بسم الله الرحمن الرحيم

Endocrinology 0202313
Third-hour Exam
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Al-Quds University **Name: _____Key_____**
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Department of Medical Laboratory Sciences **Dr. Akram Kharroubi**

I. Multiple-choice questions. Choose the single best answer (40 points, 2 points each)

1. Zona glomerulosa is unable to synthesize glucocorticoids due to the absence of the enzyme
    a. Side chain cleavage enzyme.
    b. 17 α-hydroxylase.
    c. 11 α-hydroxylase.
    d. 18 β-hydroxylase.
    e. 21 α-hydroxylase.

2. A two-day dexamethasone suppression test is a useful diagnostic tool to distinguish between
    a. Cushing's hypercortisolemia and Addison's disease.
    b. Addison's disease and autoimmune destruction of adrenal cortex.
    c. Pituitary tumors and ectopic tumors that secrete ACTH.
    d. Aldosterone secreting tumors and cortisol secreting tumors.
    e. All of the above are correct.

3. The renin-angiotensin system
    a. Is the major system regulating aldosterone production.
    b. Is stimulated when blood flow to the kidney is increased.
    c. Is mainly under ACTH control.
    d. Stimulates the sympathetic nervous system and causes vasoconstriction.
    e. Both (a) and (d) above are correct.

4. Angiotensin I is converted to angiotensin II by
    a. Renin.
    b. Angiotensin-converting enzyme (ACE).
    c. Side chain cleavage enzyme.
    d. Chymase.
    e. Both (b) and (d) above are correct.

5. Methyltyrosine is used in the therapy of pheochromocytomas because it is an effective inhibitor of
    a. Tyrosine hydroxylase.
    b. Dopamine β hydroxylase.
    c. 4-phyenylethanolamine-N-methyltransferase.
    d. Dopa decarboxylase.
    e. All of the above are correct.

6. The effects of the hormone epinephrine include all of the following **except**
    a. Increase rate and force of heart contraction.
    b. Bronchial constriction.
    c. Increase glycogenolysis.
    d. Increase lipolysis.
    e. Increase gluconeogenesis in liver.

7. Epinephrine affects intermediary metabolism by:
    a. Increasing glycogen breakdown.
    b. Stimulating glycogen phosphorylase activity.
    c. Stimulating lipolysis.
    d. Inhibiting glycogen synthesis.
    e. All of the above are correct.

8. Hypertension and hypokalemia in Cushing's syndrome are due to increased levels of
    a. Aldosterone.
    b. Cortisol.
    c. Deoxycorticosterone.
    d. DHEA.
    e. Both (b) and (c) are correct.

9. Among the major adrenal sex hormones is(are):
    a. Testosterone.
    b. DHEA.
    c. Androstenedione.
    d. Both (b) and (c) above are correct.
    e. All of the above are correct.

10. All of the following are true concerning Cushing's disease **except**
    a. A small pituitary adenoma is present in the majority of cases.
    b. ACTH production is not normally suppressed by physiologic doses of glucocorticoids.
    c. ACTH production cannot be suppressed even by very large doses of glucocorticoids.
    d. The levels of ACTH and cortisol are usually high.
    e. The adrenal glands typically show bilateral hyperplasia.

11. The sources of cholesterol used in steroidogenesis include
    a. De novo synthesis from acetyl CoA.
    b. Uptake of LDL.
    c. Hydrolysis of stored cholesterol esters.
    d. Free cholesterol.
    e. All of the above are correct.

12. The regulatory enzyme that is activated by ACTH during steroidogenesis is
    a. 17 α hydroxylase.
    b. 21 α hydroxylase.
    c. 3 β hydroxysteroid dehydrogenase.
    d. Cytochrome P450 side chain cleavage enzyme.
    e. 18 hydroxylase.

13. Metyrapone is used to test the hypothalamic pituitary adrenal axis because
    a. Metyrapone is an analogue of CRH thus stimulates ACTH secretion.
    b. Metyrapone is an inhibitor of 11 β hydroxylase thus inhibiting cortisol synthesis, this causes ACTH increase.
    c. Metyrapone is analogue of cortisol thus causes feed-back inhibition of ACTH.
    d. Metyrapone causes hypoglycemia thus stimulating ACTH secretion.
    e. Metyrapone affects the transcription of enzymes involved in steroidogenesis.

14. Salivary cortisol is used to diagnose Cushing's disease because
    a. Saliva is easier to get than blood.
    b. Saliva contains higher amounts of cortisol than blood.
    c. Saliva contains free cortisol whereas in blood total cortisol is measured.
    d. Both (a) and (c) above are correct.
    e. All of the above are correct.

15. The calcium which is most precisely regulated by PTH is
    a. Content of total calcium in bone mineral.
    b. Concentration of total calcium in plasma.
    c. Concentration of ionized calcium in plasma.
    d. Concentration of total calcium in urine.
    e. Concentration of intracellular calcium.

16. Osteoblasts
    a. Are primarily responsible for the bone resorption.
    b. Have receptors for PTH and vitamin D.
    c. Are frequently recognizable as large multinucleated cells.
    d. Can bring about the rapid mobilization of calcium from the skeleton seen after an acute hypocalcemia.
    e. Contain large quantities of acid phosphatase and other lysosomal enzymes.

17. The direct biological effect of PTH include
    a. Mobilization of calcium and phosphorous from bone.
    b. Decreased formation of 1,25 $(OH)_2$ D_3 by the kidney.
    c. Decreased calcium reabsorption by the kidney tubules.
    d. Increased phosphate reabsorption by the kidney tubules.
    e. Increased intestinal absorption of calcium.

18. Low calcium levels induce PTH secretion by the following mechanisms **except**
    a. Binding of calcium to calcium receptors.
    b. Increasing intracellular calcium levels that cause exocytosis.
    c. Increasing intracellular magnesium levels that cause exocytosis.
    d. Regulating the synthesis of PTH.
    e. Stabilization of prepro PTH mRNA and enhancing gene transcription.

19. 1,25 $(OH)_2$ D_3 production is
    a. Stimulated by PTH.
    b. Inhibited by PTH.
    c. Inhibited by high levels of calcium and phosphate.
    d. Both (a) and (c) above are correct.
    e. Both (b) and (c) above are correct.

20. Primary osteoporosis
    a. Refers to reduced bone mass and bone fracture in postmenopausal women.
    b. Reflects relative increase in bone resorption over formation activity.
    c. Is probably due to loss of estrogen.
    d. Is probably due to increase in cytokines that stimulate osteoclasts.
    e. All of the above are correct.

II. Complete the following sentences (you may use abbreviations): (12 points)

1. The mitochondrial enzymes in cortisol biosynthesis from cholesterol are side chain cleavage and 11 βhydroxylase.
2. Osteoblasts are the bone forming cells and osteoclasts cause bone resorption.
3. The active hormone derived from vitamin D is 1,25 (OH) D_3.
4. Examples of catecholamines secreted by the adrenal medulla are epinephrine and norepinephrine.
5. The major source of cholesterol used in steroidogenesis is derived from LDL.
6. The hormone secreted from thyroid gland and affects calcium metabolism is calcitonin.
7. Bone formation requires collagen matrix and the enzyme alkaline phosphatase.

III. Short answers. Answer the following questions <u>briefly</u>:

1. Concerning the cortisol-cortisone shunt:

a. What is meant by the cortisol-cortisone shunt? (6 points)

Ans: It is the pathway of converting cortisol to cortisone in kidney by the enzyme 3 β hydroxysteroid dehydrogenase II. Cortisone that is released from the kidney is converted in liver by the enzyme 3 β HSD I to cortisol.

b. Why this shunt important? (4 points)

Ans: it is important because it prevents cortisol from binding to mineralocorticoid receptors in the kidney and affecting Na and K, since cortisone does not bind to mineralocorticoid receptors.

c. How can you explain the deleterious (or harmful) effects of the cortisone creams using this shunt even though cortisone is inactive? (3 points)

Ans: cortisone in the skin can be converted to cortisol by the effect of 3 β HSD I. The cream has high levels of cortisone which could produce high levels of cortisol. High levels of cortisol have deleterious effects.

2. **Concerning glucocorticoids:**

a. What are they mainly used for in medicine? (3 points)

Ans: Glucocorticoids are used as antiinflammatory, suppression of the immune system in transplantation, and in many other diseases.

b. Explain briefly why glucocorticoid excess is harmful and glucocorticoids should not be used except as a last resort? (discuss only the deleterious effects on bone and muscle). (8 points)

Ans: Excess glucocorticoids are harmful because they cause bone resorption by affecting Ca absorption, increase PTH levels, Ca resorption from bone, decrease collagen synthesis, osteoporosis. In muscles excess glucocorticoids inhibit protein synthesis, cause protein wasting.

3. **Give two tests to differentiate between primary and secondary adrenal hypersecretion. Explain how these tests differentiate between the two cases. (6 points)**

Ans: Primary adrenal hypersecretion: high cortisol, low ACTH.
Secondary adrenal hypersecretion: high cortisol, high ACTH.
Test 1. Measure ACTH. High in secondary and low in primary.
Test 2. CT scan for adrenal and pituitary.
Test 3. Dexamethasone suppression test will inhibit ACTH if pituitary is normal (primary) and has no effect or slight effect if there is pituitary tumor (secondary).
Metyrapone test and stress tests will increase ACTH. But if ACTH is high as in secondary adrenal hypersecretion, the increase due to stress could not be measured because ACTH is already high.

4. **Write the structure of cholesterol and cortisol, indicate the position of carbon 17, 11 and 21. (5 points)**

Ans: look it up.

5. **What is the importance of having the parathyroid hormone receptors present on the osteoblasts even though the effect of the hormone is on the osteoclasts? (5 points)**

Ans: this will give the message to bone forming cells that bone resorption will occur due to high PTH so bone remodeling will follow to fix the resorbed bone.

Note: most of you have problem writing (resorption, reabsorption).

6. **How is calcium homeostasis achieved when calcium levels in the blood decreases (i.e. what hormones are affected and what are the effects of these hormones that bring calcium back to normal levels?) (8 points)**
   Ans: when ionized calcium in the blood decreases PTH increase, this causes the following:
   - **Increases bone resorption (this increases calcium and phosphate levels)**
   - **Increases reabsorption of calcium and secretion of phosphate in kidney.**
   - **Increases the production of $1,25(OH)_2$ D_3 which causes and increase in calcium absorption from the intestine.**