivity occurs in 10% to 15% of patients. This means that someone who has had a reaction to penicillin is also at risk for a reaction to cephalosporins.

Pharmacokinetics

- ✓ Many cephalosporins are administered parenterally and others are given orally.

Distribution

- ✓ Cefuroxime (second-generation) and the third-generation drugs cefotaxime, ceftriaxone cross the blood-brain barrier after I.V. or I.M. administration.

Excretion

- ✓ All cephalosporins are excreted primarily unchanged by the kidneys with the exception of ceftriaxone, which is excreted in stool via bile.

Pharmacotherapeutics

- **First-generation** : acts primarily against gram-positive organisms, may be used as alternative therapy in the patient who's allergic to penicillin
- **Second-generation**: acts against gram-negative bacteria. Cefoxitin is the only cephalosporin effective against anaerobes.
- **Third-generation**: acts primarily against gram-negative organisms.
- **Fourth-generation**: active against many gram-positive and gram-negative bacteria.

Adverse effects

1. Hypersensitivity: (cross-allergy with penicillin).
2. Nephrotoxicity especially if used with aminoglycosides.
3. Local irritation g severe pain after IMI and thrombophlebitis after IVI.
4. Hypoprothrombinemia & bleeding with warfarin

Carbapenems & Monobactam

Imipenem	Aztreonam
<ul style="list-style-type: none"> • Broadest-spectrum beta lactams: effective against Gram +ve, -ve organisms and anaerobes. • Given IV • Increase cross-allergy with penicillin 	<ul style="list-style-type: none"> • Narrow spectrum: effective against aerobic gram -ve organisms (as aminoglycosides). • Given IV & IM
<ul style="list-style-type: none"> ✓ Nephrotoxic ✓ Increase risk of convulsion → avoided in meningitis ✓ Meropenem & Etrapanem less adverse effect 	<ul style="list-style-type: none"> ✓ No cross-allergy with beta lactams (penicillin).

Vancomycin

- ✓ **Mechanism:** Bactericidal inhibits cell wall synthesis
- ✓ **Uses:** ORSA or MRSA & Serious infections
- ✓ Given by IV infusion

Adverse effects

1. Fever, chills, rigors and phlebitis.
2. Shock with rapid infusion g red man syndrome (due to histamine release), avoided by slow infusion & pretreatment with antihistamines.
3. Ototoxic.
4. Nephrotoxic.



Clindamycin

- ✓ It used specifically against anaerobic infections.
- ✓ It used in bone infection (good penetration into bone).

Adverse Effects: Pseudomembranous colitis (diarrhea) treated by metronidazole (flagyl) or vancomycin

Quinolones

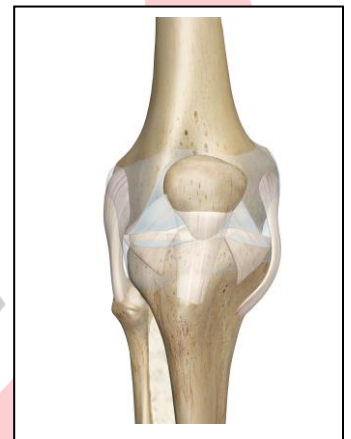
- ✓ **Action:** inhibit DNA synthesis
- ✓ **Preparations:** ciprofloxacin- ofloxacin - Levofloxacin

Uses of quinolones

1. Typhoid fever & infective diarrhea (ciprofloxacin: 1st choice for empiric therapy).
2. Urinary tract infections.
3. Gonorrhea.

Adverse Effects and Contraindications (CI)

1. GIT: Nausea, vomiting & diarrhea (most common).
2. CNS: Headache, dizziness, insomnia, convulsions.
3. **Reversible arthropathy (children < 18 years).**
 - Quinolones are contraindicated in pregnancy & lactation.
 - Not routinely recommended in patients <18 years.
4. Drug interactions



- ✓ Enzyme inhibitor increase levels of warfarin, theophylline.
- ✓ Arrhythmias (increase risk with hypokalemia & with drugs that increase QT interval e.g., erythromycin, antiarrhythmic drugs.
- ✓ Antacids → decrease absorption of quinolones.

Intravenous antifungal

Antifungal: Amphotericin - B

- **Mechanism of action:** fungicidal
- **Indications:** Most important antifungal in deep infections especially:
 - ✓ Severe life threatening (IV- not absorbed orally).
 - ✓ Meningitis (intrathecal- does not reach CSF after IVI).

Side effects & toxicity:

1. Fever, rigor, vomiting, hypotension & shock after IVI
2. Convulsions if given (intrathecally)
3. Nephrotoxic: decrease level of erythropoietin and induce anemia.
4. Hypokalaemia and cardiac arrhythmias.

Azole antifungals

Preparations: Ketoconazole - fluconazole - Itraconazole

Mechanism of action: Inhibition of synthesis of cell membrane by inhibiting cytochrome P450.

✓ 1st oral broad spectrum antifungal for:

- Deep fungal infections
- Candidal infection.

Avoid its combination with:

1. Antacids or H2 blockers → ↓ gastric acidity → ↓ ketoconazole absorption.
2. Amphotericin B: ketoconazole → ↓ amphotericin effect.

Adverse effects

1. Nausea - vomiting - rash (common).
2. Hepatotoxic (serious).
3. ↓ Steroid synthesis which depends on cytochrome P450:
 - a. Decrease corticosteroids → adrenal suppression (used in Cushing's disease).
 - b. Decrease Testosterone → gynecomastia, impotence (used in cancer prostate).
 - c. Decrease Female sex hormones → menstrual irregularities, infertility.
 - d. Decrease Metabolism of drugs → drug interactions: decrease Level of oral anticoagulants, antiepileptics
 - e.

Chapter 7

Anticoagulants – Thrombolytics- Antiplatelet

Objectives

- Identify and understand the pharmacological actions, indications, route of administration, common adverse effects, common drug interactions, precautions during administration, common contraindications and specific antidote of anticoagulants

Classification of Anticoagulants

I. Parenteral anticoagulants:

1. Indirect thrombin inhibitors: Heparin - LMWHs.
2. Indirect selective inhibitor of factor Xa: fondaparinux.
3. Direct thrombin inhibitors: bivalirudin¹ - argatroban.

II. Oral anticoagulants:

1. Inhibitor of synthesis of clotting factors (II, VII, IX, X): warfarin.
2. Direct thrombin inhibitor → Dabigatran.
3. Direct inhibitor of factor Xa: Rivaroxaban- apixaban.

I. Parenteral Anticoagulants

Indirect thrombin inhibitors

Heparin

Pharmacological Actions: anticoagulant action (effective both in vitro and in vivo)

- Mechanism: combines with antithrombin (natural anticoagulant factor) forming heparin-antithrombin complex which accelerates the inhibitory effect of antithrombin on activated clotting factors specially: Factor IIa (Thrombin)- factor IXa- factor Xa.

Pharmacokinetics

- Immediate onset of action after IV injection and short duration (4-6 h).
- 80 % metabolized in the liver by heparinase enzyme.
- 20 % excreted unchanged via the kidney.
- Does not cross placenta & is not secreted in milk (high MW) → can be used during pregnancy or lactation.

Routes of Administration & Doses

- IV bolus (5,000 IU), followed by IV infusion (1,000 IU/h); guided by aPTT).
- SC: 5,000 IU (low dose of heparin) for prophylaxis, 2 hours preoperative and every 12 hours postoperative for 5-7 days.

Heparin should not be given by IMI as hematoma can occur

Control of Therapy

- aPTT (activated partial thromboplastin time) should be kept as close as possible to twice normal value (normal value 30-35 seconds).

Adverse Effects

1. Hemorrhage.
2. Hair loss (alopecia).

3. Hematoma if given by IMI.
4. Hypersensitivity.
5. Osteoporosis (on long term use, especially in pregnancy).
6. Thrombocytopenia (so regular platelet count is required):
 - a) Early: mild due to direct effect on platelets.
 - b) Late: severe due to immunoglobulin-induced platelet aggregation.

Management of thrombocytopenia:

- Stop heparin.
- Give direct thrombin inhibitor or fondaparinux

Heparin Antidote

(Protamine sulfate)

- Highly basic with low MW carrying electropositive charge.
- Neutralizes heparin (each 1 mg neutralizes \approx 100 IU heparin).
- Partially antagonizes Low-Molecular-Weight Heparins.
- Does not antagonize fondaparinux.
- Has a slight anticoagulant effect \rightarrow avoid overdose.

2. Low-Molecular-Weight Heparins “LMWHs”: (Dalteparin - Enoxaparin)

- ✓ They are fractions of the standard heparin thus they have a low molecular weight.
- ✓ They are mostly given subcutaneously.

Mechanism of Action

They bind to antithrombin increasing its inhibitory effect on factor Xa

Advantages of LMWHs

1. Equal efficacy to unfractionated heparin.
2. Greater bioavailability from sc sites.
3. Long $t_{1/2}$ → given subcutaneously once or twice/day.
4. Less thrombocytopenia & osteoporosis.
5. Less risk of bleeding.

3. Fondaparinux

- Binds to antithrombin with high specificity → efficient inactivation of factor Xa.
- Long $t_{1/2}$ → given once daily sc.
- Used in venous thromboembolism & heparin - induced thrombocytopenia.
- Effect not antagonized by protamine sulfate.

2. Direct Thrombin Inhibitors

(Lepirudin - Bivalirudin - Argatroban)

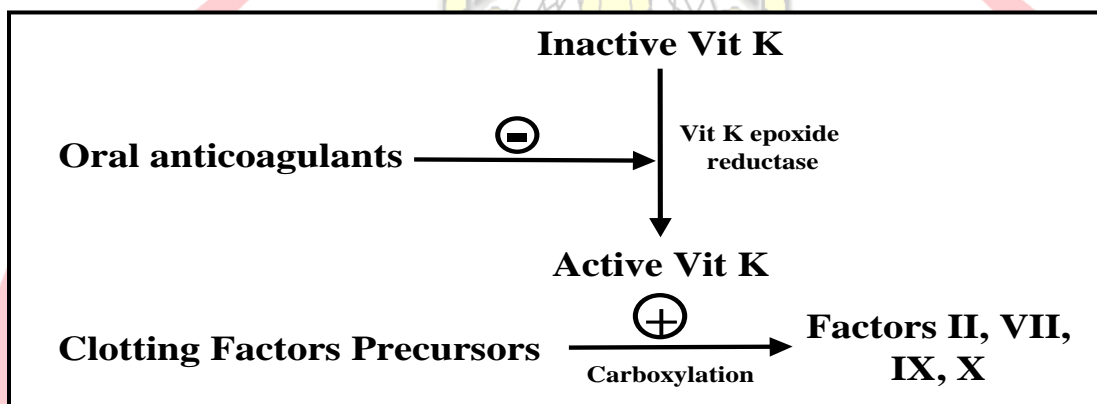
- Directly bind to thrombin independent of antithrombin → more inhibition of fibrin-bound thrombin.
- Given IV.
- Used in heparin - induced thrombocytopenia

III. Oral Anticoagulants

(Warfarin)

Mechanism of Anticoagulant Action (effective only in vivo):

- Inhibition of vitamin K epoxide reductase enzyme → prevention of reactivation of vitamin K → interference with hepatic synthesis of vitamin K-dependent clotting factors (II, VII, IX, X).



Pharmacokinetics

- Well absorbed after oral administration.
- More than 99 % bound to plasma proteins.
- Metabolized by liver & excreted by kidney.
- Long duration of action (up to 6 days).
- Crosses placenta (contraindicated in pregnancy)
- Secreted in milk (negligible amounts → safe during lactation).

Control of Therapy

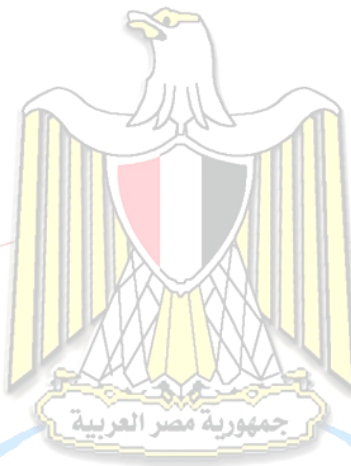
- ✓ PT (Prothrombin Time): should be kept as close as possible to twice normal value (12 s).
- ✓ INR (International Normalized Ratio): should be kept at 2-3.

Antidotes for oral anticoagulants

- ✓ Fresh frozen plasma.
- ✓ Vitamin K1.

Adverse Effects

1. Hemorrhage.
2. Skin necrosis
3. Teratogenic
4. Hemorrhage in fetus



Newer Oral Anticoagulants

Rivaroxiban - Dabigatran

Advantages over warfarin:

1. More rapid onset and offset.
2. No monitoring is required.
3. Less drug interactions

Indications of Anticoagulants

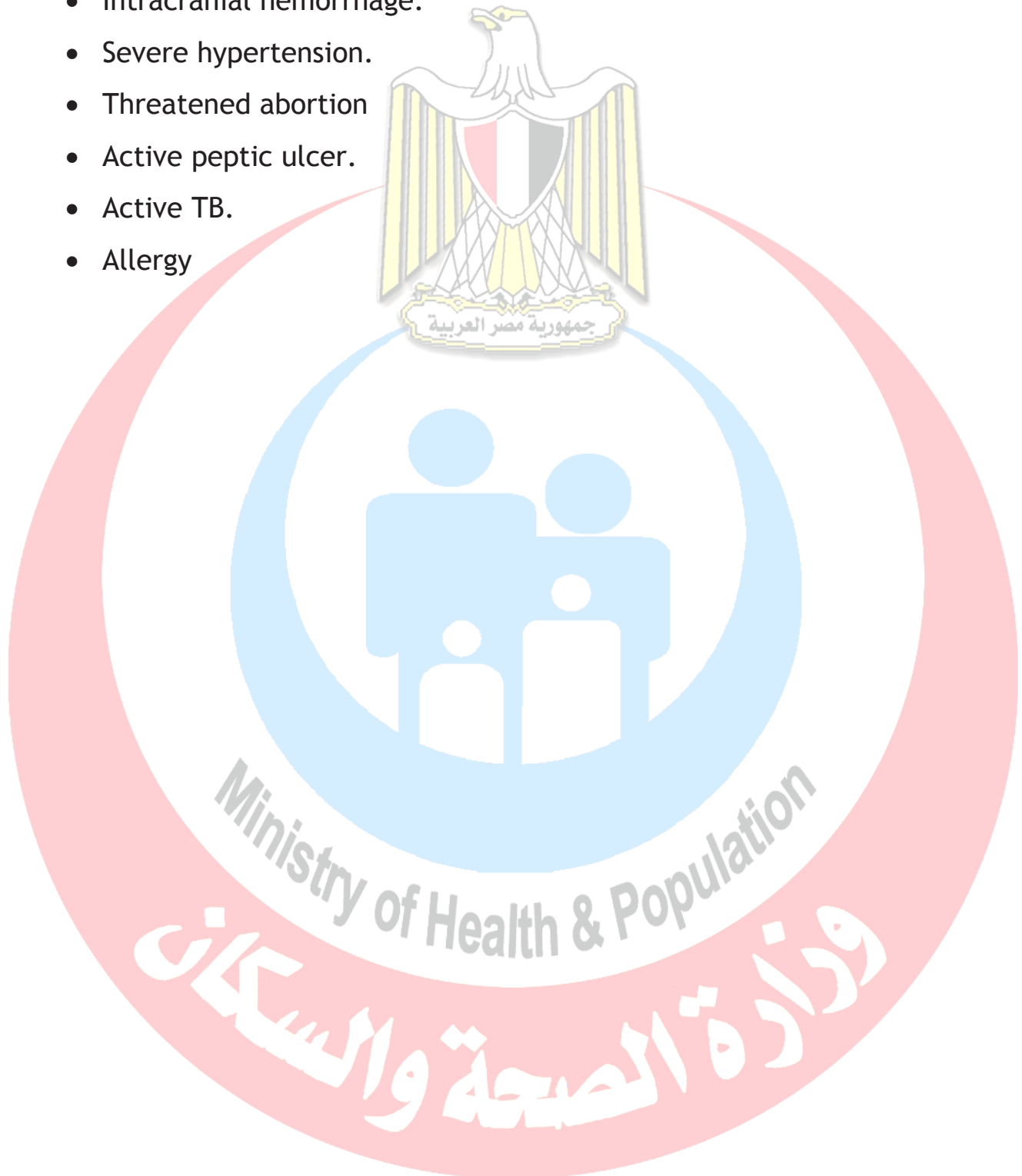
Aim of Therapy (limits propagation & prevents formation of new thrombi)

1. Deep venous thrombosis & pulmonary embolism (treatment & prophylaxis).
2. Cerebral or retinal arterial embolism.
3. Myocardial infarction & coronary thrombosis.
4. Cardiac & vascular surgery.
5. Hemodialysis (heparin).

Contraindications of Anticoagulants

- Increased risk of bleeding
- Hemophilia, purpura.

- Head injuries.
- Intracranial hemorrhage.
- Severe hypertension.
- Threatened abortion
- Active peptic ulcer.
- Active TB.
- Allergy



Chapter 8

Thrombolytics – Hemostatics

Fibrinolytics (Thrombolytics)

Drugs that cause lysis of clot (thrombus). They are given IV.

Indications of Fibrinolytics

1. Acute myocardial infarction (most effective if given early within 6 hours).
 2. Massive pulmonary embolism.
 3. Acute peripheral arterial occlusion.
 4. Deep venous thrombosis.
 5. Obstructed arteroivenous shunt & occlusion of intravascular catheter.
- ❖ Fibrinolytic therapy should be started as soon as possible after the onset of thrombosis or embolism (since they become resistant to lysis as they age).

Classification of Fibrinolytics

1-Fibrin-Nonspecific (1st generation)

A. Streptokinase (SK) B. Urokinase (UK)

- -Non-clot-selective: activate both circulating & clot (fibrin)-bound plasminogen:
- A. streptokinase: acts indirectly forming a complex with plasminogen which then activates free plasminogen
 - Advantage: (cheapest & most widely used).
- B. Urokinase : directly activates plasminogen
 - Advantage: (non-antigenic).

Disadvantages

1. ↑bleeding risk (non-clot-selective)
2. Antigenic (SK).
3. Given as intravenous infusion→loading dose followed by maintenance dose.

2-Fibrin-specific (2nd generation)

- ❖ Tissue Plasminogen Activators (tPA): Alteplase - Tenecteplase
- ❖ Clot-selective: greater affinity for activating clot (fibrin)-bound plasminogen than circulating plasminogen.

Advantages

1. ↓bleeding risk (clot-selective).
2. Nonantigenic.
3. Tenecteplase is given as a single IV bolus dose (longer $t_{1/2}$).

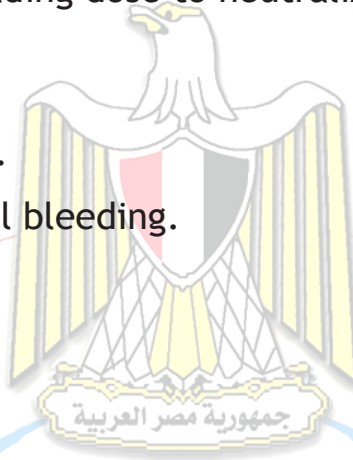
Adverse effects of fibrinolytics

- Bleeding (more with fibrin-nonspecific agents →treated by stopping infusion, fresh blood & antifibrinolytics).

- Antigenicity (fever, allergy & hypotension) with streptokinase→ start therapy with a large loading dose to neutralize antibodies).

Contraindications

- Recent surgery.
 - Gastrointestinal bleeding.
 - Hypertension.
 - Cancer.
 - Pregnancy.
 - Children & old age.
- ❖ Fibrinolytics should be followed by anticoagulants & antiplatelets because as the clot dissolves local thrombin increases→↑platelet aggregation & thrombosis



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Chapter 9

Magnesium – Potassium - Calcium

Magnesium

Magnesium serves many functions in the human body. It's important for:

- ✓ protein synthesis
- ✓ healthy bone formation
- ✓ regulating blood pressure
- ✓ maintaining heart health
- ✓ energy production
- ✓ nerve function
- ✓ blood sugar control

Uses:

1. 1-Magnesium is effective for treating eclampsia and preeclampsia.
2. 2-IV magnesium is effective for treating torsade de pointes and managing rapid AF.
3. 3-In severe acute asthma, parenteral magnesium

supplementation improves peak expiratory flow rate and forced expiratory volume in one second, and reduces hospital admissions.

4. 4-Oral and parenteral magnesium is possibly effective in improving symptoms of migraine.
5. 5-Magnesium is a widely accepted and effective approach to treat dyspepsia.

Common side effects

- Low blood pressure
- Skin flushing
- Low blood calcium
- Vomiting
- Muscle weakness
- Decreased breathing

Potassium

- ❖ Potassium is a mineral that plays many important roles in the body. Potassium is essential for the proper functioning of the heart, kidneys, muscles, nerves, and digestive system.

Uses & Effectiveness

- a. A-Effective for hypokalemia (oral or IV)
- b. B-Possibly effective for high blood pressure and Stroke (↑ potassium intake →20% reduced risk of stroke).

Side effects

1-nausea and vomiting, diarrhea, and bleeding of the digestive tract.

2-Overdoses cause hyperkalemia, which can lead to paresthesia, cardiac conduction blocks, fibrillation and arrhythmias.

Calcium

- ❖ Calcium is the most abundant mineral in the human body, making up about 2% of the total body weight.
- ❖ The main role of calcium in the body is to provide structure and strength to the skeleton.

Uses of Calcium

1. 1-Oral calcium is used to treat and prevent low blood calcium, osteoporosis, and rickets
2. 2-IV calcium is used for low blood calcium that is resulting in muscle spasms and for high blood potassium or magnesium toxicity

Common side effects

- Constipation
- Nausea
- ↑ risk of kidney stones

Chapter 10

Bronchodilators

Objectives

- ❖ Identify the different groups of bronchodilator drugs. Understand the mechanism of actions, indications, route of administration, side effects, drug interactions and possible precautions and contraindications of different groups of bronchodilator drugs.

Groups of bronchodilators:

- Short and long -acting beta-adrenergic bronchodilator
- Anticholinergic bronchodilators
- Xanthine derivatives (theophylline - aminophylline)

Uses:

- Bronchial asthma.
- Bronchospasm due to bronchitis or emphysema.
- Parenteral for treatment of status asthmaticus.

Side effects:

- Anxiety
- Tremors
- Tachycardia
- Tolerance
- Hypokalemia
- Hyperglycemia
- Hypoxemia



Nursing considerations:

- Don't exceed the recommended dose.
- The contents of the container are under pressure, don't store near heat or open flames.
- NEVER give the solution prepared to be given as inhalation by the IV route. It may cause severe tachycardia.

Anticholinergic bronchodilators

Ipratropium (short acting) & Tiotropium (long acting)

- Cholinergic receptors blockers
- Atropine substitute useful in treatment of bronchial asthma and is taken by inhalation
- Has less systemic side effects than atropine
- Effective in COPD and patient taking beta blockers
- Tolerance is common with Ipratropium



Side effects and precautions:

- Given cautiously in patient with benign prostatic hyperplasia
- Worsening symptoms of narrow-angle glaucoma
- Other side effects :Dry mouth - Cough -Dizziness

Theophylline Derivatives

Action:

- ✓ They belong to the xanthine family.
- ✓ They stimulate the CNS, relax the smooth muscles of the bronchi and pulmonary blood vessels which result in relieve of bronchospasm.
- ✓ They also have a slight diuretic effect, stimulate gastric acid secretions & increase the force and rate of the heart.

Uses:

- ✓ Prophylaxis and treatment of bronchial asthma.
- ✓ Reversible bronchospasm associated with C.O.P.D

Route of administration:

- Oral - injection- rectal

Side effects & precautions:

1. Anorexia -Nausea -Vomiting & proctitis (rectal)
 - Precautions: oral preparation taken with meal -avoids oral preparations in peptic ulcer- avoid suppositories
2. Insomnia & headache & convulsion
 - Precautions: add pyridoxine (vitamin B6)
3. Hypotension & arrhythmia& cardiac arrest
 - Precautions: intravenous should be very slowly to avoid cardiac arrest





4. Low therapeutic & saturable kinetics & increase risk of drug interactions

- Precaution: monitor plasma level & adjust dose in certain patients

Factors affecting theophylline plasma level requiring dose adjustment

- **Decrease dose in:**
 - extreme of age
 - liver & heart failure
 - with enzyme inhibitors drugs : erythromycin-ciprofloxacin-oral
 - contraceptive pills
- **Increase dose in:**
 - children
 - heavy smoker
 - with enzyme inducer drugs : rifampicin- phenytoin

Corticosteroid in bronchial asthma

Mechanism:

- Anti-inflammatory - potentiate the effect of Beta 2 agonist

Preparations:

- inhalation (beclomethazone- fluticasone)

- Oral (prednisolone)
- Parenteral (hydrocortisone)

Side effects:

- Oropharyngeal candidiasis
- Horsiness of voice
- Eye: cataract- glaucoma
- Bone: osteoporosis - growth retardation
- CVS: hypertension -edema
- Endocrine: Diabetes - Cushing syndrome

How to avoid these side effects:

- Patient should gargle and spit after inhalation
- Use by inhalation→ decrease systemic side effects
- Avoid sudden withdrawal

Chapter 11

Antiemetic - Acid suppressant

Acid suppressant

Ranitidine Hcl:

Action: It competitively inhibits gastric acid secretion by blocking the effect of histamine on histamine H₂-receptors.

Uses:

- Short-term (up to 8 wks) & maintenance treatment of duodenal ulcer & treatment of benign gastric ulcer.
- Management of hypersecretion of gastric acid.
- Reflux esophagitis.

Contraindications:

- Impaired renal & hepatic function.

Side effects:

- ✓ Constipation, nausea , vomiting, diarrhea, headache
- ✓ Dizziness , malaise , vertigo
- ✓ bradycardia or tachycardia
- ✓ Pancytopenia

Nursing considerations:

- ✓ Dilute for I.V. use (50 mg in 20 ml of 0.9% NaCl) .
- ✓ Note any evidence of renal or liver disease.
- ✓ Obtain baseline liver & kidney function.

Omeprazole

Action:

- Inhibits activity of acid (proton) pump and binds to hydrogen-potassium adenosine triphosphatase at secretory surface of gastric parietal cells to block formation of gastric acid.

Uses:

- Gastroesophageal reflux disease
- Esophagitis,
- Duodenal ulcer (short-term treatment),
- Eradicate H. Pylori

Side effects:

- ✓ CNS: headache, dizziness.
- ✓ GIT: diarrhea, abdominal pain, nausea, vomiting, constipation, flatulence.
- ✓ Musculoskeletal: back pain.
- ✓ Respiratory: cough, upper respiratory tract infection.
- ✓ Skin: rash.

Contraindications & cautions

- ✓ Contraindicated in patients hypersensitive to drug or its components.
- ✓ Use cautiously in patients with hypokalemia and respiratory alkalosis.

Nursing considerations

- ✓ Dosage adjustments may be necessary in patients with hepatic impairment.
- ✓ Tell patient to swallow tablets or capsules whole and not to open, crush, or chew them.

- ✓ Instruct patient to take drug 30 minutes before meals.
- ✓ Caution patient to avoid hazardous activities if he gets dizzy.

Intravenous Antiemetic

Metoclopramide Hcl:

Action:

- It is dopamine receptor antagonist acts both centrally & peripherally:
 - ✓ centrally due to the effect in the CTZ (inhibition)
 - ✓ Peripherally it stimulate the motility of the upper GIT without affecting gastric & biliary or pancreatic secretions.
- It relaxes the pyloric sphincter & increases the peristalsis of the duodenum resulting in accelerated gastric emptying & intestinal transit.

Indications:

- 1- Digestive disorders leading to relief GIT pain , Dyspepsia & regurgitation in peptic ulcer, reflux esophagitis
- 2- Postanesthetic vomiting
- 3- Nausea & vomiting as in chemotherapy.
- 4- Facilitate diagnostic procedure e.g. barium meal.

Side effects:

- ✓ GI disturbances: diarrhea
- ✓ dizziness & extrapyramidal effect “convulsion”

Contraindications:

- ✓ Seizure (epilepsy)
- ✓ Pheochromocytoma
- ✓ Intestinal obstruction.

Nursing considerations:

- 1- Don't give pramin to patients with epilepsy, patients with intestinal obstruction.
- 2- Administer oral medication 30 minutes before meal & at bed time .
- 3- Administer I.V. injection slowly over 1-2 minutes.
- 4- Be aware of the extrapyramidal symptoms specially in children .

Ondansetron:

Action:

- Block serotonin receptors in vomiting center

Uses: Prevention and treatment of:

- Postoperative nausea and vomiting
- Cancer chemotherapy induced nausea and vomiting

Side effects:

- Diarrhea
- Liver function test abnormalities
- pruritus, headache, tachycardia, myalgia, anorexia, fatigue

Precautions:

- Monitor cardiac rhythm.
- They're contraindicated in patients with prolonged QT intervals
- Monitor liver function.
- Correct hypokalemia and hypomagnesemia before administering.

Chapter 12

Antiepileptic drugs

Antiepileptic Drugs

Members:

I. Classic agents (major or older agents)

Phenytoin (prototype) - carbamazepine - valproate (valproic acid) - ethosuximide.

Phenobarbital - benzodiazepines.

II. Newer agents

Lamotrigine - levetiracetam - oxcarbazepine.

Topiramate - gabapentin- pregabalin.

Mechanism of Action:

- Anti-epileptics block initiation or spread of seizures by ↓hyper-excitability of
- Cerebral neurons by acting on neurotransmitters or by blocking ion channels.

Therapeutic Uses:

1. Epilepsy.
2. Mood stabilizers in bipolar depression: Lamotrigine - valproate - carbamazepine.
3. Neuropathic pain (trigeminal neuralgia, post herpetic & diabetic neuralgia): Carbamazepine- gabapentin - pregabalin.
4. Migraine: Valproate - topiramate.

5. Antiarrhythmic: Phenytoin.

Adverse Effects & Precautions of Major (classic) Anti-epileptics

	Phenytoin	Carbamazepine	Valproate
Hypersensitivity	Skin rash → stop drug		
GIT Disturbances	Nausea - vomiting - epigastric pain (most common with valproic acid) → give small dose after meals.		
Neurological Disturbances (specially in toxic doses)	Nystagmus, diplopia. Ataxia. Drowsiness. ↓ Learning in children.	Diplopia. Ataxia. Drowsiness.	Fine hand tremors. Ataxia. Less sedative.
Effects on Hepatic Microsomal Enzymes (monotherapy is preferred)	-Enzyme inducer ↑ Metabolism of other antiepileptics. -Osteomalacia: ↓ vitD metabolism (→ vit D & Ca ²⁺ supplements).	Enzyme inducer ↑ Metabolism of antiepileptics, warfarin & other drugs.	Enzyme inhibitor ↓ Metabolism of antiepileptics & other drugs.
Hematological Effects (→ regular blood picture)	-Megaloblastic anemia 'supplement folic acid' - Lymphadenopathy	Leukopenia Agranulocytosis	Thrombocytopenia
Teratogenicity → give folic acid	Cleft palate & lip-heart anomalies.	Less teratogenic.	Spina bifida. Neural tube defect.
Others	1. Cosmetic changes -Gingival	Water intoxication & dilutional	Hepatotoxicity (rare but fatal). Hair loss.

	hyperplasia -Coarse facial features. -Hirsutism - acne. 2. Unpredictable serum level → monitor serum level.	hyponatremia (potentiates ADH).	↑Appetite. ↑Body weight.
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N.B.: Ethosuximide (safest): GIT upset, skin rash, dizziness, drowsiness, headache.

Specific adverse effects of newer antiepileptics:

- ❖ Newer agents are generally better tolerated with fewer drug interactions than the older agents. Specific adverse effects include:
 - Lamotrigine: rash → fatal dermatitis (Stevens Johnson syndrome), hypersensitivity.
 - Topiramate: renal stones- myopia (→glaucoma)- weight loss- hypohydrosis.
 - Levetiracetam: mood & behavioral changes.
 - Gabapentin /Pregabalin: sedation, ataxia, weight gain- peripheral edema.

Chapter 13

Nonsteroidal anti-inflammatory drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are a heterogeneous group having anti-inflammatory, analgesic & antipyretic effects. They include:

- I. Prototype NSAID: acetylsalicylic acid (aspirin).
 - II. Non-selective NSAIDs: (ibuprofen, naproxen, diclofenac, piroxicam, indomethacin).
 - III. Selective COX-2 Inhibitors: Celecoxib.
- Paracetamol is an analgesic-antipyretic with weak anti-inflammatory action.

Cyclooxygenase Enzymes (COX)

- COX-1: present normally in tissues regulating its physiologic functions, responsible for forming protective PGs in GIT & kidney.
- COX-2: increase in inflammation, present normally in endothelium & kidney.

Mechanism of Action of NSAIDs & Paracetamol

Acetylsalicylic acid irreversibly inhibits (acetylates) cyclooxygenase enzymes (COX-1, COX-2) → inhibits PG & TXA₂ production.

Other NSAIDs cause competitive reversible inhibition of COX enzymes.

Celecoxib is a selective inhibitor of COX-2 enzyme.

I. Aspirin

Pharmacological Actions & Therapeutic Uses

A- Low-Dose (75-150 mg/d): Prophylactic Antiplatelet

Uses: prophylaxis for transient ischemic attacks, unstable angina, acute MI

B-Intermediate dose (325 mg tab) 1-2 tab/4 h

Analgesic

1. Mild to moderate pain 2ry to inflammation, e.g. arthritis, dental pain
2. Headache, dysmenorrhea.
3. Postpartum pain, postoperative & cancer pain (added to opioids to ↓their dose).

Antipyretic: in fever (paracetamol preferred).

C- High-Dose (4-8 g/d) Anti-inflammatory

1. Rheumatic fever
2. Rheumatoid arthritis & other inflammatory joint diseases.

Pharmacokinetics

Bound to albumin → displaces warfarin potentiating its effect.

Alkalinization of urine: ↑its excretion (useful in toxicity).

Adverse Effects

A. Effects Common to all NSAIDs (particularly in the elderly)

1. GIT (most common): dyspepsia, nausea, vomiting, gastritis, ulceration with ↑ risk of bleeding.
2. Nephrotoxicity (less frequent with aspirin): in renal insufficiency or in hypovolemic patients (e.g. heart failure or extensive diuretic therapy)
3. Hypersensitivity reactions: skin rash, rhinitis, asthma especially in asthmatics & patients with nasal polyps
4. ↑Bleeding tendency (stop aspirin 1 week before surgery)

B. Effects Specific to Aspirin

1. Reye's syndrome: encephalopathy and liver damage in children with fever due to viral infection (CI as antipyretic in children < 12 years).
2. Chronic toxicity (salicylism): prolonged administration of large doses → dizziness, tinnitus, nausea & vomiting.
3. Acute toxicity

Advantages over opioid analgesics:

- i. No dependence.
- ii. No respiratory depression (in therapeutic doses)

II. Non selective NSAIDs

Possess analgesic, antipyretic & anti-inflammatory effects (see aspirin).

They are increasingly used in inflammatory joint diseases (osteoarthritis, rheumatoid arthritis, & gouty arthritis), dysmenorrhea, renal colic & postoperative pain; in patients not responding to aspirin or intolerant to it. They are ineffective as antiplatelets since they inhibit COX reversibly leads to short antiplatelet effect.

Individual NSAIDs

Ibuprofen: (first-choice in inflammatory joint disease).

Naproxen: (least risk of CV events).

Diclofenac: (stronger than ibuprofen)

Piroxicam: (↑risk of GIT bleeding).

Indomethacin : (limited use due to its serious adverse effects)

Drug interactions of NSAIDs

1. ↓ Effects of ACEIs.
2. ↓ Effects of diuretics.
3. Displace warfarin & oral hypoglycemics from plasma proteins.
4. ↑ Risk of gastric ulceration with glucocorticoids.

III. Selective COX-2 Inhibitors

Celecoxib

Uses: Anti-inflammatory: used in chronic inflammatory musculoskeletal disorders (with less risk of gastric ulceration).

Adverse Effects of COX-2 Inhibitors

1. Nephrotoxicity
2. Stroke & infarction
3. Skin rash with celecoxib (structurally related to sulfonamides).

PARACETAMOL (Acetaminophen)

-It is an analgesic antipyretic with weak anti-inflammatory action.

-It is preferred to aspirin in:

1. Patients allergic to aspirin.

2. Peptic ulcer (no GIT disturbances).
3. Viral infections in children (to avoid Reye's syndrome with aspirin).
4. Bleeding disorders (does not affect platelet function).

Adverse Effects and Toxicity

- Minimal adverse effects - well tolerated.
- Paracetamol hepatotoxicity (in toxic doses [150 mg/kg]: nausea and vomiting, followed in 24-48 h by liver damage)

Iv paracetamol (PERFALGAN)

1. Analgesic: in mild to moderate postoperative pain
2. Antipyretic: in acute fever of infectious origin requiring IV therapy.



Chapter 14

Oxygen therapy - blood components

Oxygen

- ✓ Oxygen supplementation is used in medicine.
- ✓ Administered through nasal cannula, a mask or a breathing tube, oxygen therapy provides a concentration of oxygen directly to the patient.
- ✓ Treatment not only increases oxygen levels in the patient's blood but has the secondary effect of decreasing resistance to blood flow in many types of diseased lungs, easing work load on the heart.

Uses of Oxygen therapy

- a. A-Treatment of emphysema, pneumonia and some heart disorders (congestive heart failure)
- b. B-Long term oxygen is often useful in people with chronically low oxygen such as from severe COPD or cystic fibrosis.
- c. C- Hyperbaric oxygen therapy is one of the most advanced ways to treat wounds and infection. The increase in oxygen rich blood helps heal and improve these conditions:
 - Carbon monoxide poisoning
 - Gangrene
 - Wounds
 - Infections
 - Skin grafts

- Radiation injury (many times from cancer treatment)

Side Effects of Oxygen Therapy

- ✓ Bloody nose or skin irritation where oxygen is administered
- ✓ Morning headaches
- ✓ Fatigue
- ✓ Side effects of trans-tracheal oxygen therapy, including infection, tube slipping, injury to the windpipe and mucus balls blocking the tube

Blood and blood components

The components of human blood are:

Plasma: The liquid component of the blood in which the following blood cells are suspended:

- Red blood cells (erythrocytes): these carry oxygen from the lungs to the rest of the body
- White blood cells (leukocytes): these help fight infections and aid in the immune process. Types of white blood cells include:
 - Lymphocytes
 - Monocytes
 - Eosinophils
 - Basophils
 - Neutrophils
 -
- Platelets (thrombocytes): these help in blood clotting.

Acid base disturbance treatment

Treatment of respiratory acidosis

- Treatment is targeted to the cause.
- Bronchodilator medications may be given to correct some forms of airway obstruction.
- If your blood oxygen level is too low, you may require oxygen.
- Noninvasive positive pressure ventilation or a breathing machine may be necessary.
- Treat the underlying cause.
- The cause could be from an organ deformity, an infection, or some type of inflammation.
- Antibiotics.
- Stop smoking.

Treatment of metabolic acidosis

- Sodium bicarbonate is prescribed to return the blood to a normal pH.

Treatment for alkalosis

- Some medications (such as chloride and potassium) can help correct chemical losses.
- Further treatment will depend on the cause. Your physician will need to monitor your vital signs and create a proper plan to correct your pH imbalance.

Chapter 15

Antihistamines - corticosteroids

Antihistamines “H1 Blockers”

Action:

- The effect of histamines may be reversed either by drugs that block histamine receptors (antihistamine) or by drugs that have effects opposite to those of histamine e.g. epinephrine.
- Antihistamines used for the treatment of allergic conditions.
- They prevent or reduce increased permeability edema & itching & bronchospasm.
- H1-blockers manifest varying degrees of CNS depression, anticholinergic & antiemetic effect.

Uses:

- ✓ Treatment of seasonal allergic rhinitis, allergic conjunctivitis.
- ✓ Treatment of urticarial transfusion reactions.
- ✓ Treatment of topic dermatitis.
- ✓ Treatment of insect bites.
- ✓ Sneezing & rhinorrhea due to common cold.
- ✓ Prophylaxis & treatment of motion sickness “nausea & vomiting”.
- ✓ Night - time sleep aid.

Contraindications:

- Hypersensitivity
- Pregnancy.
- Glaucoma
- Prostatic hypertrophy
- CNS depression.
- Bone marrow depression



Side effects:

- Sedation - deep sleep - Dizziness - Headache - muscle weakness - disturbed coordination
- Epigastric distress - dry mouth - nausea - vomiting
- Paradoxical excitation (especially in children & elderly)
Restlessness, irritability, insomnia, hysteria, tremors euphoria, nervousness, hallucinations, disorientation & convulsion usually caused by overdose (acute toxicity).

Corticosteroids

Mechanism of action:

1. CHO metabolism:
 - Deposition of glucose as glycogen in the liver & conversion of glycogen to glucose when needed. (Gluconeogenesis).
2. Protein metabolism:
 - The stimulation of protein loss from many organs.
3. Fat metabolism:

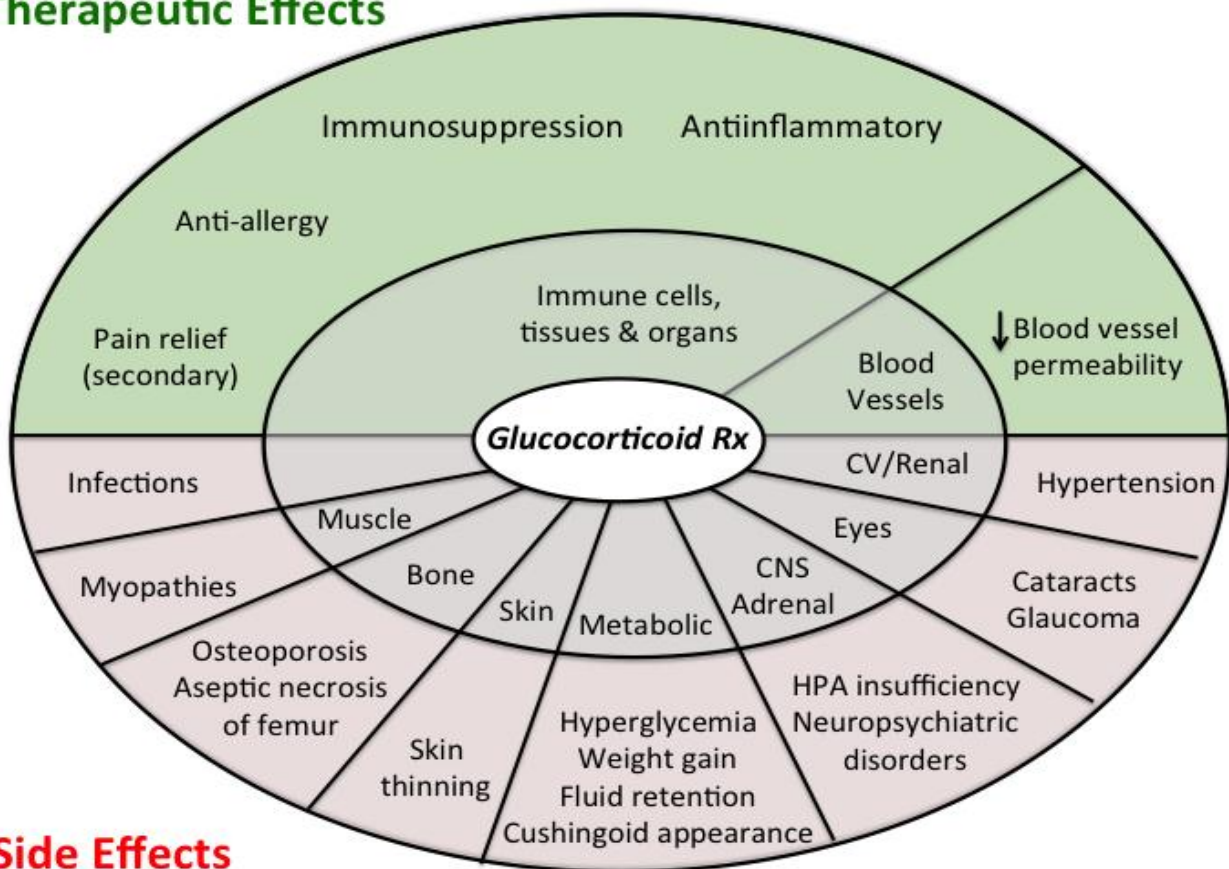
- The deposition of fatty tissue in facial, abdominal & shoulder regions.
4. Water & electrolyte balance:
 - Alteration of glomerular filtration rate, increase sodium & fluid retention, also affect the excretion of potassium, calcium & phosphorus.
 5. Have anti-inflammatory effect:
 - They decrease prostaglandin synthesis.
 6. The immunosuppressant effect:
 - They decrease number of T-lymphocyte, monocytes, and eosinophils.
 7. Anti-stress effects e.g. trauma & sever illness.

According to their chemical structure, they fall into 2 classes.

- Glucocorticoids e.g. cortisone & hydrocortisone: regulate the metabolism of CHO, protein & fat.
- Mineralocorticoids e.g. hydrocortisone: increase reabsorption of Na^+ (+water) & excretion of potassium & hydrogen.

Uses and side effects:

Therapeutic Effects

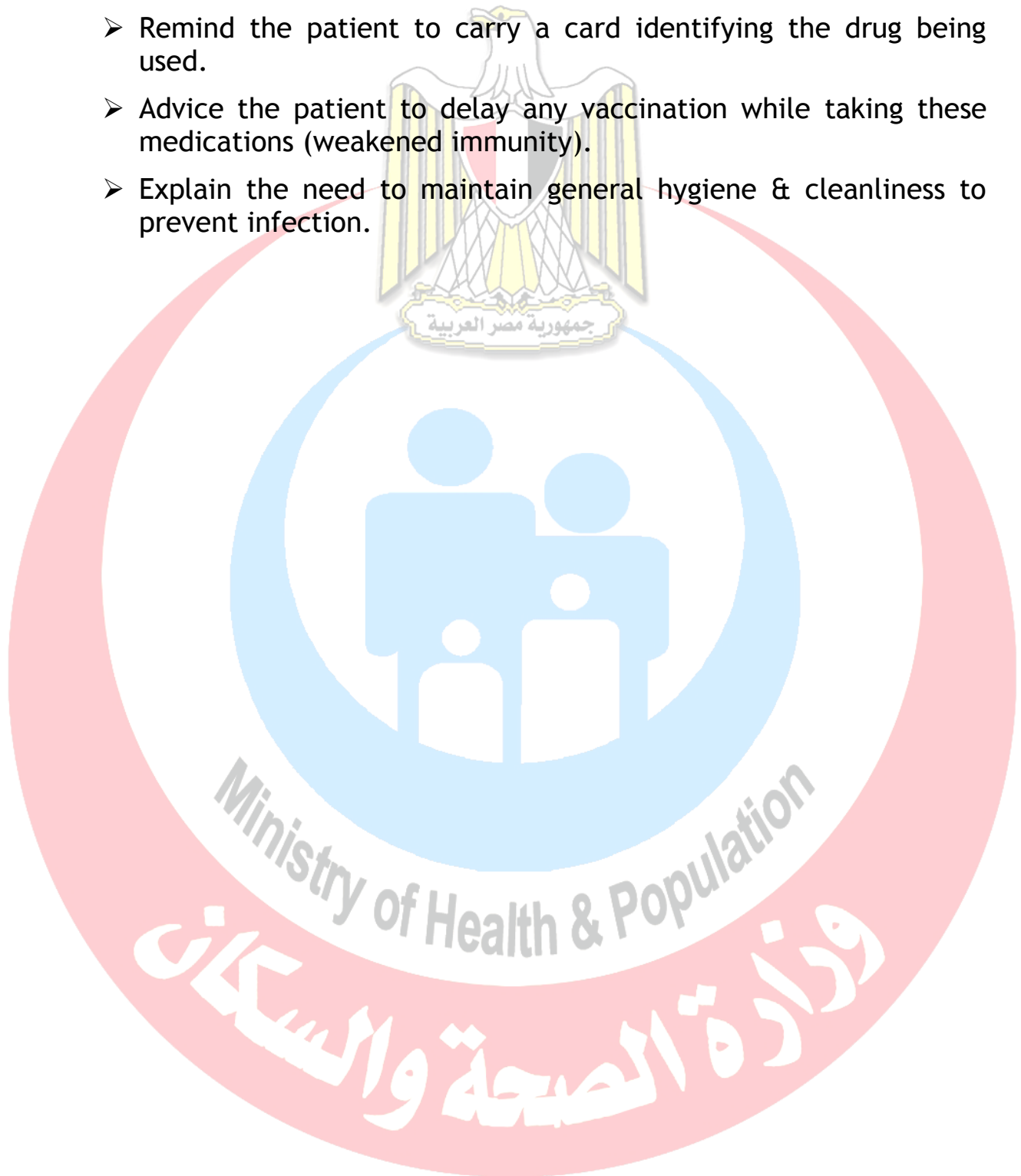


Side Effects

Nursing Considerations:

- Administer oral forms with food to minimize ulcerogenic effect.
- For chronic use, give the smallest dose possible.
- Gradual withdrawal if used more than 2 weeks
- Document blood pressure, Pulse, temperature, monitor body weight (signs of Na⁺ & H₂O retention).
- Periodic serum electrolytes, blood sugar monitoring.
- Report signs & symptoms of side effects (Cushing-like syndrome).
- Discuss with female patient about the potentials of menstrual difficulties.
- Instruct the patient to take diet high in protein & potassium.

- Instruct the patient to avoid falls & accidents (osteoporosis causes pathological fracture).
- Remind the patient to carry a card identifying the drug being used.
- Advise the patient to delay any vaccination while taking these medications (weakened immunity).
- Explain the need to maintain general hygiene & cleanliness to prevent infection.



References:

1. Pharmacology book 3rd year medical students
2. <https://en.wikipedia.org/wiki/Oxygen>
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