**tolerance** and **hyperglycemia** may occur during the paroxysms, later after fasting are also present.

In untreated patients with sustained arterial hypertension **orthostatic hypotension** is often present. It is manifested by a significant postural fall in blood pressure (more than 30 mmHg in comparison with current values of the patient) accompanied by dizzinesses. In some patients with orthostatic hypotension collapse may sometimes originate. Hypotension may last several minutes. During trauma or surgical intervention in untreated patients with pheochromocytoma unexplained hypotension or circulatory shock may develop.

In the patients with untreated pheochromocytoma several factors probably participate in the origin of orthostatic hypotension. It may be partly a consequence of hypovolemia (as a result of increased diuresis which is secondary to arterial hypertension and glycosuria), and partly a consequence of blunted postural reflexes due to a prolonged excess of catecholamines. According to some authors orthostatic hypotension occurs mainly in the patients with oversecretion of adrenaline and enkephalins from pheochromocytoma.

## 5.7 Endocrine disorders of the ovaries

Endocrine disorders of the ovaries are the third most common endocrinopathy, more frequent are only the thyroid gland disorders and the disorders of the endocrine portion of the pancreas. Their classification has not been yet sufficiently transparent and uniform. At present **pathogenetic classification** has been considered most convenient. It is based on the following four criteria:

1. The type of intensity of hormonal secretion, i.e., hyposecretion or hypersecretion of ovarian hormones, respectively secretion of hormones atypical for ovaries.

2. The place of origin of an endocrine disorder, i.e., primary, secondary, or tertiary disorder of hormonal secretion.

3. The basic cause of endocrine disorder, i.e., inborn or acquired endocrine disorder.

4. Number of hormones of which secretion is impaired, i.e., disorder of only some or all ovarian steroid hormones.

### 5.7.1 Ovarian endocrine hypofunction

Hyposecretion of ovarian hormones is denoted as **female hypogonadism** (hypogonadismus femininus). Its etiopathogenesis is rather variable. The cause of ovarian hormone deficiency may be within the ovaries themselves (**primary** female hypogonadism), in the adenohypophysis (**secondary** female hypogonadism), or in the hypothalamus (**tertiary** female hypogonadism). The clinical picture of ovarian hypofunction depends on the age of a patient in the time of its origin. If the ovarian endocrine hypofunction originates prior to puberty in girls its consequences begin usually to appear at the time of expected onset of puberty. Insufficient sexual maturation (sexual infantilism) develops. If the ovarian endocrine hypofunction originates in adult female it is manifested by menstrual abnormalities and infertility.

#### 5.7.1.1 Primary ovarian hypofunction

Primary (peripheral) ovarian hypofunction is **a complete disorder** of ovarian hormone secretion, i.e., the production of all ovarian steroid hormones is insufficient. Primary ovarian hypofunction can result from multiple causes, but principally it may be inborn or acquired. The menopause is a special form of primary ovarian hypofunction (physiological cessation of ovarian function). However, cessation of ovarian function can occur at any age, even in utero. If it occurs before puberty, the presentation is as primary amenorrhea; after pubertal development and menarche the presentation is as secondary amenorrhea. Due to decreased plasma ovarian hormone concentrations hypothalamic-adenohypophyseal area is stimulated to increased secretion of gonadotropins by feedback mechanism. The pituitary gonadotropin concentrations in circulating blood are, therefore, increased (**hypergonadotropic female hypogonadism**).

### A. **Inborn primary ovarian hypofunction**

It may originate due to ovarian agenesis, gonadal dysgenesis with abnormal karyotype (most common Turner syndrome), gonadal dysgenesis with normal karyotype (pure gonadal dysgenesis), or ovarian 17$\alpha$-hydroxylase deficiency (adrenal cortex is usually simultaneously affected by this hereditary enzymopathy as well). Inborn primary ovarian hypofunction occurs in about 30 % of female patients with a disorder of sexual maturation.

#### Turner syndrome

It is the best known form of inborn primary ovarian hypofunction and most common among gonosomal anomalies causing the disorder of sexual maturation of adolescent girls. Its incidence in female population is about 0.03 %.

From the cytogenetic point of view it is **a simple monosomy X** manifested by the 45,X karyotype of all cells of the patient (symbolic sign is 45,X0). **Mosaic monosomy X** is also known. In the patients with mosaicism the cells with the normal 46,XX karyotype occur along with the cells with the 45,X0 karyotype (the 45,X0/46,XX karyotype). Other mosaic patterns, e.g., 45,X0/47,XXX or 45,X0/46,XX/47,XXX, are rarer. Genotype and phenotype of the affected individual is female. Due to gonosomal anomaly only bilateral streak rudimentary gonads (dysgenetic gonads) are present instead of the ovaries. Neither oogenesis nor biosynthesis of steroid hormones are realized in these fibrous gonadal streaks. Therefore, it is characterized primarily by hypogonadism in phenotypic female.

**The clinical picture** of simple monosomy X (**typical Turner syndrome**, the classic form of the 45,X0 gonadal dysgenesis) is characterized by short stature, multiple congenital anomalies, and disorder of sexual maturation.

In adult affected women, the average height rarely exceeds 150 cm, the legs are usually shorter compared with the trunk (**disproportional stature**). The growth retardation and disorder of skeletal maturation appear in about 8th year of age. They are supposed to be the secondary changes conditioned by deficiency of estrogens, probably secondary to the lack of the estrogen-induced rise in plasma growth hormone concentration and consequently insufficient production of IGF I at puberty. As yet, the exact cause of the progressive growth failure has not been defined. It is also considered that the abnormality resides in the response of the chondrocyte to the somatomedins.

The most common **congenital somatic anomalies** of Turner syndrome include: short and broad neck (even bilateral neck webbing) with a low posterior hairline; redundant skin folds on the back of the neck (pterygium colli); micrognathia (shortened upper jaw); prominent, low-set, rotated or deformed ears or both; a fish-like mouth; a narrow, high arched palate (Gothic palate); ptosis; a square shield-like chest with widely spaced nipples; and increased number of pigmented nevi. Additional anomalies which are less common include: cubitus valgus, short fourth metacarpals, strabismus, congenital heart disease and renal abnormalities, lymphedema of the dorsum of the hands and feet, puffiness of the dorsum of the fingers, and hypoplastic nails. Sometimes also further skeletal anomalies may be present.

The genital ducts and external genitalia are female in character (female phenotype) but immature. The external and internal genitalia remain infantile, there is no breast development, uterus and tubes are hypoplastic, and menstruation is absent (primary amenorrhea). The secondary sexual characteristics have not been developed. In an affected subject the clinical picture of **sexual infantilism** originates. Psychosexual feeling of an affected subject is female. The mental status of these patients is usually normal, but a few may exhibit some signs of mental retardation.

The clinical picture of **mosaic variants** of monosomy X is variable. The 45,X0/46,XX mosaicism is the most common. Some patients with the 45,X0/46,XX karyotype may have the some clinical features as those with the 45,X0 karyotype, however, the patients without an evident clinical symptomatology may be also found. A gonadal differentiation may vary from that of a gonadal streak to that of an ovary. More women with this form of mosaicism usually exhibit fewer of the associated somatic anomalies, are not invariably short stature, and may menstruate and even be fertile. In some individuals with the 45,X0/46,XX karyotype its clinical manifestation may appear as late as after puberty as postpubertal female hypogonadism. Various degrees of Turner's stigmatization, and gonadal dysgenesis and dyshormogenesis are most common. These introduced differences in intensity of the clinical features in individuals with the presence of the

45,X0/46,XX mosaicism probably depend on mutual quantitative ratio of the cells of both lines, e.g., the cells with the 45,XO karyotype and those with the 46,XX karyotype in the gonads and in peripheral tissues.

### B. Acquired primary ovarian hypofunction

Etiology of acquired primary ovarian hypofunction is usually miscellaneous. The foundation of its origin may be an impairment of the gonads already in utero, e.g., due to a viral disease of the mother. Another cause of acquired primary female hypogonadism may be autoimmune oophoritis, which participates in the origin of about 20 % of acquired primary ovarian hypofunction. Antiovarian autoantibodies are present in circulating blood, the ovaries are infiltrated by the lymphocytes. The result of autoimmune inflammatory process is the origin of hypoplastic ovaries and insufficient secretion of ovarian hormones. Ovarian failure due to ovarian antibodies is often associated with other autoimmune endocrinopathies and also with autoimmune diseases of other organ systems. Acquired primary ovarian hypofunction may be induced also by other factors, such as gonadal damage by radiation therapy or cytotoxic chemotherapy, polycystic ovarian disease, and rarely by mumps oophoritis. The cause of peripheral ovarian hypofunction may be also bilateral ovariectomy.

**The clinical picture** of acquired primary ovarian hypofunction depends on the age at which the ovarian hormone deficiency develops (before or after puberty).

At present, **prepubertal** primary ovarian hypofunction ranks among a common term **the disorder of sexual maturation** (delayed puberty and sexual infantilism), which originates in girls before puberty not only in the consequence of peripheral, but also of central (pituitary or hypothalamic) ovarian hypofunction and as a consequence of inborn primary ovarian hypofunction as well. The disorder of sexual maturation is clinically manifested in the time of expected puberty, when its signs begin to appear. All signs of the onset of puberty (thelarche, pubarche, adrenarche, and menarche) are usually absent. Puberty does not appear spontaneously, external and internal genitalia remain infantile. In affected female primary amenorrhea and infertility originate. Secondary sexual characteristics are immature. Epiphyseal plates remain open for a long-time leading to disproportional linear growth (eunuchoidal habitus).

At present, **postpubertal** primary ovarian hypogonadism is included among **disorders of the menstrual cycle and infertility**, which besides peripheral comprise also central (hypothalamic and pituitary) ovarian hypofunction originating during reproductive years of women. Principally **premature menopause** originates (women cease menstruating prior to age 40). In affected women secondary amenorrhea and infertility occur. Internal genitalia and mammary gland atrophy, and sparse pubic hair may appear. In most affected women changes similar to those typical for the period of the female climacteric, mainly osteoporosis, symptoms of vegetative vasomotor lability, and psychological changes, may occur.

#### 5.7.1.2 Central ovarian hypofunction

In women with central ovarian hypofunction plasma gonadotropin concentrations are low, therefore, it is also denoted as **hypogonadotropic female hypogonadism**. It may be associated with only insufficient secretion of progesterone (a partial disorder of ovarian hormone production) or with insufficient secretion of all ovarian steroid hormones (a complete disorder of ovarian hormone production).

**Partial** central ovarian hypofunction is characterized by insufficient production of progesterone. Its cause may be hyperprolactinemia or insufficient secretion of gonadotropins in the time of ovulation or during luteal phase of menstrual cycle. It may be manifested as luteal phase dysfunction, respectively as **estrogen breakthrough bleeding** which is one of the forms of anovulatory bleeding (anovulatory cycles). Estrogen breakthrough bleeding occurs when continuous estrogen stimulation of the endometrium is not interrupted by cyclic progesterone secretion and withdrawal.

Etiology of **complete** central ovarian hypofunction has been partialy mentioned in the chapter on pathophysiology of hypothalamic-adenohypophyseal system. In the following text, therefore, general survey of central ovarian hypofunction will be presented.

Female hypogonadotropic hypogonadism may be induced either by organic or functional disorders of the CNS-hypothalamic-pituitary axis. **Organic lesions** of the hypothalamic-adenohypophyseal area include, e.g., tumors (craniopharyngioma, germinoma, astrocytoma, glioma, hamartoma, and metastatic

tumors), granulomas, aneurysms, cysts, inflammatory process, and head trauma. Hypogonadotropic hypogonadism may be associated with some inborn syndromes, as such Laurence-Moon-Biedl-Bardet syndrome and Kallmann syndrome. Hypogonadotropic hypogonadism may be also a part of panhypopituitarism. Combinated deficiency of growth hormone and gonadotropins (combinated hypopituitarism) is rare. More commonly, female hypogonadotropic hypogonadism arises from **functional disorders** of the hypothalamus or higher nerve centres. They include psychoemotional stress (psychogenic amenorrhea), weight loss associated with dieting or malnutrition, rigorous excercises (such as long-distance running or other athletic disciplines, ballet, dance, or swimming), and anorexia nervosa. Delayed puberty may be also evoked by idiopathic hypogonadotropic hypogonadism or it may occur as constitutional delay in growth and puberty.

Central ovarian hypofunction may be caused also by other endocrine and nonendocrine diseases primarily not afecting reproductive system of a woman. Other **endocrine diseases** include mainly severer hypothyroidism or hyperthyroidism, insufficiently compensated diabetes mellitus, Cushing syndrome, Addison disease, hyperprolactinemia, congenital adrenal hyperplasia, and all virilizing syndromes. **Nonendocrine diseases** include obesity, congenital heart diseases, severer anemia, pulmonary tuberculosis, collagenosis, and chronic renal failure. Prognosis of ovarian hypofunction in the patients with these endocrine or nonendocrine diseases depends on the development and on the treatment of the primary disease.

**The clinical features** of central ovarian hypofunction depend on the age at the time of its origin. If it originates **before puberty**, it evokes the disorder of sexual maturation manifested by delayed puberty or sexual infantilism. Central ovarian hypofunction originated **after puberty** is manifested by menstrual irregularities even by secondary amenorrhea and infertility. The signs and symptoms of female hypogonadotropic hypogonadism are usually associated with other clinical features (e.g., symptoms of deficiency of other adenohypophyseal hormones, symptoms resulting from compression of structures of hypothalamic-pituitary area, symptoms of other endocrine or nonendocrine primary diseases, and the like) depending on the cause of its origin.

## 5.7.2 Ovarian endocrine hyperfunction

Hypersecretion of ovarian hormones is denoted as **female hypergonadism** (hypergonadismus femininus). The cause of its origin may reside in the ovaries (primary female hypergonadism), in the adenohypophysis (**secondary** female hypergonadism), or in the hypothalamus (**tertiary** female hypergonadism). The clinical picture of ovarian hyperfunction depends on the age of a patient at the time of its origin. Primary (peripheral) ovarian hypergonadism occurs mainly after puberty, central (secondary and tertiary) hypergonadism occurs prevailingly before puberty.

### 5.7.2.1 Primary ovarian hyperfunction

The cause of the origin of peripheral ovarian hyperfunction may be the ovarian hormonally active benign or malignant tumors. According to the kind of produced hormones they are divided into feminizing and virilizing tumors. The concentrations of circulating gonadotropins are decreased by feedback mechanism (**hypogonadotropic female hypergonadism**).

A. **Feminizing ovarian tumors**

Excess estrogens may be produced by hormonally active granulosa cell neoplasms, theca cell neoplasms, primary ovarian carcinoma, and rarely by cystadenofibroma. The cells of these estrogen-secreting ovarian tumors produce estrogens autonomously.

**Granulosa cell tumors** are the most frequent hormonally active ovarian neoplasms. They account for about 1–3 % of all ovarian neoplasms. About 55 % of granulosa cell tumors originate during reproductive years of women, 40 % in post-menopausal women, and 5 % before puberty. They are composed of cells resembling granulosa cells of Graafian follicle. These tumors belong to malignant tumors, but their malignity and hormonal activity are variable. The tumors originated before puberty are malignant only very rarely. Granulosa cell ovarian tumors are usually unilateral. Besides estrogens they may produce also gestagens, and occasionally androgens. Sometimes these tumors may contain a mixture of granulosa and theca cells.

**Theca cell tumors** occur more rarely than granulosa cell tumors. In 70 % of cases they may be discovered in the post-menopausal period. During reproductive years of women they occur mainly after the

age of 30. In younger females they are seen rarely. They do not occur before puberty. They are prevailingly benign. Histologically, they are composed of the cells resembling those of theca interna of ovarian follicle. They are usually unilateral. Along with estrogens they may produce also progestogens and occasionally androgens. Sometimes, theca cell tumor may coexist with granulosa cell tumor.

**The clinical features** of feminizing tumors are conditioned by hypersecretion of estrogens and depend on the age of a female in the time of their origin.

**In childhood** they result in the origin of precocious sexual maturation of prepubertal girls (**isosexual precocious pseudopuperty**, pseudopubertas praecox isosexualis) with irregular uterine bleeding and hypoplastic endometrioma. The increased plasma estradiol level inhibits secretion of pituitary gonadotropins by feedback mechanism. In the consequence of low plasma GTH concentrations the ovaries remain immature, ovulation is not present, female is infertile. Breast development appears precociously (precocious thelarche), the vaginal mucosa thickenning originates, vaginal cytology examination reveals various degrees of estrogenism, labia minora are enlarged. The rate of skeletal maturation, height velocity, and somatic development increase, but epiphyseal fusion is premature. These changes lead to the paradox of tall stature in childhood but short adult height. The stature of the adult affected man is short and disproportional (the legs are short in relation to the trunk).

If feminizing tumor originates **in reproductive years** of a woman, various manifestations of hyperestrogenism appear. Abnormal uterine bleeding, interrupted by amenorrhea of various duration, is most frequent. A feminizing tumor originated **in the postmenopausal period** is associated with enlargement of mammary glands, endometrial hyperplasia, and abnormal uterine bleeding. On laboratory examination an increased plasma estradiol concentration is found. Plasma FSH and LH levels are low.

#### B. Virilizing ovarian tumors

They are also denoted as masculinizing ovarian tumors. They produce androgens, mainly testosterone. They form a heterogenous group of neoplasms, the classification of which has not been standardized yet. The best known of them are arrhenoblastoma and hilar cell tumors.

**Arrhenoblastoma** (androblastoma) recapitulates, to a certain extent, the cells of the testis (Sertoli-Leydig cells) at various stages of development. They are the most common virilizing ovarian tumors. They are malignant in about 20 % of cases. They usually originate during reproductive years of women, mainly between the ages 20 and 40.

**Hilar cell tumors** are almost always benign. They usually occur in the perimenopausal period. These tumors originate rarely and are unilateral.

**The clinical picture** of virilizing ovarian tumors is conditioned by overproduction of androgens. It is usually the same as the clinical picture in the patients with virilizing neoplasms of adrenal cortex. At the onset of the disease hirsutism originates. It gradually progresses to striking virilization and masculinization. Plasma testosterone and sometimes also androstenedione concentrations are increased. In the patients with virilizing ovarian tumors, unlike those with virilizing neoplasms of adrenal cortex, plasma adrenal androgen concentrations are normal.

### 5.7.2.2 Central ovarian hyperfunction

Central ovarian hyperfunction is conditioned by the increased secretion of adenohypophyseal gonadotropins and by the successive increase of their concentrations in circulating blood. It is, therefore, also denoted as **hypergonadotropic female hypergonadism**. It may be associated with hypersecretion of all ovarian hormones (complete central ovarian hyperfunction) or with only some ovarian hormones (partial central ovarian hyperfunction). The complete ovarian hyperfunction originates only before puberty, the partial ovarian hyperfunction may originate before or after puberty.

#### A. Complete central ovarian hyperfunction

It may be induced by functional (more common) or organic disorders of the hypothalamic-hypophyseal area. In affected girls it is clinically manifested by the origin of **true precocious puberty** (pubertas praecox vera). Etiology and clinical features of precocious secretion of hypothalamic gonadotropin-releasing hormone (LHRH), as well as etiology of primary induced precocious secretion of pituitary gonadotropins have been described in the chapter on the pathophysiology of hypothalamic-adenohypophyseal system. The causes of true precocious puberty in girls are almost the same as those

in boys. However, while in boys the organic cause of the origin of true precocious puberty is discovered in about 60 % of cases, in girls the organic lesion can be proved only in 15–20 % of the patients. In both sexes the rest of the cases accounts for idiopathic true precocious puberty.

### B. Partial central ovarian hyperfunction

It has three forms: follicular cyst, luteal cyst, and Stein-Leventhal syndrome.

1. **Follicular cyst**.
It originates from a cystic formation of atretic follicles which arise due to involution of the original primordial, primary, secondary or Graafian follicle. The cystic formation contains pure liquid and is a normal part of atretic follicles. Probably due to excess stimulation by gonadotropins a cystic formation of one or more atretic follicles may be evidently enlarged. One or several follicular cysts being able to produce estrogens. In a short time follicular cysts usually regress spontaneously by resorption, disruption, or by hemorrhage into the cyst. However, some of them may persist and cause a permanent overproduction of estrogens (**persisting estrogen-secreting follicular cyst**). In girls it is **manifested** by premature thelarche, true precocious puberty, or by transient or incomplete sexual precocity. In adult women it is manifested by abnormally severe and long menstrual bleeding (menorrhagia) or by bleeding from the uterus in other than normal menstrual periods (metrorrhagia, acyclic vaginal bleeding).

2. **Luteal cyst**
It originates spontaneously or may be iatrogenic due to long-lasting administration of clomiphene (antiestrogen). **Spontaneous luteal cyst** is considered as the corpus luteum persisting after unnoticed early miscarriage. **Iatrogenic luteal cysts** are usually multiple and cause enlargement of the ovary. Luteal cyst may also originate due to stimulative effect of human chorionic gonadotrophin (hCG) produced by ovarian choriocarcinoma. Luteal cyst autonomously and permanently produces estrogens and progestogens usually in larger amounts than they are produced by the corpus luteum during luteal phase of the normal menstrual cycle. In the prepubertal girl it is **manifested** by sexual precocity. In adult woman it is manifested by a sudden origin of amenorrhea, hyperemic cervix uteri, hyperemic vagina, and enlarged and sensitive breasts.

3. **Stein-Leventhal syndrome**
About 1.5–3.5 % of female population are affected by this syndrome. It is probably a familial, geneticly conditioned disease. Type of heredity is not exactly known, but X-linked type inheritance is supposed.

**From morphological point of view** it is characterized by evidently enlarged ovaries (usually twice normal size), with whitish colour and nacrous lustre of their smooth surface. Albuginea tunica is thickened, subcortical multiple follicles in various stages of atresia are present. In women with Stein-Leventhal syndrome, the classic term polycystic ovaries is, therefore, misleading, because the ovaries are studded with atretic follicles, not with cysts. The ovarian stroma and theca cells are hyperplastic. Corpora albicans are rare or absent.

**From endocrinological point of view** the syndrome is characterized by twofold even threefold increase of LH/FSH ratio in plasma. The increase of this ratio is conditioned mainly by the evident increase of plasma LH level. Plasma FSH concentration may be normal or decreased.

Pathogenesis of Stein-Leventhal syndrome is not exactly known. The increase in both the pulse amplitude and the frequency of LH pulses, which is the fundamental pathogenetic mechanism, is conditioned by an abnormality of the LHRH pulse generator located in the hypothalamus. The most plausible explanation is that the increased secretion of LH occurs secondary to disturbances in steroid feedback in the hypothalamic-pituitary unit. On biochemical examination several days lasting irregular waves of increased plasma LH concentrations have been found. However, in an affected woman typical ovulatory peak of plasma LH concentration is missing. Permanently increased plasma LH level stimulates synthesis of androgens in the cells of the theca interna and in the interstitial cells of the ovary (both kinds of these cells have LH receptors and enzymes catalyzing the biosynthesis of androgens). Plasma androgen (mainly testosterone and androstenedione) concentrations are, therefore, permanently increased. But, plasma adrenal androgen concentrations are normal. In about 15–20 % of affected women plasma prolactin level is also moderately increased. Hyperprolactinemia is probably the result of dopamine deficiency in hypothalamus, which is the most important prolactin-inhibiting factor (PIF). Dopamine deficiency may be the evidence of the existence of more

extensive dysfunction of hypothalamus in women with Stein-Leventhal syndrome.

Because the plasma androgens are a substrate for peripheral aromatization (mainly in the cells of fat tissue) their permanently elevated concentration in circulating blood usually results in an increased **formation of extraglandular estrogens**. The increased plasma estrogen concentration, conditioned by the mentioned mechanism, is considered as the cause of inhibition of FSH secretion by a negative feedback, and the cause of stimulation of LH secretion by a positive feedback, giving the characteristic LH/FSH ratio in plasma. In women with Stein-Leventhal syndrome (with or without obesity) insulin resistance has been discovered. The increased plasma insulin concentration is supposed to stimulate androgen secretion in ovarian stroma. Insulin may probably act on the ovary via IGF receptors.

Stein-Leventhal syndrome begins clinically manifest usually in the period of adolescence or in young women (in 2nd or 3rd decennium). Varying degrees of **hirsutism** appear. In adolescent girls it may cause late onset of menarche, but uterine bleeding is dysfunctional and is unpredictable in onset, duration, and amount. **Oligomenorrhea** (prolonged menstrual cycle over 35 days), **hypomenorrhea** (weak menstrual bleeding), and **amenorrhea** ensue after a variable time. About 5–10 % of affected women present with primary amenorrhea. Due to hormonal inbalance ovarian follicles mature insufficiently, and, therefore, multiple atretic follicles are found. These women have persistent anovulation and are infertile. About 40 % of affected women are obese.

Stein-Leventhal syndrome is considered a special type of **polycystic ovarian syndrome**. The term polycystic ovarian syndrome includes those endocrine states which lead to the origin of multiple ovarian cysts associated with similar functional abnormalities to those occuring in the patients with Stein-Leventhal syndrome. Such diseases include: classic and nonclassic virilizing adrenal enzymopathies, virilizing tumors of adrenal cortex, Cushing syndrome, hyperthyroidism, hypothyroidism, and acanthosis nigricans. Heterogenity of polycystic ovarian syndrome points up the fact that polycystic ovaries may also occur in about 20 % of healthy and fertile women.

### 5.7.3 Secretion of hormones atypical for the ovaries

The ovaries may produce human chorionic gonadotrophin (hCG), thyroid hormone, or serotonin. Thyroxine is secreted by some specialized ovarian teratomas. High level of hCG is caused by ovarian choriocarcinomas, occasionally dysgerminomas, and rare immature malignant teratomas. Serotonin may secrete primary or metastatic intestinal ovarian carcinoids.

**Ovarian choriocarcinomas**. They are very malignant tumors. Most of them exist in combination with other germ cell tumors, pure ovarian choriocarcinomas are extremely rare. Ovarian choriocarcinoma usually originates in girls before puberty. As hCG itself (also LH itself), without simultaneous presence of FSH, does not stimulate ovarian estrogen production. Therefore, the increased plasma level of hCG does not induce precocious sexual maturation of affected girls. Precocious pseudopuberty cannot originate unless estrogens have been simultaneously produced by ovarian choriocarcinoma.

**Specialized ovarian teratomas**. The most common of them are struma ovarii and carcinoid. They are unilateral. Teratomas that contain mature thyroid tissue (**struma ovarii**) may secrete thyroxine, although rarely in sufficient quantities to cause thyrotoxicosis. This type of teratomas is usually benign. Primary ovarian and metastatic intestinal **carcinoids** may secrete serotonin (5-hydroxytryptamine) in quantities sufficient to produce the carcinoid syndrome. The primary ovarian carcinoid presumably rises from intestinal epithelium in a teratoma. Metastatic ovarian carcinoid is virtually always bilateral. A combination of struma ovarii and carcinoid in the same ovary is very rare.

## 5.8 Endocrine disorders of the testes

Classification of endocrine disorders of the testes, similarly as classification of endocrine disorders of the ovaries, has not been yet sufficiently transparent