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# محاضرات الادوية والسموم

# Pharmacology and toxicology

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## Pharmacology

Is the science which deals with drug from all its aspects.

**Drug** : any chemical agent that affect biological system

**Pharmacodynamics** is the action of drug on living tissues

**Pharmacokinetics**: is the action of living tissues on drug. This action include :

a- absorption ,
b- distribution
c- metabolism
d- excretion.

**Pharmacognosy**: the science which deals with the source of the drugs and physical and chemical properties of the drugs.

**Pharmacotherapeutics** : the science which deals with the usage of drugs in the prevention , diagnosis and treatment of the disease.

**Toxicology**: describe undesirable or adverse effect of drugs or chemicals on the body.

**Pharmacy**: is deals with collection, preparation , standardization and dispensing of drug

**Source of drugs:**

1- Plant source (atropine from leave of belladonna)
2- Animal source (insulin from pancreas of different animals).
3- Mineral : (magnesium sulphate and iodine)

4- Microorganisms (antibiotics from fungi and bacteria isolated from soil).
5- Synthetic drugs(produced in laboratory such as sulfonamide).

**Routs of drug administration:**

1- Alimentary:
   a- oral(per mouth).
   b- rectal .
2- Parenteral:
   a- Intravenous (i.v): rapid action and avoid destruction of drug in stomach.
   b- Intramuscular(i.m)
   c- Subcutaneous (s/c)
   d- Intraperitoneal (i.p)
   e- Intrathecal
3- Inhalation.
4- local.

**oral administration:**

1- less common in vet medicine.
2- no strict sterilization
3- safe

disadvantage:

a- delay onset of action.
b- irregular absorption and destruction of drug by gastric juice
c- irritation of gastrointestinal tract.

**Intravenous:**

a- water soluble
b- immediate action
c- avoid chemical destruction
d- suitable for irritant drugs
e- best route for replacement fluid( normal saline, ringer solution and glucose saline)

disadvantage:

a- sterile
b- slow administration
c- risky

**Intramuscular**

a- suitable for water insoluble drugs
b- absorption is greater than subcutaneous and and lesser than i.v
c- less sensitive to pain than s/c

disadvantage

a- sterile.
b- volume of soluble drug less than 30 ml.

**Subcutaneous s/c:**

a- commonly used in vet medicine
b- can be used for replacement fluid

**Intraperitoneal**

a- alternative route for i.v

b- fast

c- non irritant

d- sterile

**Intrathecal**: commonly used for spinal anesthesia.

**Inhalation:**

a- volatile substance (ether, chloroform and halothen)

b- spray

c- commonly used in general anesthesia

**Type of drug action on the body:**

1- Local action: drug act at its site of administration (eye drop and skin ointment)
2- Systemic action : after absorption and circulation it affect various tissues.
3- Reflex action the drug act locally to produce reflex action elsewhere (injection of camphor subcutaneously cause reflex stimulation of respiration.

**Mechanism of drug action**

1- Physically: e.g by adsorption (kaolin in diarrhea) and osmosis (osmotic diuretics)
2- Chemically: e.g neutralization (sodium bicarbonate in hyperacidity)
3- Interference with cell division(cytotoxic effect).

4- Action of enzymes; inhibition of enzyme (choline esterase inhibitors).
5- Interference with normal metabolic pathways: eg sulphanomide compete with para-amino benzoic acid which is essential metabolite for bacteria.
6- Action on cell membrane: e.g. local anesthetics.
7- Action on cell receptors. Acetyl choline act on cholinergic receptors.

**Factors affect response to drug.**

1- Dose: there are 2 type of response to drug
   a- Graded response : mean increase in dose lead to increase in response.
   b- Quantal response: response does not occur until the concentration of drug reach certain level.
2- Drug interaction : presence of two or more dugs are combined together we observe one of the following:
   a- Addition or summation (1+1=2)
   b- Synergism(1+1=>2).
   c- Potentiation: one drug had no apparent action but its potentiate the action of another drug.
   d- Antagonism: the action of one drug opposite the action of another drug.
3- Sex: female require smaller dose the male also difference in hormone may affect drug action.
4- Rout of administration.
5- Time of administration : rapid absorption on an empty stomach.

6- Genetic factors.
7- Drug allergy.
8- Drug tolerance.
9- Diseases.
10- Age and weight.

## DRUGS USED IN GASTROINTESTINAL DISEASES

The pharmacologically treatable disorders of impairments of normal motility, digestion, absorption, secretions of the gastrointestinal tract include peptic ulcer, esophagitis, constipation, diarrhea, inflammatory diseases and infections.

1- **Antiacid** : the drug that neutralize or decrease acidity of stomach which act by:
   a- Neutralize gastric acid (HCl) e.g. magnesium and aluminum hydroxide.
   b- Reduce gastric acid secretion e.g. cimetidine
   c- Enhance mucosal defenses e.g sucralfate and colloid bismuth compound.
2- **Laxatives and cathartics (purgatives) :** are drugs used orally to evacuate the bowels or to promote bowel elimination (defecation):
   a- Lubricant such as liquid paraffin which is non absorbable coating the GIT and consider as laxative.
   b- Simple bulk purgatives: substances which swell in the presence of water forming non absorbable gel and help in removal of ingesta. such as agar agar and methylcellulose.

c- Saline purgatives: water soluble salts increase osmotic pressure in GIT. ("magnesium sulphate).

d- Irritant purgatives: cause irritation to intestinal mucosa and increase motility such as caster oil.

e- neuro muscular purgatives: stimulate parasympathetic system and increase motility.(acetylcholine and carbachol).

**Uses of laxatives:**

1- To relieve constipation .

2- To empty the bowel in preparation for bowel surgery or diagnostic procedures.

3- elimination of potentially toxic substances from the GI tract .

4- excretion of parasite after anthelmintic drugs .

**5- Astringent (Antidiarrhoeals):** Are used in the treatment of diarrhea . they are two types:

1- Adsorbent – demulcent products such as kaolin – pectin is non absorbable materials that believed to adsorb large numbers of bacteria and toxins and reduce water loss and to coat the GI mucosa, they given with other antidiarrhetic drugs..

2- • Anticholinergic agents e.g. atropine are occasionally used to decrease intestinal movement and spasm associated with diarrhea.

6- **Protectant**: substances which coat GIT mucosa forming protective layer between toxic substances and epithelial layer. Sucralfate This is a sucrose sulfate-aluminum hydroxide complex .it is covert to a viscous gel. The sulfate groups bind to proteins in ulcerated tissue and protect ulcers from acids and pepsin.

7- **Adsorbent**: substances which bind to toxic materials and prevent absorption of them such as ca carbonate and aluminum silicate and pectin .

8- **Emetics**: the drug which produce vomiting by stimulation of vomiting center. They are used in case of poisoning and is of two types:

   **a-** Local emetics : stimulate nerve ending in GIT such copper sulphate and zinc sulphate.

   **b-** Directly stimulate vomiting center and produce vomiting such as apomorphin.

9- **Antiemetic:** Are drugs used to prevent or treat nausea and vomiting. Vomiting occurs when the vomiting center in the medulla oblongata is stimulated. Dopamine and acetylcholine play a major role in stimulating the vomiting center. To a certain extent, vomiting is a protective mechanism which can result from various noxious stimuli. antiemetic agents acting inhibit the vomiting center and cerebral cortex. Antiemetic drugs include: Phenothiazine such as chlorpromazine and Antihistamines – such as promothazine, dimehydrinate etc. Are especially effective in prevention and treatment of motion sickness.

10- **Appetite stimulant**: bitters stimulate salivary gland and gastric secretion by acting on taste buds and gastric mucosa. Such as tincture of vomica and orange peel extract and cinnamon.

11- **Digestant**: substances which promote digestion such as:

   a- pancreatic enzymes

b- cholirectic :stimulate bile secretion(sodium and potassium Salts of bile acids.

12- **Carminative:** preparation intended to either prevent formation of gas in the GIT or facilitate the expulsion of gas. This include volatile oil such as turpentine oil, eucalyptus and peppermint.

## Local anesthetics

Local anesthetics produce loss of sensation to pain in specific area of body without loss of consciousness(awareness).

Lidocaine ,xylocaine , procain are some examples of local anesthetics.

Local anesthetics are used in minor surgery, dentistry, abdominal surgery and painless childbirth. The unwanted effects are due the entrance of LA into systemic circulation and these are: CNS effects (agitation, confusion, respiratory depression, and convulsion), CVS effects (myocardial depression, hypotension) and occasional hypersensitivity reactions.

**Its divided into:**

1- Surface anesthesia : anesthetic substance applied on the mucous membrane of mouth , nose and urinary system.
2- Infiltration anesthesia: Direct injection into tissues to reach nerve braches and terminals.
3- Regional anesthesia: intravenous injection for arm and leg anesthesia.
4- Nerve block anesthesia LA injected close to nerve trunks (Dentistry).
5- Spinal anesthesia LA injected into subarachinoid space. Pelvic surgery.
6- Epidural anesthesia LA injected into epidural space. (Labour).

## General anesthesia

General anesthesia involves the physiological changes: Reversible loss of response to painful stimuli, loss of consciousness and loss of motor and autonomic reflexes.

Stage of anesthesia:

I. Analgesia stage

- Patient conscious
- Spontaneous respiration
- Reflexes present
- Possible small surgery procedures like dressing change in burns

II. Excitation stage

- Possible uncontrolled movements, vomiting
- Increase in respiratory rate

III. Anesthesia for surgery

- It begins with lack of lid reflex

IV. intoxication, overdosing.

- Respiratory arrest
- If anesthesia not discontinued possible cardiac arrest.

## Type of general anesthesia:

### 1- Inhalation anesthetics

**a. Halothane:** Is the most widely used agent, highly lipid soluble, potent. It causes arrhythmia, hangover and the risk of liver damage is high if used repeatedly.

**b. Nitrous oxide:** Odorless and colorless gas. It is rapid in action and also an effective analgesic agent. Its potency is low, hence must be combined with other agents. It is a relatively free of serious unwanted effects.

**c. Enflurane:** Halogenated ether (similar to halothane). Poorly metabolized in the liver, thus less toxic than halothane. It is faster in its action, less liable to accumulate in the body fat compared to halothane. It causes seizure during induction and following recovery from anesthesia.

**d. Ether:** Has analgesic and muscle relaxant properties. It is highly explosive, causes respiratory tract irritation, postoperative nausea and vomiting. It is not widely used currently.

**2- Intravenous anesthetics.**

Intravenous anesthetics act much more rapidly, producing unconsciousness in about 20 seconds, as soon as the drug reaches the brain from the site of its injection. These agents used for induction of anesthesia followed by inhalation agent. The main induction agent in current use is: thiopentone, etomidate, propofol, ketamine and short acting benzodiazepine (midazolam).

**a- Thiopentone:** After intravenous administration the drug enters to tissues with a large blood flow (liver, kidneys, brain, etc) and more slowly to muscle. Uptake into body fat occurs slowly because of the low blood flow to this tissue, which may cause prolonged effect if given repeatedly. It causes cardiovascular depression.

**b- Etomidate:** It is more quickly metabolized and the risk of cardiovascular depression is less compared to thiopentone. Etomidate suppresses the adrenal cortex, which has been associated with an increase in mortality in severely ill patients.

**c- Ketamine:** acts more slowly than thiopentone and produces a different effect, known as dissociative anesthesia in which there is a marked sensory loss and analgesia, as well as amnesia and paralysis of movement, without actual loss of consciousness. Ketamine causes dysphoria, hallucinations during recovery.

3- **Combined, balanced(intravenous + inhalation)**.

**Preanesthetic medication:**

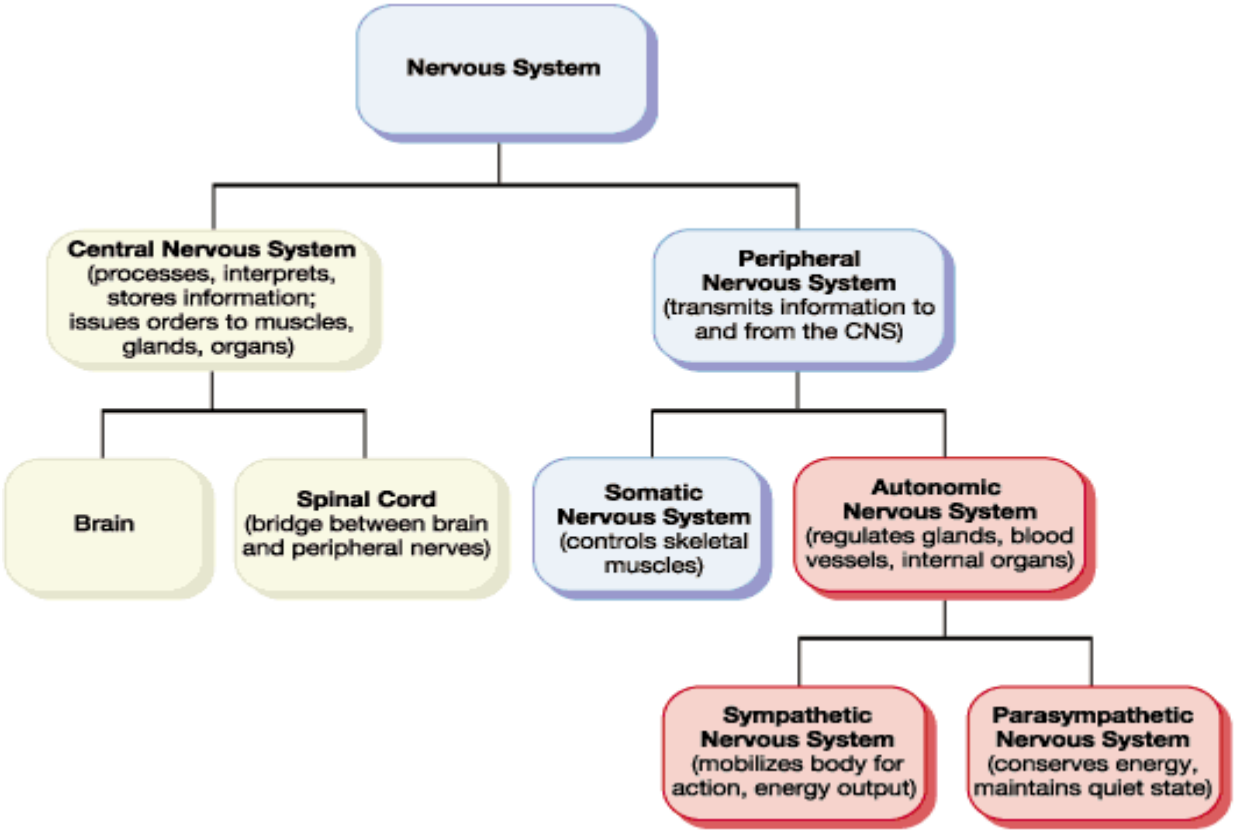
It is the use of drugs prior to the administration of anesthetic agent with the important objective of making anesthesia safer and more agreeable to the patient. The drugs commonly used are, opioid analgesics(fentanyl), barbiturates, anticholinergics, anti-emetics and glucocorticoids.

**Sedatives and hypnotic drugs .**

**sedatives** are used to treat the symptoms of anxiety, whereas **hypnotic drugs** used to treat insomnia. The same drugs are used for both purposes. examples of these drugs:

1. Benzodiazepines.*(* diazepam, chlordiazepoxide, clonazepam)
2. Barbiturates (phenobarbitone).
3. chloral hydrate.

## Drugs acting on nervous system.




the parasympathetic nervous system is concerned primarily with rest and digest.

In contrast, the sympathetic nervous system is concerned with the expenditure of energy, i.e., it has almost opposite functions with parasympathetic nerve stimulation and it is usually associated with emergency situations, i.e., prepares the body for fight-or-flight responses.

There are two important neurotransmitters in the autonomic nervous system. These are acetylcholine and adrenalin and noradrenaline (epinephrine and norepinephrine).

Acetylcholine is a neurotransmitter which is released after stimulation of the parasympathetic nervous system to act on effector organs (cells) to elicit their response.

Cholinergic receptors are classified into muscarinic and nicotinic cholinergic receptors.

adrenalin and noradrenaline is a neurotransmitter which is released after stimulation of the sympathetic nervous system.

Receptors for adrenalin and noradrenaline called adrenergic receptors.

## AUTONOMIC DRUGS

There are several drugs affecting the autonomic nervous system which, for a better understanding of specific drugs, are classified into groups.

### 1. Drugs acting on the sympathetic nervous system

a) Sympathomimetic or adrenergic drugs: are drugs that mimic the effects of sympathetic nerve stimulation.

b) Sympatholytic: are drugs that inhibit the activity of sympathetic nerve or that of sympathomimetic.

### 2. Drugs acting on the parasympathetic nervous system

a) Para sympathomimetic or cholinergic drugs: are drugs which mimic acetylcholine or the effects of parasympathetic nerve stimulation.

b) Para sympatholytic: are drugs that inhibit parasympathetic nervous system activity or that of cholinergic drugs.

### Cholinergic drugs

There are 2 groups of Cholinergic drugs (Para sympathomimetic drugs)

1. *Direct-acting*: bind to and activate muscarinic or nicotinic receptors (mostly both) and include the following subgroups:

a. Esters of choline: methacholine, carbachol, betanechol.

b. Cholinergic alkaloids: pilocarpine, muscarine, arecoline, nicotine.

2. *Indirect-acting*: inhibit the action of acetylcholinesterase enzyme.

a. Reversible: neostigmine, physostigmine.

b. Irreversible: Organophosphate compounds.

**Action of Cholinergic drugs**

1- slow heart rate
2- vasodilation
3- Low blood pressure
4- stimulates the tone and motility of the Gl tract but the sphincters will be relaxed.
5- stimulates the detrusor muscle and relaxes the internal urethral sphincter resulting in evacuation of bladder
6- increase bronchial secretion and brings about bronchoconstriction
7- Eye miosis and accommodation for near objects.
8- stimulates salivary, gastric, bronchial, lachrymal and sweat gland secretions.

**ANTICHOLINERGICS**

Anticholinergics block the effects of acetylcholine and other cholinergic drugs at cholinergic receptors of effector cells.

a- Antimuscarinics such as atropine, scopolamine
b- Antinicotinics :hexamethonium, gallamine, tubocurarine,

## ADRENERGIC DRUGS

Adrenergic drugs, like cholinergic drugs, can be grouped by mode of action and by the spectrum of receptors that they affect.

a. *Direct mode of action:* directly interact with and activate adrenoreceptors, e.g., adrenaline and noradrenaline

b. *Indirect mode of action:* their actions are dependent on the release of endogenous catecholamine. This may be:

i. cause release of stored catecholamine from the adrenergic nerve endings, e.g., amphetamine, tyramine and ephedrine .

ii. Inhibition of reuptake of catecholamine already released, e.g. cocaine, tricyclic, antidepressants.

**ADRENERGIC BLOCKERS** the drugs that block adrenergic receptors such as propranolol.

## DRUGS ACTING ON THE RESPIRATORY SYSTEM

The respiratory system includes the upper airway passages, the nasal cavities, pharynx and trachea as well as the bronchi and bronchioles. Respiration is the exchange of gases between the tissue of the body and to outside environment.

The chapter will focus on drugs used to treat some of the more common disorders affecting the respiratory system particularly bronchial asthma, allergies and congestions associated with certain respiratory disorders.

### Stimulant of respiratory system:

Are drugs which accelerate or deepen respiratory movement mainly through stimulation of respiratory center which are classified into:

1- Central stimulant: these stimulate respiratory center in the medulla oblongata which belongs to analeptics such as caffeine and picrotoxin.

2- Reflex stimulant: these cause mild irritation to the nerve ending or mucous membrane of the nasal cavity or skin producing reflex stimulation of the respiratory center such as camphor , ammonia. $CO_2$ stimulate chemoreceptors in the carotid sinuses.

**ANTI-TUSSIVES :**Cough is a protective reflex, which serves the purpose of expelling sputum and other irritant materials from the respiratory airway.

1. Central anti- tussives: Suppress the medullary cough center e.g. codeine, hydrocodeine, dextromethorphan

2. Peripheral antitussives: Decrease the input of stimuli from the cough receptor in the respiratory passage. e.g: Demulcents ( licorices roots, honey), Local anesthetics e.g. lidocaine aerosol.

**Demulcents:** coat the irritated pharyngeal mucosa and exert a mild analgesic effect locally.

**Expectorant:** is a drug that aid in removing thick tenacious mucus from respiratory passages, e.g. Ipecac alkaloid, sodium citrate, saline expectorant, guaifenesin, potassium salts.

**Mucolytics:** are agents that liquefy mucus and facilitate expectoration, e.g.acetylcysteine.

## DECONGESTANTS:

Decongestants are the drugs that reduce congestion of nasal passages, which in turn open closed nasal passages and enhances drainages of the sinuses. e.g phenylephrine, oxymetazoline etc.

**Bronchodilators:** are drugs used to remove bronchoconstriction. Constriction of bronchial and bronchiolar smooth muscle is known as **asthma** which is different from other causes of bronchial obstruction such as vascular congestion , edema and tumors.

**Bronchodilators are classified into**:

1- Direct relaxant of smooth muscle such as methylxanthene derivatives(caffeine and aminophylline).
2- Sympathomimetic drugs (adrenaline, ephedrine, salbutamol and isoprenaline).

   Note : you should be careful when give adrenaline because it may cause heart shock.
3- Anticholinergic drugs (atropine and hyoscine hydrobromide).
4- Anti-inflammatory agent They are presumed to act by their broad anti-inflammatory effect through inhibition of production of inflammatory mediators (histamine and leukotriene). Example of

Anti-inflammatory agent are hydrocortisone, predinisolone, betamethasone and triamcinolone.

## Respiratory antihelminthics

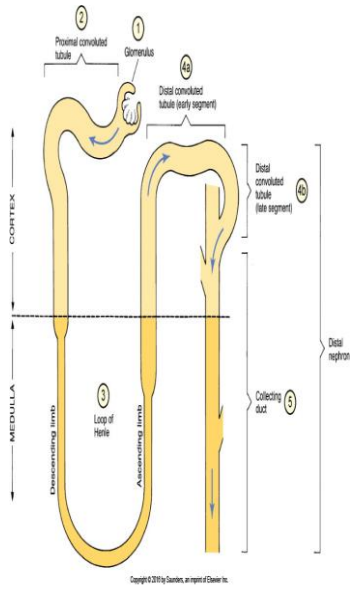
1- Ivermectine
2- Piperazine
3- Albendazole
4- Livamizole
5- Tetramizole

# Drugs affect urinary system

The nephron is the functional unit of kidney

Each kidney has about one million nephrons

- Glomerulus
- Bowman's Capsule
- Proximal convoluted tubule
- Loop of Henle
  - Descending
  - Ascending
- Distal convoluted tubule
- Collecting duct




**Basic nephron processes**

- **<u>Filtration</u>**:~ 20% of the plasma that flows through the glomerular capillaries gets filtered into Bowman's Capsule (180 liters filtrate produced daily)

  → Occurs only at glomerulus

- **<u>Reabsorption</u>**: more than 99% of the water, nutrients and ions get reabsorbed.
  - Na reabsorption creates osmotic gradient.

    → Cl may be co-absorbed or passively follow the sodium

    → **"Water follows salt."**
  - By reabsorbing sodium from the tubular fluid, water also gets reabsorbed from tubular fluid.
- **<u>Active secretion</u>:** various wastes, drugs and toxins

  → Occurs at PCT
- **Net result:** 1.5 – 2 liters of urine produced daily .

**Four major classes of diuretics**

1- **Osmotic diuretics**:

- Highly osmotic molecules that are freely filtered at the glomerulus, and drag water into the filtrate too (mannitol and glycerin)

2- **Loop diuretics-**

- Block reabsorption of Na, Cl in the Loop of Henle (furosemide).

3- **Thiazides**

- Block reabsorption of Na, Cl in the early Distal Convoluted Tubule
  (hydrochlorothiazide, chlorothiazide)

4- **Potassium-sparing diuretics**

- Block reabsorption of sodium and prevent the excretion of potassium in the collecting duct(spironolactone).

**Uses of diuretics:**

1- Increase the volume of urine excreted by the kidneys and promote release of water from tissues.

2- Lower the fluid volume in tissues; are used to decrease edema and lower blood pressure

3- May also be used to reduce udder edema in cattle and enhance removal of toxins from the body.

**Urolith treatment**

Uroliths are abnormal mineral masses in the urinary system.

Types of uroliths include: struvite, calcium oxalate, calcium phosphate, urate, cysteine.

Some drugs used to treat uroliths:

a- Urinary acidifiers are used clinically to produce acid urine, which dissolves and helps prevent formation of struvite uroliths. Their use has declined with the use of urinary acidifying diets. Examples include methionine and ammonium chloride

b- Urinary alkalinizers are used clinically to treat calcium oxalate, cystine, and ammonium urate uroliths. An example is potassium citrate.

c- Xanthine oxidase inhibitors decrease the production of uric acid, which helps decrease the formation of ammonium urate uroliths. An example is allopurinol.

## Drugs acting on reproductive system:

1- Gonadotrophic hormones:
   a- FSH (follicle stimulating hormone).
   b- LH(luteinizing hormone).
2- Sex hormones:
   a- Testosterone
   b- Estrogen
   c- Progesterone
3- Drugs which contract and relax uterus.

- **Gonadotrophic hormones**

**1- FSH**: secreted from anterior pituitary gland. The function are:

a- Stimulate formation of ovarian follicle (Graafian follicle).

b- Stimulate spermatogenesis (so is called SSH).

**PMSG**: The hormone has FSH activity in most species

**2- LH**: secreted from anterior pituitary gland. The function are:

a- Ovulation of mature Graafian follicle.

b- Formation of corpus luteum.

c- Stimulate interstitial cells(leydig cell)to produce testosterone.

**HCG(**Human chorionic gonadotropin**):** HCG exerts mainly luteinizing-hormone-like effects in domestic animals.

- **Sex hormones**

**1- Testosterone**: secreted from leydig cells. The functions are:

a- Development of genital organs.

b- Development of secondary sex characteristics of male.

c- Spermatogenesis.

d- Anabolic effect so male is stronger than female.

**2- Progesterone:** is secreted primarily by the corpus luteum and the placenta.

a- Prepares uterus for implantation

b- pregnancy maintenance.

c- development of mammary tissue for milk production.

**3- Estrogen**: its secreted from growing ovarian follicle before ovulation (ovary).

a- Stimulates growth of accessory reproductive organs and secondary sex characteristics.

b- Induces estrus (heat).

c- Mammary gland: stimulates development of the duct system.

- **Drugs which contract and relax uterus.**

1- **Oxytocin:** is secreted from posterior lob of pituitary gland and the functions are:

a- stimulates contraction of uterus .

b- ejection of milk through contraction of the myo-epithelial cells around the alveoli of the mammary gland.

**2- Prostaglandins:**

In female reproductive system prostaglandin E & F are found in ovaries, endometrium and menstrual fluid.

**a-** Causes regression of corpus luteum in sheep, cattle and swine

**b-** Contaction of uterus during parturition.

3- **Relaxin :** is secreted from corpus luteum(ovary). It is relaxes pubic bones and cervix (birth).

**4- Ergometrine:** It is one of the ergot alkaloids which cause contraction of the uterine smooth muscle.