

3. Some hormones can be produced also in the cells of organs which do not belong to the glands of internal secretion. It is **an ectopic production of hormones**, which is autonomous and causes the origin of ectopically conditioned endocrine hyperfunction (ectopic endocrine syndrome). As a rule it is the consequence of production of hormones from non-endocrine neoplastic tissue, and, therefore, this clinical syndrome is also called paraneoplastic endocrine syndrome (**paraneoplastic endocrinopathy**).

4. In unique cases, an endocrine disorder can arise in the consequence of **a defect of hormonal transport** from the place of its origin to the place of its action. This disorder is caused by deficiency or by abundance of a plasma transport protein for the hormone or it is due to the defect of hormone binding to the specific carrier protein.

5. The endocrine disorder can also originate as the consequence of **a defect in target tissue** for the hormone or in the place of hormone degradation. This endocrine disorder can be due to:

- A. A change of number or function (structure) of receptors for individual hormones.
- B. A presence of antibodies against receptors for individual hormones.
- C. A defect on the level of postreceptor effector mechanisms for individual hormones.
- D. An accelerated or slowed conversion of prohormone to active hormone.
- E. A defect of inactivation (degradation) of hormone in peripheral tissues.

The above mentioned defects on the level of target (peripheral) tissues are called pseudohypofunctional or pseudohyperfunctional endocrine disorders (**pseudoendocrinopathies**).

6. Adenomas or carcinomas originated from the cells of dispersed endocrine system, known as Amine Precursor Uptake and Decarboxylation (APUD) system, are called **multiple endocrine neoplasia (MEN)**. Adenomas or carcinomas can be found in several endocrine glands or other endocrine structures. They are typical familial diseases with autosomal dominant type of heredity.

The common characteristic of the APUD cells is ability of secretion of polypeptide hormones with local or general effects, in less extent also ability of secretion of biogenic amines, and in special cases also ability to produce prostaglandins and kinins. A neoplasm of the APUD system (apudoma) can produce not only larger amount of hormone, but usually also more kinds of hormones which cause a variety of the clinical picture of this disease.

5.2 Etiology of endocrine disorders

The causes of endocrine disorders can be acquired or genetic.

1. Acquired causes

- A. **Tumors** of endocrine glands. *Adenomas* (benign neoplasms) are one of the main causes of hyperfunctional endocrine syndrome. They occur more frequently than malignant neoplasms. Adenomas may also cause combined endocrine disorder characterized by the excess of one hormone and by the deficiency of other hormones (e.g., adenoma arising from one type of cells of adenohypophysis causes destruction of other types of its cells). *Malignant neoplasms* of endocrine glands are less frequent. The production of hormones by malignant tumors depends on the degree of differentiation of their cells. If the cells are insufficiently differentiated they usually lose their hormonal activity.
- B. **Inflammatory lesions** of endocrine glands. There are a very frequent cause of hypofunctional endocrine syndromes. Etiological factor of these lesions may be autoimmune process or viral and bacterial infection.
- C. **Disorders of nutrition.** The most frequent cause is the deficiency of iodine needed for the synthesis of thyroid hormones. The increased strumigen intake

in food, which inhibits synthesis of thyroid hormones, may be also a cause of endocrine disorder.

- D. **Iatrogenic causes.** Endocrine disorders may occur as a complication of various kinds of therapy (e.g., surgical intervention, radiotherapy, inadequate hormone treatment, or therapy with some non-hormone drugs).
- E. **Primary hyperplasia** of endocrine gland cells. As its consequence, a hyperfunctional endocrine syndrome develops.
- F. **Other acquired causes.** They are rather rare. They include, e.g., destruction of endocrine cells by hormone inactive neoplasma, various kinds of vascular disorders (mostly aneurysm or hemorrhage), cyst, trauma, degenerative process, metabolic defect, and by toxic influences.

2. Genetic causes

Relatively frequent genetic causes of endocrine disorders are defects of various enzymes (**enzymopathies**) taking part in a hormone biosynthesis. The other inherent cause can be the synthesis of a defective prohormone or hormone or the disorder of conversion of prohormone to active hormone. The existence of genetic **disorder of cell receptors** for hormones is assumed as well. Inborn causes of endocrine disorders can also include **hypoplasia** or **aplasia** of endocrine gland as well as **chromosome anomalies** concerning X or Y chromosomes (gonosomes).

5.3 Pathophysiology of hypothalamic-hypophyseal system

Hypothalamus has an important integrative influence on the function of vegetative nervous system and also it is a place of various vital centres. It has a key role in regulation of basic biological rhythms and it is the place of production

of various hormones (hypothalamic releasing hormones, hypothalamic inhibiting hormones or factors, antidiuretic hormone, and oxytocin). Hypothalamus, therefore, has an important role in the regulation of endocrine system as well. In the hierarchy of endocrine glands hypothalamus has a role of a control centre and along with hypophysis it forms a functional unit. In the consequence of its organic or functional disorder, a hypothalamic syndrome develops. In the clinical picture of this syndrome only endocrine symptomatology is present, or its endocrine symptomatology may be combined with neurovegetative symptomatology. These disorders are usually distinguished as: disorders of hypothalamic-neurohypophyseal system and disorders of hypothalamic-adenohypophyseal system.

5.3.1 Pathophysiology of hypothalamic-neurohypophyseal system

Antidiuretic hormone (ADH, vasopressin) and oxytocin are the hormones of hypothalamic-neurohypophyseal system. They are produced in the nuclei of the front hypothalamus, i.e., in nucleus supraopticus and in nucleus paraventricularis. They are transported to neurohypophysis via the axons of the cells of these nuclei, where they are stored and released into the circulation when needed. Clinical symptoms of deficiency or overproduction of ADH are known only in human being. Disorders of oxytocin secretion are unknown at present.

5.3.1.1 Central diabetes insipidus

Central diabetes insipidus (neurogenic diabetes insipidus, diabetes insipidus verus) is a rare disease caused by partial deficiency or total absence of ADH. The kidneys of a patient, therefore, are not able to produce hypertonic urine and thus to prevent excessive loss of water from the organism. Most often it develops in the consequence of the damage of front hypothalamus, namely of nucleus supraopticus, e.g., by severe head trauma, intracranial tumors (craniopharyngioma, Rathke's pouch tumor, germinoma, pinealoma, pituitary adenoma, and metastatic tumors), cysts, inflammatory lesions, vessel lesions (hemorrhage or aneurysm), sarcoidosis, or by surgical intervention in the area of hypothalamus. Diabetes insipidus, which is due to any organic lesion mentioned above, is called **symptomatic** (secondary)