DIPLOMA IN REGISTERED NURSING

eLEARNING TRAINING PROGRAM

Course Title: Pharmacology II

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INTRODUCTION

Welcome to Pharmacology II. In previous module you had an introduction to pharmacology in which you learnt about the principles of pharmacology; legal, ethical and cultural aspects of pharmacology; ordering, control and classification drugs. We also discussed drugs acting on the gastrointestinal tract, cardiovascular system and the respiratory system. We ended the discussion on cytotoxic drugs and drugs used to treat tuberculosis. You will continue to be equipped with knowledge and understanding of pharmacology in pharmacology II in order for you to complete the course.

Pharmacology II has 7 units as outlined in the course content.

COURSE AIM

To equip you with knowledge and skills in pharmacology

COURSE OBJECTIVES

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

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1. Describe the actions, contra-indications and side effects of commonly used drugs
2. Demonstrate skills in calculating, measuring, preparing and administering drugs.
3. Prescribe and dispense commonly used drugs.
4. Describe the responsibilities of the nurse in drug administration

COURSE CONTENT

UNIT 1: DRUGS ACTING ON THE ENDOCRINE SYSTEM

In this unit, you will describe drugs that act on the endocrine system and their effect on the body cells and how they influence body activities.

UNIT 2: DRUGS ACTING ON THE NERVOUS SYSTEM

In this unit, you will acquire knowledge and explain the drugs used to treat diseases of the nervous system and their effect on the body.

UNIT 3: DRUGS ACTING ON THE EYE, EAR AND NOSE

In this unit, you will gain knowledge on the drugs used to treat eye, ear and nose conditions.

UNIT 4: DRUGS ACTING ON THE SKIN

In this unit, you will gain knowledge on the drugs acting on the skin for treatment of various skin conditions. You will also learn different organisms which cause skin infections and how the drugs are administered.

UNIT 5: DRUGS ACTING ON THE IMMUNE SYSTEM

This unit will provide you with valuable information on drugs that act on the immune system of an individual. These drugs are divided into two classes and these are Immunosuppressant and anti-retroviral drugs. You will also learn the difference between immunosuppressant and anti-retroviral drugs and when each class is supposed to be administered.

UNIT 6: DRUGS ACTING ON THE URINARY SYSTEM

This unit discusses drugs you will be using to treat infections of the urinary system. You will gain knowledge on the drugs that exert antibacterial activity on the urinary system but have little or no systemic anti-bacterial effect.

UNIT 7: DRUGS USED IN OBSTETRICS

In this unit, you will acquire knowledge on drugs used in treating conditions commonly found in women during pregnancy, labour and delivery of the fetus. You will also explore your role when administering drugs to pregnant women, doses and why you should keep the said doses as low as possible.

LEARNING TIPS

It will probably take you a minimum of 50 hours to work through this whole course. The time should be spent on studying the Course and the readings, doing the activities and self-help questions and completing the assessment tasks. Be informed that sections are not all the same in length; therefore, plan your work and pace to give yourself time to complete all of them. . For example, units, 2, 3 and 5 have heavy reading schedule. Again, we wish to remind you that good review and understanding of basic anatomy and physiology is a pre-requisite to appreciating pharmacology

ACTIVITIES, SELF-HELP QUESTIONS AND CASE STUDIES

You will find activities, self-help questions and case studies in this course. These are part of a planned distance education programme and they are intended to help you make your learning experience more active and effective. They will help you to engage with ideas and check your own understanding. It is important that you take the required time to complete them in the order that they occur in the course. Make sure you write full answers to the activities, or take notes of the discussions.

READINGS

There is a list of further reading at the end of this course. This includes books, web sites and articles referred to in the course and there are suggestions in case you wish to explore topics further. You are encouraged to read as widely as possible during and after the course.

ASSESSMENTS

Your work in this course will be assessed in the following three ways;

Continuous Assessment which is divided into two has - 40%.

Tests (2) - 20%

Assignments (2) - 20%

Final exam Written - 60%

UNIT 1: DRUGS ACTING ON THE ENDOCRINE SYSTEM

1.1 Introduction

Hello, welcome to unit I of pharmacology II. In this unit, you will learn about the drugs that act on the endocrine system. The unit will equip you with the much needed knowledge for the betterment of the clients/ patient who will be under your care. Please pay attention to the content of this material.

1.2 Unit Objectives

Unit Objectives

By the end of this unit you should be able to describe the following drugs that act on the endocrine system:

1. Corticosteroids
2. Androgens and anabolic steroids
3. Estrogens and progesterones
4. Anti-diabetic drugs and glucagon
5. Thyroid hormones and antagonists
6. Pituitary hormones
7. Parathyroid like drugs

Before going through the drugs acting on the endocrine system, it is important that you refresh your memory on the meaning of the endocrine system.

The word endocrine derives from the Greek words 'endo,' meaning within, and 'crinis' meaning secrete. The endocrine system is the collection of glands (eight), each of which secretes different types of hormones that regulate metabolism, growth and development, tissue function, sexual function, reproduction, sleep and mood, among other functions (Zimmermann K.A, 2013).

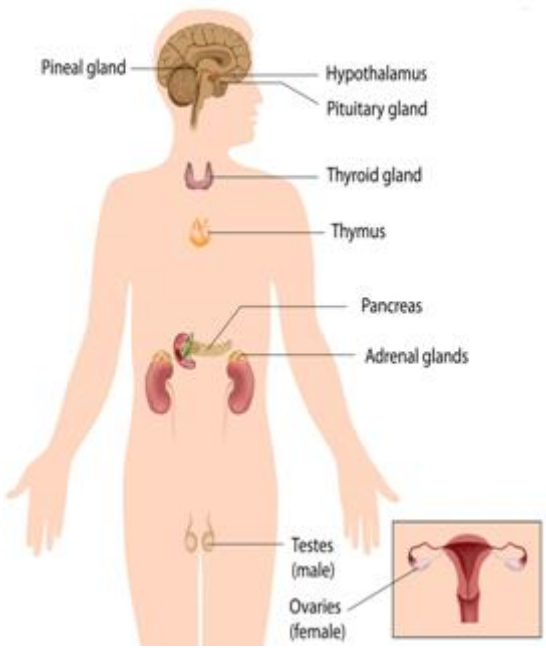

Figure 1: The Endocrine Glands

Endocrinology refers to study of the coordination of body functions by chemical messengers. The multiple activities of cells, tissues and organs of the body are coordinated by the interplay of several types of chemical messengers (neuro transmitter) such as;

- Neural endocrine
- Paracrines
- Autocrines
- Cytokines

Now, let us describe and give examples of the drugs used to treat conditions of the endocrine system.

1.3 Corticosteroids

They are naturally secreted by the adrenal cortex as Cortisol and Cortisone. However, some of the hormones can be synthesized

Examples of synthetic corticosteroids (Glucocorticoids)

- Prednisolone
- Betamethasone
- Dexamethasone
- Hydrocortisone

Pharmacological action

Activity

Do you remember the influence of corticosteroids on growth and development?

Well, let us have a look at the following actions of corticosteroids:

1. Metabolic Effects

- Increase blood glucose levels by facilitating the conversion of stored glycogen, especially in the liver
- Increase lipolysis and fatty redistribution
- Promote catabolic effects except in the liver
- Have an anabolic effect in the liver

2. Immune response and regulation of inflammation
- Have an anti-inflammatory effect on the body system by reducing vasodilatation and oedema
- Inhibit prostaglandins synthesis which is a vasoactive substance.
- Inhibit platelet activation leading to bleeding disorders
- Reduce healing by inhibiting inflammation (immunosupression)

3. They are immunosuppressive

- They reduce antibody production thereby reducing white cell migration and inhibit inflammation.

4. Action on the GIT

- They reduce gastric mucus secretion and increase hydrochloric acid and pepsin production leading to ulceration

Mode of action

Decreases inflammation, suppresses the immune response, stimulates the bone marrow and influences protein, fat and carbohydrates metabolism

Indications

- They are used to treat a number of different disorders especially inflammatory or immunologic disorders
- Adrenal insufficiency
- Arthritis
- Immunosuppressant in organ transplants
- Dermatitis
- Allergic reactions that is, anaphylactic shock, Asthma,
- Hepatitis
- Hypercalcaemia
- Leukaemia
- Anti-stress
- Lupus erythematosus
- Inflammatory bowel disease: ulcerative colitis and Crohn's disease
- Uveitis – inflammation of eye
- Cerebral oedema
- Respiratory distress syndrome
- Premature labour
- Babies born less than 32 weeks and in premature labour

Contraindications

- Patients with Diabetes Mellitus
- Patients with osteoporosis
- Use with caution in patients with elevated blood pressure.
- Avoid in ulcers
- Avoid in TB patients

Adverse Effects
- Thinning of the skin
- Peptic ulcers
- Hypocalcaemia
- Poor wound healing
- Osteoporosis
- Moon face.
- Trunk obesity
- Immune suppression
- Thinning of the limbs
- Growth retardation in children
- Cataract formation
- Glaucoma
- Hyperglycaemia
- Adrenal atrophy
- Psychosis
- Depression
- Diabetes mellitus.

Activity
Explain how corticosteroids can predispose someone to have diabetes mellitus. Write the answer in your note book

Well done for successfully doing this activity.

Drug interaction: aspirin, indomethacin, brufen (NSAIDs), barbiturates, phyntoin and rifampicin, oral anticoagulants, thiazide diuretics

Take Note

Glucocorticoids are tapered down (dosages are adjusted downward) before being discontinued in order to allow for the feedback mechanism in the regulation of glucocorticoid secretion by the body

Examples of glucocorticoids

1. **Prednisolone:**

It has less mineralocorticoid activity. Longer duration of action than cortisol and it is an anti-inflammatory and immunosuppressant.

Presentation:

Supplied as 5mg tablet or injection 25mg/ml, 100mg/ml; suppository.

Pharmacokinetics: It is readily absorbed after oral administration. Widely distributed to muscle, skin, intestines and kidneys and it is metabolized in the liver. Excreted as inactive metabolites and small un-metabolized drug mostly in urine..

Dosage

- Severe inflammation or immunosuppresion: Adults; 2.5-15mg PO 2- 4 times a day. 2-30mg I.M or I.V q 12 hours.
- Proctitis (inflammation of the rectum): 1 suppository bid preferably in the morning.
- Ulcerative colitis.

2. **Dexamethasone**

A glucocorticoid with anti-inflammatory and immunosuppressive effects.

Presentation; Supplied as tablet and injection of various strengths. It is readily absorbed after oral administration.

Pharmacokinetic; Absorption after an injection depends on site of injection. It is distributed to muscle, liver, skin, intestines and kidneys and metabolized in the liver to inactive metabolites.

Inactive metabolites and small amounts of un-metabolized drug are excreted by kidneys.

Dosage

- Cerebral oedema: Use dexamethasone sodium phosphate. Adults; 10mg I.V, then 4 to 6 mg I.M q 6 hours until symptoms subside then dose tapered over 5-7 days.
- Inflammatory conditions, allergic reactions, neoplasia; Adults; 0.75-9mg/day PO 0.5-9mg/day I.M (phosphate). 4-16mg I.M if acetate is used.
- Shock; Adults 1-6mg/kg I.V. as a single dose or 40mg I.V q 2-6 hours when necessary.

3. **Hydrocortisone**

Hydrocortisone is used to treat people who lack adequate naturally generated cortisol.
Presentation: 100mg per vial (injectable) 50mg and 100mg per tablet.
Dosage: 100mg to 200mg IM/IV tds or qid depending on the indication**:** In children 0.16 or 1 bd, tds or qid mg per kg body weight

Nursing consideration/implication of corticosteroids

1. Patient receiving long – term steroids require double their usual dose if they develop a moderate infection or triple the usual dose for severe illness to compensate for the deficient production by the body.
2. Before surgical operation, the surgeon and the anaesthetist must be informed if the patient is receiving /taking steroids due to anti-inflammatory and immunosuppressive effects. `
3. If treatment with steroids lasts more than 10 days, withdrawal must be gradual (tapered) as adrenal suppression will have occurred.
4. Patients must be taught not to stop taking steroids suddenly to prevent glucocorticoid deficiency.
5. Careful monitoring of side effects of steroids is important.
6. Random blood sugar should be checked regularly if the patient is on long steroid treatment. Patient on long term steroid should avoid contact with patient with infectious conditions such as Pulmonary Tuberculosis (PTB).
7. Prednisolone is often the steroid of choice because it has relatively little salt retaining activity.
8. Steroids are best taken in the morning with breakfast. At this time natural steroid production is at the maximum so causes less suppression of adrenal function.
9. All patients receiving long term steroids should carry a card detailing their treatment.

10. Nurses should wear gloves when applying steroids and wash afterwards because these drugs are easily absorbed through the skin (Greensten, 2013).

Self assessment – test 1

Where are cortical steroids secreted?

A. Adrenal cortex
B. Medulla cortex
C. Kidney
D. Adrenal tissue

2..... is **not** an example of a corticosteroid.

A. Betamethasone.
B. Dexamethasone.
C. Levonergestol
D. Hydrocortisone

Answers to self assessment - test 1

Multiple choice questions

1	2
A	C

1.4 Androgens and Anabolic Steroids

I. Androgens

You must always remember that androgens are secreted by the testes though there are weak androgens secreted by the adrenal cortex and the ovaries.

In males, they are responsible for the development and maintenance of sex organs, secondary sexual characteristics, normal reproductive function and sexual performance ability.

They also stimulate the growth and development of the skeleton and skeletal muscles during puberty.

Androgens promote development of sex organs and development of secondary sexual characteristics and stimulation of spermatogenesis. They also work to increase protein synthesis and increased bone and muscle development (anabolic effect).

The commonly available preparations of androgens are:

- Testosterone
- Methyltestosterone

Testosterone

Mode of action: Stimulates target tissues to develop normally and suppresses the production of oestrogen.

Presentation: 25mg/ml, 50mg/ml, 100mg/l

Dosage: 5-25mg IM injection 2-3 times per week for 2 – 6 weeks

Indication

- Androgens are used for palliative treatment in post-menopausal women
- Hypogonadism
- Androgen responsive metastasis of breast cancer

Androgenic effects

- Development and maintenance of sex organs in males.
- Development of secondary sexual characteristics in males.
- Stimulation of spermatogenesis

Anabolic effects

- Increases protein synthesis
- Increases bone and muscle development

Table 1: Side effects of androgens in males and females

In females	**In males**
Acne	Azoospermia
Hirsutism	Increased libido
Muscularisation	Testicular atrophy
Vaginal bleeding	Decrease ejaculatory volume
Weight gain	Impotence
Reversible oedema	
Bladder irritation	

Contra indications

- It is contraindicated in elderly males with breast cancer
- Patients with hypocalcaemia

- Patients with hepatic, cardiac and renal disease
- Males with prostate cancer
- Pre pubertal males

Drug interactions

- Insulin
- Oral anti diabetic agents
- Oral anticoagulants

Nursing considerations

- Avoid use in women of child bearing age until pregnancy is ruled out.
- Report any signs of hypocalcaemia
- It enhances hypoglycemia hence patients should be taught on the signs of hypoglycemia
- Instruct men to report priapism, reduced ejaculatory volume and gynaecomastia. If these occur you must report to the doctor to withdraw the drug.
- Monitor weight routinely to rule out obesity.
- Unless contraindicated, use with diet high in calories and protein.

Activity 1.2

Compare and contrast testosterone and methyltestosterone. Write your work in the note book (at least indicate 5 points)

II. Anabolic Steroids

Anabolic steroids are synthetic androgens with high anabolic effects and low androgenic effect.

Mode of action

Anabolic steroids potentiate tissue building processes.

The following are examples of anabolic drugs;

- Stanozolol
- Nandrolone
- Methanolone
- Methandiolone
- Ethylestranol

Indications

Anabolic steroids are used in:

i. Senile osteoporosis or post-menopausal osteoporosis
ii. Chronic debilitating diseases such as cancer or renal failure
iii. Major surgical operation after they have been conducted to enhance tissue repair
iv. Chronic immobilization due to muscle atrophy
v. Corticosteroid catabolism.

Side effects, drug interactions, contra indications and nursing consideration: same as for androgens

Self-Assessment Test 2: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. Androgens are responsible for secondary sexual characteristics in females …..

2. Anabolic steroids produce weight gain …..

ANSWERS:

1. F

2. T

1.5 Oestrogens and progesterones

In this section you will cover both oestrogen and progesterone.

a) Oestrogens

Oestrone and Oestradiol are both natural Oestrogens. Estrogens are the main ovarian oestrogens.

Oestrogens are responsible for the normal development of the female genital tract, breasts and of the female secondary sexual characteristics. Pubertal growth spurt is less marked in females than in males due to less anabolic effects of oestrogens than the androgens. However they are effective in promoting closure of epiphysis. The blood oestrogens concentration must be above the critical levels for the maintenance of both proliferative (together with progesterone) and secretive phase of uterine endometrium. If oestrogen levels

fall too low then the endometrium can no longer be maintained and uterine bleeding follows. Oestrogen is concerned with the normal maintenance of pregnancy accompanied by breast hypertrophy.

Natural sex hormones are rapidly metabolized in the liver therefore they are not used clinically.

Examples of synthetic oestrogen

- Ethyinyl estradiol
- Mestronal
- Di-ethyl stilbosterol (stilbosterol)
- Estropipate

Di-ethyl stilbosterol (stilbosterol)

Mode of action

It increases the synthesis of DNA, RNA and protein in the responsive tissues and reduces release of follicle stimulating hormone (FSH) and luteinizing hormone (LH).

Presentation: Tablets 1mg, 5mg. Injection: 50mg/ml

Dosage and indication

- Post coital contraception: 25mg per oral bd for 5 days
- Prostate cancer: 50-200mg IV daily for 5 days then once weekly.
- For breast cancer: 15g per oral daily

Side effects

The side effects include; Sodium retention and oedema, gynaecomastia, impotence, hypocalcaemia, depression, hypertension, lethargy, weight changes, increased appetite, altered menstrual cycle and cervical secretions, loss of libido, headache and dizziness.

Drug interaction

Cabamazepine, phynobarbitone, rifampicin, cortical steroids and ancitcoagulants

Contraindication
Patients with thrombophlebitis, pregnancy, undiagnosed genital disorders.
Use with caution in patients with hypertension, asthma, diabetes mellitus, cardiac, hepatic and renal disease.

Nursing implications/considerations

- Ensure that the patient has a thorough medical examination before initiation of oestrogen
- Warn the patient to stop taking immediately they become pregnant
- Warn patients to report abdominal pain, numbness, chest pain, shortness of breath, severe headache, visual disturbance and sudden weight gain
- Give drug with or immediately after meal.
- Teach women how to perform routine breast examination

Take Note
Ethyinyl estradiol is a very powerful synthetic oestrogen and is widely used in oral contraceptives

Activity

Read about ethyinyl estradiol, mestronal and estropipate in relation to indications, mechanism of action, side effects and nursing implications

Indications

- The drugs are used in oestrogen responsive prostate and breast cancer
- Used to suppress lactation
- Replacement hormone therapy (post menopause) in primary hypogonadism in girls.
- Reduce post-menopausal symptoms for example, hot flushes mood swings and headaches.

b) Progesterone

It is a hormone that is produced by the corpus luteum and converts uterine epithelium from the proliferative to the secretory phase. It is thus necessary for successful implantation of the ovum and is essential throughout pregnancy. In the last two trimesters it is secreted in large amounts by the placenta. It acts primarily on tissues which are sensitive to oestrogen but some synthetic progesterone types are less selective having varying oestrogenic and androgenic activity and these may inhibit ovulation though not very reliable.

Mode of action

It suppresses ovulation, possibly by inhibiting pituitary gonadotropin secretion, forms thick cervical mucus.

Examples

1. Progesterone derivatives
   - Depo-provera (medroxy progesterone)
   - Hydroxyl progesterone
2. Testosterone derivatives
   - Levonergestol
   - Noristhisterone (Noestherat)

Depo-provera (medroxy progesterone)

- Presentation:Tablets 2.5mg,5mg,10mg
- Injection: 100mg/ml, 150mg/ml 400mg/ml

Indications

- Hormonal contraception
- Dysmenorrhoea
- Endometriosis
- Long ovulation suppression
- Uterine bleeding
- Secondary amenorrhoea
- Endometrial carcinoma

Side effects, contra indications, drug interactions and nursing considerations: same as for oestrogen.

Self assessment test 3 : MCQ
Choose the most appropriate answer
1. The following are side effects of androgen drugs except----
---
A. Impotence
B. Secondary sexual characteristics
C. Increased libido
D. Infertility in females
1. Which of the following is not a side effect of using oestrogen:
A. Oedema
B. Weight gain
C. Hypertension
D. Suppression of lactation
2. Which hormone is produced by the corpus luteum:
A. Prolactin
B. Oestrogen
C. Progesterone
D. Oxytocin

Answers

1	2	3
B	A	C

1.6 Anti-diabetic drugs and glucagon

The pancreas is an exocrine as well as an endocrine gland. It has two main functions:

- To produce pancreatic endocrine hormones (for example,, insulin and glucagon) which help regulate many aspects of our metabolism and
- To produce pancreatic digestive enzymes – exocrine function.

Insulin is secreted from beta cells of the islet of Langerhans of the pancreas. Its action provides for storage of glucose, amino acids and fatty acids. The presence of glucose in the blood stimulates the release of insulin and it is in biphasic. This means that the initial release of stored insulin is rapid while the release of newly formed insulin is slow.

The initial phase is absent in patients with Non-insulin dependent Diabetes Mellitus (NIDDM) (Type II) common in adults and both phases are absent in Insulin dependent Diabetes Mellitus (IDDM) common in children (Type I)

Diabetes mellitus (DM) is a chronic disorder of carbohydrate, protein and fat metabolism characterized by hyperglycaemia, polyuria, polydypsia and polyphagia due to deficiency or diminished secretion or effectiveness of insulin (Berkow R, 1997). Diabetes Mellitus can be Type I or Type II. Type I diabetes often called insulin-dependent diabetes or juvenile diabetes always requires insulin therapy. The primary treatment for diabetes type I is insulin. This is because;

- Insulin functions as a substitute for the endogenous hormone.
- It replaces the insulin that is either not made or is made defectively in the body.

Type II DM is also referred to as Non-Insulin Dependent Diabetes Mellitus (NIDDM) or late/adult onset and the primary treatment is oral hypoglycaemics.

Take Note

Medical treatment of Diabetes mellitus involves the use of Insulin and Oral hypoglycaemic drugs

Activity

Outline common clinical features of diabetes mellitus

A. Insulin

Mode of action

Insulin is responsible for transporting blood glucose into the cells after a meal by facilitating uptake, utilization, storage and acts on three principal tissues. Glucose is the primary source of energy for the cell in the body. Insulin binds to specific insulin receptors on the cell membrane and triggers the cells' response. Insulin will transport glucose across the cell membrane in the presence of potassium there by controlling the blood glucose levels of between 3.3g/dl and 6.5g/dl(80-120mg/100ms of blood (mg%)

However, when circulating blood glucose is low there is need to convert stored glycogen in the liver and muscles to glucose and the process is called glycogenolysis.

The hormone glucagon starts this process and it is released by the alpha cells of the pancreas to ensure the normal levels of blood glucose are maintained. It mobilizes stored glucose, amino acids and fatty acids in the blood stream to maintain blood glucose. Glucagon stimulates hepatic glyconeolysis and gluconeogenesis.

Mode of action of insulin according to target structures

In the liver insulin increases glucose storage by stimulating glycogenesis

- It reduces hepatic glucose output by inhibiting glycogenolysis and gluconeogenesis
- It reduces production of ketone bodies

In the muscles, insulin:

- It increases glucose up take, glycolysis and glycogenesis on the other hand.
- It increases amino acid uptake with increased synthesis of proteins.

In the adipose tissues:

- It increases glucose uptake with increase synthesis of fatty acids glycerol and triglycerides.
- It also inhibits lipolysis and mobilization of fatty acids.
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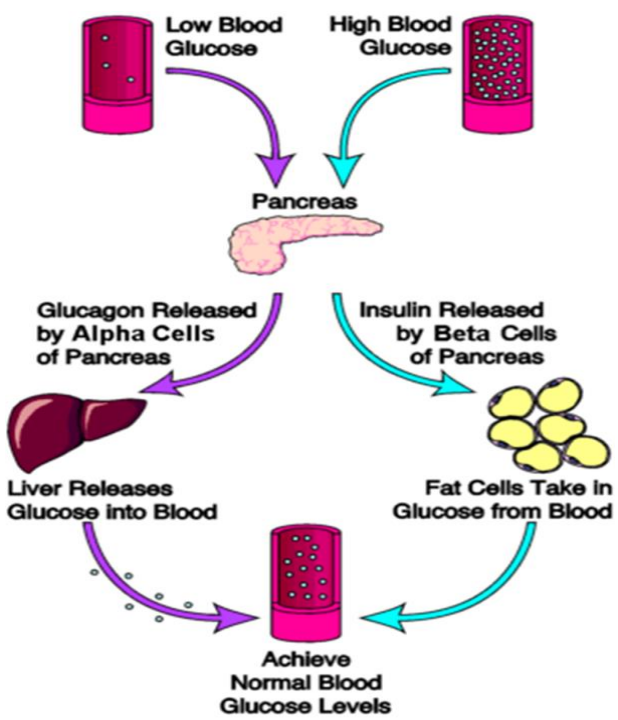

Figure 2: The Glucose Control Mechanism -*Source (***www.d.m.com**, 2013)

Types of insulin

There are four major classes of insulin:

a. **Rapid acting (Soluble)**: It is used to cover extra carbohydrates. Dosage is adjusted according to number of carbohydrates ingested. It is best given 15 minutes before a meal. It has a peak action of 1-3 hours and has the duration of 3-5 hours. Therefore you must be alert before giving this drug to prevent the patient from going into hypoglycaemia.
b. **Short acting (regular):** It is best given 30 to 60 minutes before a meal. It has a peak action of 2-4 hours and the duration of 8-12 hours
c. **Intermediate acting (lente**): This is a combination of long-acting 70% and rapid-acting 30%. Its effect is slower and more prolonged. It has a peak action of 4 – 12 hours and has a duration of 24 hours.
d. **Long-acting (lantus**): It contains rapid-acting and slower-acting insulin in 70/30 or 50/50 proportion.

Indications for insulin administration

It is indicated in the following conditions;

i. IDDM
ii. NIDDM to stabilize the patient
iii. After failure of diet control and full dose of oral hypoglycaemics
iv. Diabetic acidosis
v. Patients with hyperkalaemia
vi. For testing the pituitary function.

Side effects of insulin

i. Too much insulin can result in hypoglycemia (Abnormally low blood glucose level of below 50 mg/dL)
ii. Hypokalaemia
iii. Lipodystrophy
iv. Insulin overdose can result in shock and possible death.

Administering insulin

a. Insulin may be administered in several ways such as by syringe and needle, by a micro fine needle or a jet injection system. An insulin pump may also be used for insulin administration.
b. The doctor may prescribe insulin using a brand name or trade or generic name, for example, Insulin zinc suspension (lente).
c. It is therefore very important that the nurse understand the different types of insulin.
d. The nurse should never substitute one type of insulin for another because some patients might be sensitive to the other brands for example, protamine zinc sulphate insulin cannot be substituted by insulin zinc suspension.
e. The nurse should read the label on the bottle of the drug carefully for the name and the source.
f. A vial containing insulin in suspension form should be gently rotated between the palms of hand and tilted gently from end to end to help in distribution of the particles.
g. Check the doctor's orders again before withdrawing the drug.

h. Calculate the correct dose and collect the correct syringe.

B. Oral hypoglycaemics

Oral hypoglycaemics or oral anti-diabetic drugs are used as primary treatment of diabetes type II along with life style modifications. Newly diagnosed patients must not be subjected to anti diabetic drugs but must be educated on life style modification such as control of diet, doing some exercise, smoking cessation and monitoring of blood glucose levels. If these measures do not significantly reduce the blood glucose levels, then oral anti- diabetic drugs can be used

Oral hypoglycaemics are mainly divided into 2; sulfonylureas and biguanides

1. Sulfonylureas

Mode of action

The drugs require presence of at least 60% functional beta cells of the Islet of Langerhans in the pancreas. They help to stimulate insulin secretion from the beta cells of the pancreas and improve tissue sensitivity to insulin thereby helping to transport glucose out of the blood into the cells. The drugs further increase the sensitivity of insulin receptors.

Examples of Sulfonylureas include:

- Tolbutamide
- Chlorpropramide
- Glipicide
- Gliquidone
- Glibenclamide (Doanil)

Chlorpropamide (Diabinase)

Presentation:

Dosage: Initially 250mg daily. Elderly patients adjust according to response (100-125mg). Max dose 500mg daily taken with breast fast.

Glibenclamide (Daonil)

Presentation: 5mg, 10mg tablets
It is a long acting oral hypoglycaemic, given with caution in elderly patients.
Initially 5mg daily, elderly 2.5mg, maximum adjusted according to response, 15mg taken with food.

Side effects of sulfonylureas:

i. Hematologic system: anaemia, thrombocytopenia
ii. Fluid retention
iii. Skin rashes
iv. Gastrointestinal: nausea, epigastric fullness and heartburn
v. Hypoglycaemia especially with long acting agents especially there is a problem of kidney failure where they are cleared

Take note
Chlopropamide (diabenese) has a prolonged duration of action therefore has more side effects.

Contra indication

- Severe hepatic impairment.
- Severe renal impairment
- Porphyria
- Breastfeeding
- In pregnancy
- In ketoacidosis

Drug interactions
Aspirin, Thiazide diuretics

Activity:

Read and write short notes about tolbutamide, chlorpropramide, glipicide, gliquidone. State the presentation and the dosages of each.

2. Biguanides

They are the most commonly used oral drug in treating diabetes type II.

Mode of action

They work by decreasing the production of glucose (inhibit gluconeogenesis) as well as increasing peripheral utilization of insulin

Example of biguanide:

Metformin (Glucophage)

Presentation: 500mg tab

Dosage: Adults and children over 10 years initially 500mg with breakfast for one week, then 500mg with breakfast and evening meals for one week, then 500mg with breakfast, lunch and evening meals usually maximum dose of 2g daily in divided doses.

Side effects

Gastrointestinal upset, anorexia, nausea, vomiting, diarrhoea, abdominal pains, metallic taste. Others are decreased vitamin B-12 absorption, erythema, pruritis, urticaria and lactic acidosis.

Contraindications: renal impairment, ketoacidosis, pregnancy and breastfeeding.

3. Other oral hypoglycaemics:

Meglatides

Have similar mode of action as sulfonylureas: increase insulin secretion from the pancreas.
Side effects: headache, hypoglycemic episodes, weight gain, joint pain

Acarbose

It is an alpha glucosidase enzyme inhibitor which breaks down carbohydrates into smaller molecules found in the intestines. It inhibits glucosidase enzyme and reduces absorption of carbohydrates in the GIT.

Indication: Diabetes mellitus type II.
Side effects: Abdominal cramps, diarrhoea, flatulence, hypoglycaemia.

Thiazolidinediones

This group of drugs belongs to a group of chemicals called glitazones. They are part of the newer generation of drugs.

Mode of action
The drug work to decrease insulin resistance by enhancing the sensitivity of insulin receptors in liver, skeletal muscle and adipose tissue thereby reducing conversion of carbohydrates to glucose. Examples of these drugs are rosiglitazone and pioglitazone.

Side Effect
Can increase low density lipid (LDL) and high density lipid (HDL), GIT upsets, weight gain, hepatoxicity.

Contraindications
i. You must not give these drugs in pregnant women and breastfeeding mothers.
ii. You must also not administer to people with liver disorders, heart and those with renal failure
iii. Do not give with insulin

Drug interaction
Oral hypoglycaemics interact with Calcium channel blockers, erythromycin, ciclosporin, glucocorticoids for example prednisolone

Nursing consideration for oral hypoglycaemic agents
- The use of metformin with iodine containing radiologic contrast can lead to acute renal failure.
- Confirm that blood glucose test is done and that glucose levels are within acceptable limits.
- Elderly patients may be more sensitive to drugs adverse effects
- Instruct patients about nature of disease, importance of follow up, therapeutic regimen, adhering to specific diet, weight reduction, exercise, personal hygiene etc.
- Make sure patients know that therapy relieves symptoms but does not cure disease
- Patients transferring from another oral antidiabetic agent require blood glucose level testing at least three times a day before meals.

Glucagon
Glucagon, is a hormone secreted by the alpha cells of the pancreatic islets of langerhans.

Mode of action

- Stimulates glycogen breakdown to glucose in the liver
- Stimulate gluconeogenesis
- Inhibits glycogen synthesis
- Inhibits glucose oxidation
- Causes increased release of insulin

The overall result is to increase blood glucose.

> **Take note**
> Glucagon`s actions oppose those of insulin. It also limits its own actions by stimulating insulin release.

Indication: Hypoglycaemia for example, after an overdose of insulin
Dosage: 0.5 to 1 mg SC, IM or IV 1 hour after coma develops may repeat within 25 minutes, if necessary.
Side effects: Nausea, vomiting, hypersensitivity reactions, rash, dizziness, light headedness
Drug interaction: Phenytoin
Contra indication: Insulinoma – a benign adenoma of the islet cells of the pancreases, causing hypoglycaemia

Nursing consideration

- Unstable hypoglycemia diabetic patients may not respond to glycagon, give dextrose iv instead.
- It is vital to arouse patients from coma as quickly as possible and give additional carbohydrates orally to prevent secondary hypoglycemic reactions.
- Instruct patients and their family members on recognition of hypoglycaemia and urgency of calling the doctor or going for medical attention.
- For IV drip infusion, use dextrose solution which is compatible with glucagon.

Self-Assessment Test 4: TRUE OR FALSE
State whether true (T) or false (T) against the following statements in the spaces provided

1. Insulin is not used to treat NIDDM …
2. Glibenclamide is an example of a biguanide ……
3. Mertiformin is an example of a biguanine --------

ANSWERS:
1. F
2. F
3. T

Well done!

1.7 Thyroid Hormones and Antagonists

The thyroid gland

It is a gland that is situated in the neck in front of the larynx and trachea at the level of the 5th, 6th and 7th cervical and 1st thoracic vertebrae. It is a highly vascular gland which weighs about 25 measuring about 5 cm long and 3 cm wide and it is surrounded by a fibrous capsule. It has a shape of a butterfly with two lobes, one on either side of the thyroid cartilage and upper cartilaginous rings of the trachea. The lobes are joined by a narrow isthmus, lying in front of the trachea. The gland has two parathyroid glands on the posterior surface of each lobe which are sometimes embedded in thyroid tissue. Functionally the thyroid gland is made up of follicles (acini) made of a single layer of epithelial cells enclosing the follicular lumen. The lumen is packed with colloidal protein called thyroglobulin which is a storage place of thyroid hormone.

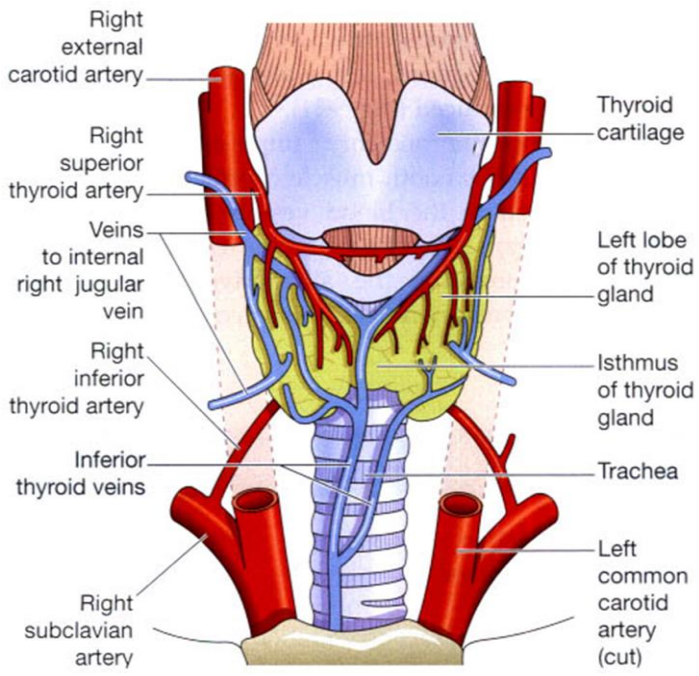

Figure 3: Anterior view of the Thyroid Gland
(Ross and Wilson 2004)

Functions of the Thyroid gland

Thyroid gland is responsible for the secretion of three hormones essential for proper regulation of metabolism.

i. Thyroxine (T4)
ii. Triodothyronine (T3)
iii. Calcitonin

Thyroid-stimulating hormone

TSH production is stimulated by TRH (thyrotropic releasing hormone) and inhibited by somatostatin, both of which are produced by the hypothalamus. TSH stimulates the secretion of the thyroid hormone thyroxine from the thyroid gland and the uptake of iodine when the blood levels of T3 and T4 are low.

T3 and T4

Both produced in the thyroid gland through the iodination and coupling of the amino acid tyrosine. The body needs about 1 mg of iodine per week from the diet.

Action of the thyroid hormone

Under physiological conditions, exposure to cold stimulates the hypothalamus to secrete thyrotropin releasing hormone (TRH) which increases the size, vascularity and function of the thyroid gland and stimulates the thyroid stimulating hormone whose actions are as follow:

i. The thyroid hormone antagonises the effects of thyrotropin releasing hormone by a negative feedback.
ii. It increases oxygen consumption leading to increased heat production and increased basal metabolic rate
iii. There will be pyrexia and these people experience flushing and heat intolerance.
iv. Causes susceptibility to both sympathetic and parasympathetic nervous system.
v. Increased sympathetic activity leads to anxiety and tremors of the skeletal muscles and sweeting
vi. There is an increase in diuretic action.
vii. Increased appetite but loss of weight
viii. Rapid glucose absorption and utilization
ix. Causes lipolysis
x. There is increased catabolic effect

Thyroid Hormone

Examples
Levothyroxine sodium (T4 or L-thyroxine sodium)

Presentation: Tablets: 25 mcg, 75 mcg, 100mcg, 150mcg, 200mcg; Injection: 200mcg/vial, 500mcg/vial
Dosage
In cretinism – 25 mcg to mcg p.o daily for 2 to 3 weeks
In myxeodema – 400mcg IV then 100 to 300mcg daily for 2-3 weeks
Thyroid hormone replacement 25 mcg, 100mcg, p.o daily for 4 weeks

Liothyronine sodium (T3)

Presentation: Tablets: 5mcg, 25mcg, 50mcg
Dosage
In myxeodema -5mcg p.o daily increased by 5mcg to 10 mcg 1 – 3 weeks
In non-toxic goiter - 5mcg initially then increase to 10 mcg daily for 2 weeks
Thyroid replacement -25mcg p.o daily for 1 to 2 weeks maintenance dosage is 25mcg to 75 mcg
Mode of action
Stimulates metabolic processes in all body tissues by accelerating the rate of cellular oxidation
Side effects
Nervousness, insomnia, tremor, tachycardia, palpitations, arrhythmias, angina, pectoris, hypertension, appetite change, nausea, diarrhoea, headache, leg cramps, weight loss, diaphoresis, heat intolerance, fever, menstrual irregularities.
Drug interaction
Insulin, oral antidiabetic agents, phenytoin, oral anticoagulants epinephrine
Contra indications
Thyrotoxicosis, adrenal insufficiency, angina pectoris, hypertension, cardiovascular disorders, renal insufficiency, ischemia
Nursing consideration

- Intravenous (IV) administration - use prepared IV dose immediately before injection. Do not mix with other solution.
- Warn patients to tell the doctor at once if chest pain, palpitations, sweating nervousness, shortness of breath
- Make sure patient understands the importance of compliance
- Tell patient to take thyroid hormones at the same time each day.
- Monitor pulse and blood pressure every day.

Thyroid hormones antagonist
Antithyroid agents prevent or suppress the biosynthesis of thyroid hormones. They are used to treat hyperthyroidism by inhibiting the excessive production of thyroid hormones or by decreasing thyroid hormone activity.

Examples of thyroid hormones antagonists include:

i. Methimazole
ii. Carbimazole
iii. Propylthioracil

Mode of action of thyroid hormones antagonists
They inhibit oxidation of iodine in the thyroid gland, blocking iodine's ability to combine with tyrosine to form thyroxine.
May also prevent the coupling of monoiodotyrosine and diiodotyrosine to form thyroxine and triodothyronine.
Propylthioracil has the added ability to inhibit the conversion of T4 to T3 in the peripheral circulation

Carbimazole

Presentation: Tablets containing 5 mg, 20mg
Dosage 30-60mg daily as a single dose until patient becomes euthyroid (4-8 weeks) then progressively reduce dose to a maintenance dose of 5 to 15 mg daily

Methimazole (thiamazole)

Presentation: Tablets 5mg, 10 mg
Dosage: 10-60mg daily in 2 divided doses. Propylthiouracil 300-900mg in 3 divided doses per day in adults. 50mg -150 mg in children

Indication for thyroid hormone antagonists

- Hyperthyroidism
- Thyrotoxic crisis

Side effect
Headache, drowsiness, vertigo, loss of taste, diarrhoea, nausea, vomiting, salivary gland enlargement, leucopenia, jaundice, hepatic, dysfunction (anorexia, pruritis, right upper quadrant pain, rash, urticaria, skin discoloration
Drug interaction: None significant
Contra indication: Use with caution in pregnancy and breast feeding patients.

Nursing consideration

- Watch for signs of hypothyroidism (mental depression, cold intolerance) adjust dosage as necessary
- Warn patients to immediately report fever, sore throat, or mouth sores (possible signs of developing agranulocytosis)
- Teach patients to recognise and immediately report signs and symptoms of hepatic dysfunction such as anorexia, pruritis, right upper quadrant pain, yellow skin or sclera
- Pregnant women may require fewer drugs as the pregnancy progresses. Drug may be stopped during last few weeks of pregnancy
- Give with meals to reduce adverse gastrointestinal tract reactions
- Store in light resistance container

Other Drugs

- **Thionamide**: they block the synthesis of thyroid hormone
- Radio-iodine used to destroy cells making thyroid hormone.
- **Iodine solution**: Used to reduce production of thyroid hormone temporarily. This is the drug of choice in the treatment of thyroid crisis and premedication before thyroid surgery.

Adverse effects:
Patient may develop allergic responses such as skin rashes, sneezing and conjunctivitis.
Many of the common symptoms of hyperthyroidism such as palpitations, tremors, and anxiety are mediated by increase in beta adrenergic receptors on cell surfaces.

These can be controlled by using beta blockers such as:

- Propranolol 10-40mg tds
- Metoprolol 50mg qid

Whenever you are administering beta blockers you have to look out for the following due to crisis that may occur;

i. Tachycardia and cardiac Arrhythmias,
ii. Fever
iii. Heart failure
iv. Flushed skin
v. Confusion / apathetic attitude / behavioral changes
vi. Hypotension.

You have to be alert and do not discontinue treatment abruptly but monitor the dosing and therapeutic effects of the drug used.

Self-Assessment Test 5: TRUE OR FALSE
State whether true (T) or false (F) against the following statements
1. Thyroid hormones are essential to life …..
2. Carbimazole is an anabolic steroid …..
ANSWERS:
1. T
2. T

1.8 Pituitary Hormones

If you remember very well in your anatomy and physiology, you discussed the endocrine system. This is the system which regulates body activities through hormonal directive.
The pituitary is a small endocrine gland attached to the brain by a stalk surrounded by the sphenoid bone in the base of the skull. It consists of the anterior and the posterior lobes. The lobes secret a number of hormones that affect not only various processes in the body but also activities of most other endocrine glands. The pituitary gland also is regulated by the master gland the Hypothalamus through the negative feedback mechanism.

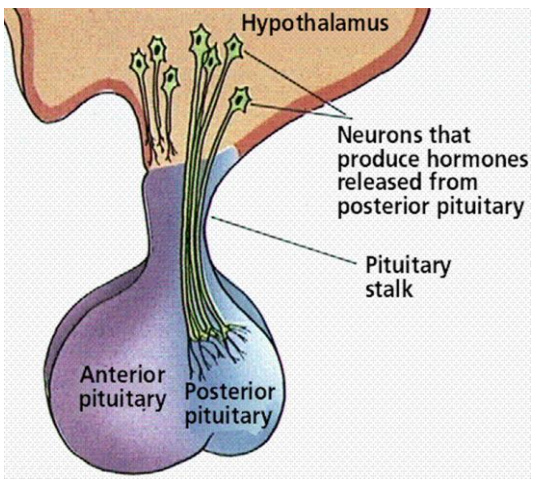

Figure 4: Pituitary and Hypothalamus glands (www.whfreeman.com)

Control of pituitary hormone release
There are two groups of hormones and these are:
1 Anterior lobe hormone
2 Posterior lobe hormone

Anterior Pituitary hormones
Do you remember the number of hormones?
The anterior pituitary is an endocrine gland that responds to signals from the hypothalamus to make and secrete hormones. Each hormone released by the hypothalamus is either a releasing or inhibiting hormone and either promotes or inhibits hormone release by the anterior pituitary. Hormones secreted by the anterior pituitary aid regulation of a varied set of functions within the human body (metabolism, osmo-regulation, reproduction).
The anterior pituitary receives releasing and inhibiting hormones from the hypothalamus by way of a capillary network and a portal vein, which empty into a second capillary network in the anterior pituitary.
These hormones stimulate the anterior pituitary to produce its own hormones. These are tropic hormones (for example, FSH, TSH, and ACTH), which control other endocrine glands.
Many of the hormones produced by the anterior pituitary are tropic hormones, or tropins, which affect the growth, nutrition, or function of other endocrine glands . Hormones released by the anterior pituitary control a wide range of functions, including growth and metabolism, reproduction, and osmo-regulation. Most types of secretory cells in the anterior pituitary are specialized to secrete only one hormone each when stimulated by a specific releasing factor from the hypothalamus.

The Hypothalamus
The hormones produced by the hypothalamus and their respective anterior pituitary hormones are:

i. Thyrotropin-releasing hormone (TRH) ---> thyroid-stimulating hormone (TSH)
ii. Corticotropin-releasing hormone (CRH) --->adrenocorticotrophc hormone (ACH)

iii. Dopamine (DA), also called 'prolactin inhibiting factor' (PIF) ---> prolactin
iv. Gonadotropin-releasing hormone (GnRH) ---> follicle-stimulating hormone (FSH) and luteinizing hormone (LH) and
v. Growth hormone releasing hormone (GHRH) ---> growth hormone (GH)

Control of secretion of hormones
Hormone release from the pituitary is controlled by negative feedback from the target gland. For example, TSH from the anterior pituitary is released in response to release of TRH from the hypothalamus. TSH then causes the thyroid gland to release thyroid hormones. As the levels of thyroid hormones build up in the blood, they assert negative feedback on the hypothalamus and anterior pituitary, thereby suppressing the release of TRH and TSH.

Growth Hormone
It is a polypeptide hormone (secreted by the pituitary gland) that promotes growth and regulates the metabolism of carbohydrates, proteins and lipids. Growth hormone (GH) has both nontropic and tropic effects and targets the liver, which responds by releasing insulin-like growth factors (IGFs) which directly stimulate bones and cartilage growth and also influences aging. It promotes linear growth in children but does not accelerate bone maturation, sex maturation and closure of the bone epiphysis.

Preparation: Somatrem and somatotropin
Used to promote growth in Growth hormone deficiencies
Over secretion of GH results in disorders, including gigantism and acromegaly
Under secretion of GH in childhood retards bone growth and can result in dwarfism.
Individuals with this disorder tend to be very short. If diagnosed before puberty, this disorder can be treated with human GH.

Adrenocorticotrophic Hormone
ACTH stimulates secretion of glucocorticoid steroid hormones from adrenal cortex cells, especially in the zonafasciculata of the adrenal glands. ACTH promotes the growth of the cells that produce cortisol and also of the production of the enzymes to synthesise cortisol.
Indications
i. Diagnosis in the patients with abnormal corticosteroid production.
ii. Anti-inflammatory and immunosuppressive agent.

Gonadotropins
Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are called gonadotropins because they stimulate the gonads –Luteinizing hormone promotes testosterone production in males, and in females, the ovaries. Follicle stimulating hormones in males stimulate spermatogenesis and testosterone secretion while in females they stimulate ovulation including oestrogen and progesterone production from ovaries.
They do not necessary support life, but are essential for reproduction. These two hormones are secreted from cells in the anterior pituitary called gonadotrophs. Most gonadotrophs secrete only LH or FSH, but some appear to secrete both hormones.
The hormone human chorionic gonadotropin (HCG) is produced during pregnancy. It is made by cells that form the placenta, which nourishes the egg after it has been fertilized and becomes attached to the uterine wall. Levels can first be detected by a blood test about 11 days after conception and about 12 - 14 days after conception by a urine test.

Preparations
Human menopausal gonadotrophins
i. Menotrophins (Folicle stimulating and leutinizing hormone).
ii. Urofollitropin (FSH)
iii. Human chorionic gonadotrophins (HCG)
Indication
i. Treatment of infertility in male and female
ii. In vitral fertilization
iii. Ammenorrhoea due to lack of gonadotrophins
Side effects
i. Hyperstimulation syndrome .for example, ovulation enlargement, ascitis.
ii. Multiple births in one pregnancy
iii. Spontaneous abortions
iv. Gynaecomatsia in males.

Prolactin
It stimulates lactation (milk Production) and has a direct effect on the breasts immediately after parturition. It is stimulated by prolactin releasing hormone (PRH) released from the hypothalamus and it is lowered by prolactin inhibiting hormone (PIH, dopamine).Suckling stimulates prolactin secretion and lactation. Hormones such as oestrogens, corticosteroids, insulin and thyroxine help in initiating and maintaining lactation.
Prolactin also inhibits the effect of ovarian function and high blood levels of prolactin during lactation period are responsible for the delayed return of menstruation after pregnancy.

Self-Assessment Test 6: MCQ
Choose the most appropriate answer
1. How many hormones does the posterior pituitary gland produce?
A. 4
B. 3
C. 2
D , None

2. Which gland stimulates the production of hormones by other glands in the human body?
A. Anterior pituitary gland
B. Posterior pituitary gland
C. Hypothalamus
D. None of the above
ANSWERS:
1. D
2. C

1.9 Parathyroid drugs

Parathyroid hormone and analogs (a synthetic form of parathyroid hormone) control the distribution of phosphate and calcium in the body. High levels of parathyroid hormone triggers transfer of calcium from the bones to the blood. It increases absorption of calcium by the intestine and increases re-absorption of calcium by the renal tubules. A low level of parathyroid hormone reduces calcium levels in the blood.
The parathyroid glands are embedded behind the thyroid gland and are responsible for regulation of calcium and phosphorus in the blood and their excretion in the kidneys. A fall in the level of blood calcium concentration stimulates the parathyroid to release the parathyroid hormone which mobilizes calcium from the bones and decrease its loss through the kidney hence returning the calcium levels to normal.

Action of parathyroid hormone
The parathyroid hormone mobilizes calcium from the bones and increases the production of calcitriol, a member of vitamin D which increases calcium absorption from the GIT. It increases active bone desorption and enhances calcium re-absorption from the kidney tubule.

Parathyroid hormone deficiency
Its deficiency results in an increase in blood phosphorous and decrease in blood calcium. Low calcium levels causes a condition called *tetany* which is characterized by increased irritability of muscles with spasms of the head and feet and the larynx.

Calcium may be decreased due to:

- PTH deficiency
- Lack of calcium in diet especially if vit D is missing
- Alkalosis
- Increase phosphorous excretion

Treatment of Tetany
You must administer calcium gluconate or calcium chloride IV. Calcium salts can also be used to treat tetany as well as to prevent chronic calcium deficiency especially in menopause.
Poor calcium re-absorption may be due to;

- Vitamin D deficiency
- Gastrectomy
- Age
- Stetorrhoea

Self assessment Test 7: TRUE OR FALSE
State whether true (T) or false (F) against the following statements in the spaces provided
1. Calcitonin is an hypocalcaemic agent …
2. Vitamin D deficiency may lead hypocalcaemia ….
ANSWERS:
1. T
2. T

You have come to the end of the unit where we were discussing drugs acting on the endocrine system. You have learnt about several drugs and the hormones that influence activities of the body and I hope you found it interesting. Let us now review what you have learnt.

1.10 Summary

In this unit you have learnt about drugs acting on the endocrine system.
In this unit we discussed corticosteroids (which can be glucocorticoids or mineralcorticoid), androgens and anabolic steroids, oestrogens and progesterones. We also discussed anti-diabetic drugs, which we said are divided into Injectable Insulin and oral hypoglycaemics. We discussed that oral hypoglycaemics are mainly divided into sulfonylureas and biguanides. We further discussed thyroid hormones and their antagonistic agents, pituitary and parathyroid hormones. We emphasized that the secretion of hormones is controlled by the feed-back mechanism. Well done for completing this unit. I hope you found it interesting.
In the next unit, which is Unit 2, we will look at drugs that act on the nervous system.

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UNIT 2: DRUGS ACTING ON THE NERVOUS SYSTEM

2.1 Introduction

Welcome to yet another interesting unit. In the previous unit, we discussed and gave examples of drugs acting on the endocrine system. In this unit we will discuss the drugs that act on the nervous system. The nervous system and the endocrine system are related because their functions are interdependent. The unit discusses drugs that act on the central nervous and autonomic nervous system

The nervous system coordinates rapid and precise responses to stimuli using action potentials. The endocrine system maintains homeostasis and long-term control using chemical signals. Drugs acting on the nervous system (NS) were among the first to be discovered by primitive humans and are still the most widely used group of pharmacologic agents .However, the NS works hand in hand with the endocrine system growth and maturation of the body system along with homeostasis.

2.2 Unit Objectives

Unit Objectives

By the end of this unit you should be to;

1. Describe drugs acting on the Central Nervous system including;

a) sedatives

b) Anticonvulsants

c) Antidepressants

d) Antipsychotics

e) CNS stimulants

f) Ant parkinsonism

2. Describe drugs acting on the Autonomic Nervous System including:

a) Adrenergic and adrenergic blockers

b) Skeletal muscle relaxants

c) Neuromuscular blockers

d) Cholinergics

e) Anticholinergics

Do you remember the non-narcotics, analgesics and anti-pyretics, non-steroidal anti-inflammatory drugs narcotic and opiate analgesics that were covered in Unit 4 of Pharmacology 1 under Classification of Drugs? These drugs act on the central nervous system. You will need to refresh your memory on these drugs that you learnt about earlier in unit 4 of the previous module. You can make reference to your notes.

ACTIVITY :

List four non-steroidal anti-inflammatory drugs (NSAIDS)
Differentiate between narcotic and opiate analgesics
Write your answers in your note book.

That was a very good attempt. You learn very fast.

Now, because we already discussed non-narcotics, analgesics and anti-pyretics, non-steroidal anti-inflammatory drugs, narcotic and opiate analgesics, we will now proceed to discuss sedatives / anxiolytics / hypnotics and other drugs in this unit.

2.3 Drugs acting on the central nervous system

2. 3.1. Sedatives (Anxiolytics / hypnotics/ anti-depressants)

These are drugs used mainly for the treatment of insomnia and anxiety. Anxiolytic drugs are used to treat the symptoms of anxiety, whereas hypnotic drugs used to treat insomnia, thereby inducing sleep. The degree of central nervous system depression caused by a sedative should be the minimum consistent with therapeutic efficacy. A hypnotic drug should produce drowsiness and encourage the onset and maintenance of a state of sleep (Katzung, 2006).

Sedatives are classified into different types depending on the circumstance that produce the symptoms.

You have to know the different symptoms for you to come up with the right treatment in time. The symptoms are as follows:-

General anxiety disorder (GAD).

This is when the patient feels apprehensive and tense for no apparent reason due to minor problems. The patient may present with the following signs and symptoms: Muscle aches, nausea, sleep and problems.

Panic attacks

These are unexpected attacks of anxiety, often marked with physical signs and symptom such as tremors, palpitations and dry mouth.

Obsessive compulsive disorders

This is a condition characterized by repetitive anxiety driven behaviour such as checking if the door has been locked or not.

Post- traumatic stress disorder

This is a condition where anxiety is as a result of a traumatic experience (physical, emotional or psychological) such as death of a family member or being raped.

Phobic states

It is a state in which the patient fears certain situations; the commonest being hydrophobia, where an individual is afraid of water. Treatment is through counselling, sensitization and desensitization

Sedatives comprise:

- Benzodiazepines (These are widely used sedative-hypnotics).
- Buspirone (It is recently introduced anxiolytic)
- Beta-blockersβ -adrenoceptor antagonists (for example propranolol). They are used to treat some forms of anxiety, where physical symptoms (sweating, tremor, and tachycardia), are troublesome. They are not used as hypnotics.

Antidepressants
Mechanism of action of benzodiazepines

These drugs reduce anxiety by stimulating the action of an inhibitory neurotransmitter called gamma-aminobutyric acid (GABA) improving symptoms of sleep disturbances, tremor and muscle tension.

Therapeutic uses

You have to be aware that the use of these drugs has effects of the central nervous system. Hence use them with caution in people operating machines and driving.

Anxiolytic and euphoria actions

Diazepines potentiates the action of GABA in the limbic system therefore they are used for treatment of;

- Anxiety
- Panic attacks
- Withdrawal from alcohol

Sedative –hypnotic actions

Due to the potentiating/activation of the GABA action in the reticular formation which promotes sleep onset increase sleep duration and reduce rapid eye movements.

Therapeutic uses

- Insomnia
- Sleep walking

Anaesthetic action
Potentiate the action of GABA in the reticular formation of the brain stem thereby producing amnesia and sedation.

Therapeutic uses

- For endoscopic examinations
- Adjuvant and antedote to anaesthetic agents

Anticonvulsant actions
Benzodiazepine potentiates the action of GABA in the motor cortex.

Therapeutic uses

- Epilepsy
- Status epilepticus

Adverse effects

- Drowsiness and confusion
- Ataxia (poor coordination of skeletal muscles)
- Memory difficulties
- Hang over

Examples of Sedatives

Chlodiazepoxide (Librium)

Presentation: 5mg, 10mg, 25mg Cap, Inj. 1oomg ampoule

Therapeutic uses: Anxiolytic

Indications: Anxiety (short term use), delirium tremens

Dose: Anxiety, 10mg t.i.d increased in severe anxiety to 100mg daily in divided doses (elderly half the adult dose)

Side effects

Impairment of alertness, fatigue, dependence and respiratory depression

Contraindications

Respiratory depression, pulmonary insufficiency

Buspirone

Presentation: 5mg, 7.5mg, 10mg, 15mg, 30mg Tab

Mechanism of action

It acts by inhibiting the action of serotonin by binding to serotonin and dopamine receptors, also increases norepinephrine metabolism. It has delayed effect/onset of action and requires one week to act.

Therapeutic uses

In anxiety and panic state (suitable for patients liable to abuse the drug).

Dose

The usual starting adult dose is 5 mg daily in 2 or 3 divided doses. The dose may be increased by 5 mg every 2 to 4 days until an effective dose is found.

The maximum adult dose is 60 mg daily, but most patients respond to 15-30 mg daily in 2 or 3 divided doses.

Adverse effects

They occasionally cause nausea and headache, nervousness, light headedness, excitement, and insomnia. Less frequent side effects include unsteady gait, diarrhea, excitement, weakness, hostility, skin rash, and tremors.

Diazepam (Valium)

Presentation: Tablet containing 5mg and injection containing 10mg.

Action: Anxiolytic, sedative, anaesthetic antedote

Indications: Short term treatment of anxiety states, psychiatric disorders associated with anxiety, epilepsy, delirium tremens, Panic attack and tetanus

Dose: 5 to 30mg per day in 3 divided doses.

Side effects

- They include drowsiness, dizziness, and decreased alertness and concentration.
- Lack of coordination may result in falls and injuries, in particular, in the elderly.
- Impaired judgement.
- Decreased libido and erection problems are a common side effect.

Contra-indications: Respiratory depression, pulmonary insufficiency.

Nursing implications of sedatives

- Assess degree of anxiety, what precipitate anxiety and whether drug controls symptoms.
- Asses for alcohol withdrawal symptoms including hallucinations, delirium, irritability, agitation, fine to coarse tremor.
- Monitor blood pressure (BP) with patient lying down or standing.

Self-Assessment Test 8: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. Antidepressants are anxiolytics drugs …..

2. Sedatives are mainly used to treat insomnia and anxiety …..

ANSWERS:

1. T

2. T

2. 3. 2 Anticonvulsants/ anti-epileptic

Epilepsy is a chronic brain disorder characterized by repeated attacks of abnormal discharge of electrical impulses resulting into seizures and temporal sensory, motor, psychotic changes (http://www.merriam-webster.com/dictionary/epilepsy).

Seizure is associated with the episodic high frequency discharge of impulses by a group of neurons in the brain.

Seizure may be partial or generalized depending on the location and the spread of the abnormal neuronal discharge.

The cause of epilepsy is-idiopathic however, it is associated with secondary causes such as hypoglycaemia, fever and hypocalcaemia, trauma, meningitis and tumours.
Anti-consultants are drugs that are used to treat epilepsy. Treatment is aimed to prevent the occurrence of seizures by maintaining an effective plasma concentration of the drug, with careful adjustment of doses if necessary, starting with the low doses and increasing until seizures are controlled. Avoid abrupt withdrawal of anti epileptics to prevent precipitate of severe rebound seizures.

ACTIVITY
Mention three drugs which can be used to treat epilepsy

Write you answers in your note book.

Compare your answers to the notes.

Very good. You are a good learner.

Mode of action

The main target is to reduce the hyper excitability of cerebral neurons by;-

- Increasing the inhibitory transmission by potentiating the action of gamma amino-butyric acid (GABA) for example, phenobarbitone and benzodiazepines.
- Increasing GABA levels by reducing its breakdown through enzyme inhibition for example, Valproate and vagabatin.
- Reducing membrane ion permeability through sodium channel for example, phenytoin and valproate
- The objective of treatment is to prevent the occurrence of seizures by maintaining an effective plasma concentration of the drug.
- However, there are disadvantages of multiple therapies that occur between the various anti-epileptics and other drugs. Abrupt withdrawal of anti-epileptics, particularly the barbiturates and benzodiazepines, should be avoided, as this may precipitate severe rebound seizures.

The following are examples of anticonvulsant drugs.

1. **Carbamazepine (Tegretol)**

Presentation: tablet containing 100mg, 200mg and 400mg. liquid sugar containing 100mg/5ml and suppository containing 125mg.

Mode of action

It stabilizes neuronal membranes and limit seizure activity by either increasing efflux or decreasing influx of sodium ions across cell membranes in the motor cortex during generation of nerve impulses.

Indications: seizures and idiopathic trigeminal neuralgia.

Dose: 200 mg /day once per oral or 100mg b.d per oral

Side effects: nausea, vomiting, dizziness, bone marrow depression, Steven-Johnson's syndrome, impotence, sedation, drowsiness, blurred vision, speech disturbances and abnormal anti arrhythmic action

Contraindications

- With previous bone marrow depression
- Those hypersensitive to tricyclic anti-depressants

Use cautiously in patients with cardiac problems and liver disease

Nursing considerations

- Assess blood studies such as Full Blood Count (FBC), at least weekly, in long term therapy
- Monitor liver function tests (LFTs), including urinalysis
- Monitor and record blood sugar levels during treatment

2. **Phernobarbitone (Luminal)**

Presentation: Tablet containing 15mg and injection containing 15mg/ml

Mode of action: Depresses activity in brain cells primarily in reticular activating system in brainstem, also selectively depresses neurons in posterior hypothalamus, limbic structures.

Indications: Grandmal seizures, psychomotor attacks

Dose: Adult; by mouth, 30-360mg daily in 1 or 2 doses by IM 100-200mg as single dose, repeated 6 hourly as required. Max. 600mg daily

Child: by mouth, 3-5mg/kg daily in 1 or 2 doses by IM or slow IV 3.5mg/kg as single dose

Side effects: Drowsiness, lethargy, mental depression, ataxia and allergic skin reactions, insomnia, distractibility, aggression, poor memory, decreased libido, impotence, folate deficiency, neonatal haemorrhage, hypocalcaemia and osteomalacia.

Contra-indications: Respiratory depression

Nursing consideration

- Assess mental status, mood, affect and memory especially the elderly.
- Assess respiratory dysfunction, respiratory depression, character, and rate.
- Assess for blood dyscrasias, fever, sore throat, bruising, rash, jaundice, epistaxis.

3. Phenytoin (Epanutin)

Presentation: Capsule containing 25mg, chewable tablets 50mg and suspension containing 30mg/5ml.
Mode of action: Inhibits spread of seizures activity in motor cortex by altering ion transport, increases AV conduction to decrease dysrhythmias.
Indications: All forms of epilepsy except absence seizures.
Dose: Adult; 50-600 mg daily in 1 or 2 doses
Child; 3-8mg/kg daily in 1 or 2 doses

Side effects: Gum hypertrophy and tenderness; nystagmus, ataxia, slurred speech, confusion, hallucinations and lymphoid hyperplasia

Contra-indications: Seizures due to hypoglycaemia

Nursing considerations

- Assess drug level: toxic level 30-50mcg/ml; therapeutic level is 7.7-20mcg/ml.
- Assess mental status, mood, affect, memory especially in the elderly.
- Monitor kidney function through urinalysis, blood urea nitrogen (BUN) and creatinine tests.

4. Sodium valproate (Epilim)

Presentation: Tablet 100mg-200mg and oral solution 200mg/5ml.

Indications: All forms of epilepsy

Dose: Adult; initially, 600mg daily in divided in doses after food, increasing by 200mg/day at 3 day intervals to a max of 2.5g daily in divided doses, according to the patient's needs

Side effects: Gastric irritation, nausea, increased appetite and weight gain; transient hair loss, oedema

Contra-indications: Acute liver disease.

Nursing considerations

- In pregnancy encourage mothers to take folic acid.
- Coagulation abnormalities may occur-give vitamin K one month before expected day of delivery.
- If on contraceptives –encourage use of additional contraceptive methods due to increased metabolism of hormones.
- Regular and timely administration of doses.

Self-Assessment Test 9: MCQ

Choose the most appropriate answer

1. Which of the following drugs is not used to treat epilepsy?
A. Phernobarbitone
B. Phenytoin
C. Diazepam
D. Sodium valproate
4. The following are nursing considerations for patients taking anticonvulsants except?
A. They make the patient become drowsy and can cause an accident
B. They are not useful for machine operators
C. They alter a person's judgment
D. They are used to treat epilepsy

2.3.3 Anti-depressants

'Depression is one of the most common psychiatric disorders. At any given moment, about 3–5% of the population is depressed (point prevalence), and an estimated 10% of people may become depressed during their lifetime. The symptoms of depression are often subtle and unrecognized both by patients and by physicians.' (Katzung, 2006).

Antidepressants are used to treat depression and manic-depressive disorders.

Depression is classified according to the origin. The following are the categories of depression.

- Endogenous depression 25% has no obvious cause
- Secondary cause 60% results from stressful events, death of loved ones.
- Depression associated with maniac

The brain contains biogenic amines. Norepinephrines (5HT) which are responsible for the mood and any reduction in their activity lead to depression and any elevation leads to mood elevation or mania.

Mechanism of action

The amine hypothesis states that antidepressant drugs help to block the amine transporters known as the norepinephrine and serotonin transporters, respectively. These transporters terminate amine neurotransmission. Blockade of these transporters presumably permits a longer rest of neurotransmitter in the intrasynaptic space at the receptor site. Monoamine oxidase inhibitors (MAO) inhibitors block a major intraneuronal degradative pathway for the amine neurotransmitters, which permits more amines to accumulate in presynaptic stores and more to be released. Presynaptic autoreceptors respond to increased synaptic transmitter by down-regulating transmitter synthesis and release. (Katzung, 2006).

The main target is to elevate the brain biogenic amines (within 12 hrs). Anti-depressants are classified according to their mechanism of action.

1. **Amine pump inhibitors**

They inhibit neuronal uptake of biogenic amines allowing accumulation of the biogenic amines in the synaptic cleft thereby increasing the action of at post synaptic receptors Examples include: Flouxity and trazodone

2. **Mono Amine Oxidase Inhibitors**

They inhibit mono enzyme oxidase for metabolism of biogenic amines in the nerve endings thereby increasing the biogenic amine stores in the cleft for example, maclobemide

3. **Presynaptic alpha 2 blockers**

They function to inhibit the release of biogenic amines into the synaptic cleft for example, mianserine

4. **Tricyclic Antidepressants**

These prolong the action of norepinephrine, dopamine and serotonin to varying degrees by blocking the reuptake of these neurotransmitters in the synaptic cleft between neuron.

These are classified into 2 groups that are: Tertiary and secondary amines

Types of tertiary amines are:

- Imipramine
- Amytryptline
- Clopramine

Types of secondary amines:

- Desipiramine

Adverse effects of anti-depressants

a) Autonomic side effects
- Histamine blockade that results into sedation and fatigue
- Atropine like side effects and these are dry mouth and blurred vision.
- Urine retention

b) Cardiac toxicity

They block impulse conduction in the heart which leads to arrhythmia.

c) Mania in bipolar mania depressive disorders

Various examples of anti-depressants

Amitryptyline (Elavil)

Presentation: tablet containing 10mg, 25mg and 50mg, Syrup containing 25mg/5ml. Injection containing 10mg/ml

Indication: depression neuropathic and functional pain

Dose: 10- 100mg daily dose range

Side effects: sedation, dry mouth, blurred vision, nausea, constipation, difficulty in micturation, postural hypotension, syncope etc.

Contraindications: severe liver disease, manic phase, cardiac arrhythmias, recent heart block and myocardial infarction.

Carbamazepine –Tegretol

Drug action: Mood stabilizer and anticonvulsants
Dose: 200 mg /day once per oral or 100mg b.d per oral.
Side Effects: as above

Fluoxetine

Presentation: Tab 10, 20 40mg; Cap 10, 20mg; Oral solution 20mg/5mls

Mechanism of Action

It is serotonin selective re-up take blocker. It acts by inhibiting the reuptake and destruction of serotonin from the synaptic cleft, thereby prolonging the action of the neurotransmitter.

Dose: 10-20mg p.o

Indication

- Depression
- Panic
- Chronic pain
- Nocturnal enuresis
- Obsessive compulsive disorder

Side effects: Sexual dysfunctional, nausea and vomiting.

Mono Amine Opiod Inhibitors

These drugs interfere with enzyme mono amine oxidase and thus interfere with the breakdown of epinephrine and norepinephrine and serotonin (5HT) in the brain. This leads to the accumulation of the amines.

Such drugs include:

- Tranylcypromine,
- Phenelzine,
- Nialamid
- Iproniazid

Indication

- Atypical depression
- Panic attacks
- Phobic disorders
- Refractory cases or endogenous depression

Adverse effects

- Postural hypotension
- Insomnia
- Nervousness
- Micturition difficulties

Self-Assessment Test 10: MATCHING ITEMS

Match the anti-depressants in Column I with their action in Column II

Column I	**Column II**
1. __ Iproniazid	A. Mono amine oxidase inhibitor
2. __ Maclobemide	B. Mono amine opioid inhibitor
	C. Miscellaneous

ANSWERS:

1. A

2. B

2.3.4 Anti-psychotics (neuroleptics)

The term 'antipsychotic' refers to several classes of drugs which includes conventional antipsychotic drugs (often referred to as 'neuroleptics'). These drugs vary in potency and propensity to induce side effects.
The Psychotic disorders include schizophrenia, the manic phase of bipolar (manic-depressive) illness, acute idiopathic psychotic illnesses, and other conditions marked by severe agitation, change in mood and affect. All exhibit major disturbances in reasoning, often with delusions and hallucinations. Antipsychotic agents also are useful alternatives to electroconvulsive therapy (ECT) in severe depression with psychotic features, and sometimes are used in the management of patients with psychotic disorders associated with delirium or dementia or induced by other agents.

Mechanism of action of antipsychotics

All antipsychotic drugs block the dopamine (D2) receptors in the mesolimbic system

Classification of antipsychotics

1. Typical antipsychotics
    - Chlorpromazine
    - Haloperidol.
2. Atypical antipsychotics
    - Resperidone
    - Clozapine
    - Olazapine

Pharmacological action

- Blockade of D2 receptors in the central nervous system (Meso limbic system).They are used as psychosis suppressants.
- Anti-emetic effect by suppressing the chemoreceptor trigger zone. 3.

Examples of anti-psychotic drugs

Chlorpromazine hydrochloride (Largactil)

Presentation: tablet containing 25mg, 50mg and 100mg. Injection containing 25mg/ml

Indications: Behavioural disturbances, intractable hiccup, nausea and vomiting.

Dose: Adult: in psychiatric conditions up to 600mg daily in 3 divided doses.

Acute excitement states, 50mg-100mg IM to a max of 300mg in 24 hours.

Anti-emetic, 25 to 50mg IM

Side-effects: Postural hypotension; jaundice and sensitivity reactions.

Contra-indications: Coma caused by CNS depressants.

Nursing implications

1. Assess for constipation, urinary retention and if these occur increase on bulk and water intake.
2. Monitor billrubin, FBC and other liver function tests.
3. Monitor any potentially reversible cause of behaviour problems in the elderly before and during therapy.

Fluphenazine (Modecate)

Presentation: 1, 2, 5, 10mg Tab; Inj 2.5mg/ml
Indications: Schizophrenia and related psychoses
Dosage: 12.5mg to 25mg by deep IM injection every 2 to 5 weeks
Side-effects: As for Chlorpromazine

Contra-indications: As for Chlorpromazine

Nursing implications: as for chlorpromazine

Haloperidol (Serenace)

Presentation: 0.5, 1, 2, 5, 10, 20mg Tab; Inj 5mg/ml
Indications: Schizophrenia; mania; tranquillization and emergency control in behavioral disturbances.

Dosage: Adult; 3 to 20mg daily in divided doses, up to 100mg daily may be given in clinically healthy cases.

Side effects: Muscle hypotonia, hypotension.

Nursing implications: as for Chlorpromazine

Trifluoperazine (Stelazine)

Presentation: 1, 2, 5, 10mg Tab; Inj 2mg/ml
Indications: Schizophrenia and related psychoses, tranquillization in behavioral disturbances, short-term adjunction treatment of severe anxiety

Dose: Adult; Psychoses, initially 5mg twice daily, increased by 5mg after 1 week, then at intervals of 3 days according to the response.

Adult; Severe anxiety, 2mg to 4 mg daily in divided doses increased if necessary to 6mg daily.

Adult; by deep IM injection (for acute symptoms) 1mg to 3mg daily in divided doses to a max of 20mg t.i.d

Side effects and nursing implications: As for Chlorpromazine.

Take Note:

Anticholinergic drugs are routinely given with antipsychotic as prophylaxis against extra pyramidal side effects.

Self-Assessment Test 11: MATCHING ITEMS

Match the anti-psychotics in Column I with their classification in Column II

Column I	**Column II**
1. __ Largactil	A. Atypical
2. __ Clozapine	B. Typical
	C. Miscellaneous

ANSWERS:

1. B

2. A

2.3.5 Central nervous system (CNS) stimulants

ACTIVITY:
Name the three parts or divisions of the central nervous system
Write your answers in your note book

Well done, keep it up.

Central nervous system (CNS) stimulants are medicines that speed up physical and mental processes. They are used to treat attention-deficit hyperactivity disorder (ADHD), narcolepsy (poor control of sleep-wake cycles), and other disorders of the central nervous system.

Therapeutic indications for stimulants include the following:

- To counteract lethargy and fatigue.
- To reduce sleepiness and to keep the person awake when necessary, as well as to treat narcolepsy.
- To decrease appetite and promote weight loss, as well as to treat obesity.
- To improve concentration and focus, especially for those with attention disorders such as Attention Deficit Hyperactivity Disorder (ADHD).

Examples of CNS stimulants

- The most commonly used central nervous system stimulant is caffeine (also known as an analeptic drug).
- Other stimulants include amphetamines, such as dextroamphetamine sulfate and methamphetamine hydrochloride, and nonamphetamine drugs such as, pemoline and methylphenidate.

Amphetamines

Increase the levels of norepinephrine and dopamine in the brain by inhibiting re-uptake. They cause stimulation through the direct release of catecholamines from storage vesicles in cells. Amphetamines are known to cause elevated mood and euphoria as well as rebound depression and anxiety**.**

Pharmacological action: increases arterial blood pressure with reflex bradycardia.

CNS stimulant action results in

- Wakefulness, alertness, decreased sense of fatigue.
- Mood elevation and self-confidence.
- Suppression of appetite.

Therapeutic uses and doses:

a. **Narcolepsy** (excessive sleep disorder) adults; 5 to 60mg PO daily in divided doses.
b. **Attention deficit disorder in children** Children 3 to 5years; 2.5mg Po daily increased by 2.5mg weekly prn. 6 and above; 5mg PO with 5mg increments weekly as necessary.
c. **Obesity-** 5 to 30mg PO daily in divided doses 30 to 60 minutes before food.

Side effects

- Psychological dependence
- Schizophrenia like syndrome
- Restlessness, anxiety, weakness and insomnia.
- Fatigue and depression follow cerebral stimulation.
- Tachycardia, palpitations, arrhythmias, increased blood pressure.
- Fatal poisoning terminates into convulsions, coma and cerebral haemorrhage.
- Loss of weight
- Altered libido.

Contraindications

- Hypersensitivity to drug.
- Use cautiously in elderly, debilitated, or hyper excitable patients, history of suicidal tendencies and pregnant women.
- Not recommended in children below 12 for treatment of obesity and in children under 3 years for treatment of ADD with hyper activity.

Nursing implications

- History of underlying condition.
- Be alert for adverse reactions and drug interactions.
- Monitor dietary intake when drug is used for obesity.
- Educate patient on amphetamine
- Drug not recommended for treatment of obesity in children below 12.
- Drug should be given 30 to 60 minutes before food.
- Make sure obesity patients are on weight reduction program.
- Administer drug at least 6 hours before bed time to avoid sleep disturbances.
- Evaluation of patient's health is maintained during amphetamine use.
- Patient is able to sleep without difficulty.

Other drugs include ephedrine

2.3.6 Anti-Parkinsonian drugs

Parkinson's disease is a progressive degenerative disease of the brain characterized by static tremors, postural instability and mood changes. It is due to the imbalance between the cholinergic and dopaminergic influences on the basal ganglia.

Causes

- Age related degenerative changes in the nerve cells in the basal nuclei of the brain
- Drug induced brain damage
- Cerebral ischemia
- Viral encephalitis

Anti-parkinsonian drugs relieve rigidity tremors of parkinsonism but they have less or little effect on bradykinesia. The aim of the treatment is either to increase dopaminergic activity (by dopamine agonist) or to decrease cholinegic (antimuscarinic drugs) influence on the basal ganglia.

Mechanism of action

They are effective against drug induced parkinsonism and cause enhancement of dopaminologic activities by depleting neuronal dopamine. Thus inhibit dopamine metabolism by selective mono amine oxidase B enzyme (selegiline).

Anti-parkinsonian drugs

Antimuscarinic drugs exert antiparkinsonism effect by correcting the relative central cholinergic excess thought to occur in parkinsonism as a result of dopamine deficiency.

The synthetic parasympatholytic drugs used for inhibition of the extra-pyramidal system include benzhexol, benztropin and procyclidine. Apart from their central action, their effects include paralysis of ciliary muscles of the eye resulting in poor accommodation, dilatation of pupils, tachycardia, dry mouth, constipation and urinary retention. In drug induced Parkinsonism the dose should be adjusted to eliminate symptoms.

Examples of anti-parkinsonian drugs

Benzhexol Hydrochloride (Artane)

Presentation: tablet containing 2 and 5mg.

Indications: Parkinsonism

Dose: 1mg daily, gradually increased; usually maintenance dose 5-15 mg daily in 3-4 divided doses

Side Effects: Dry mouth, dizziness, blurred vision, less commonly urinary retention, tachycardia, hypersensitivity, nervousness and with high dose insusceptible patients, mental confusion, excitement and other psychiatric disturbances

Caution: Cardiovascular disease, hepatic and renal impairment

Contra-indications: Untreated urinary retention, closed angle glaucoma and intestinal obstruction.

Contra-Indications: Children under 3 years and pregnancy

Nursing implications

1. Assess for mental status; affect mood, depression and worsening symptoms during therapy.
2. Monitor for urinary hesitance, retention. Palpate bladder if this occurs.

Procyclidine Hydrochloride

Presentation: Tablet containing 5mg procyclidine hydrochloride. Syrup containing 2.5mg/5ml

procyclidine hydrochloride. Injection containing 5mg/ml procyclidine hydrochloride

Indications: See under benzhexol hydrochloride

Dose: Oral; 2.5mg 3 times daily gradually increasing to a maximum of 30mg daily (60mg in exceptional cases). Elderly; preferably lower end of the dosage range.

By injection in acute dystonia; 5-10mg intramuscularly if necessary repeat after 20 minutes. Maximum dose 20mg daily.

Side effects, caution and nursing considerations are as for Benzhexol Hydrochloride

Benztropine Mesylate (Cogentin)

Presentation: 0.5, 1, 2mg; Inj. (IM/IV) 1mg/ml

Indications: Parkinsonism

Dose: By mouth, 500 micrograms-1mg daily usually at bed time, gradually increased max. 6mg daily, usual maintenance dose 1-4mg daily in single or divided doses.

By IM or IV injection; 1-2 mg repeated if symptoms reappear
Side Effects: As for Benzhexol hydrochloride

Procyclidine Hydrochloride (Kemadrin)

Indications: Parkinsonism

Dose: 2.5mg tid, gradually increased if necessary, usual max 30mg daily.

Side Effects: As for Benzhexol hydrochloride.

ACTIVITY :

Why are people taking drugs that act on the CNS not allowed to operate heavy machines?

Write your answer in your note book.

Well done. You are learning fast. Am sure you will give right advice to patients taking these drugs.

Self-Assessment Test: MCQ

Choose the most appropriate answer

1. Cerebral stimulants…

A. Reduce sleepiness

B. Promote appetite

C. Promote weight loss

D. Improve concentration

2. The following are examples of cerebral stimulants EXCEPT?

A. Caffeine

B. Amphetamines

C. Diazepam

D. Pemoline

ANSWERS:

1. B

2. C

2.4 Drugs acting on the autonomic nervous system (ANS)

ACTIVITY :
1. Which are the 2 major divisions of the autonomic nervous system?
2. What are the main functions of the ANS which support life?

Keep these at the back of your mind
Well done, if you are able to recall. You can now progress to discuss the drugs that act on the ANS.

The autonomic nervous system is an involuntary system which regulates body functions without conscious control. Its activity regulates the heart rate, contraction and relaxation of smooth muscles, respiratory and uro-genital processes and stimulates various secretory glands.

This system is divided into 2 main groups:

- **Sympathetic pathway**
- **Parasympathetic pathway**

There are three main catecholamines namely; epinephrine, norepinephrine, and dopamine DA. A physiological and metabolic response follows stimulation of sympathetic nerves which is usually mediated by the neurotransmitter norepinephrine. The pathways have antagonistic effects. The sympathetic activities predominate in stress (flight and fight responses) while the parasympathetic system is organized for localized and discrete discharge for example digestion and absorption. It is concerned with energy conservation and maintenance of organ function.

The main autonomic nervous system transmitters are acetylcholine (ACh) and norepinephrine. The transmission in which the acetylcholine is a principle transmitter are called **cholinergics** transmission while the transmission where norepinephrine is a principle neural transmitter is known as **adrenergic**

Drugs that act on the ANS either modulate through cholinergic or adrenergic pathways

A. CHOLINERGIC TRANSMISSION

Neural transmitter –Acetylcholine
Receptor - Cholinergic receptor.
Examples of cholinergic receptors include;

i) Muscarinic receptors (mAChRs)—bind both acetylcholine and muscarine, an alkaloid present in certain poisonous mushrooms (it was first isolated in Amanita muscaria). Cholinergic transmission (acetylcholine-mediated) that activates muscarinic receptors occurs mainly at autonomic ganglia, organs innervated by the parasympathetic division of the autonomic nervous system and in the central nervous system. Binding studies have identified five subclasses of muscarinic receptors: M1,M2, M3, M4, and M5. (Pharmacology Corner, 2015 http://pharmacologycorner.com/acetylcholine- receptors-muscarinic-and-nicotinic/ Accessed on 11/03/15 @13:00hrs)

ii) Nicotinic Acetylcholine receptors (nAChRs)- are neuron receptor proteins that signal for muscular contraction upon a chemical stimulus. They are cholinergic receptors that form ligand-gated ion channels in the plasma membranes of certain neurons and on the presynaptic and postsynaptic sides of the neuromuscular junction. Like the muscarinic acetylcholine receptor (mAChR)—the nAChR is triggered by the binding of the neurotransmitter acetylcholine (ACh). Just as muscarinic receptors are named such because they are also activated by muscarine, nicotinic receptors can be opened not only by acetylcholine but also by nicotine —hence the name ‘nicotinic’ (Purves. D et al (2008).

B. ADREGENIC TRANSMISSION

The major neural transmitter is norepinephrine and other neural transmitters include epinephrine and dopamine.
Adrenergic receptors are also divided into 2;
a) Alpha adrenergic receptors which are further divided into 2, Alpha 1 and Alpha 2 adrenergic receptors.

b) Beta adrenergic receptors. They are also divided into 2 groups Beta 1 and 2 adrenergic receptors.

Alpha 1 receptors occur on the target tissue and they constrict blood vessels leading to increased blood pressure and pupil dilatation.

The Alpha 2 receptors occur on the nerve terminals from which norepinephrine is released thereby forming a release control mechanism. They also dilate both the bronchi and the central blood vessels. Alpha 1 blocker drugs are used in the treatment of elevated blood pressure by removing vasoconstriction action of norepinephline leading to arterial dilatation thereby reducing the BP and it also reduces the secretion of adrenaline in pheochromacytoma (adrenal tumours)

2.4.1 Adrenergic and adrenergic blockers

A. Adrenergic Drugs

Adrenergic drugs are also called adrenergic amines or sympathomimetic drugs. They are medicines that work by stimulating the sympathetic nervous system (SNS), a division of the automatic nervous system (ANS) which helps to regulate your body's reaction to stress or an emergency.

Adrenergic drugs stimulate the sympathetic nerves by either mimicking the action of the neurotransmitter norepinephrine or stimulating its release. They are used for many life-threatening conditions. These include cardiac arrest, shock, or opening the airways during an asthma attack or allergic reaction. These are drugs which have excitatory properties on the sympathetic division of the A.N.S neurons.

Examples of adrenergic drugs

Adrenergic drugs used for bronchodilation include:

- Epinephrine
- Ephedrine
- Albuterol
- Bitolterol
- Isoproterenol
- Pirbuterol (NIH)

Sometimes an allergic reaction to insect stings, foods, or other substances can cause swelling that tightens up the air passages. Epinephrine can be injected in these emergency situations to open up the airways.

Adrenergic drugs used as Vasopressors

The vasopressors stimulate smooth muscle contraction of the blood vessels leading to vasoconstriction. Vasoconstriction is the narrowing of the blood vessels. The narrowing of the blood vessels will cause a rise in blood pressure. The increased blood pressure can be used to treat patients with hypovolaemic shock. Constriction of the blood vessels can also be useful to stop bleeding as well as to keep anesthetics to a specific area of the body.

Vasopressors can act on the alpha-1, beta-1, and beta-2 adrenergic receptors. Examples of vasopressors include:

- Phenylephrine
- Ephedrine
- Pseudoephedrine (Sudafed)
- Phenylpropanolamine
- Xylometazoline
- Dopamine
- Oxymetazoline (Elmhurst)

Adrenergic drugs used as nasal decongestants

Adrenergic drugs may also be used when swelling of the blood vessels in the mucous membranes of the nose blocks up the nasal passage and causes discharge which might happen if you have a cold or allergies. They act on sympathetic nerves to shrink the swollen membranes and provide relief for a few hours. Adrenergic drugs used as nasal decongestants include:

- Epinephrine
- Ephedrine
- Salbutamol (Ventolin)

Adrenergic drugs used as cardiac stimulators

Adrenergic drugs are also used to stimulate and restore the heart beat if a person's heart stops beating. This might occur due to drowning, electrocution, suffocation, or other causes. Epinephrine, for example, can be injected directly into the heart to make the heart start beating again

Common side effects of adrenergic drugs include:

- anxiety
- restlessness or wakefulness
- dizziness
- headache
- nausea

Self-Assessment Test: TRUE OR FALSE

State whether true (T) or false (F) against the following sentences

1. Adrenergic agonists are sympathomimetic in action ….

2. Sympathomimetic means they antagonize sympathetic nerve stimulation ….

ANSWERS:

1. T

2. F

B. Adrenergic Blockers (antagonists)

Adrenergic antagonists are drugs that act to inhibit the action of catecholamines such as adrenaline and epinephrine at the adrenergic receptors. They have the opposite effect as adrenergic agonists are also referred to as sympatholytic.

They are divided into:

Alpha-blockers dilate both arteries and veins because both vessel types are innervated by sympathetic adrenergic nerves; however, the vasodilator effect is more pronounced in the arterial resistance vessels. Examples of alpha-blockers include prazosin terazosin, doxazosin, trimazosin

Side effects of alpha-blockers

The most common side effects are related directly to alpha-adrenoceptor blockade. These side effects include:

- dizziness, orthostatic hypotension (due to loss of reflex vasoconstriction upon standing)
- nasal congestion (due to dilation of nasal mucosal arterioles)
- headache, and reflex tachycardia (especially with non-selective alpha-blockers)
- Fluid retention is also a problem that can be rectified by use of a diuretic in conjunction with the alpha-blocker

Take Note

Alpha blockers have not been shown to be beneficial in heart failure or angina, and should not be used in these conditions.

Beta-blockers are drugs that bind to beta-adrenoceptors and thereby block the binding of norepinephrine and epinephrine to these receptors. This inhibits normal sympathetic effects that act through these receptors. Examples of beta-blockers include atenolol, prapronolol, and timolol

Side effects Beta-blockers and contraindications

Cardiovascular side effects

Many of the side effects of beta-blockers are related to their cardiac mechanisms and include bradycardia, reduced exercise capacity, heart failure, hypotension, and atrioventricular (AV) nodal conduction block. These effects result from excessive blockade of normal sympathetic influences on the heart.

Beta-blockers are therefore contraindicated in patients with sinus bradycardia and partial AV block. Considerable care needs to be exercised if a beta-blocker is given in conjunction with cardiac selective calcium-channel blockers (for example, verapamil) because of their additive effects in producing electrical and mechanical depression.

Other side effects

Bronchoconstriction can occur, especially when non-selective beta-blockers are administered to asthmatic patients because sympathetic nerves innervating the bronchioles normally activate β2-adrenoceptors that promote bronchodilation. Therefore, non-selective beta-blockers for example propranolol, are contraindicated in patients with asthma or chronic obstructive pulmonary disease.

Bronchoconstriction occurs can also mask the tachycardia that serves as a warning sign for insulin-induced hypoglycemia in diabetic patients; therefore, beta-blockers should be used cautiously in diabetics.

Take Note

Both alpha and beta-blockers can either be selective (have affinity for specific adrenergic receptors) or non-selective (may not have affinity for specific adrenergic receptors) in their action

SCENARIO 1:

A 70 year old man is admitted to your ward with malignant hypertension. On history taking, you establish that he is also asthmatic. The doctor wants to prescribe a beta-blocker as part of treatment of his hypertension

In your opinion, which beta-blocker should the doctor avoid and explain why. Write the answers in your note book

2.4.2 Skeletal muscle relaxants/ Neuro-muscular Blockers

These drugs are mainly used as an adjunct to general anaesthesia to enable muscle relaxation to be achieved using a minimal dose of anaesthetic. General anaesthesia (G.A) is a reversible state of unconsciousness produced by anaesthetic in which motor, sensory, mental and reflex functions are lost (**http://medical-dictionary.thefreedictionary.com/general+anesthesia**. Accessed on 11/03/2015 @17:00hrs)

Muscle relaxants are divided into 2 groups, namely; non-depolarizing and depolarizing.

Depolarizing Agents:

Act by binding to the acetycholine receptors and blocking Ach from accessing post-synaptic receptors at the neuro-muscular junction. In the process of binding, the receptor is actually stimulated, thereby causing fasciculations. Suxamethonium (Scoline) is the commonly used drug by most anesthesia providers today

Suxamethonium Chloride (Scoline)

Presentation: injection 50mg/ml

Indications: Endotracheal intubation, Endoscopic examinations after general anaesthesia has been induced.

Dose: IV 700 mcg-1.4mg/kg

Side-effects: Prolonged apnoea, bradycardia, bronchospasm, hyperpyrexia and sensitization.

Nursing implications

Assess electrolyte imbalances as these may lead to increased action of the drug.

1. Monitor for recovery decreased paralysis of face, diaphragm, leg, arm, rest of the body.
2. Assess for hypersensitive reaction, anaphylaxis, rash, fever, respiratory distress, pruritus, then drug should be discontinued.

Non-depolarizing muscle relaxants

They act by binding to ACh receptors in a reversible manner and act by blocking access to the post-synaptic receptors. However, they do not 'stimulate' the receptor in the process of binding and, therefore, do not produce fasciculations. The common used short-acting agents include mivacurium and rapacuronium. Rocuronium, vecuronium, atracurium and others and intermediate-duration while pancuronuim and d-tubocurarine are the commonly used long-acting depolarizing muscle relaxants

Examples of non-depolarizing agent

Pancuronium bromide (Pavulon)

Presentation: Inj. 1, 2mg/ml

Indications

a) For endotracheal intubation
b) For muscular relaxation during surgery
Dose: IV initially for intubation 50-100 mcg/kg

Side-effects: Tachycardia, raised blood pressure, over dosage causes respiratory failure and vomiting.

Tubocurarine Chloride

Presentation: Inj 3mg/ml (20U/ml)

Indications: Muscular relaxation during surgery, and mechanical ventilation

Dose: IV initially 10-15 mg

Side-effects: Very few side effects. Over dosage causes respiratory failure and vomiting.

Contra-indication: Respiratory insufficiency, pulmonary disease.

Following the use of non-depolarization agents, muscle depolarization is prolonged since disengagement from the receptor site and subsequent breakdown is slower than it is for Acetylcholine. The effects of these drugs are reversed with anticholinesterase agents such as Neostigmine, a potent drug that inhibits the action of acetylcholinesterase (an enzyme that breaks down ACh.

Anticholinesterase used in surgery

Neostigmine Methyl Sulphate

Presentation: Tab 15mg; Inj. 1:000, 1:2000, 1:4000

Indication: Reverse the muscular relaxation produced by non-depolarizing muscle relaxants

Dose (Adult): 2.5-5mg with Atropine sulphate by slow IV injection over 60 seconds

Side effects: Rash, anaphylaxis, bradycardia, increased blood pressure

Nursing Implication

- Monitor for hypersensitivity reaction
- Monitor and record vital signs
- Monitor electrolyte imbalances – electrolyte imbalance may lead to increased action of the drug
- Monitor recovery – residual weakness and respiratory problems may occur

Nursing implications for non-depolarizing agent

1. Monitor for recovery decreased paralysis of face, diaphragm, leg, arm, rest of the body.
2. Assess for hypersensitive reaction, anaphylaxis, rash, fever, respiratory distress, pruritus, then drug should be discontinued.

Self-Assessment Test 12: MATCHING ITEMS

Match the muscle relaxants in Column I with their classification in Column II

Column I **Column II**

1. __ Suxamethonium A. Miscellaneous

2. __ Pancuronium B. Depolarizing

C. Non-depolarizing

ANSWERS:

1. B

2. C

2.4.4 Cholinergics

Cholinergic drugs are medications that produce the same effects as the parasympathetic nervous system. They produce the same effects as acetylcholine, most common neurotransmitter of the parasympathetic nervous system, which deals with everyday activities such as salivation, digestion, and muscle relaxation.

Mode of Action

Cholinergic drugs usually act in one of the two ways. Some directly mimic the effect of acetylcholine, while others block the effects of acetylcholinesterase, an enzyme that destroys naturally occurring acetylcholine. By blocking the enzyme, the naturally occurring acetylcholine has a longer action.

Indications

The cholinergic drugs may be used in several ways.

- The cholinergic muscle stimulants are used to diagnose and treat myasthenia gravis, a disease that causes severe muscle weakness.
- Cholinergic drugs are also used in the control of glaucoma, a disease that is caused by increased pressure inside the eye.

Side Effects

The possible adverse effects of cholinergic drugs are:

- slow heart beat, possibly leading to cardiac arrest.
- muscle weakness, muscle cramps, and muscle pain
- convulsions
- weak breathing, inability to breath
- increased stomach acid and saliva
- nausea and vomiting
- dizziness, drowsiness, and headache

Precautions

- Cholinergic drugs should be avoided when the patient has any sort of obstruction in the urinary or digestive tracts, such as a tumor, or severe inflammation which is causing blockage
- They should be used with caution in patients with asthma, epilepsy, slow heart beat, hyperthyroidism, or gastric ulcers
- Patients with slow heartbeat, increased secretions including the digestive acids of the stomach, saliva and tears

Examples of Cholinergics

1. Cholinergics which are used to diagnose and treat myasthenia gravis include ambenonium chloride (Mytelase), edrophonium chloride (Tensilon), neostigmine (Prostigmine), and piridogstimina (Mestinœn). These drugs are also widely used in surgery, both to reduce the risk of urinary retention, and to reverse the effects of the muscle relaxant drugs that are used in surgery.

2. Cholinergic drugs that are used in the control of glaucoma include humorsol and echthiophate, phospholine iodide, pilocarpine.

.

Self-Assessment Test 13: MCQ

Choose the most appropriate answer

1. Cholinergic drugs act in one of the following ways EXCEPT?

A. Mimic action of acetylcholine
B. Inhibit the action of acetylcholinesterase
C. All of the above
D. None of the above

2. Which of the following is an example of a cholinergic drug …

A. Atropine

B. Hyoscine butylbromide

C. Neostigmine

D. None of the above

ANSWERS:

1. C

2. C

2.4.5 Anti-cholinergics

ACTIVITY :

Mention two uses of atropine. Write your answers in your note book.

Well done. Now you can learn more about Anti-cholinergics.

Anticholinergic, also called antispasmodic, agents inhibit the action of acetylcholine. They stop the transmission of parasympathetic nerve impulses in the central peripheral nervous system. Mechanism of action :

Anticholinergics inhibit parasympathetic nerve impulses by selectively blocking the binding of the neurotransmitter acetylcholine to its receptor in nerve cells. The nerve fibers of the parasympathetic system are responsible for the involuntary movement of smooth muscles present in the gastrointestinal tract, urinary tract, and the respiratory tract. They, therefore, lessen the spasms of smooth muscles. In the respiratory tract, anticholinergics relax and enlarge (dilate) the airways in the lungs, making breathing easier They may protect the airways from spasms that can suddenly cause the airway to become narrower (bronchospasm). They also may reduce the amount of mucus produced by the airways. In the GIT, anticholinergics help to reduce the amount of secretions produced such as saliva by suppressing vagal stimulation. In the eyes, they paralyse the ciliary muscles thereby achieving pupil dilatation

There are two types of anticholinergics and these are short-acting and long-acting. The short-acting type relieves symptoms and the long-acting type helps prevent breathing problems. Short-acting anticholinergics are used for treating stable chronic obstructive pulmonary disease (COPD) in a person whose symptoms come and go (intermittent symptoms). Long-acting anticholinergics are effective and convenient for preventing and treating COPD in a person whose symptoms do not go away (persistent symptoms). Combining an anticholinergic with a beta2-agonist help to improve the lung function compared to a single drug (tiotropium).

Side Effects

- A mild cough and dry mouth are the most common side effects.
- Reports of closed-angle glaucoma after using inhaled ipratropium have been made.
- Urinary retention
- Tachycardia
- Diplopia
- Transient increased body temperature

Caution: renal disease, gastric ulcers, hyperthyroidism etc.

Contraindications: hypersensitivity to belladonna alkaloids, GIT obstruction, asthma, urinary retention

Nursing implications:

- Explain the possible side effects such as dry mouth and mild cough to the patient
- Watch for urinary retention
- Discourage client from operating heavy machine during treatment

Examples of anti-cholinergics used in the respiratory tract

These drugs include: - Albuterol, Tiotropium and Ipratropium.

Ipratropium

Presentation: Aerosol 18mcg/actuation; Nasal spray 0.03%, 0.06%; Inhaler solution 0.02%

Dose and route: Adult Inhaler – 2 puffs QID, not to exceed 12 puffs/24hrs

Examples of anti-cholinergics used in the gastrointestinal tract (GIT)

The commonly available anticholinergic drugs acting on the GIT are atropine and hyoscine butylbromide (Buscopan). Atropine is mainly used as a pre-operative medication and may be used in the management of cases of poisoning to dry up the secretions and to prevent bronchial spasms.

Hyoscine butylbromide (Buscopan) – Refer to drugs acting on the GIT in Pharmacology I

Atropine Sulphate:

Presentation: Inj. 0.05, 0.1, 0.3, 0.4, 0.5, 0.8, 1mg/ml; Tab. 0.4mg

Dose/Route:

Adult: IV bolus 0.5-1mg given q3-5min, not exceed 2mg

Child: IV bolus 0.01-0.03mg/kg given q3-5min, not exceed 2mg

Examples of Anti-cholinergics used in treatment of eye conditions

Anti-cholinergics used to paralyse ciliary muscles and dilate pupils are also called cycoplegics. The commonly used cyclopegics are atropine and tropicamide and mostly used for eye examination or as a premedication.

Self-Assessment Test 14: MCQ
Choose the most appropriate answer
1. Anti-cholinergics drugs act in one of the following ways EXCEPT?
E. Mimic action of acetylcholine
F. Inhibit the action of acetylcholine
G. None of the above
H. All of the above
2. In anaesthesia, atropine is administered in order to …

A. Dilate pupils

B. Relieve muscle spasms

C. Dry secretions

D. None of the above

ANSWERS:

1. D

2. C

2.5 Summary

We have come to the end of the unit. In this unit we were looking at the drugs acting on the nervous system, specifically the central nervous system and the autonomic nervous system. You have learnt that these drugs can either slowdown or enhances the normal transmission of impulses in the brains and ultimately their effects on the specific organ or muscles. The drugs you looked at include; anxiolytic, anticonvulsants, buspirone, anti-depressants, amitryptyline, anti-psychotics and anti-parkinsonian drugs. You also looked at the autonomic nervous system and the drugs which are used in conditions that affect the autonomic nervous system include adrenergic and adrenergic blockers, skeletal muscle relaxants and neuro-muscular blockers. Others are polarizing and depolarizing muscle relaxants, cholinergics and anti-cholinergics. In the next unit you will be looking at the drugs on the eye, ear and nose.

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UNIT 3: DRUGS ACTING ON THE EYE, EAR AND NOSE

3.1 Introduction

Welcome to this unit once again. As already alluded to, in this unit we are going to discuss drugs acting on the eye, ear and nose. As you may be aware, these organs fall under the special senses and they deserve special attention when treating conditions affecting them.

3.2 Unit objectives

Unit Objectives

At the end of this unit you should be able to:

1. Describe ophthalmic antibiotics
2. Describe ophthalmic anti-inflammatory drugs
3. Describe miotics
4. Describe mydriatics
5. Describe ophthalmic vaso-constrictors
6. Describe autic drugs
7. Describe nasal drops

Before proceeding it is important to review your knowledge on eye infections. Eye infections can be caused by viruses, bacteria, or fungi. Eye infections can cause changes in vision, pain, swelling, discharge, and itching. Infections can affect different parts of the eye such as the eyelid. Treatment for eye, ear and nose infections include using eye drops, ointments, and oral medications. Eye, Ear and Nose infections are also treated with Antibiotics, Anti-inflammatory and Analgesic drugs. These drugs are used to combat infections, reduce inflammations and relieve pain in order to prevent complications and promote health. You must therefore be knowledgeable with the drugs to treat conditions of these special senses for you to appreciate your role as a nurse.

Let us first review the anatomy of the eye. In your anatomy and physiology you learnt about the eye structures and their functions.

The eyes are encased in 3 connective tissue coatings - the sclera, choroid, and retina. The most outward coating is the sclera, the 'white of the eye' which admits no light. The anterior portion has the cornea, which is transparent and refracts 90% of light entering the eye while the lens refracts 10%. The optic nerve (cranial nerve II), which transmits perceptual impulses to the brain, pierces the back of the sclera.

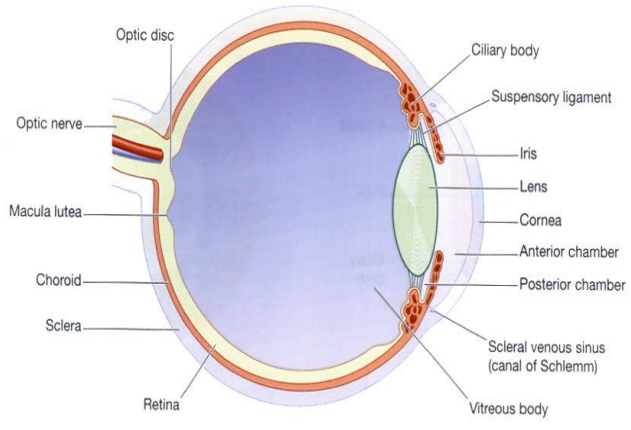

Figure 5: Section of the Eye

Source: (Ross and Wilson, 200 1)

Eye disorders include tramautic eye, Conjunctivitis, Uveitis, trachoma, Glaucoma, Cataract.

The following are preparations used in the local treatment of eye diseases.

- Eye lotions
- Eye drops
- Eye ointments
- Sub conjunctival injection and injection in the anterior chamber at operation.

3.3 Ophthalmic Antibiotics

The correct antibiotic in the case of bacterial infections can be selected as a result of clinical observations and must be validated by bacterial or viral diagnostic tests.

Antibiotics are used in the prophylaxis of endophthalmitis. The following are some antibiotics that are used to treat eye infections.

Ciprofloxacin 0.3% drops and ointment

A quinolone with broad spectrum of activity and is supplied as a 0.3% solution

Indications

Corneal ulcers**-:** application especially in the 1st two days is required throughout the day and night as well as in superficial bacterial infections

Azithromycin

Presentation – tablets, eye drops, Eye ointments

Indication – Trachoma, Corneal ulcer
Dosage: Apply eye drops throughout the day and night. Apply every 15 minutes for 6 hours then every 30 minutes on the 1st day. 2nd day- apply every hour. Days 3- 14; apply every 4 hours. Maximum duration of treatment 21 days.

Apply ointment throughout day and night every 1-2 hours for 2 days then every 4hours for next 12 days

Side effects- local burning and itching, lid margin crusting, hyperaemia, taste disturbances, corneal staining keratitis (inflammation of the cornea). Lid oedema, lacrimation, photophobia, nausea and visual disturbances.

Chloramphenicol

Presentation: 1% Eye drops

Indications: Infection of conjunctiva, lid and lachrymal sac

Administration: Instill one drop 3 or 4 times daily

Erythromycin eye ointment 0.5%

Indications: Chlamydial conjunctivitis

Administration: Apply four times daily.

Gentamycin 1%,2%(Gentacidine, Garamycin).

It is an aminoglycoside that provides coverage for most gram-negative organisms causing endophthalmitis. It is commonly used in combination with both an agent against gram-positive organisms and one that covers anaerobes. Gentamycin eye drops 1 to 2 drops in the eye 4 hourly. Gentamycin eye drops are applied to the lower conjunctival sac 8 hourly or 12 hourly.

Side effects: headache, lethargy, encephalopathy, nausea, vomiting, nephrotoxicity, rash, urticaria, skin irritation and seizures.

Nursing implications

- Use with caution in patients with nephrotoxicity and those hypersensitive to the drug.
- Use with caution in neonates, infants, the elderly and or patients with renal or neuromuscular disorders.

Tetracycline Hydrochloride

Presentation: 1% Eye ointment

Indications: Conjuctivial and corneal infection

Administration: Apply 2-4 times a day or every 2 hours (acute infections)

Oxytetracycline/Polymyxin/Hydrocortisone (Terra-Cortril)

Indications: Eye inflammation and sensitivity reactions

Administration: Apply 2-4 times daily

Side Effects: Aggravates viral and fungal corneal infections

Contra-Indications: Herpatic Keratitis.

Sulphacetamide

Presentation: 10% Eye ointment

Indications: Conjunctiva and secondary infection in trachoma

Administration: Instil one drop 3 to 4 times daily

Side Effects: Local sensitization

Eye drops prescribed as Guttae

A number of drugs are applied to eyes by means of drops which should be instilled into the lower conjuctival sac. They are good for treatment of superficial inflammation such as conjunctivitis. When two or more eye drop preparations are used at the same time of the day, 3-5 minutes should be left between instilling the two preparations to prevent dilution and the overflow effects.

Eye ointments prescribed as Oculentum

These are usually supplied in 4g-5g tubes with a long plastic nozzle. To apply the lower eyelid is pulled down and the ointment placed in the lower fornix of the eye.

A corneal laceration is a very serious injury and requires your immediate medical attention to avoid severe vision loss.

Self-Assessment Test 15: MATCHING ITEMS

Match the ophthalmic antibiotics in Column I with their classification in Column II

Column I	**Column II**
1. __ Ciprofloxacin	A. Macrolide
2. __ Azithromycin	B. Aminoglycoside
	C. Quinolone
	D. Sulphonamide

ANSWERS:

1. B

2. A

3.4 Ophthalmic anti-inflammatory drugs

Ophthalmic anti-inflammatory agents are products formulated to be applied in the eyes to suppress inflammation, thereby reducing pain as well. These agents act against one or more of the mediators that cause inflammation and reduce irritation and swelling in the eyes.

Anti-inflammatory eye drops are used when someone is allergic to the some substances including the environment or after surgery such as cataract extraction to suppress inflammation. Ophthalmic anti-inflammatory drugs may either be non-steroidal or steroidal in nature

Flurbiprofen eye drops

Flurbiprofen drops is a nonsteroidal anti-inflammatory drug (NSAID) eye drop. It works by inhibiting the production of chemical mediators such as prostaglandins that are involved in the inflammatory reaction, thereby suppressing inflammation

Hydrocortisone Acetate

This is a steroidal anti-inflammatory drug eye drop

Presentation: 1% Eye ointment and drops

Indications: Local sensitivity reactions in skin and eyes and non-infective inflammation of the cornea (keratitis), scleritis and iridocyclitis

Administration: Apply 2-3 times a day, as per doctor's prescription

Side Effects: May aggravate infection or mask inflammatory reaction and increase intra ocular pressure

Contra-Indications: Herpetic Keratitis, active trachoma

Dexamethasone Eye Drops

It is a steroid given to reduce inflammation

Dose:1-2 drops 4 hourly until the inflammation is controlled

Side effects: thinning of the cornea and sclera

Nursing implications: Avoid prolonged use as it may lead to 'steroid cataract'.

Prednisolone 1% Eye drops

Indications: Local sensitivity reactions in skin and eyes and non-infective inflammation of the cornea (keratitis), scleritisiritis and iridocyclitis

Administration: Apply 2-3 times a day

Side Effects: May aggravate infection or mask inflammatory reaction and increase intra ocular pressure

Contra-Indications: Herpetic Keratitis, active trachoma.

Nursing implications: as for dexamethasone

Nursing Consideration

- Advise patient on long term therapy to have frequent tonometric examination
- Remind patients to discard drug when it is no longer needed and not use leftover medication
- Warn patients to call the doctor immediately and stop drug if visual acuity changes and visual field diminishes.
- Teach patients how to instill eye drops or apply ointment

Sodium cromoglicate

This drug is used to treat eye conditions caused by allergy to pollen in the hay fever season. Other causes are less common such as allergies to house dust mite, cosmetics, and problems with contact lenses. Sodium cromoglicate eye drops is a membrane stabilizer used to relieve the symptoms of allergic conjunctivitis by reducing the amount of histamine produced

Preparation: Eye drops

Self-Assessment Test 16: MCQ

Choose the most appropriate answer

1. The appropriate treatment of conjunctivitis due to allergy is …….
A. Antibiotics
B. Miotics
C. Antifungals
D. Steroids
2. The following are steroidal ophthalmic anti-inflammatory drugs EXCEPT?
A. Dexamthasone
B. Hydrocortisone
C. Betamethasone
D. None of the above
ANSWERS:
1. D
2. D

3.5 Miotics

Miotic drugs act on the sphincter muscle of the iris either directly or indirectly constricting the pupil. These drugs are intended to reduce intraocular pressure by enhancing aqueous humor outflow, decrease its production, or both in the treatment of Glaucoma

Examples

Pilocarpine hydrochloride: 1, 2 or 4% eye drop, given 3-4 times daily.

Mode of Action

This is a cholinergic drug which constricts pupils (miosis) by directly stimulating sphincter muscles and increase outflow of aqueous humor by ciliary muscle pull on trabecular meshwork.

Side effects

They include a small pupil, blurred vision, an aching brow, and an increased risk of retinal detachment

Drug interaction

Ophthalmic belladonna alkaloids

Phenylephrine

Contra indication

Acute iritis, acute inflammatory disease, secondary glaucoma

Use cautiously in patients with bronchial asthma

Nursing implication

- Warn patient that transient brow pain and myopia are common at first but usually within 10-14 days
- Instruct patient to apply gel at bed time because it will blur vision

Other example of a cholenergic

Acetylcholine Chloride

Carbonic Anhydrase Inhibitors (Systemic Preparations)

Acetazolamide or Diamox

Indications: Glaucoma of all types

Dose: 500mg initially, then 250mg 2-3 times daily

Action: Inhibit the action of carbonic anhydrase (an enzyme necessary for the production of aqueous humor in the ciliary processes), thereby decreasing aqueous humor production and increase outflow,

Side effects: Including reduction of body potassium, kidney stones, numbness or tingling sensations in the arms and legs, fatigue, and nausea.

Contra-indications: Acidosis, sodium and potassium depletion.

Nursing implications

- Assess patient tinnitus, hearing loss; ear pain periodic hearing test is needed. Monitor for sign of hypokalaemia.
- Assess for cross sensitivity between other sulfonamides.

Beta-Adrenergic Antagonists

Timolol maleate 0.25 or 0.5% eye drop (1 drop) given twice a day.

Action: Decrease aqueous humor production and increase outflow by inhibiting sympathetic effects on ciliary processes, thereby decreasing intraocular pressure (IOP).

Side effects: Such as the worsening of asthma or emphysema, bradycardia (slow heart rate), low blood pressure, fatigue, and impotence prohibit their use in some patients.

Hyperosmotic Agent

Mannitol (Osmitrol) 15% to 30% IV over 30 to 60 minutes

Action: Hyperosmotic agents such as oral glycerine and intravenous mannitol can rapidly lower IOP by decreasing vitreous volume. They do not cross the blood-ocular barrier and therefore exert oncotic pressure that dehydrates the vitreous, thereby decreasing IOP

Side effects: Including nausea, fluid accumulation in the heart and/or lungs (congestive heart failure and/or pulmonary oedema), bleeding in the brain, and kidney problems (Pearson, 1998 and Monahan et al., 2007).

Self-Assessment Test 17: MCQ

Choose the most appropriate answer

1. Miotics are used to treat glaucoma because they……..
A. Paralyze the ciliary bodies
B. Reduce intra ocular pressure by enhancing aqueous humor outflow
C. Indirectly dilate the pupil
D. Directly dilate the pupil
2. Which of the following miotics inhibit the action of carbonic anhydrase, an enzyme necessary for the production of aqueous humor in the ciliary processes, thereby decreasing aqueous humor production and increase outflow
A. Mannitol
B. Timolol
C. Pilocarpine Hcl
D. None of the above
ANSWERS:
1. B
2. D

3.6 Mydriatics

Mode of action

They are anticholinergic preparations which block the responses of the sphincter muscle of the iris and the accommodative muscle of the ciliary body to cholinergic stimulation, producing pupillary dilation (mydriasis) and paralysis of accommodation (cycloplegia).

Indication

Mydriatics are used to dilate the pupil for eye examinations to allow the eye specialists to see into the eye in detail. The optic nerve and retina as well as the whole lens can be examined after administration of mydriatics. Dilating drops work either by temporarily paralyzing the muscle that makes the pupil smaller (iris sphincter muscle) or by stimulating the iris dilator muscle.

Maximal cycloplegia occurs within 25 to 75 minutes after instillation. Complete recovery of accommodation usually takes 6 to 24 hours. Complete recovery from mydriasis in some individuals may require several days. Heavily pigmented iris may require more doses than lightly pigmented iris.

Dosage and administration

Adults: Instill one or two drops of 1% or 2% solution in the eye which may be repeated in five to ten minutes if necessary. Complete recovery usually occurs in 24 hours. Complete recovery from mydriasis in some individuals may require several days.

Children: Instill one or two drops of 1% or 2% solution in the eye which may be repeated five to ten minutes later by a second application of 1% solution if necessary.

Contraindications

The drug should not be used in patients with untreated narrow-angle glaucoma, or untreated anatomically narrow angles are present, or if the patient is hypersensitive to any component of this preparation.

Side effects: Acute angle closure, glaucoma, irritability, confusion, eye dryness, photophobia

Drug interaction

None significant

Nursing considerations

- Watch for signs of glaucoma: increase intra ocular pressure, ocular pain, headache, progressive blurred vision.
- Warn patients to avoid hazardous activities
- Advise patients to ease photophobia by wearing dark glasses
- Tell patients to use sugarless candy or gum for dry mouth

Examples include

Atropine

An anti-muscarinic indicated for; refraction procedure in young children and anterior uveitis.

Preparations: 0.5% and 1% eye drops and 1% eye ointment.

Other drugs include: Cyclopentolate 1%

Self-Assessment Test 18: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. Mydriatics are dilate pupils …..

2. Mydriatics affect accommodation …..

ANSWERS:

1. T

2. T

3.7 Ophthalmic Vaso-constrictors

These are drugs that mimic the action of adrenaline and noradrenaline in the presynaptic nervous system Thereby increasing the out flow of aqueous humour

Penylephrine hydrochloride ophthalmic solution 2.5% is an example of an alpha receptor sympathetic agonist used in local ocular disorders because of its vasoconstrictor and mydriatic action. It exhibits rapid and moderately prolonged action, and it produces little rebound vasodilation.

Mode of action

Vasoconstrictors provide temporary relief from tissue congestion. The mechanism by which vasoconstrictors act is adrenergic receptor activation. Ocular vasoconstrictors include naphazoline, tetrahydrozoline, phenylephrine and oxymetazoline and act as adrenergic receptor agonists. Adrenergic Receptors mediate the physiological response to catecholamines, norepinephrine and epinephrine, and are central to cardiovascular and central nervous system activity. When administered topically, ocular decongestants (or vasoconstrictors) constrict the superficial conjunctival blood vessels and thus reduce congestion and redness.

They alsomediate stimulation of smooth muscle contraction and, systemically, play a role in control of blood pressure. α1- adrenergic receptors (ARs) are excitatory post-synaptic receptors, constricting larger arterioles. α2- adrenergic receptors often work in opposition to α1 receptors, mediating nociception, blood pressure and spinal reflexes. α2- adrenergic receptors mediate smooth muscle contraction, and also inhibit release of norepinephrine by sympathetic post-ganglionic fibers.

There are two classes of vasoconstrictors:

1. Sympathomimetic amines
2. Imidazoles.

Sympathomimetic amines mimic the actions of the sympathetic nervous system through the pre-synaptic release of norepinephrine in sympathetic nerves. Norepinephrine then binds post-synaptically to α-ARs, resulting in vasoconstriction.

The imidazoles can be α2-AR agonists (for example,, brimonidine), or mixed α1-AR/α2-AR agonists (for example, naphazoline), and act post-synaptically on sympathetic nerves to cause vasoconstriction. They may also lower production of norepinephrine, thus decreasing blood flow and reducing congestion.

Example of Ophthalmic vaso-constrictor

Brimonidine tartrate eye drop 0.2%

Action: It is an alpha 2 stimulant and can be used when beta blockers are contraindicated

Self-Assessment Test 19: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. Ophthalmic vasoconstrictors are indicated in increased intraocular pressure …..

2. Ophthalmic vasoconstrictors sympathomimetic in in their mechanism of action …..

ANSWERS:

1. T

2. T

3.8 Autic (Ear) Drugs

Most ear infections are treated with antibiotics used to treat eye infections. The commonly used drugs for infections that involve the ear drum include systemic administration of penicillins, cephalosporins, sulfonamides, and macrolides. Amoxicillin is the most common antibiotic used to treat ear infections due to streptococcus pneumonia or haemophillus influenza. However the use of ear drops is be considered under several ear disorders/conditions individuals present with.

Instillation of drops

You have to consider the following before you instill ear drops:

- Mop ear discharge away gently.
- Warm the ear drops to approximately body temperature
- Turn the head in such a way that the affected ear is the in the uppermost position
- Instill 2-3 drops while you ensure that the head id held in position for two minutes.

Impacted wax treatment

If the patient/client has wax (hard and impacted) in the ear, which resists the effort of ear syringing, you must treat the condition by instilling 5% solution of sodium bicarbonate or warm almond or olive oil for a few days. This will help to soften the wax before ear syringing is attempted again.

Wax softeners

Cerumen (Earwax) provides protection to the meatal skin and need only be removed if it causes deafness or interferes with a proper view of the eardrum. As a general rule syringing is best avoided in patients with a history of recurring otitis externa, perforated eardrum or previous ear surgery.

Wax may be removed by syringing with warm water. If necessary, wax can be softened with simple remedies such as vegetable oil.

Vegetable Oil
Presentation: Eardrops
Indications: Earwax
Dose: Warm to body temperature and instill 4 -5 drops into the ear wait 5-10 minutes with ear upwards and then syringe with warm water.
Caution: Hypersensitivity to oil report

Management of patients with severe ear infections

Severe infections of the ear are managed with appropriate agents the organisms are sensitive to. Treatment should be continued for longer than a week due to drug sensitization and development of fungal infection.

You must **not** use gentamicin or neomycin ear drops for conditions with ear drum perforation as this may result in deafness.

Otitis externa

Treatment of otitis externa requires you to regularly do aural (ear) cleansing to remove debris and instilling of treatment agents such as:-

Clioquinol 1% with flumetasone 0.02%

This drug has a mild antibacterial and antifungal action and can be used to treat bacterial and fungal infections of the ear.

Gentamicin 0.3% with hydrocortisone 1% / Neomycin

This drug can be used to treat bacterial and inflammatory ear conditions.

Treat eczema of the ear with steroids such as prednisolone 0.5% or betamethasone 0.1% to relieve irritation and inflammation.

Neomycin sulphate

Indication: bacterial infection in Otitis externa.

Contra-indications- perforated tympanic membrane (risk of ototoxicity)

Side effects- local sensitivity

Chloramphenicol

Indication-bacterial infection in Otitis externa

Side effects-high incidence of sensitivity to propylene glycol (vehicle)

Take Note

Solution containing a corticosteroid can be used where infection is present with infection and eczema.

Anti-inflammatory preparations

Topical corticosteroids are used to treat inflammation and eczema in otitis externa and prolonged use must be avoided. Avoid corticosteroids in the presence of untreated ear infection. If infection is present, the steroid should be used in combination with a suitable anti-infective.

Side effects; Local sensitivity reactions may occur.

Examples of autic drugs

Betamethasone or Betamethasone with neomycin eye/ear drops.

Dose: apply 2-3 drops in the ear 3-4 times a day.

Dexamethasone

Indications: eczematous inflammation in Otitis externa.

Dose: apply 2-3 drops 3-4 times daily in the ear.

Self-Assessment Test 20: MCQ

Choose the most appropriate answer

2. Instillation of steroids is discouraged in active ear infection or perforation because

A. It is painful

B. It may delay healing

C. It requires an expert

D. None of the above

2. Principles of instilling ear drops include the following EXCEPT?
A. Mop ear discharge away gently.
B. Instil ear drops to approximately lower body temperature

C. Turn the head in such a way that the affected ear is the in the uppermost position
D. Instil 2-3 drops while you ensure that the head id held in position for two minutes.

ANSWERS:

1. B

2. B

Well done!

3.9 Nasal Drops

Drugs used in nasal allergy

Oral antihistamines and systemic nasal decongestants are used to control mild cases. Topical corticosteroids and sodium cromoglycate may be used in severe cases.

Topical nasal decongestants

Common cold has no specific treatment as it viral in most cases. Therefore, the use of nasal drops in common cold should be done with caution. Sodium chloride 0.9% given as nasal drops may relieve nasal congestion by helping to liquify mucus secretions.

Sodium Chloride

Presentation: Solution containing 0.9% sodium chloride administered as nasal drops
Indications: Nasal congestion
Dose: Use as required

This medication is used for temporary relief of congestion in the nose caused by various conditions including the common cold, sinusitis, hay fever, and allergies. It works by narrowing the blood vessels in the nose area, reducing swelling and congestion.

Topical Nasal Decongestants

Ephedrine Hydrochloride

Presentation: Ephedrine nasal drops, 0.5%

Indication: Nasal decongestant not recommended for infants

Administration: Instil 1-2 drops into each nostril when required

Side effects: Temporary burning, stinging, dryness in the nose, runny nose, and sneezing may occur. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.

Pseudoephedrine (Sudafed)

Pseudoephedrine is a decongestant that shrinks blood vessels in the nasal passages. Dilated blood vessels can cause nasal congestion (stuffy nose).

Pseudoephedrine is used to treat nasal and sinus congestion, or congestion of the tubes that drain fluid from your inner ears, called the Eustachian tubes.

Indications: Nasal Congestion

Dose: 60 mg every 6 hours p.o.

Side Effects: Tachycardia, insomnia, severe dizziness or anxiety, easy bruising or bleeding, unusual weakness, fever, chills, body aches and flu symptoms;

Self-Assessment Test 21: MATCHING ITEMS

Match the nasal drops in Column I with their most appropriate indications in Column II

Column I Column II

1. __ Ephedrine A. Nasal congestion in children
2. __ Sodium chloride B. Nasal congestion in adults
C. Nasal congestion in comatose patients

ANSWERS:

1. B

2. A

3.10 Summary

Thank you for your attention. You have come to the end of the unit 3. In this unit, we discussed and gave examples of drugs used to treat conditions affecting the eye, ear and nose I hope you now appreciate the importance of treating infections of these special senses to prevent disabilities. In the next unit you will be looking at the drugs acting on the skin.

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UNIT 4: DRUGS ACTING ON THE SKIN

4.1 Introduction

Hello dear student, welcome to unit 4. In the previous unit you learnt on drugs that act on the Eye, Ear and Nose. However, in this unit you will be looking at drugs that act on the skin. I hope you will enjoy the lesson.

If you remember very well in your anatomy and physiology, you learnt about the skin under special senses.

Patients who present with a skin problem often complain of 'itchy rash all over the body'. After taking history and performing a proper skin examination you may find he or she is suffering from anything as varied as eczema, urticaria, a drug reaction, a skin infection, scabies or any other skin disease. A proper skin examination should be performed in good light, preferably daylight. Ideally the whole skin should be examined. The aspect, extent and localisation of all the lesions is essential for making a diagnosis and will influence your management.

Drugs applied to the skin are usually used for their local effects and thus are most commonly used to treat superficial skin disorders, such as psoriasis, eczema, skin infections (viral, bacterial, and fungal), itching, and dry skin. The drug is mixed with inactive substances. Depending on the consistency of the inactive substances, the formulation may be an ointment, cream, lotion, solution and powder.

4.2 Unit objectives

Objective
At the end of this unit you should you should be able to;

1. Describe how topical antibiotics act on the skin
2. Describe how scabicides and pediculicides act on the skin:
3. Describe how topical corticosteroids act on the skin
4. Describe how antifungals act on the skin

Before going through the drugs that act on the skin, start with a brief on the skin. The skin is the largest organ of the body and weighs about 5 kilograms. It has a surface area of about 1.5 to 2m² in adults and it includes glands, hair and nails. The skin consists of three layers: the epidermis, the dermis and the hypodermis or subcutaneous fatty tissue. It has three main functions: protection, regulation and sensation. The skin can become infected with bacteria, viruses and fungi and this may affect all its functions hence the need to treat such infections.

When drugs are applied to the skin, the term topical treatment is used to denote the application of the drug direct to the affect area of the skin to combat infection. It is important to use the correct base to achieve the best results.

The most commonly used bases are:-

- Ointments
- Creams
- Pastes
- Lotions
- Dust Powders

i. Ointments

The distinction between ointments and creams is not obvious due to various bases used to for both ointments and creams. However, the distinction between the two is that ointments are generally greasy while creams are thinner and consists of emulsions.

Ointments and creams bases are classified as:

- Hydrocarbon bases
- Fat and fixed oil bases
- absorption bases
- Emulsifying base
- Water soluble bases

Water soluble ointments: These bases have the advantage that they do not stain the skin.

Emulsifying ointments: These emulsify (combine) with water.

Non-emulsifying ointments: These do not mix with water and paraffin form the basis of most of greasy ointments. They are good for treatment of chronic dry skin disorders such as chronic atopic eczema, psoriasis and ichithyosis (dry skin with fish scales).

ii. Creams

These are emulsions which are either water dispersed on oil (oil cream) or oil dispersed in water (aqueous cream). Oil dispersed creams are commonly accepted by patients cosmetically and they are used to moisten and soften the skin.

Some creams act as barrier creams and they protect the skin against physical agents such as sunlight.

iii. Pastes

These can be greasy or dry and contain large amounts of powder. They are useful for localized lesions such as psoriasis. Care must be taken not to apply pastes on normal skin areas to prevent sensitization. Pastes are also applied to protect inflamed or excoriated skin.

iv. Lotions

Water lotions are used to cool acutely inflamed skin and need frequent application to achieve the desired effects. The lotions help to cool the body by evaporation thereby leaving the inert powder on the skin surface For example, calamine lotion.

v. Dusting powder

These are drying agents and increase the effective evaporating surface. They are used especially in the folds of the skin. For example, Talc, starch and zinc oxide are commonly used powders. Other active agents can be added such as antiseptics for bacterial infections and antifungal agents for athletes foot (tinea pedis).

Activity :
Name any drugs that can be applied topically to treat skin infections
Write your answers in the note book

Well done.

If you did not find the answers correctly, do not worry because this lesson will help you understand.

4.3 Topical antibiotics

As earlier discussed, you now appreciate that topical application of an antibacterial agent is used as remedy for localized infection of the skin. Early treatment of infected lesions and wounds helps in reducing colonization of the area by staphylococci, in axillary deodorization, and in the management of acne vulgaris. However, prolonged use of most antibacterial agents such as neomycin has a risk of sensitization to the agent. It causes other complications such as contact dermatitis.

To determine the best treatment for bacterial infection of the skin, isolation of the causative organism will help to come up with the topical antibacterial to be used.

Examples of topical antibiotics

Neomycin plus bacitracin ointment

Indications: Skin infections

Administration: Apply tid

Side Effects: Local hypersensitivity reactions

Caution: Large open wounds

Neomycin & Gentamicin

Neomycin and gentamicin are aminoglycoside antibiotics active against gram-negative organisms, including E coli, proteus, klebsiella, and enterobacter. Gentamicin generally shows greater activity against P aeruginosa than neomycin. Gentamicin is also more active against staphylococci and group A -hemolytic streptococci.

Presentation: Cream containing neomycin sulphate 0.5%.
Indications: Skin infections due to sensitive organism.
Side effects: Allergic hypersensitivity, ototoxicity, nephrotoxicity with prolonged use.
Contraindications: Hypersensitivity to neomycin, cross-sensitisation with aminoglycosides.
Administration: Apply up to 3 times daily; maximum 60g daily for 3 weeks. Do not repeat for at least 3 months.

Caution: Neomycin frequently causes sensitization, particularly if applied to eczematous dermatoses or if compounded in an ointment vehicle.(Zambia National formulary, 2013)

Tetracycline

Presentation: Ointment 3%

Indications: Impetigo, infected burns and abrasions. Apply 1-2 x/day

Side effects: Allergic hypersensitivity, ototoxicity, nephrotoxicity with prolonged use.

Contraindications: Hypersensitivity to neomycin, cross-sensitisation with aminoglycosides.

Administration: Apply up to 3 times daily

Side Effects: Local hypersensitivity reactions

Self-Assessment Test 22: MCQ

Choose the most appropriate answer

1. Topical antibiotics are indicated in ….

A. Fungal infections

B. Viral infections

C. Viral and fungal infections

D. None of the above

2. The following are examples of topical antibiotics EXCEPT?

A. Gentamycin cream

B. Neomycin cream

C. Dexamethasone cream

D. Cetrimide cream

ANSWERS:

1. D

2. C

4.4 Scabicides and Pediculicides

A. Scabicides

Scabicides are drugs that are used to treat scabies. Scabies, also known as the itch, is a contagious ectoparasitic skin infection characterized by superficial burrows and intense pruritus (itching).

The word scabies itself is derived from the Latin word for 'scratch' (scabere). Scabies is an infection caused by the mite Sarcoptes Scabiei, which lives and moves in the skin producing burrows (S-shaped ridges), small blisters and papules. Itching is especially severe at night, and causes scratch marks and very commonly secondary infection with pustules and crusts. Lesions occur preferentially between the fingers, on the sides of the hands and feet, on the flexor sides of the wrists, in the armpits and on the genitals and buttocks. In infants and small children palms, soles, head and neck are often affected. Scabies is primarily spread through direct contact but may be transmitted through clothing, linen, or towels.

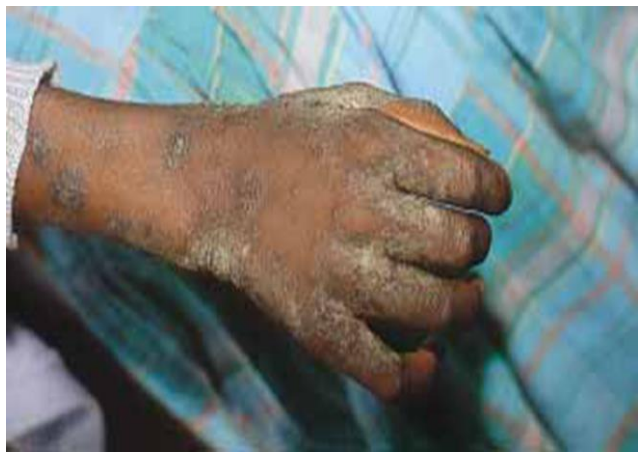

Figure 6: Scabies infection

(www.skin infection.co 1)

Scabies can be treated with the following topical solutions after bathing throughout the night.

Benzyl Benzoate

Presentation: Application cream containing 25% benzyl benzoate

Indications: Scabies

Administration: The patient should scrub well preferably in warm water and immediately after drying, the application should be applied over the whole body below the neck; a second application should be made on the following day without washing the previous application; same personal clothing and linen should be used during these two days which is changed after a wash on the third day; all affected family members should be treated at the same time.

Side Effects:
Skin irritation, burning sensation especially on genitalia and excoriation, occasionally rashes, may cause convulsions when ingested.
Caution: Avoid in children, avoid contact with eyes and mucous membrane, pregnancy and breast feeding.
Administration: Apply over whole body (omit head and neck), repeat without bathing on the following day. Wash off on the third day. Third application may be required.

Transient burning of the skin; when ingested may cause convulsions.

Permethrin
Presentation: Cream rinse containing permethrin 1%. Dermal cream containing permethrin 5%
Indications: (Cream rinse) head lice and (dental cream) scabies.
Side effects: Pruritis, erythema, and stinging; rarely rashes and oedema.
Caution: Avoid contact with eyes, pregnancy and breast feeding, children under 6 months, medical supervision required for cream rinse, children aged 2 months – 2 years, medical supervision required for dermal cream.
Administration: Cream Rinse (Head lice). Apply to clean damp hair, leave on for 10 minutes, rinse and dry.
Dermal Cream (Scabies) – Apply over whole body (excluding head in adults) and wash off after 8 – 24 hours. Child; apply over whole body, including face, neck, scalp and ears. If hands are washed with soap within 8 hours of application, cream should be re-applied.

Toxicity may resemble allergic reactions. It is usually applied to the skin before bedtime and left on for about 8 to 14 hours, then showered off in the morning.

Malathion
Presentation: Lotion containing malathion 0.5% in alcoholic basis or liquid containing malathion 0.5% in aqueous basis.
Indications: Crab lice, head lice and scabies.
Side effects: Skin irritation
Caution: Avoid contact with eyes, alcoholic lotions not recommended for pediculosis in asthmatics or small children, or for scabies or crab lice. Do not use lotion for more than once a week for 3 weeks at a time; medical supervision required when used in children under six months.
Administration: Pediculosis – rub lotion into dry hair, scalp, and affected area, comb, allow to dry naturally. Remove by washing after 12 hours.
Scabies – apply liquid preparation over whole body, omitting head and neck, and wash off after 24 hours. (Zambia National Formulary, 2013)

Lindane

Presentation: Application containing 100mg lindane

Indications: Scabies and Pediculosis,

Treatment of Scabies: Apply 1% application over whole body, omitting the head and neck, and wash off after 24 hours. Repeat after 1-3 days.

B. Pediculicides

Pediculicides are drugs that are used to treat pediculosis (lice infestation)

Treatment of pediculosis: Rub 0.1-2% application into hair and scalp or affected area; allow drying, and removing by washing after 24 hours (kills parasites within a few days).

When using shampoo, leave on hair for 5 minutes, rinse, allow drying, comb, repeat once after 7 days.

Side Effects: Rarely skin irritation

Caution: Avoid contact with eyes.

Self-Assessment Test 23: MCQ

1. The drug of choice for treating scabies is……..
A. Benzyl Benzoate
B. Permethrin
C. Tetracycline
D. Lindane
2. Which is the best time of applying benzyl benzoate?
A. In the morning
B. In the afternoon
C. At night
D. At mid-morning

ANSWERS:

1. A

2. C

4.5 Topical corticosteroids

Anti-inflammatory agents often produce dramatic effects in the treatment of skin diseases in which inflammation is a prominent feature for example, eczema, atopic dermatitis and psoriasis. Symptoms may return when the treatment is withdrawn if the underlying cause is not removed. Topical corticosteroids should not be used for trivial rashes and irritation but should be reserved for more recalcitrant (unmanageable) conditions. Systemic or potent corticosteroids should be avoided or given only under specialist supervision.

Examples of topical corticosteroids

1. Betamethasone (Betnovate)

Presentation: Cream/ointment 0.1%

Indications: Severe non-infected inflammatory conditions of the skin

Administration: Apply very thinly 2-3 times daily, reducing frequency as condition responds

Side Effects: Severe pituitary adrenal axis suppression and hypercorticism and immunosuppression on prolonged use.

Contra-Indications: Stasis ulcers and infective conditions. It should not be used on the face for long periods

2. Hydrocortisone acetate

Presentation: Cream containing 0.5% and 1% hydrocortisone, ointment containing 0.5% and 1% hydrocortisone.

Indications: Eczema and other inflammatory skin disorders

Administration: Apply thinly 1-2 times daily, reducing frequency as condition responds

Side Effects: Thinning of skin with prolonged use, increased hair growth, peri-oral dermatitis, acne at site of application, mild pigmentation and vellus hair.

Contraindications: Untreated bacterial, fungal or viral infections; stasis ulcers and infected conditions. It should not be used on the face for long periods

3. **Clobetasol**

Presentation: Cream, Ointment, Scalp application containing 0.05% clobetasol propionate
Indications: Short term treatment of severe resistant inflammatory skin disorders such as recalcitrant eczema unresponsive to less potent corticosteroids, psoriasis.
Side effects: See betamethasone
Contraindications: See betamethasone
Caution: This is a high potency corticosteroid.
Administration: Apply thinly 1 – 2 times daily for up to 4 weeks reducing frequency as condition responds.

Self-Assessment Test 24: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. The patient with complaints of irritations of the skin due to allergic reaction can best be treated with steroids …….
2. Neomycin cream is an example of a topical steroid ……..

ANSWERS:
1. T
2. F

4.6 Antifungals

Fungal infections are very notorious and need copious treatment in order to achieve the required effects. Tinea or ringworm presents in typical round lesions, which show scaling at the periphery, or in concentric rings. Usually one or a few lesions are seen and only topical treatment is necessary. Multiple, large or widespread lesions may be seen if a patient delays seeking treatment for a long time or is malnourished or immunosuppressed. Skin scrapping can help identify the fungi before commencing treatment. However, systemic treatment is used to for widespread, unresponding fungal infection and for nail care (tinea ungiuium) and scalp ringworm.

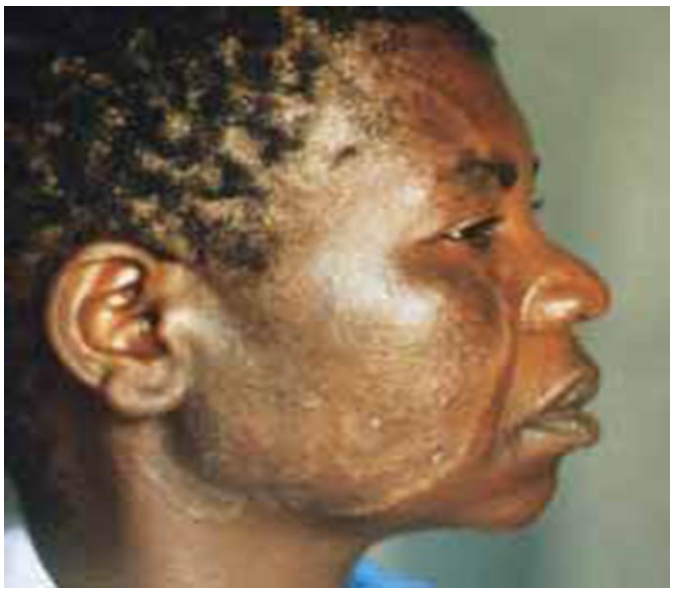

Figure 7: Tinea corporis

(www.skin infection.com 2 1

Topical antifungal preparations

Benzoic acid (Whitfield ointment)

Presentation: Ointment containing 6% benzoic acid and salicylic acid 3%.

Indications: Tinea

Administration: Apply bid for 6 weeks

Caution: Application on face and other tender areas should be avoided. It should not be applied on eczematized areas.

Clotrimazole

Presentation: Cream containing 1% clotrimazole

Indications: Fungal skin infections

Side effects: Occasional skin irritation or sensitivity.

Contraindications: Hypersensitivity to clotrimazole.

Administration: Apply once daily until a few days after disappearance of all symptoms.

Miconazole Nitrate

Presentation: Cream 2%

Indications: Fungal skin infections, hair and nails.

Administration: Apply bid continuing for 10 days after lesions have healed

Side Effects: Occasional skin irritation or sensitisation

Contraindications: Hypersensitivity to miconazole

Nystatin

Presentation**:** Ointment, 100,000 units/g

Indications: Skin infections due to candida spp.

Administration: Apply 2-4 times daily for seven days after lesions have been healed

Side Effects: Local sensitivity reaction

Antiprutitics (Soothing Preparations)

Calamine

Presentation: Lotion containing calamine 15% and zinc oxide 5%. Ointment containing calamine 15% in white soft paraffin.

Action: Mildly astringent and soothing preparation

Indications: Pruritis; Apply to affected areas

Zinc Oxide

Presentation: Cream containing 32% zinc oxide

Action: Mildly astringent, soothing and protecting preparation.

Indications: Mild eczema, excoriations, nappy rash and skin irritation.

Administration: Massage lightly into affected parts bid or t.i.d.

Systemic antifungals

These are antifungals that are administered either orally or parenterally. Examples of systemic antifungals include:

Griseofulvin

Mechanism of action: The drug binds to tubulin (globular proteins), interfering with microtubule function, thus inhibiting mitosis. It also binds to keratin in keratin precursor cells and makes them resistant to fungal infections

Presentation: Tab 125mg

Indications: Tinea capitis, tinea pedis, tinea barbae, tinea corporis

Dose: 10mg/kg in 2 divided doses daily x minimum of 6 weeks

Side Effects: Hepatotoxic, hypersensitivity, headache, GI upset

Contraindications: Liver Failure

Nursing considerations:

- Monitor liver function tests
- Give with or after meals
- Observe for sensitivity reaction

Ketoconazole (Nizoral, Diflucan)

Mechanism of action: alters cell membrane and inhibits action of several fungal enzymes thereby preventing fungal metabolism

Presentation: Tab 200mg; Susp. 100mg/5mls

Indications: Systemic candidiasis, chronic oesophageal candidiasis, oral thrush, histoplasmosis

Dose: Adult (oral): 200-400mg OD x 1-6 weeks; Child (>2yrs): 3.3-6.6mg/kg OD

Side Effects: Headache, nausea/vomiting, impotence, gynaecomastia, anaphylaxis

Contraindications: Hypersensitivity, lactation, fungal meningitis

Nursing considerations:

- Monitor for hypersensivity reactions
- Monitor for hepatotoxicity

Amphotericin B

Mechanism of action: Alter permeability of cell membrane leading to loss of essential cell constituents

Presentation: Inj. 50mcg/ml usually in 50mg vials

Indications: Arspegillus, candida species, cryptococci, histoplasma

Dose:

- A single intravenous test dose of 1 mg in 20 mL of 5% dextrose solution administered over 20 to 30 minutes may be preferred. The patient's temperature, pulse, respiration, and blood pressure should be recorded every 30 minutes for 2 to 4 hours
- If tolerated, an initial intravenous infusion of 1 to 5 mg of Amphotericin B per day, gradually increased to 0.4 to 0.6 mg/kg daily

Side Effects: extravasation, nephrotoxic, nausea/vomiting, anaphylaxis, anaemia

Contraindications: renal failure, hypersensitivity,

Nursing considerations:

- Give a test dose before commencement of therapy
- Closely monitor client on parenteral therapy
- Ensure good IV access
- Rule out anaemia before commencement of treatment
- May require administration of antihistamine prior to commencement of therapy

Self-Assessment Test 25: MCQ
Choose the most appropriate answer

1. Tinea infections can respond well to…….
A. Benzoic Acid (Whitfield ointment)
B. Lindane
C. zinc oxide
D. Hydrocortisone acetate
2. Which of the following drugs can be used to sooth the skin?
A. Betamethasone
B. Calamine lotion
C. Benzyl Benzoate
D. Lindane
ANSWERS:

1. A

2. B

4.7 Summary

You have come to the end of the unit. In this unit you were looking at the drugs acting on the skin. There are different preparations of these drugs and work against different pathogenic organisms. There are those that act against bacterial and fungal infections. Others are used to treat scabies and allergic reactions.

In the next unit, you will learn about drugs acting on the immune system.

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UNIT 5: DRUGS ACTING ON THE IMMUNE SYSTEM

5.1 Introduction

Welcome to yet another interesting unit where you will learn about the drugs acting on the immune system. In the previous unit you were looking at the different drugs that are used to conditions of the skin and I hope you found it interesting and you have gained some knowledge.

In this unit you will go learn about the drugs that act on the immune system. What do you understand by the term immunity? Well, the drugs you will look at are used to enable the body fight infection hence rendering the body healthy.

5.2 Unit Objective

By the end of this unit you should be able to

1. Describe immuno-suppressants as they act on the immune system
2. Describe anti- viral drugs as they act on the immune system
3. Describe vaccines and toxoids as they act on the immune system
4. Describe anti-toxins and anti-venoms as they act on the immune system
5. Describe immune serums; immunoglobulin as they act on the immune system
6. Describe vitamins as they act on the immune system

Just before we talk about the drugs let us briefly review the anatomy and physiology of the immune system. The immunity is the body's ability to fight invading pathogens (disease-causing infections) and destroy them thereby keeping the body free from infection. It is therefore a network of cells, tissues, and organs that work together to defend the body against infections. These infections are primarily caused by pathogenic microorganisms such as bacteria, parasites, and fungi.

5.3 Immune-Suppressants

Definition

Immuno suppressants are potent medicines that dampen the activity of the body's immune system. They are helpful for controlling abnormal growths of body tissues by suppressing the over-activity of the immune system that causes inflammation of the involved tissues. These drugs are only prescribed by hospital specialists.

Immuno suppressants are, therefore, agents that lower or reduce the body's immune response foreign materials in the body. They may be either exogenous, as immunosuppressive drugs, or endogenous such as testosterone. When the immune system function is suppressed, there is an increased susceptibility to infectious diseases and cancers.

Indications

i) They are useful in organ transplant surgery to prevent organ rejection. When an organ, such as the liver, heart or kidney, is transplanted from one person (the donor) into another (the recipient), the immune system of the recipient triggers the same response against the new and foreign organ just as it would have done to any foreign material, setting off a chain of events that can damage the transplanted organ. This process is called rejection and it can occur rapidly (acute rejection), or over a long period of time (chronic rejection). Rejection can occur despite cross matching of the donated organ and the recipient.

ii) Immunosuppressant drugs are also used to treat skin disorders such as psoriasis and such other diseases as rheumatoid arthritis, Crohn's disease (chronic inflammation of the digestive tract) and patchy hair loss (alopecia areata).

Mode of action

Immunosuppressant drugs can be classified according to their specific molecular mode of action. The three main immunosuppressant drugs currently used in organ transplantations are the following:

- Cyclosporins (Neoral, Sandimmune, Sang Cya). These drugs act by inhibiting T-cell activation, thus preventing T-cells from attacking the transplanted organ.
- Azathioprines (Imuran). These drugs disrupt the synthesis of DNA and RNA and cell division.
- Corticosteroids such as prednisolone (Deltasone, Orasone). These drugs suppress the inflammation associated with transplant rejection.

Most patients are prescribed with a combination of drugs after transplant surgery, one from each of the above main groups; for example cyclosporin, azathioprine and prednisolone. Over a period of time, the doses of each drug and the number of drugs taken may be reduced as the risks of rejection decrease. However, most patients need to take at least one immunosuppressive for the rest of their lives.

Other classifications

Immunosuppressants can also be classified depending on the specific transplant:

- Basiliximab (simulect) or daclizumab (zenapax) are used, in combination with other drugs such as cyclosporin and corticosteroids, in kidney transplants
- Muromonab CD3 (Orthoclone OKT3) is used, along with cyclosporin, in kidney, liver and heart transplants
- Azathioprine (Imuran) is used not only to prevent organ rejection in kidney transplants, but also in treatment of rheumatoid arthritis. It has been used to treat chronic ulcerative colitis, but it has been of limited value for this use.
- Cyclosporin (Sandimmune, Neoral) is used in heart, liver, kidney, pancreas, bone marrow and heart/lung transplantation. The neoral form has been used to treat psoriasis and rheumatoid arthritis. The drug has also been used for many other conditions including multiple sclerosis, diabetes and myesthenia gravis.
- Glatiramer acetate (Copaxone) is used in treatment of relapsing-remitting multiple sclerosis. In one study, glatiramer reduced the frequency of multiple sclerosis attacks by 75% over a two-year period.
- Mycopehnolate (cell cept) is used, along with cyclosporin, in kidney, liver and heart transplants. It has also been used to prevent the kidney problems associated with systemic lupus erythematosis.
- Sirolimus (rapamune) is used in combination with other drugs including cyclosporin and corticosteroids, in kidney transplants. The drug is also used for the treatment of psoriasis

After organ transplantation, the body will nearly always reject the new organ(s) due to differences in human leukocyte antigen haplotypes between the donor and recipient. As a result, the immune system detects the new tissue as 'hostile', and attempts to remove it by attacking it with recipient leukocytes, resulting in the death of the tissue. Immunosuppressants are applied as a countermeasure; the side-effect is that the body becomes more vulnerable to infections and malignancy, much like in an advanced HIV infection.

Self-Assessment Test 26: TRUE OR FALSE

State whether true (T) or false (F) against the following statements

1. Immunosuppresants are indicated in pregnancy __

2. Steroids are immunosuppressants __

ANSWERS:

1. F

2. T

5.4 Anti-viral Drugs

Most viruses have no known specific treatment and are, therefore, treated symptomatically. These are drugs that are used to treat certain viral infections, other than HIV, and called antiviral drugs. Drugs that are used to treat infection by HIV are called because HIV is a retrovirus. In this sub-unit we shall discuss both antiviral and antiretroviral drugs

Antiviral drugs

Activity :

Review the life cycle of viral replication which you learnt in Microbiology and Public Health Nursing

Antiviral drugs are a class of medication used specifically for treating viral infections, just like antibiotics for bacteria. Unlike most antibiotics, antiviral drugs do not destroy their target pathogen; instead they inhibit their development

The commonly used antiviral drug is **Acyclovir**

Mechanism of action: It interferes with DNA synthesis thereby slowing down viral replication and growth

Indications: Is used to treat infections caused by herpes viruses, such as genital herpes, cold sores, shingles, and chicken pox.

Presentation: Cap 200mg, Tab 400, 800mg; Inj. IV 500mg, Ointment 5%

Dose: Adult – 200-800mg Q4H, depending on the indications

Side effects: hypersensitivity reaction, nausea, vomiting, diarrhea, general ill feeling, headache

Contraindications: Hypersensitivity

Nursing considerations:

- Monitor patient sensitivity
- Monitor fluid intake and output ratios
- Monitor bowel motions before, during and after treatment

Other antiviral drugs include rapivab, relenza and tamiflu

Antiretroviral drugs (ARVs)

Activity :

Review the life cycle of HIV infection in the human being. The diagram below will help you to do this

Review of HIV life cycle

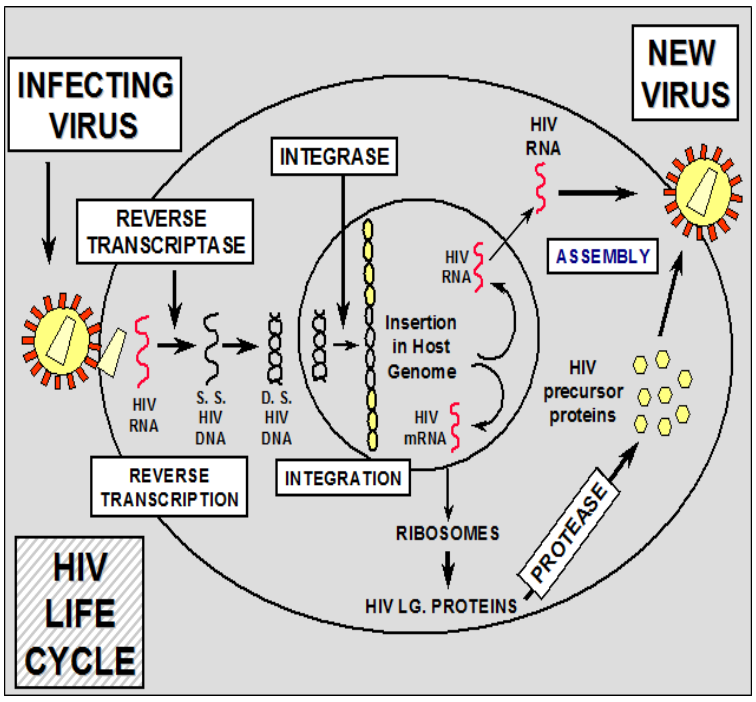

Figure 8: HIV life cycle

(MOH 2004) 1

Anti-retroviral drugs are a class of medication used specifically in treatment HIV/AIDS infection. Unlike most antibiotics, anti-retroviral drugs do not destroy their target pathogen; instead they inhibit their replication and growth rates. Anti-retroviral agents are used to inhibit production of viruses that would further attack other CD4 cells and weaken an individual's immunity.

Currently, antiretroviral drugs are broadly classified into 2 groups

1. **Reverse Transcriptase Inhibitors**:

Once HIV has locked onto and invaded a human cell, it uses an enzyme known as Reverse Transcriptase to convert its genetic code into the same form as the genetic code of the host human cell. The viral DNA then merges with the host human DNA, converting the cell into a factory for making the building blocks for new viruses.

Reverse Transcriptase Inhibitors (RTIs) work by inhibiting the action of the enzyme reverse trancriptase, thereby interfering with HIV RNA transcription. There 2 different classes of RTIs. These are:

A. Nucleoside Reverse Transcriptase Inhibitors (NRTIs) – They are sometimes called 'nucleoside analogues' or 'nukes'. They competitively inhibit the enzyme that facilitates the conversion of HIV RNA into HIV DNA. NRTIs contain faulty versions of the building blocks (nucleotides) used by reverse transcriptase to convert RNA to DNA. When reverse transcriptase uses these faulty building blocks, the new DNA cannot be built correctly. In turn, faulty HIV's genetic material cannot be incorporated into the healthy genetic material of the cell and prevents the cell from producing new virus. Some examples of the currently available NRTIs in Zambia include zidovidine, diadosine, lamuvidine, abacava, zalcitabine and stavudine

B. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): They are also known as 'non-nucleosides' or 'non-nukes'. NNRTIs attach themselves to reverse transcriptase enzyme and prevent the enzyme from converting RNA to DNA. In turn, HIV's genetic material cannot be incorporated into the healthy genetic material of the host human cell DNA. This prevents the host human cell from producing new virus. Some examples of the currently available NNRTIs in Zambia are nevirapine (NVP) and efavirenz (EFV)

Take Note:

In Zambia, at least 2 NRTIs + 1 NNRTI are currently used as first line treatment of HIV/AIDS infection

Table 2: RTIs and Mode of Action

Drug Class	**Mode of action (Both drugs inhibit reverse transcriptase enzyme)**
NRTIs	NRTIs contain faulty versions of the building blocks (nucleotides) used by *reverse transcriptase* to convert RNA to DNA. When *reverse transcriptase* uses these faulty building blocks, the new DNA cannot be built correctly
NNRTIs	NNRTIs inhibit viral DNA synthesis by attaching itself directly (binding) to *reverse transcriptase* enzyme and thereby preventing it from converting RNA to DNA.

2. Protease Inhibitors:

When HIV infects a CD4 cell in a person's body, it copies its own genetic code into the cell's DNA. The CD4 cell is then 'programmed' to make new HIV genetic material and HIV proteins. The proteins must be cut up by the HIV protease, a protein-cutting enzyme, to make functional new HIV particles.
PIs block the protease enzyme and prevent the cell from producing new viruses. Some examples of PIs currently available in Zambia include Indinavir, nelfinavir, saquinavir and ritonavir
Protease inhibitors became available in the 1990s and have proven effective, though they can have unusual side effects, for example causing fat to build up in unusual places.

Take Note:

In Zambia, PIs are currently used as second line treatment of HIV/AIDS infection

Table 3: Classes of ARVs available in Zambia 1

NRTIs *(Nucleoside and Nucleotide)*	**NNRTIs**	**PIs**
Zidovudine (AZT) Lamivudine (3TC) Stavudine (d4T) Didanosine (ddI) Abacavir (ABC) Emtricitabine (FTC) **NtRTI** Tenofovir(TDF)	Nevirapine (NVP) Efavirenz (EFV) Rilpivirine (TMC 278) RDEA806	Ritonavir (RTV) Indinavir (IDV) Saquinavir (SQV) Nelfinavir (NFV)

Table 4: Classes of ARVs available in Zambia 1

Generic name	**Acronym**	**Trade name(s)**
Nucleoside reverse transcriptase inhibitors (NRTI)		
Zidovudine	ZDV, AZT	Retrovir
Lamivudine	3TC	Epivir
Stavudine	d4T	Zerit
Didanosine	Ddi	Videx
Abacvir	ABC	Ziagen
Non-Nucleoside reverse transcriptase inhibitors (NNRTI)		
Nevirapine	NVP	Viramune
Efavirenz	EFV	Sustiva
Rilpivirine	(TMC 278)	
Protease Inhibitors (PI)		
Indinavir	IDN	Crixivan
Ritonavir	RTV	Novir
Nelfinavir	NFV	Viracept
Saquinavir	SQV	Invirase (Hard gel) Fortovase (soft gel)
Lopinavir+Ritonavir	LPV/r	Kaletra

ARV-Fixed Drug Combinations (FDCs) in Zambia

To reduce the pill-burden associated with ARVs and increase compliance to Highly Active Antiretroviral Therapy (HAART), most ARVs have been combined in FDCs, just like anti-TB drugs. The FDCs range from combinations of 2 to 4 drugs. Some of the currently available FDCs include the following:

- ZDV/3TC (Combivir)
- d4T/3TC
- ZDV/3TC/NVP (Duovir-N)
- d4T/3TC/NVP (Triomune)
- Lopinavir/ritonavir-LPV/r-(Kaletra)

Management of patients on ARVs

You need to prepare patients predictable and unpredictable side effects that may occur. Some of the side effects are mild and often self-limiting while others are severe and life threatening.

The following are side effects according to the class of ARVs

Suspect adverse effects due to NRTI if the patient has:-

- Peripheral neuropathy
- Pancreatitis
- Lipoatrophy
- Hepatitis
- Lactic acidosis
- Mitochondrial toxicity

Suspect adverse effects due to NNRTI if the patient has:-

- Rash
- Fever
- Nausea
- Diarrhea
- Hepatoxicity

Suspect adverse effects due to NNRTI if the patient has:-

- Lipodystrophy
- GI Intolerance
- Hyperglycemia
- Lipid abnormalities

Common overlapping adverse effects

- Bone Marrow depression may be due to: AZT,Ganciclovir and Cotrimoxazole
- Nephrotoxicity may be due to: Indinavir which may cause renal stones and Aminoglycosides
- Peripheral Neuropathy may be due to: ddI,d4T ,Cotrimoxazole and Isoniazid
- Diarrhoea may be due to: ddI,NFV and RTV
- Rash may be due to: ABC, EFV, NVP,dapsone, and cotrimoxazole
- Hepatotoxicity may be due to: EFV, NVP, NRTIs, rifampicin/ rifabutin, isoniazid and fluconazole /ketoconazole/Itraconazole,
- Pancreatitis may be due to: ddI, 3TC in children,d4T,RTV
- Occular effects may be due to**:** ddI, rifabutin and ethambutol

Nursing considerations for Patients on ARVs

- ARVs are taken for life
- Report on any drug side effects using the tools provided so that the patient can be helped in time. You must continue giving supportive/symptomatic treatment if need arose.
- Inform the doctor immediately you notice any side effect so that he may either discontinue treatment or change it (rarely required) if serious and/or life threatening.

Principles in management of adverse drug reactions

If you observe the above stated adverse effects:

i. Determine the Severity

ii. Establish cause – ARVs (consider ation) or other drug (including self-medication)

iii. Consider other diseases (hepatitis, viral, immune reconstitution)

Well done. We have come to the end of antiviral and antiretroviral drugs. Before we discuss vaccines and toxoids, here is a self-assessment test for you

Self-Assessment Test 27: TRUE OR FALSE

State whether true (T) or false (F) against each question in the spaces provided

1. Acyclovir is a broad spectrum antifungal __

2. All Reverse Transcriptase inhibitors have same mechanism of action ___

3. Ritonavir is a Protease Inhibitor ___

ANSWERS:

1. F

2. F

3. T

5.5 Vaccines and Toxoids

ACTIVITY:

Review the information which you learnt in microbiology about vaccines – the different types, their schedules and how they work

Write the answers in your book

A. Vaccines

In Zambia immunization includes vaccination against Tuberculosis, polio, diphtheria, whooping cough (Pertussis), tetanus, haemophilus influenza type B, hepatitis B and measles. It is a requirement that all children should receive all doses of the antigen before their first birth day.

Vaccination: This is the inoculation with the vaccine in order to protect against a disease.

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins.

Mode of action of vaccines

The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and 'remember' it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

Examples of vaccines
BCG vaccines
Cholera vaccines
Hemophilus b. conjugate vaccines
Hepatitis B vaccine
Influenza virus vaccine
Measles virus vaccine
Polio vaccine
Pneumococcal vaccine
Yellow fever vaccine

B. Toxoids

A toxoid is a bacterial toxin (usually an exotoxin) whose toxicity has been inactivated or suppressed either by chemical (formalin) or heat treatment, while their immunogenicity properties are maintained. It is harvested from a pathogenic organism toxin and treated so as to destroy its toxicity but leave it capable of inducing the formation of antibodies on injection. Toxoid vaccines are made from inactivated toxic compounds that cause illness rather than the micro-organism. It exposes the individual to a small amount of the bacteria (or to a protein from the bacteria) causing the body to develop immunity to the disease. Thus, when used during vaccination, an immune response is mounted and immunological memory is formed against the molecular markers of the toxoid without resulting in toxin-induced illness. Toxoids are used as vaccines because they induce an immune response to the original toxin or increase the response to another antigen since the toxoid markers and toxin markers are preserved. For example, the tetanus toxoid is derived from the tetanospasmin produced by Clostridium tetani. Toxoids are used for prevention of diphtheria, tetanus and botulism.

Table 5: Vaccines and toxoids

VACCINE	DISEASE	AGE	TYPE OF VACCINE	DOSE	ROUTE OF ADMINISTRATION	SIDE EFFECTS	CONTRAINDIACTION
BCG	**TB**	At birth (0 to 13 days) if no scar after 12 weeks repeat dose	Live attenuated bacteria	0.05ML	Intradermal injection in the left under arm.	Severe local inflammation Swelling under the arm pits or near the elbow Deeper abscess – need treatment with antibiotic for example, cloxacillin 50mg/kg/bwt/day.	Symptomatic HIV/AIDS infection.
OPV (Oral Polio Vaccine)	***Polio***	0-13 days 1.At 6 weeks 2.At 10 weeks 3.At 14weeks	Live attenuated virus.	2 to 3 drops	oral	No side effects.	Immunosuppressed patients
DPT-HepB+Hib Vaccination	Deptheria, pertussis, Tetanus, Hepatits B, heamophyl us influenza type B	1.At 6weeks, 2.At 10weeks 3.At 14weeks	Live attenuated	***0.5mls***.	***intramuscularly*** into the ***antero-lateral*** aspect of the thigh of infant.	*Fever*- usually subside after some time. Give paracetamol. *Local soreness*- reassures the mother that some children may get a red, tender lump at the site of injection that is not serious and needs no treatment.	Immunosuppressed patients Children with pre-existing disorders must not receive pertussis components
Measles Vaccination	Measles	9 Months 18 Months booster dose	Live attenuated (weakened) form of measles virus.	0.5mls	Subcutaneously into upper arm.	Fever Rash	Immunosuppressed patients

Self Assessment – Test 28: MCQ

Choose the most appropriate answer

1. The following Vaccine should be given in a confirmed case of HIV/AIDs infection **except**

A. Measles vaccine
B. BCG Vaccine
C. Hepatitis B vaccine
D. DPT vaccine

2. The route of administration for measles vaccine is

A. Subcutaneously
B. Intramuscularly
C. Orally
D. Subdermal

Answers to self assessment – Test

1	2
B	A

5.6 Anti-toxins and Anti-venoms

A. Antitoxin

An antitoxin is an antibody with the ability to neutralize a specific toxin. Antitoxins are produced by certain animals, plants, and bacteria. Although they are most effective in neutralizing toxins, they can kill bacteria and other microorganisms.

An antitoxin is a preparation of antibodies against a toxin such as diphtheria or botulism or against animal venoms such as black widow spider venom or various snake venoms. They are produced by injecting the harmful toxin into an animal such as a horse in gradually increasing amounts. If the doses are correctly chosen, the animal may not be harmed. The animal then produces its own antibodies to the toxin. The blood is then withdrawn from the animal, and these antibodies are extracted from the blood and purified. When injected into a human patient, the antitoxin selectively attack and neutralize the toxin present within the patient's system. Natural antitoxins are useful in counteracting the poisonous effects of being bitten by certain animals or insects, such as a venomous snake or spider. However, antitoxins are also effective against the toxic effects of bacteria and other microorganisms, such as clostridium botulinum and corynebacterium diphtheriae, which cause botulism and diphtheria, respectively.

Example of antitoxin

- Botulism antitoxin
- Diphtheria antitoxin
- Antitetanus immunoglobulin

Presentation

Injection not less than 500units/ml in 10,000 unit and 20,000 units vials

Mode of action

Neutralizes and binds toxin

Indication

Diphtheria prevention

Diphtheria treatment

Dosage

1,000 to 5,000 units IM for diphtheria prevention

Side effects

Fever, malaise

Contra indications

Patients hypersensitive to the drug

Nursing consideration

Store the antitoxin in a refrigerator at 2 ºc to 10 ºc

B. Anti-venoms

An Antivenom is a biological product used in the treatment of venomous bites or stings. Antivenom is created by milking venom from the desired snake, spider or insect. The venom is then diluted and injected into a horse, sheep or goat. The subject animal will undergo an immune response to the venom, producing antibodies against the venom's active molecule which can then be harvested from the animal's blood and used to treat envenomation.

Snake antivenoms are the only specific treatment for envenoming by snakebites. They can prevent or reverse most of the snakebite venomous effects, and play a crucial role in minimizing mortality and morbidity. Antivenom is produced by injecting a small (safe) amount of that particular venom into an animal and once that animal makes antibodies against the venom, the blood is drawn, purified and used to treat bites, etc. by the venomous organism (for example snake).

Example of antivenins

- Black widow spider antivenin
- Crotaline antivenin
- Micrunus fulvinus antivenin

- Crotaline antivenin

Presentation: Injection diluted 1:10
Mode of action; Neutralizes and binds venom of snakes

Indication: Snake bites – crotalids including rattle snakes, water moccasus and copper heads

Dosage: Initially 10 to 50mls IV depending on severity of bite and patient response.

Side effects: Hypersensitivity

Interactions: Antihistamines enhances

Contra indication: Hypersensitivity to the drug

Nursing consideration

Immobilize the patient immediately. Splint the bitten extremity.

Self-Assessment Test 29: MATCHING ITEMS

Match the anti-toxins/anti-venom in Column I with their indications (conditions) in Column II

Column I	**Column II**
1. __ Tetanus Toxoid	A. Diphtheria
2. __ Antivenom antitoxin	B. Tetanus
	C. Snake bite

ANSWERS:

1. B

2. C

5.7 Immune serums; immunoglobulin

Immunoglobulins are glycoprotein molecules that are produced by plasma cells in response to an antigen. Immunoglobulins function as antibodies.

Examples of immunoglobulin
Tetanus immunoglobulin
Hepatitis B immunoglobulin
Rabies immunoglobulin

1. Tetanus immunoglobulin Human

Presentation: Injection 250 units per vial

Mode of action: Provides passive immunity to tetanus

Indications

Tetanus exposure

Tetanus treatment

Dosage: 250 to 500 units Im

Side effects: Fever, pain at injection site

Drug interaction: None significant

Contra indication: Hypersensitivity

Nursing consideration

Use tetanus immunoglobulin only if a wound is more than 24 hours old.

2. Hepatitis B Immunoglobulin human

Presentation: Injection 1ml, 4ml,5ml vial

Mode of action: Provides passive immunity to hepatitis B

Indication: Hepatitis B exposure in high risk patients

Dosage: 0.06 ml with 7 days after exposure. Repeat after 28 days.

Side effects: Anaphylaxis

Drug interaction: Live –virus vaccines

Contra indication: Hypersensitivity

Nursing consideration

Inject in a deltoid muscle in adults and lateral aspect of the thigh in children.

4. **Rabies immunoglobulin (human)**

Presentation: Injection 150 iu/im in 2 ml, 10ml vials

Mode of action: Provides passive immunity to rabies

Indication: Rabies exposure

Dosage: 20iu/kg im at time of first dose. Use half dose to infiltrate wound area.

Side effects: Fever, angioedema

Drug interaction: Corticosteroids

Contra indication: Hypersensitivity

Nursing consideration

Give regardless of interval between time of exposure and initiation of therapy.

Self Assessment – Test 30: MCQ

Choose the most appropriate answer

1.Antitoxins are prepared from……

A. Toxins
B. Organisms
C. None of the above
D. All of the above

2.After an organ transplant, which drugs can be used to reduce the chances of organ rejection?

A. Anti-viral drugs
B. Immunosuppressant
C. Toxoids
D. Immunoglobulin

Answers to Self Assessment – Test

1	2
B	B

5.8 Vitamins

Vitamins are used for the prevention and treatment of specific deficiency states or where the diet is inadequate. They may be prescribed to prevent or treat deficiency but not as a dietary supplement.

Ascorbic Acid (Vitamin C)

Presentation: Tablet containing 50mg, 100mg, 200mg, ascorbic acid. Effervescent tablet containing 1g ascorbic acid. Injection containing ascorbic acid 100mg/ml.
Indications: Supplementation and deficient states. Prevention and treatment of Scurvy.
Effects of deficiency: Scurvy, irritability, slow growth, decreased resistance to infections, haemorrhagic tendencies, poor wound healing.
Physiological requirements: *Up to 1 year;* 35mg daily. *1 – 12 years*; 40mg daily. *Over 12 years*; 40 – 60mg daily.
Therapeutic dose: 200 – 400mg daily.
Natural sources: Citrus fruits, tomatoes, green vegetables, black currant and rose fruit.
Side effects: Large doses cause diarrhoea, other GIT disturbances, hyperoxaluria, renal calcium, oxalate calculi, haemolysis in patients with G6PD deficiency.
Caution: Destroyed by usual cooking temperatures. Hyperoxaluria, deficiency of G6PD.

Ergocalciferal (Vitamin D)

Vitamin D comprises compounds used in treatment and prevention of rickets. The margin of safety between therapeutic and toxicity concentration is narrow. Therefore, vitamin D dietary supplementation may be detrimental in patients already receiving adequate dietary intake. Furthermore, Vitamin D is the most likely of all vitamins to cause toxicity.
Presentation: Effervescent and chewable tablet containing 10,000 units (250mcg), 50,000 units (1.25mg) ergocalciferal. Injection containing 300,000 units/ml ergocalciferal in oil.
Indications: Vitamin D deficiency including that caused by intestinal malabsorbtion, chronic liver disease, hypoparathyroidism.
Dose: therapeutic dose – deficiency due to malabsorption or liver disease – up to 40000 units daily. Hypocalcaemia due to hypothyroidism – doses up to 100,000 units daily. Monitor calcium levels initially weekly then every 2 to 4 weeks to optimize clinical response and avoid hypercalcaemia.
Effects of deficiency: Rickets and osteomalacia
Physiological requirements: *Child*; 400i.u. daily. *Adult*; 100 i.u. daily
Therapeutic dose: 40,000 – 100,000 units daily
Natural sources: Milk, fish, liver, oil, sunlight
Side effects: Excess leads to hypercalcaemia, hypercalcaeuria, renal damage and cardiovascular damage.
Caution: Infants, renal and heart disease,hypercalcaemia. Infants breast-fed by mothers taking therapeutic doses of vitamin D. **Contraindications**: Hypercalcaemia

Retinal (Vitamin A)
Retinol (Vitamin) A is a fat soluble vitamin and essential for growth, development and maintenance of epithelial tissue and for vision. Deficiency state develops with inadequate dietary intake. This is common in children.
Presentation: Capsule containing 50,000 i.u., 100,000 i.u., 200,000 i.u. vitamin A
Indications: Night blindness, xerophthalmia, xeromalacia. Adjunct treatment in measles, diarrhoea, malnutrition and primary biliary cirrhosis.
Effects of deficiency: Night blindness, xerophthalmia, xeromalacia, abnormal bone and teeth formation, dry skin and mucous membrane, retarded growth, decreased resistance to infections, significant increased risk of child mortality.
Physiological requirements: *Up to 1 year*; 1500 i.u. daily. *1 – 12 years*; 2000 – 4500 i.u. daily. *Over 12 years*; 5000 – 8000 i.u. daily.
In deficient populations children should receive a high dose supplement every 6 months as follows; 6 – 11 months, 100,000 i.u. 1 – 6 years 200,000 i.u.
Therapeutic dose: 50,000 daily.
Dose: Primary biliary cirrhosis
Intravenous doses of 10,000 units every 2 to 4 months
Xerophthalmia.
Over 1 year of age 200,000 units by mouth immediately on diagnosis.
6 – 12 months 100,000 units**)**
Less than 6 months 50,000 units**)** given by mouth immediately on diagnosis, then on the following day and repeated 2 weeks later.
Effects of overdose: Drying and cracking of skin, pain in long bones, sparse hair growth, growth retardation, increased intracranial pressure.
Natural sources: Dietary vitamin is derived from two sources, namely animal and plan. Animal sources include Liver, kidney, dried fish, oils, whole milk, egg yolk. Plant sources include carrots, whole grain, yellow fruits, dry/dark green or yellow vegetables.
Side effects: Excessive amounts may lead to hyper vitaminosis A, raised intracranial pressure, tinitus, visual disturbances, acute vitamin A intoxication.
Caution: Destroyed by exposure to strong sunlight. Pregnancy, women of child-bearing age and breast feeding. Resistant to usual cooking temperatures,

Vitamin B Group
The Vitamin B. Group comprises the following substances Vitamin B1 (Thiamine), Vitamin B2 (Riboflavine), Vitamin B6 (pyridoxine and derivatives) and Vitamin B12 (cobalamines). To these are added nicotinic acid and derivatives, folic acid and pantothermic acid.
The term vitamin B complex is a term generally used when individual Vitamin B substances and other components are commercially prepared. The ingredients and doses, are according to the manufacturers' instructions.
Indications, side effects and Caution are as for the individual components of the formulation. The presentation of the Vitamin B complex is in form of tablets, capsules, elixir and injection.

Nicotinamide
Naturally occurs as a water-soluble vitamin B substance which is converted to nicotinamide odemine dinucleotide (NADP). These co-enzymes play a major role in electron transfer reactions in the respiratory chain. Their deficiency leads to a syndrome of pellagra which is characterized by skin lesions especially to areas exposed to sunlight with hyperpigmentation and hyperkeratinisation. Nicotinic acid deficiency may occur in association with other Vitamin B complex deficiency states for example, in alcoholism.
Presentation: Tablet containing 50mg nicotinamide
Indications: Pellagra, especially in alcoholism.
Effects of deficiency: Pellagra
Natural sources: Milk, fish, poultry, liver, whole grain, green vegetables and groundnuts.
Dose: Daily requirements are not definitely known but daily human requirement is required for optimum amounts of nicotinic acid to be absorbed.
Side effects: Vasodilation, dryness of the skin, pruritus hyperpigmentation, abdominal cramps, peptic ulcer disease, amblyopia, jaundice, impaired liver function, decrease in glucose tolerance, hyperglycaemia, hyperuricaemia.
Caution: Peptic ulcer disease, diabetes mellitus, gout or impaired liver function.

Pyridoxine (Vitamin B6)
A water soluble vitamin involved principally in amino acid, carbohydrate and fat metabolism and also required for haemoglobin formation. Deficiency is rare but may occur during drug therapy for example, isoniazid therapy. Deficiency causes sideroblastic anaemia, dermatitis, cheillosis and neurologic symptoms such as peripheral neuritis, convulsions especially in neonates.
Presentation: Tablet containing 10mg, 20mg, 50mg pyridoxine hydrochloride

Indications: Pyridoxine deficiency such as may occur in isoniazid therapy or metabolic disorders for example, hyperoxaluria, in sideroblastic anaemia, peripheral neuropathy.

Effects of deficiency: Irritability, convulsions especially in neonates, hypochromic anaemia, polyneuritis.
Side effects: Large dose and long term therapy leads to severe peripheral neuritis (neuropathies).
Physiological requirements: Up to 1 year; 200 – 400micrograms. 1 – 12 years; 500mcg.
Over 12 years; 1.2 – 1.8mg daily.
Deficiency states; 50 – 150mg daily in divided doses. Prophylaxis of isoniazid neuropathy; 10mg daily. *Therapeutic dose*; 50mg 3 times daily. Idiopathic *sideroblastic anaemia*; 100 – 400mg daily in divided doses.
Natural sources: Meat, liver, kidney, whole grain, groundnuts and soya beans.
Caution: Destroyed by heat, intestinal synthesis occurs.

Riboflavin (Vitamin B2)
It is a water-soluble vitamin. It is used as a coenzyme in the various metabolic reactions. It is also necessary for the normal functioning of pyridoxine and nicotinic acid. Riboflavin deficiency mainly results from insufficient intake. The deficiency state is called ariboflavinosis. In addition, there may also be normocytic anaemia and some ocular symptoms. It may also occur in other deficiency states with other B vitamins
Presentation: Tablet containing 5mg riboflavin
Indications: Aviboflavinosis characterized by conditions such as glossitis, stomatitis, photophobia and blurred vision.
Physiological requirements: Up to 1 year; 400 – 600micrograms. 1 – 12years; 600mcg – 3mg. Over 12 years; 1.3mg – 1.5mg daily. Therapeutic dose: 5 – 10mg daily
Natural sources: Milk, cheese, liver, meat, eggs, fish, green vegetables, whole grain.
Caution: Resistant to normal cooking temperatures.

Thiamine (Vitamin B1)
This is a water-soluble vitamin. It is essential in carbohydrate metabolism. Its deficiency leads to a syndrome known as beri-beri.
Presentation: Tablet containing 25mg, 50mg, 100mg, 300mg thiamine hydrochloride. In high potency vitamin B Co. injections containing 25mg/ ml (intravenous), 50mg/ml (intramuscular)
Indications: Treatment of thiamine deficiency, beri-beri, adjunct in treatment of alcohol abuse.
Physiological requirements: *Up to 1 year*; 200 – 500mcg daily. *1 – 12 years;* 500mcg – 1.3mg. *Over 12 years*; 1.5mg daily

Therapeutic dose: 25 – 100mg intramuscularly or orally. In severe cases up to 300mg, higher doses acceptable in Wernicke-Korsakoff syndrome by intravenous route.

Effects of overdose: Sudden death with injection. Hypersensitivity reactions which may be fatal.
Natural sources: Liver, meats, milk, legumes, cereals and nuts
Caution: Destroyed by normal cooking heat. Because of possibility of potentially serious allergic reaction, use by injection should be restricted to those patients in whom parenteral treatment is essential, intravenous injection should be given slowly (over 10 minutes).

Vitamin B12
This is a water-soluble vitamin. It occurs in various forms of cobalamins. Deficiency is commoner in those strict vegetarians who do not ingest any animal and dairy products. It is also common in patients after gastrectomy or ileal resection. Deficiency causes megaloblatic anaemia, demyelination and other neurological damage.
Presentation: Oral form of cyanacobalamin. Injectable forms of cynanocobalamin and hydroxy cobalmin.
Therapeutic dose: (I) Pernicious anaemia and other macrocytic anaemia without neurological involvement: intramuscular cyanocobalamin and hydroxycobalamin 250 - 1000mcg on alternate days for one to two weeks. Then 250mcg weekly until blood levels are normal.
Maintenance doses: 1000mcg cyanocobalamin monthly or 1000 mcg hydrocobalamin every 2 to 3 months.
Prophylaxis for Vitamin B12 deficiency following gastrectomy or malabsorption syndromes: intramuscular cyanocobalmin 250 – 100mcg monthly and intramuscular hydroxycobalamin 100mcg every 2 to 3 months.
For vitamin B12 deficiency of dietary origin – oral cyanocobalamin 50 – 150 mcg daily in between meals.
Side effects: Allergic hypersensitivity following parenteral administration, arrhythmias secondary to hypokalaemia.
Caution: Avoid use in hebers disease or tobacco amblyopia since these optic neuropathies may degenerate further.
Interactions absorption of Vitamin B12 is reduced when administered together with neomycin, aminosalicylic acid, H^2 receptor antagonist, and colchicines

Folic Acid (vitamin B9)
Presentation: Tablet containing 5mg folic acid
Indications: Prevention and treatment of folic acid deficiency
Dose: 5 – 20mg daily
Contraindications: Sub acute combined degeneration of spinal cord.

Phytomenadione (Vitamin K)
Presentation: Injection containing 10mg/ml Phytomenadione. Tablet (sugar coated) containing 10mg phytomenadione
Indications: Vitamin K deficiency particularly in neonates and also in liver disease. Reversal of effects of anti-coagulants.
Dose: Neonatal prophylaxis 1mg immediately after birth. Liver disease 1-2mg repeated as desired.
Side effects: Shock-like reactions, cyanosis, bronchospasm, rapid pulse, pain and swelling at injection site.
Caution: Pregnancy, store in the dark, do not use if separation has occurred or oil droplets have appeared.

Multivitamin tablets and Syrup
These are available in different formulations.
The constituents and dose are according to manufacturer's instructions. Indications and side effects are as for constituents mentioned above.

Self-assessment Test 31: MCQ

Choose the most appropriate answer

1. Which vitamin helps in the formation of prothrombin an element which is important for haemostasis

A. Vitamin A

B. Vitamin D

C. Vitamin E

D. Vitamin K

2. Vitamin B6 is used to treat……

A. Beriberi

B. Peripheral neuropathy

C. Poor sight

D. Scurvy

Answers

1	2
D	B

5.9 Summary

We have come to the end of the unit. In this unit we were looking at drugs acting on the immune system. We specifically discussed and gave examples of immune-suppressants, antiviral and antiretroviral drugs, vaccines and toxoids, anti-toxins and anti-toxoids, Immunoglobulins and vitamins. You now appreciate the importance of this class of drugs in improving the health of individuals. Thank you very much. You have been an excellent student. In the next unit you will be looking at drugs acting on the urinary system.

5.10 References

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UNIT 6: DRUGS ACTING ON THE URINARY SYSTEM

6.1 Introduction

Welcome to another yet interesting unit where you will be looking at drugs that act on the urinary system. In the previous unit you were learning about drugs that act on the immune system. You saw how important these drugs are especially to patients who have received an organ from a different donor. In this unit, you learn in detail on the drugs that act on the urinary system. If you remember very well in your anatomy and physiology, you learnt about the urinary system. Do you remember its functions? Well, let us explore on the drugs together so that lives can be saved.

6.2 Unit Objective

At the end of this unit you should be able to ;

1. Describe urinary antiseptics as they act on the urinary system.
2. Describe diuretics as they act on the urinary system.
3. Describe sulphonamides as they act on the urinary system.

The urinary system performs the essential function of getting rid of metabolic wastes which if they are left to accumulate to toxic levels they can harm the body.

The main structures that make up the urinary system are two kidneys. Within each kidney are millions of individual structures, called nephrons that do the actual work of the kidney (which are the functional unit of the kidney), two ureters, one urinary bladder, and one urethra. A nephron consists of a glomerulus, Bowman's capsule, proximal convoluted tubule, loop of Henle, distal convoluted tubule, and a collecting duct. The Ureter connects the kidney to the bladder. The bladder is the temporal storage for urine. Urine is excreted to the outside of the body through the urethra. You have reviewed the anatomy and physiology of the kidney. Now let us look at the drugs that act on it.

ACTIVITY :
Are urinary tract infections the same as the sexually transmitted infections?

Write your answers in the note book with rationales
Well done! Now go through the module for you to understand the lesson.

6.3. Urinary Antiseptics

These are drugs that exert antibacterial activity in the urinary system but have little or no systemic anti-bacterial effect. These are generally effective against most gram negative bacteria and some gram positive bacteria. They must be used with caution in patients with epilepsy, in hepatic or renal impairment, in pregnancy and breast feeding. They are concentrated in urine.

Examples of commonly used urinary antiseptics include:

Nalidixic Acid

Presentation: Tab 250, 500mg

Action: It inhibits microbial DNA synthesis

Indications: It is effective in uncomplicated urinary tract infections, patients with Ecoli, staphylococcal infections and dysentery.

Dosage: 1g 6 hourly for 7 days in acute conditions while in chronic cases 500mg 6 hourly. Children over 3 months maximum dose is 50mg /kg body weight daily in divided doses; reduced in prolonged therapy to 30mg/kg body weight daily. (Quinolones can cause arthropathy in young animals hence not recommended in children).

Side effects: Skin rashes, nausea, vomiting, dyspepsia, abdominal pain, diarrhea, neurotoxic and metabolic acidosis. Other side effects include skin rashes, pruritus, and urticaria. In larger doses- CNS disturbances for example, convulsions, confusions or epilepsy.

Caution: Patients with a history of epilepsy or conditions that predisposes to seizures, in pregnancy, breast feeding mothers, growing children.

Contraindications: Patients with hypersensitivity to drug, seizure disorders infants less than 3 months and patients on nitrofurantoin (nitrofurantoin antagonizes effects of nalidixic acid).

Nursing implications for quinolones

- Instruct patient to take drug with food to prevent GI upset.
- Advise patient to report any visual disturbances or CNS symptoms immediately.
- Do not give in children less than 3 months
- Tell patient to avoid exposure to sunlight, to wear protective clothing and to use sunscreen.

Nitrofurantoin (Furadantin)

Presentation: tablet containing 50mg and 100mg. Suspension containing 25mg/5ml

nitrofurantoin

Action: It is bacteriostatic that inhibits bacterial enzyme systems that are essential for bacterial function **Indications:** UTI due to susceptible Escherichia coli, Staphylococcus aureus, enterococci or certain strains of Klebsiella and Enterobacter.

Dosage: Adults and children over age 12: 50- 100mg P.O q.i.d. with meals.

Children ages 1 month to 12 years: 5- 7mg/ kg body weight P.O daily, divided q.i.d.

Chronic, severe or recurrent dose: 100mg q.i.d.

Prophylaxis: Adults 50-100mg nocte and children 1mg/kg body weight.

Side effects: Nausea, vomiting, diarrhea, anorexia, abdominal pain, urticaria, systemic lupus erythromatosus and hypersensitivity reactions.

With high doses; headaches, dizziness, drowsiness and ascending polyneuropathy.

Contraindications: Contraindicated in infants 1 month and under, moderate to severe renal impairment, pregnancy at term (38-42 weeks) and during labour and delivery.

Nursing Implications

- You must encourage the patient to take medicine with food to minimize stomach upset.
- Monitor intake and output; do not give in renal patients due to cumulative effects.
- Warn patient that colour of urine is likely to change to yellowish brown.

Other drugs that are used to treat urinary tract infections include antibiotics such as amoxicillin, metronidazole and ciprofloxacin

Self-Assessment Test 32– MCQ: Choose the most appropriate answer

1. Most urinary antiseptics are self-limiting in action. This means that…

A. They are ineffective

B. They are toxic

C. They act locally

D. They act systemically

2. Why is it advisable to collect urine specimens from patients taking urinary antiseptics before commencement of treatment?

A. Urinary antiseptics may alter results

B. Urinary antiseptics may worsen the infection

C. It may be difficult to collect urine from patient taking urinary antiseptics

D. The reason is not well understood

ANSWERS:

Q1. C

Q2. A

6.4 Diuretics

These are drugs that increase the volume of urine excreted by the kidneys and promote release of water from tissues. They also lower the fluid volume in tissues to decrease oedema and lower blood pressure.

ACTIVITY:

Diuretics have already been discussed in pharmacology 1 unit 6.4 under the antihypertensive drugs.

Refer to pharmacology 1 and update your knowledge on diuretics.

Self-Assessment Test 33: State whether true (T) or false (F) for each of the following statements

1. Furosemide is a potassium-sparing diuretic _____

2. Spinorolactone is better give with potassium chloride (Slow K) _____

ANSWERS:

1. F

2. F

6.5 Sulphonamides

This is a group of antibiotic drugs derived from para-amino benzoic acid (sulphanilamide) that prevent growth of bacteria (that is, they are bacteriostatic). They are antimetabolites which act by inhibiting the conversion of para-amino benzoic acid to folic acid

Sulphonamides are usually given by mouth and are effective against a variety of infections. They are insoluble in very acidic urine and so may crystallize and cause renal damage. For this case a high intake of fluids must be taken when taking the drugs. Sulphonamide are also well known for severe hypersentivity reactions, therefore, it should always be established that the patient is not allergic before commencement of treatment. Examples of sulphonamides include; sulfadiazine, sulfamethoxazole and sulfafurazole.

Indications: Sulphonamides are bacteriostatic in action and are active against a wide range of organisms including meningococci, strepcocci and gonococci and the bacillary dysentery group, for example, shigella. It is effective against both gram negative and positive organisms.

Side effects

- Renal necrosis may occur due to crystallization
- Nausea, vomiting and pyrexia
- Agranulocytosis, haemolytic anaemia
- Hypersensitivity reactions

Contraindication

- Jaundice
- Premature infants
- Pregnant women

Co-trimoxazole

It is a combination of sulphonamides and trimethoprim will provides a sequential blockage of the formation of folinic acid which is essential for DNA synthesis.

Action: It prevents growth of bacteria in the urinary tract by decreasing bacterial folic acid synthesis (bacteriostatic). It is effective against shigellosis, UTI due to susceptible strains of E coli, Proteus, Klebsiella or Enterobacter. It is also effective against staphylococci and streptococci pneumonia.

Indications: Urinary tract infections, upper respiratory tract infections, prostatitis, broncho pneumonia, bronchitis, salmonelosis, brucellosis, enteric fever and malaria.

Dosage: Adults: 160mg trimethoprim/ 800mg sulfamethoxazole (double strength tablet) P.O 12 hourly for 10- 14 days in UTIs and 15 days in Shigellosis.

Children ages 2 months and older: 8mg/kg/ day, P.O in two divided doses.

Side effects: Nausea, Steven- Johnson syndrome, toxic epidermal necrolysis, systemic lupus erythematosus, anorexia, liver damage including jaundice, hepatic necrosis, headaches, hallucinations and seizures.

Contra indications: Patients with severe renal failure, megaloblastic anaemia due to folic acid deficiency, hypersensitivity to sulphonamides, pregnant women, breast feeding women and infants under 2 months old.

Nursing implications

- Always establish that patient is not allergic before commencing treatment
- Advise the patient to take the drugs with a lot of water to aid flush out the drug from the kidneys.
- Advise patients to stop the drug and report when they observe signs of jaundice.
- Take history of allergy against sulphonamides before commencing treatment.
- Tell patient to take drug as prescribed even if he feels better.

Sulphadiazine

Action: As for Co-trimoxazole

Indications: Asymptomatic meningococcal meningitis, Rheumatic fever prophylaxis as an alternative to penicillin, toxoplasmosis usually given in combination with pyrimethamine.
Dosage: 1g, B.D, P.O for adults or patents weighing more than 30 kg and children weighing less than 30kg is 500mg, P.O, B.D.
Side effects: As for Co-trimoxazole.
Contraindications: As for Co-trimoxazole
Nursing implications: As for Co-trimoxazole

Sulphamethoxazole
Action: As for co-trimoxazole
Indications: UTIs and systemic infections.
Dosage: 2g, P.O, stat then 1g P.O, b.i.d up to t.i.d in severe infections. In children and infants over age 2 months; initially, 50- 60mg/ kg P.O; then 25- 30mg/ kg b.i.d. Maximum daily dose should not exceed 75mg/ kg.
Side effects: As for Co-trimoxazole
Contraindications: As for co-trimoxazole
Nursing implications: As for co-trimoxazole.

Trimethoprim
Presentation: tablet containing 100 to 200mg and oral suspension containing 50mg/ml

Action: Same as for co-trimoxazole

Indications: UTI, acute and chronic Bronchitis and other systemic infections.

Dosage: For acute infections; 200mg, B.i.d, P.O, in children; 25- 50mg, b.i.d. In UTIs; 300mg P.O, b.i.d, in chronic illnesses in children; 1-2mg/kg at night.

Side effects: contraindications and nursing implications as for co-trimoxazole

ACTIVITY :

Sulphonamides were already been discussed in pharmacology 1 unit 4.2 under classification of antibiotics. Refer to pharmacology 1 and read more about sulphonamides.

Self-Assessment Test 34: MCQs

SELF TEST QUESTION

1. Severe bacterial urinary tract infections are mostly treated with…….

A. ARVs

B. Antifungals

C. Antibiotics
D. All of the above
2. The most severe side effect of taking co-trimoxazole is
A. Steven- Johnson syndrome
B. Toxic epidermal necrolysis,
C. Liver damage
D. Systemic lupus erythematosus,

ANSWERS TO SELF TEST QUESTIONS

1	2
C	A

6.6 Summary

We have come to the end of the unit where you were looking at drugs acting on the urinary system. You learnt about urinary antiseptics, diuretics and sulphonamides. These drugs are used to treat different organisms that affect the urinary systems. Examples of urinary antiseptics are nitrofurantoin and nalidixic acid while examples of sulphonamides are sufadiazine and co-trimoxazole. I hope you looked up and found examples of diuretics in Pharmacology 1 unit 6.4. I hope you found the lesson interesting. In the next and last unit you will be looking at drugs used in obstetrics.

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UNIT 7: DRUGS USED IN OBSTETRICS

7.1 Introduction

Welcome to the last unit of the course in pharmacology for nurses. I must thank you for your endurance throughout the course and I hope you gained the much needed knowledge in pharmacology for the betterment of the community you will be serving.

In the previous unit you learnt about drugs acting on the urinary system. In this unit you will learn the drugs used in obstetrics, a branch of medicine that deals with conditions peculiar to the pregnant woman up to 6 weeks after delivery. I hope you will pay attention as we explore these equally important drugs in details.

7.2 Unit Objective

At the end of the unit, you should be able to;

1. Describe oxytocic drugs as used in obstetrics.
2. Describe alkalinizing agents as used in obstetrics.
3. Describe sedatives as used in obstetrics.

As mentioned earlier, Obstetrics is a branch of medicine that deals with conditions peculiar to pregnancy, labour and up to 6 weeks following the delivery of the fetus. For the purpose of understanding drugs used in obstetrics, let us briefly review the stages of pregnancy which you learnt in Integrated Reproductive Health (IRH)

Pregnancy has four main stages and it is very important to appreciate these stages because some drugs cross the placenta and can harm the fetus.

Stages of Pregnancy

1. Stage 1 (5-15 days). Implatation Stage

This is the stage of implantation. In this stage, drug toxicity results into abortion.

2. Stage 2 (15- 55 days) Embryology Stage

This is the stage at which the embryo changes from a group of cells into recognized human being and this process is achieved through binary fusion. Therefore drug toxicity at this stage may result into fetal malformation. (Teratogens).

3. Stage Three (55 days to birth) Fetagenic Stage

The fetus Continuous to grow and develop. At this stage the drugs can damage the fetus if taken in excess.

4. Stage 4 (Point of Delivery)

During this stage, certain drugs can interfere with the process and progress of labour and can seriously affect the neonate immediately at and after delivery. Therefore precautions must be taken when administering the drug pregnancy and labour.

Pharmacokinetic Changes in Pregnancy

A. Clearance:

This is the rate at which a substance such as a drug is removed from the body by the kidneys . During pregnancy, the body acquires more fluids resulting in the increased workload of the kidney. This should, therefore, be borne in mind as drugs are administered in pregnancy

B. Volume of Detoxication

Because the body is overwhelmed by and most physiological processes are slowed down in preganancy, it should further be borne in mind that even the elimination of metabolic waste is dampened. Drug dosages should, therefore, be kept to the minimum to lessen chances of toxicity

7.3 Oxytocic Drugs

These are drugs that stimulate contraction of the myometrium, the muscle layer of the uterus (http://www.reference.md/files/D010/mD010120.html Accessed on 13/03/2015). They are life-saving drugs in obstetrics and gynaecology.

The commonly used oxytocic drugs are oxytocin and ergometrine

Oxytocin (Pitocin, Syntocinon)

Oxytocin is a mammalian neurohypophysial hormone, produced by the hypothalamus and stored and secreted by the posterior pituitary gland. It acts primarily as a neuromodulator in the brain. It is released in large amounts after dilation of the cervix and distention of uterus during labour, facilitating birth, maternal bonding, and, after stimulation of the nipples, lactation

Mechanism of action: It causes potent and selective contraction of the uterine smooth muscles and mammary glands. Action of the drug occurs within 3-5 minutes after IM administration and it acts immediately after IV administration. Its effects persist for an hour after IV infusion and 2-3hours after IM.

Presentation and route:

Injection containing 5 units,10IU/ampule for slow IV injection or IM

Indications:

Induction and augmentation of labour, treatment of post-partum haemorrhage, active management of third stage of labour, incomplete abortion, and promotes lactation.

Prevention of uterine atony after caesarean section

Dose:

A .Induction of labour; 10 units in one litre of 5% dextrose solution or normal saline by IV infusion. Initially 5 drops /minute then increase the rate by 5 drops/minute every 30 minutes until efficient contractions are obtained (that is over 10 minutes 3 contraction lasting 40 seconds).Do no not exceed 60 drops/minute.

B. Stimulation of uterine contractions during labour; 1.5 units in 1 litre 5% dextrose solution by IV infusion

Control of post-partum haemorrhage; 2.5 units by SC injection.

Side effects

Uterine rupture, oedema, coma, foetal asphyxiation, maternal hypertension and subarachnoid haemorrhage. Others include sensitivity reactions, nausea and vomiting.

Contraindications

- Not to be given in cephalopelvic disproportion (CPD) presentations
- Fetal distress when delivery is eminent
- Do not give in a hypertensives

Cautions: High parity, previous caesarean section, concomitant use with prostglandins.

Ergometrine

Presentation: Ergometrine 0.5 mg/Oxytocin 5 I.U. Injection (Syntometrine). It is a combination of Ergot and Oxytocin

Mechanism of action

While it acts at alpha-adrenergic, dopaminergic, and serotonin receptors, it exerts on the uterus (and other smooth muscles) a powerful stimulant effect not clearly associated with a specific receptor type. This effect results in smooth muscle contraction, thereby facilitating delivery of the placenta and prevent bleeding after childbirth

Indications

- Prevention and treatment of post-partum haemorrhage
- Haemorrhage due to uterine atony after delivery of abortion
- Management of third stage of labour
- Heavy menorrhagia in non-pregnant women.

Side effects

- Nausea and vomiting
- Transient increase in BP

Contraindications

- Do not administer during labour (delivery).
- Do not administer to patients with hypersensitivity reactions history

Self-Assessment Test 35: True or False

1. Oxytocic drugs also induce muscle relaxation _____

2. Oxytocic drugs can also cause rupture of uterus ___

ANSWERS:

1. F

2. T

7.4 Alkalinizing Agents

These are drugs used to prevent premature labour in women of 24 -33 weeks gestation. The administration of these drugs is seen useful in postponing labour long enough to allow;

- Transfer patient for specialist treatment for operative delivery if emergencies arise such as cord prolapse and breach presentation
- Administration of corticosteroids to hasten fetal lung maturation
- The goal of the above is to reduce uterine contractions and arrest cervical dilation using the lowest effective dose of this same drugs.

Alkalinizing drugs include Beta2 adregenoreceptor agonist such as;

a) Sulbutamol
b) Ritodrine
c) Magnesium sulphate

Route

These drugs are administered IV, IM and SC

Mechanism of action

The drugs stimulate the beta 2 receptors which are present in the liver and the smooth muscles of the glands of many organs including the uterus, lungs and the GIT.

Indications

- Inhibition of uncomplicated premature labour
- Delaying delivery

Sulbutamol

It is a beta 2 -adrenoceptor agonist which relaxes the uterus and can be used to prevent premature labour in uncomplicated cases between 24 and 33 weeks of gestation. Its main purpose is to permit a delay in delivery of at least 48 hours. The greatest benefit is obtained by using this delay to administer corticosteroid therapy or to implement other measures known to improve perinatal health. Prolonged therapy should be avoided since the risks to the mother increase after 48 hours and the response of the myometrium is reduced. It acts by stimulating the adreno 2 receptor in the uterine wall.

Dose: Orally, **Dose:** 4mg

Intravenous Dose:10mg/minute VI

The rate is gradually increased according to the response with an interval of 10 minutes up to the time contractions diminish.

Maintain the rate 4-7 hours after contractions and gradually reduce by 50% every 6 hours and the switch on to oral drugs 4mg QID.

Ritodrine

Presentation: tablet 10mg and injection 10mg/ml.

Indications: uncomplicated premature labour.

Dose: IV infusion initially 50mcg/minute, increased gradually according top response by 50mcg/minute every 10 minutes until contractions stop or maternal heart rate reaches 140beats/minute; continue for 12-48hrs after contractions cease.

IM 10mg every 3-8hrs continued for 12-48hrs after contractions have ceased.

Oral 10mg 30minutes before termination of IV infusion repeated every 2hrs for 24hrs followed by 10-20mg every 4-6hrs. Maximum oral dose is 120mg.

Side effects: nausea, vomiting, flushing. Tremors, hypokalaemia, palpitations, hypotension, uterine bleeding (reversed with non-selective beta blockers), pulmonary oedema, leucopoenia.

Contraindications: cardiac disease, eclampsia and severe pre-eclampsia, intra-uterine infection and diabetes mellitus.

Magnesium Sulphate

It has a major role in eclampsia for the prevention of recurrent seizures. Monitoring of blood pressure, respiratory rate and urinary output is carried out, as is monitoring for clinical signs of overdosage (loss of patellar reflexes, weakness, nausea, sensation of warmth, flushing, double vision and slurred speech). Calcium gluconate injection is used for the management of magnesium toxicity.

The drug is also used in women with pre-eclampsia who are at risk of developing eclampsia; careful monitoring of the patient (as described above) is necessary.

Mechanism of action

Acts by reducing the uterine contraction by influencing the amplitude of the mono plate potentials and interfering with calcium functioning at myometrimal neuronal junction. Magnesium will prevent the calcium ions from reacting the muscle from the neuron because there will be no contraction in the uterine muscles.

Indication: Premature labour prevention/ control of seizures in pre-eclampsia or eclampsia (Dose 4-6grams IV over 20 minutesthen 3grams/hour. Titrate dose till patient has less than or 6 cent per hour).

Side effects

- Headache
- Hypertension
- Bronchospasms

Contraindications

- Myosthenia Gravis (Progressive muscle weakness due to reduced calcium levels in the body)
- Recent myocardial infarction
- Pre-eclampsia
- Obstructive airway disease

Nursing implications

1. Assess patient's deep tendon reflex
2. Do lung function test to assess patients breathing patterns.
3. Observe for depression which is a side effect of MgSO4
4. Give an anti-dote Calcium gluconate for severe side effects to replace calcium.

Self-Assessment Test 36: MATCHING ITEMS

Match the alkalinizing agents in Column I with the most appropriate indication Column II

Column I	Column II
1. __Sulbutamol	A. Induction of labour
2. __Magnesium Sulphate	B. Premature labour
	C. Augmenting labour
	D. Eclampsia

ANSWERS:
1. B
2. D

7.5 Sedatives

As already discussed in unit 2 on the drugs acting on the nervous system, sedatives help to allay anxiety. Sedative in obstetrics are primarily used in the promotion of comfort of a woman in Labour

Indications for sedatives

- To provide the mother with a relaxed friendly atmosphere within which her well being and that of the fetus can be closely supervised.
- To keep the mother as more comfortable as possible before delivery by administering prescribed analgesics.
- The following are the common approaches used in sedating the woman in labour

Opioid analgesia

Inhalation with entonox (A mixture of 50% nitrate and 50% oxygen and halothen)

This is usually used at the end of 1st stage of labour or during 2nd stage of labour

Tens (Transcutaneous Electrolyte Nerve Stimulation)

This is the application of electric stimuli on the mother's skin over her back by means of electrodes connected to the battery powered device. This is done in the first stage of labour.

Nacortics

These drugs are given IM to women in established labour. Avoid these drugs 2-3 hours before delivery to prevent adverse effects on the fetus such as respiratory distress.

ACTIVITY:

Narcotics were discussed as opioid analgesics in Pharmacology I unit 4 under classification of drugs. Please refer to this unit for further reading

Continuous Epidural Anaesthesia

The local anaesthetic 0.25% or 0.5% of bupivacaine

It is administered between the 3rd and 4th lumber vertabra to relieve the patient from labour pain.

NB; The above interventions are used in the following conditions or stages.

- Labour
- Vaginal delivery
- Caesarean section

Opiods and analgesics are used in moderate to severe pain

Mechanism of action

The opiods stimulate special receptors. This results in inhibition of transmission of pain impulses and thus appreciation of pain is suppressed.

Specific Preparations

Morphine sulphate

Dose 0.5-4mg /ml in an ampule and 8-10mg in an ampule im

Indications: Severe pain.

Side Effects

- **CNS**; Sedation, euphoria and seizures,
- **GIT;** Nausea, constipation and vomiting
- **Respiratory Tract**; Respiratory tract depression

Contraindication

Not to be administered to women with broncho-asthma and upper respiratory obstruction

Self-Assessment Test 37: True or False

Indicate true (T) or false (F) against each of the following statements

1. Sedatives in labour should be used with extreme caution ____

2. Continuous epidural aneasthesia is administered intravenously ____

ANSWERS:

1. T

2. F

7.6 Summary

Well, we have come to the end of the unit and indeed to the end of pharmacology course. You have been an excellent student and I thank you for your attention and time spent in studying this course. In this unit you were looking at drugs that are used in obstetrics and how they are used to serve fetal and maternal lives. You specifically looked at oxytocin as a drug which stimulates uterine muscle contractions to enhance patulation and helps to control post-partum bleeding.

You looked at ergometrine which acts as an agonist of alpha-adrenoceptor and dopamine receptor of the uterine muscles resulting into contractions of uterus. It is used in the management of third stage of labour

You further learnt about the alkalinizing agents as drugs used to prevent premature labour in women of 24 -33 weeks gestation and one of the drugs is salbutamol.

Finally we talked about analgesia used in labour. These drugs must be used with caution to prevent respiratory depression of the fetus. It is important that you follow the guiding principles as you administer various drugs that are used in obstetrics and indeed other drugs that you have learnt. Before we finally say good bye, review your understanding through a self-test below

7.7 References

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