The future gender of the individual coming into being is already fixed on a chromosomal level during the fertilization of the ovum. The determination and differentiation of the gender take place during the embryogenesis. Disturbances of the sexual differentiation can arise due to chromosome anomalies, gene mutations and exogenous or endogenous influences, which are remarkable at last in the puberty and cause patients to consult a doctor.

Definition, Epidemiology, and Etiology of Turner Syndrome

An important disorder of the genital development is Turner Syndrome which is defined by a chromosomal aberration. It is a gonosomal monosomy which means that there are only one of the two gonosomes, in this case, the X-chromosome. The result is the karyotype 45, X0 with a female phenotype.

It is the only monosomy which is bearable in a human’s life and is with a frequency of 1 : 2500 – 7500 (living girls) the most frequent gonadal chromosome anomaly for women. The syndrome accompanies a high spontaneous abortion rate. 99% of pregnancies with 45, X karyotype spontaneously abort.

The cause is the loss of a gonosome during the embryogenesis which can occur on different levels of the development (spermatogenesis or oogenesis, fertilization) and is based on a nondisjunction of the chromosomes, more specifically of the chromatids. In 70% of the cases, this gonosome is the X-chromosome of the father.

A structurally modified X-chromosome can be a cause as well. Chromosomal mosaics with unobtrusive and striking cells (e.g. 46, XX/45, X0) can also occur, but the form of the
pathology is, in this case, proportionally weakened.

While the occurrence of the Turner syndrome does not correlate with the age of the mother, a high age of the father plays a possible role in the pathogenesis.

**Symptoms and Clinical Appearance of Turner Syndrome**

In the case of Turner Syndrome, the phenotype, as well as the psychosexual setting, are female. **Main symptoms are primary amenorrhea and dwarfism** (143-147 cm). The growth spurt is absent. The patients are infertile and show sexual infantilism (hypoplastic female genitals due to a lack of hormonal stimulation). While the gonads develop normally at first, they start to degenerate and fibrosis in the third month of pregnancy, which finally causes the ovaries to exist only as tissue cords (streak gonads).

**The ABCs of Turner Syndrome are:**

- **Audiology**
- **Autoimmunity**
- **Cardiac defects**
- **Dermatologic manifestations**
- **Failure to grow**
- **Gastrointestinal disease**
- **Genetics**
- **Metabolic disorders**
- **Orthopedic complications**
- **Renal abnormalities** -> 30-50% with horseshoe kidney being most common
- **Reproductive and pubertal disorders**
- **X-linked disorders**

**Further facultative symptoms are:**

- Short neck
- Pterygium colli (webbed neck)
- Low hairline
- Lymphoedema on the back of the hand and the foot (in the first weeks of life) giving sausage like appearance to fingers
- Infants have a higher incidence of congenital hip joint dislocation
- Cubitus valgus (x-formed arms)
- Shield thorax with widely diverged nipples and funnel chest
- Multiple (benign) pigment naevi
- Nail and ear dysplasia
- Ptosis, strabismus, cataracts, red and green color-blindness may be present
- Incidence of GIT bleedings, Crohn’s disease, and ulcerative colitis is increased
- Malformations of the kidneys and the urinary system
- Malformations of the skeleton (e.g. deformities of the spine) and anomalies of the ligamentous apparatus
- Heart defect: e.g. aortic stenosis, aortic coarctation, anomalies of the pulmonary veins
- Hypertension may be present

These symptoms do not necessarily occur together and can be pronounced to a different extent according to the individual person. The intelligence of the affected persons can be
normal or reduced. There are often partly inefficiencies (e.g. mathematics, spatial orientation).

As already mentioned above, fewer corporal anomalies can occur with the presence of a chromosomal mosaic. Depending on the obtained ovarian function, a puberty development and even a spontaneous pregnancy are possible (but: elevated abortion rate, congenital malformations of the children).

**Diagnostics and Differential Diagnostics of Turner Syndrome**

The amenorrhea and the absence of puberty are often the reasons why patients consult a doctor.

Too little estrogen is produced due to the insufficiency of the ovaries, which triggers superior centers to produce more hormones. Correspondingly, there are raised levels of FSH, and LH, as well as a reduced level of estrogen found during an endocrinological examination. As the disorder lies on the level of the gonads, it is also called hypergonadotropic or primary hypogonadism.

To make a diagnosis, a chromosomal analysis is appropriate which is made on the peripheral lymphocytes. The karyotype of the patient can be examined with the karyogram.

The differential diagnosis has to exclude tumors (e.g. gonadoblastoma, dysgerminoma).

Patients with virilizing symptoms should be examined for the presence of Y chromosome material; these patients may have malignant gonadoblastoma or a testicular tissue.

<table>
<thead>
<tr>
<th>Prenatal</th>
<th>Neonatal</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound findings include fetuses who present with:</td>
<td>Physical findings include:</td>
<td>The most common presentation is:</td>
</tr>
<tr>
<td>• IUGR</td>
<td>• Low birth weight</td>
<td>• Short stature</td>
</tr>
<tr>
<td>• Large septate cystic hygromas</td>
<td>• 30% present with lymphedema of lower upper and lower extremities</td>
<td>• Amenorrhea</td>
</tr>
<tr>
<td>• Nuchal thickening</td>
<td>• Webbed neck (pterygium colli)</td>
<td>• Lack of secondary sexual characteristics</td>
</tr>
<tr>
<td>• Short femur</td>
<td>• High arched palate</td>
<td>30% of Turner patients undergo some degree of spontaneous puberty</td>
</tr>
<tr>
<td>• Total body lymphangiectasia and cardiac defects</td>
<td>• Low set prominent ears</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Low posterior hair line</td>
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<tr>
<td></td>
<td>• Micrognathia</td>
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</tbody>
</table>

**Therapy of Turner Syndrome**

Turner Syndrome is **not curable due to the disorder on the molecular level** (missing chromosome), which is the reason why the treatment only allows for a symptomatic therapy which improves the physical and psychic female characteristics.

A hormone substitution is induced at the beginning of puberty (approximately at the age of 12 or 13). Estrogens enhance the growth of the primary and secondary sexual characteristics (vagina, uterus, breast development, pubic hair) and provide prevention of osteoporosis and arteriosclerosis. A preparation which is used is, for example, estradiol valerate (1-2 mg). Gestagens should be given at least ten days a month as they trigger menstruation; hence, the endometrium is transformed and not constantly stimulated which prevents the development of an endometrium carcinoma.
The final height of the patients can be increased by up to 10 centimeters through the early dose of a synthetic growth hormone (hGH), but this should already take place in early childhood.

The infertility of affected women cannot be healed, but an egg donation can be considered when there is a desire to have children.

Note: The sterility of patients with the karyotype 45, X0 is irreversible.

A surgical therapy for the removal of disturbing stigmata (e.g. Pterygium colli) comes into question as well. A psychosocial care for the patients is important, too.

**Complications of Turner Syndrome**

Women who suffer from Turner Syndrome come down more frequently than the standard population with cardiovascular diseases, diabetes mellitus, thyroid diseases and inflammmable bowel diseases.

The lifespan of patients can be reduced by an average of 13 years.

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