بسم الله الرحمن الرحيم

Endocrinology Second-Hour Exam

First Semester, 2008/2009

Al-Quds University
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Date: 17/12/2008

Question 13: answer (none) – given to all

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

1. The most sensitive test for the detection of primary thyroid failure is measurement of
   a. Serum T_4.
   b. The free thyroxine index.
   c. Serum TSH.
   d. Serum TRH.
   e. Serum cholesterol.

2. Iodide is transported from plasma across the follicular cell to reach the colloid by
   a. Thyroglobulin.
   b. Na^+/I^- symporter.
   c. Na^+ ATPase.
   d. Pendrin.
   e. Both (b) and (d) above are correct.

3. During the synthesis of thyroid hormones, thyroidal peroxidase enzyme
   a. Catalyzes oxidation of iodide ions.
   b. Catalyzes iodination of free tyrosines.
   c. Catalyzes iodination of thyroglobulin tyrosines.
   d. Is stimulated by ACTH.
   e. Both (a) and (c) above are correct.

4. The enzyme that may protect the fetus and the brain from excess T_4 is
   a. Type 1 5'-deiodinase.
   b. Type 2 5'- deiodinase.
   c. Type 3 5 –deiodinase.
   d. Thyroperoxidase.
   e. Tyrosine hydroxylase.

5. Graves' disease and Hashimoto's disease are examples of
   a. Parathyroid diseases.
   b. Autoimmune diseases.
   c. Hyperthyroidism and hypothyroidism, respectively.
   d. Both (b) and (c) above are correct.
   e. All of the above are correct.

6. All hypothalamic hormones that regulate anterior pituitary are stimulatory **except**
    a. Somatostatin.
    b. TRH.
    c. Corticotrophin and thyrotropin.
    d. Dopamine.
    e. Both (a) and (d) above are correct.

7. Anterior pituitary hormones include
    a. Thyrotropin releasing hormone.
    b. Adrenocorticotropic hormone.
    c. Gonadotropin releasing hormone.
    d. Corticotropin releasing hormone.
    e. All of the above are correct.

8. α- and β-Melanocyte stimulating hormones (MSH) in humans
    a. Do not exist as separate hormones.
    b. Are responsible for hyperpigmentation during ACTH hypersecretion.
    c. Are parts of pro-opiomelanocortin (POMC).
    d. Both (a) and (c) above are correct.
    e. All of the above are correct.

9. Growth hormone hypersecretion causes
    a. Gigantism in children.
    b. Acromegaly in adults.
    c. Insulin resistance.
    d. Both (a) and (b) above are correct.
    e. All of the above are correct.

10. All of the following are true about ADH and oxytocin **except**
    a. Both are nanopeptides.
    b. Their receptors are bound to heat-shock proteins.
    c. Both are produced by the hypothalamus.
    d. Both are released from the posterior pituitary.
    e. Both have plasma membrane receptors.

11. Scatchard plot analysis for hormone-receptor interaction measures
    a. The affinity of the hormone to the receptor.
    b. The number of binding sites (receptors).
    c. The number of subunits of the receptor.
    d. Both (a) and (b) above are correct.
    e. All of the above are correct.

12. Binding of insulin to growth factor receptors causes all of the following **except**
    a. Dissociation of heat shock proteins associated with receptors.
    b. Dimerization of the receptor.
    c. Autophosphorylation of the receptor.
    d. Stimulation of protein synthesis.
    e. Stimulation of phospholipase Cγ.

13. All of the following hormones are associated with heat shock proteins **except**
    a. Estrogen.
    b. Progesterone.
    c. Cortisol.
    d. Androgen.
    e. Thyroid hormones.

14. Desensitization of plasma membrane receptors coupled to G protein when exposed to high ligand concentration is due to all of the following **except**
    a. Binding of arrestin to the phosphorylated receptor which prevents the receptor from binding to hormone.
    b. Glycosylation of the hormone.
    c. Internalization of the hormone-receptor complex.
    d. Degradation of hormone-receptor complex.
    e. Suppression of new receptor synthesis.

15. Plasma membrane seven-transmembrane domain receptors are coupled to
    a. G proteins.
    b. Tyrosine kinase that causes autophosphorylation.
    c. Adenylate cyclase or phospholipase C.
    d. Both (a) and (c) above are correct.
    e. All of the above are correct.

16. Cytoplasmic receptors bind all of the following hormones **except**
    a. Glucocorticoids.
    b. Mineralocorticoids.
    c. Thyroid hormones.
    d. Progesterone.
    e. Androgen.

17. Growth hormone receptors
    a. Are linked to G protein.
    b. Have intrinsic protein kinase activity.
    c. Activate cytoplasmic Janus kinase that causes autophosphorylation of the receptor.
    d. Binds insulin in addition to growth hormone.
    e. All of the above are correct.

18. Nitric oxide generated as a second messenger by hormones like acetylcholine and bradykinin
    a. Stimulates the synthesis of cGMP.
    b. Inhibits the synthesis of cGMP.
    c. Causes vasodilation (vasorelaxation).
    d. Both (b) and (c) above are correct.
    e. Both (a) and (c) above are correct.

19. Hyperprolactinemia may cause infertility or amenorrhea by
    a. Reducing the levels of LH and FSH.
    b. Decreasing the pulsatile secretion of LH and FSH.
    c. Suppressing the LH surge in women.
    d. Inhibiting the secretion of GnRH.
    e. Both (b) and (c) above are correct.

20. The Wolff-Chaikoff effect means
    a. The ability of the thyroid gland to "escape" the effect of low iodide intake.
    b. The ability of the thyroid gland to "escape" the effect of high iodide intake.
    c. The ability of the thyroid gland to synthesize large amount of thyroid hormones under low or high iodide intake.
    d. The inability of the thyroid gland to synthesize thyroid hormones under high iodide intake.
    e. All of the above are correct.

II. Complete the following sentences (you may use abbreviations): (13 points)

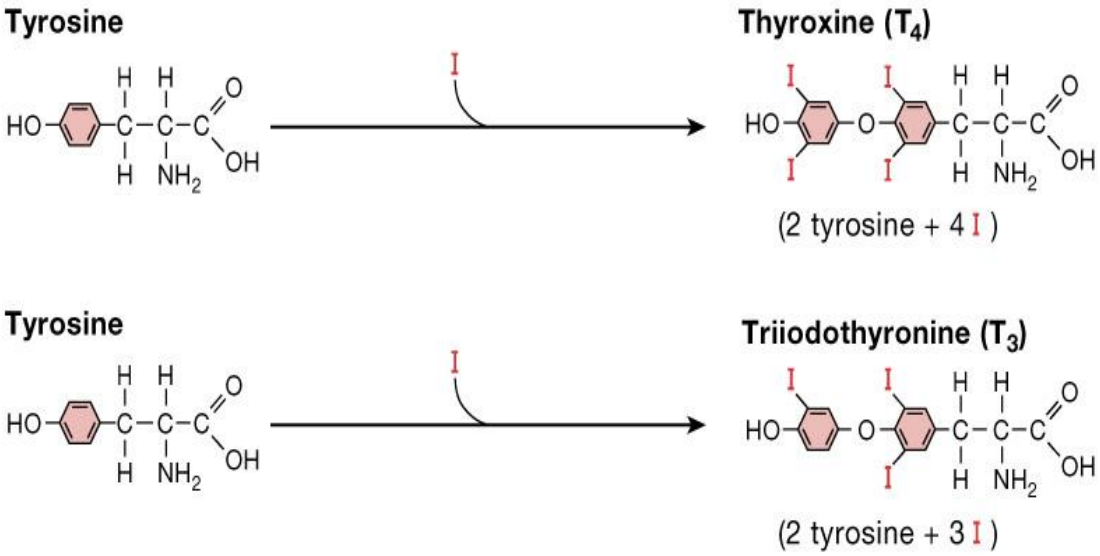
1. The neurohormone secreted by the posterior pituitary and is responsible for milk ejection is oxytocin.
2. Prolactin from anterior pituitary is regulated mainly by dopamine that inhibits prolactin secretion.
3. Growth hormone stimulates the production of IGF-1 from liver that is responsible for the growth effects of growth hormone.
4. TRH from the hypothalamus stimulates the synthesis and release of thyroid stimulating hormone from the anterior pituitary.
5. LH and FSH are known as gonadotropins and are under the regulation of GnRH from the hypothalamus.
6. Deficiency of ADH causes a disease known as diabetes insipidus.
7. The hydrolysis of phosphoinositol 4,5-bisphosphate (PIP2) by phospholipase C yields the second messengers IP3 and DAG.
8. By inhibiting GTPase activity, cholera toxin causes the activation of adenylate cyclase that results in increased intestinal water and salt loss.
9. Gonadal dysfunction and galactorrhea are the major symptoms of hyperprolactinemia.
10. Oxytocin affects mainly parturition and lactation.

III. Short answers. Answer the following questions briefly:

1. Why do you think excess growth hormone has diabetogenic effect? What are the direct and indirect functions of growth hormone? (10 points)

Ans: GH is considered a diabetogenic hormones because it increases the levels of blood glucose by decreasing carbohydrate utilization and impairing glucose uptake. This cause the continuous release of insulin to counteract the increased levels of glucose. GH also induce insulin resistance at the post receptor level. The direct effects of GH is the effect on glucose and lipids (mobilization of fat). The indirect effects of GH are to increase linear growth through IGF-1, increase amino acid uptake and protein synthesis.

2. **Draw the structure of tyrosine, T_3 and T_4. What is the role of thyroperoxidase in thyroid hormone synthesis? (6 points)**
Ans:



Thyroperoxidase: causes oxidation of iodide ions, the incorporation of iodine into tyrosine and the coupling of iodinated tyrosines to T_3 and T_4.

3. **How is measuring free T_4 levels (FT_4I) and TSH differentiate between primary hyperthyroidism and secondary hyperthyroidism? What other tests do you suggest to evaluate the hypothalamic-pituitary-thyroid axis in case of hyperthyroidism? (8 points)**

Ans: If T4 is high and TSH is low, this means that hyperthyroidism is due to a primary defect in the thyroid. If T_4 and TSH are both high then the defect is probably secondary (at the level of the pituitary). Other tests include TRH stimulation to test the pituitary response, the measurement of TSH receptor antibodies [stim] that causes Grave's disease, CT scan of the thyroid and the pituitary gland to detect if tumor exists.

4. **What are the different families of plasma membrane receptors and what are the major differences between these families? Give <u>one</u> example for each. (8 points)**

Ans: 1. Seven-transmembrane domain e.g. LH, FSH, catecholamines, ACTH, glucagon. 2. Single-transmembrane domain: (a) growth factor receptors e.g. Insulin, IGF; (b) cytokine receptors e.g. GH, prolactin; (c) guanylyl cyclase-linked receptor e.g. ANP.

5. **If growth hormone is low, why is it difficult to evaluate the defect by measuring growth hormone levels? Suggest three tests to evaluate GH deficiency? (5 points)**

Ans: Because of the diurnal rhythm of GH it is very difficult to detect low levels because of the sensitivity of the assay to detect low levels. GHRH, arginine test and insulin-induced hypoglycemia cause the release of GH.

6. **The cytoplasmic receptor family for the steroid hormone has common characteristics. Describe the structure of the cytoplasmic receptor for the steroid hormones; what is the function of each part and give three examples of steroid hormones that bind to this receptor family. (10 points)**

Ans: Structure of the receptor (1) amino terminal for ligand-independent transactivation; (2) DNA binding domain encodes two zinc finger motifs that binds DNA and contribute to dimerization; (3) carboxyl terminal domain responsible for ligand binding, receptor dimerization, association with hsp, nuclear translocation and ligand-dependent transactivation. Examples of hormones: glucocorticoids, mineralocorticoids, androgen and progesterone receptors.