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CHEMICAL PATHOLOGY

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Course Title: chemical pathology (MLT 4rth) **Instructor: Mr. Adnan Ahmad**

Time: 6 hours **Marks 50**

Q1: Write down a detail note on thyroid hormones.

Thyroid Hormones

Thyroid is an endocrine situated at the basis of the neck on either side of the trachea.

TH secretes T3 (9%), T4 (90%) and calcitonin.

The potency of T3 is four times more than that of T4.

TSH is necessary for secretory activity of the thyroid gland.

Degradation of thyroid hormones occurs in muscles, liver and kidney.

FUNCTIONS OTHYROID HORMONES

• To increase basal metabolic rate

• To stimulate growth.

• Action on fat metabolism

• Action on carbohydrate metabolism

• Action on protein metabolism

• Action on body weight

• Action on cardiovascular system

Hyperthyroidism

Hyperthyroidism is caused by:

1. Graves' disease

2. Thyroid adenoma.

Sign and symptoms

Toxic goiter, Polycythemia, Tachycardia, atrial fibrillation, Increased sweating, Decreased body weight, Diarrhea, Muscular weakness etc.

Hypothyroidism results in myxedema in adults and cretinism in children.

Sign and symptoms

Anemia, Fatigue, Extreme somnolence with sleeping disturbance, decreased cardiovascular functions such as reduction in rate and force of contraction of the heart, cardiac output and blood volume, Increase in body weight, Constipation, Depressed hair growth, Scariness of skin, Cold intolerance.

Thyroid function tests

Measurement of plasma level of T3 and T4.

Measurement of TRH and TSH.

Measurement of basal metabolic rate.

Measurement of plasma level of T3 and T4:

For hyperthyroidism or hypothyroidism, the most accurate diagnostic test is the direct measurement of concentration of "free" thyroid hormones in the plasma, i.e. T3 and T4.

Measurement of TRH and TSH

There is almost total absence of these two hormones in hyperthyroidism but increase in hypothyroidism. It is because of negative feedback mechanism, by the increased level of thyroid hormones.

Measurement of basal metabolic rate

In hyperthyroidism, basal metabolic rate is increased by about 30% to 60%. Basal metabolic rate is decreased in hypothyroidism by 20% to 40%.

Q2: Explain and classify Adrenocortical Hormone.

The two adrenal glands, each of which weighs about 4 grams, lie at the superior poles of the 2 kidneys. Each gland consists of two distinct parts, the medulla and therefore the cortex.

1. Adrenal Cortex

2. Adrenal Medulla

Adrenal medulla

The medulla, the central 20 percent of the gland, is functionally associated with the sympathetic systema nervosum. • It secretes the hormones epinephrine and norepinephrine in response to sympathetic stimulation. It secretes epinephrine and norepinephrine

Adrenal cortex

The cortex secretes a completely different group of hormones, called corticosteroids.

These hormones are all synthesized from the steroid cholesterol. And they all have similar chemical formulas. And have a slight differences in their molecular structures.

Two major types of adrenocortical hormones

The mineralocorticoids (especially affect the electrolytes (the "minerals") of the extracellular fluids, especially sodium and potassium) and the glucocorticoids, (exhibit important effects that increase blood glucose concentration) small amounts of sex hormones are secreted, especially androgenic hormones, which exhibit about an equivalent effects within the body because the male sex hormone testosterone.

More than 30 steroids are isolated from the cortex, but two are of outstanding importance to the traditional endocrine function of the human body: aldosterone, which is that the principal mineralocorticoid, cortisol, which is the principal glucocorticoid.

1. Mineralocorticoid

Mineralocorticoid includes aldosterone, 11-deoxycorticosterone, and 11-deoxycortisol. Mineralocorticoid helps the body to retain sodium and expel potassium. It is an essential hormone in maintaining the balance of electrolytes and body fluid. It also possess the d4-21-3, 20-prednenolone basic structure; but on the 11th position it lacks oxygen (like deoxycorticosterone and deoxycortisol), or on the 18th position it contain (-CHO) (like aldosterone). The 18th position of (-CHO) can obviously increase the mineralocorticoid

effect; thus the retaining sodium effect of aldosterone is 25 times stronger than that of 11-deoxycorticosterone. But, if on the 17th position, a-CHO is added, the effect is weaker. Thus sodium retention effect of 11-deoxycortisol is merely 3% of that of 11-deoxycorticosterone.

2. Glucocorticoid

Includes cortisol and corticosterone. Glucocorticoid moderates the metabolism of sugar, fat, and protein and may raise the resistance to the adverse stimulation of the body. Clinically applied steroids belong to this group, like cortisone, hydrocortisone, and their pharmaceutical derivatives: prednisone, dexamethasone etc. It is called glucocorticoid due to the first discovery of its function on the metabolism of sugar. In structure they possess the common characteristics of being able to affect physiological functions which beside require d4-21- 3, 20-prednenolone- 21- sterol-3, 20 diketone basic structure, and in site 11th possess oxygen base (like hydroxy base of hydrocortisone, and acetone base of cortisone). If in site 17th, a replacement by α-hydroxy as glucocorticoid the action are going to be much stronger than corticosterone.

Synthesis and Secretion of Adrenocortical Hormones

The zona glomerulosa:

Thin layer of cells that lies just underneath the capsule; 15% of the cortex.

Secrete Aldosterone; because these cells contain the enzyme aldosterone synthase.

The zona fasiculata:

The middle and widest layer; 75% of the cortex.

Secretes the glucocorticoids cortisol and corticosterone, also as small amounts of adrenal androgens and estrogens.

The secretion is controlled by the hypothalamic-pituitary axis via adrenocorticotrophic hormone (ACTH).

The zona reticularis:

The deep layer of the cortex.

Secretes the adrenal androgens dehydroepiandrosterone (DHEA) and androstenedione. As well as small amounts of estrogens and a few glucocorticoids.

The secretion is controlled by ACTH, although other factors such as cortical androgen-stimulating hormone (released from the pituitary) may also be involved. The mechanisms are not nearly as well understood as those for glucocorticoids and mineralocorticoids.

Adrenocortical Hormones are steroids derived from cholesterol

The cells within the cortex can synthesize de novo small amounts of cholesterol from acetate. Approximately 80% of the cholesterol used for steroid synthesis is provided by low-density lipoproteins (LDL) within the circulating plasma. Transport of cholesterol is regulated by feedback mechanisms. This initial step in steroid synthesis is stimulated by the various factors that control secretion of the main hormone.

Q3: define and explain Hyperthyroidism and hypothyroidism.

Hyperthyroidism and thyrotoxicosis are used interchangeably, however each refers to slightly different conditions. Hyperthyroidism refers to over activity of the thyroid, with resultant excessive secretion of thyroid hormones and accelerated metabolism within the periphery. Thyrotoxicosis refers to the clinical effects of an unbound hormone, no matter whether or not the thyroid is that the primary source.

Hyperthyroidism is caused by

There are variety of pathologic causes of hyperthyroidism in children and adults.

These include Graves' disease, toxic adenoma, toxic multinodular, goiter, and thyroiditis, Graves' disease accounts for about 95% of cases of hyperthyroidism, to know the pathophysiology of hyperthyroidism, it's necessary to understand the traditional physiology of the thyroid.

Sign and symptoms

- Symptoms and their severity depend upon duration and extent of hormone excess, and therefore the age of the individual. Individuals may experience:
- Nervousness and irritability
- Palpitations and tachycardia
- Heat intolerance or increased sweating
- Tremor
- Weight loss or gain
- Increase in appetite
- Frequent bowel movements or diarrhea
- Lower leg swelling
- Sudden paralysis
- Shortness of breath with exertion
- Decreased menstrual flow
- Impaired fertility
- Sleep disturbances (including insomnia)
- Changes in vision
- Photophobia, or light sensitivity
- Eye irritation with excess tears
- Diplopia, or double vision
- Exophthalmos, or forward protrusion of the eyeball
- Fatigue and muscle weakness Thyroid enlargement Pretibial myxedema (fluid buildup within the tissues about the shin bone; could also be seen with Grave's disease)

Hypothyroidism

Abnormally low activity of the thyroid, leading to retardation of growth and mental development in children and adults.

Causes of hypothyroidism

Medication: A number of medications can cause Hypothyroidism. Lithium, which is employed to treat certain psychiatric disorders, also can affect the thyroid.

Genetic dysfunction: The thyroid could also be dysfunctional at birth, or may fail at some introduce adult life.

Previous thyroid surgery: Removal of an outsized portion or the whole thyroid may reduce or stop the method of hormone production.

Treatment for Hyperthyroidism: Treatment for Hyperthyroidism may sometimes end in Hypothyroidism.

Radiation therapy: Exposure of the thyroid to radiotherapy for the treatment of cancers of the top and neck region may end in Hypothyroidism.

Damage to the Pituitary Gland: The pituitary gland may be damaged due to disease or surgery which may result in decreased level of thyroid hormones.

Autoimmune Thyroid Disease: this is often the foremost common explanation for Hypothyroidism. This happens when the body's system produces certain antibodies that attack its own thyroid resulting in a reduced hormone production.

Sign and symptoms

- Hypothyroidism signs and symptom may include:
- Fatigue
- Increased sensitivity to cold
- Constipation
- Dry skin
- Weight gain
- Puffy face
- Hoarseness
- Muscle weakness
- Elevated blood cholesterol level
- Muscle aches, tenderness and stiffness
- Pain, stiffness or swelling in your joints
- Heavier than normal or irregular menstrual periods

- Thinning hair
- Slowed heart rate
- Depression
- Impaired memory

Q4: How calcium is regulated? Define Osteomalacia.

Blood calcium levels are regulated by parathyroid hormone (PTH), which is produced by the parathyroid glands. PTH is released in response to low blood calcium levels. It increases calcium levels by targeting the skeleton, the kidneys, and therefore the intestine. In the skeleton, PTH stimulates osteoclasts, which are cells that cause bone to be reabsorbed, releasing calcium from bone into the blood. PTH also inhibits osteoblasts, cells which deposit bone, reducing calcium deposition in bone. In the intestines, PTH increases dietary calcium absorption and within the kidneys, PTH stimulates re-absorption of the calcium. While PTH acts directly on the kidneys to extend calcium re-absorption, its effects on the intestine are indirect. PTH triggers the formation of calcitriol, a lively sort of vitamin D , which acts on the intestines to extend absorption of dietary calcium. PTH release is inhibited by rising blood calcium levels.

Osteomalacia

Osteomalacia is that the softening of the bones caused by defective bone mineralization secondary to inadequate levels of obtainable phosphate and calcium, or due to overactive resorption of calcium from the bone which may be caused by hyperparathyroidism (which causes hypercalcemia). Osteomalacia in children is understood as rickets, and since of this, use of the term "osteomalacia" is usually restricted to the milder, adult sort of the disease. Signs and symptoms can include diffuse body pains, muscle weakness, and fragility of the bones.

CAUSES

Osteomalacia may be a generalized bone condition during which there's inadequate mineralization of the bone. Many of the consequences of the disease overlap with the more common osteoporosis, but the 2 diseases are significantly different.

There are two main causes of osteomalacia:

1. Insufficient calcium absorption from the intestine due to lack of dietary calcium or a deficiency of, or resistance to, the action of vitamin D; and

2. Phosphate deficiency caused by increased renal losses.

Dietary deficiency of vitamin D + lack of solar irradiation

Deficiency of metabolism of vitamin D

Chronic renal disease (most common cause)

1-hydroxylation of 25-vitamin D renal tubular disorder (vitamin D resistant rickets): high level of phosphorus in urine

SIGNS AND SYMPTOMS

- Diffuse joint and bone pain (especially of spine, pelvis, and legs)
- Muscle weakness
- Difficulty walking, often with waddling gait
- Hypocalcemia (positive Chvostek sign)
- Compressed vertebrae and diminished stature
- Pelvic flattening
- Weak, soft bones
- Easy fracturing
- Bending of bones

Osteomalacia in adults starts insidiously as aches and pains within the lumbar (lower back) region and thighs before spreading to the arms and ribs. The pain is symmetrical, non-radiating and amid sensitivity within the involved bones. Proximal muscles are weak, and there's difficulty in climbing up stairs and getting up from a squatting position.As a results of demineralization, the bones subsided rigid. Physical signs include deformities like triradiate pelvis and lordosis. The patient has a typical "waddling" gait. However, these physical signs

may derive from a previous osteomalacial state, since bones don't regain their original shape after they become deformed.

Q5: Writ a short note on sex hormones.

DEFINITION:

Hormones are chemical substances synthesized in small amounts by endocrine tissues and carried by blood stream to a different tissue, where it acts as a messenger to manage the function of the target tissue or organ.

Sex hormones

These are group of hormone that produced in the testes in males and ovaries in the female. The male sex hormones are usually referred to as androgens and the principal androgen is known as testosterone. These hormones are produced primarily by the testes and in discrete amounts by the adrenal cortex. Androgens are primarily liable for the right development and maintenance of male reproductive function and stimulation of the secondary sex characteristics. Androgens are anabolic, and used in stimulating the production of skeletal muscles and bone as well as red blood cells. In direction to strengthen the anabolic activity of androgens without increasing their masculinizing capability, anabolic steroids were developed to fight diseases marked by wasting, these synthetic hormones are harmed by individuals meaning to increase their muscle mass, like athletes seeking to recognize a competitive advantage. Overdosing has been linked to serious side effects, including infertility and coronary heart condition.

On the opposite hand, there are basically two female sex hormones which are estrogen and progestins. Estrogens are secreted mainly by the ovaries and in smaller amounts by the adrenal glands and (in men) by the testes. The most potent estrogen is estradiol. This hormone contains a similar function similarly to androgens in men, the estrogens promote the event and maintenance of the first and secondary female sexual characteristics; they also stimulate linear growth and skeletal maturation. In some other mammals these hormones have been shown to precipitate estrus (heat). The ovarian production of estrogen stops plummets during menopause.

Progestins, the foremost important of which is progesterone, are the opposite form of female sex hormone and are named for his or her role in maintaining pregnancy (pro-gestation). Estrogens and progestins are secreted cyclically during menstruation. During the menstrual cycle, the ruptured ovarian follicle (the corpus luteum) of the ovary produces progesterone, which renders the uterine lining receptive to the implantation of a fertilized ovum. Should this occur, the placenta becomes the most source of progesterone. As pregnancy headways, placental creation of progesterone increases, and these high doses defeat ovulation, stopping a second conception.