Pediatric and adolescent gynecology in gynecological surgery

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Summary
Pediatric and adolescent gynecology (PAG) is a subspecialty that involves the diagnosis and treatment of symptoms and diseases of genitalia and breasts of female children and adolescents and which is mainly performed by gynecologists and pediatricians. Specific knowledge of the age-dependent maturation process is therefore most important in order to distinguish between normal and pathologic criteria; adolescent young girls are not “small adults”. Their genital anatomy, gynecological problems, and the questions posed are quite different to those of adult women. This review of PAG specifically comprises methods of examination for differential diagnosis in all age-groups of girls and adolescents. Recommendations on contraception and the responsibility of physicians in cases of suspected sexual abuse are also dealt with.

Definition and Tasks of Pediatric and Adolescent Gynecology
Pediatric and adolescent gynecology is a medical subspecialty for the diagnosis and, if necessary, the treatment of symptoms and diseases of the genitals and breast in very young and developing girls. Specific knowledge of the age-dependent maturation process is most important in order to distinguish between normal and pathologic development. Symptoms and illnesses that span various disciplines play a large role, making interdisciplinary cooperation, particularly between gynecologists, pediatricians, pediatric surgeons, urologists, and psychologists indispensable.

The three main subjects of child and adolescent gynecology – prevention, diagnostics/therapy, and aftercare – are summarized in Table 1.
Development Stages

Three developmental stages that are dependent on hormonal stimulation should be differentiated in pediatric and adolescent gynecology: the newborn stage, the so-called resting phase (childhood) and the maturation stage, which is divided into prepubertal and pubertal phases. The age-dependent transitional stages are fluid and vary greatly according to the state of the endocrinologic development (Table 2).

Table 2: Developmental phases

<table>
<thead>
<tr>
<th>Stages</th>
<th>Clinical symptoms</th>
<th>Endocrinology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn stage up to 4th /6th week of life</td>
<td>Edematous hymen, swollen, White fluor, possibly containing blood, Possibly B2 breasts, Cytology: superficial, intermediate cells</td>
<td>Estrogens ↑, LH/FSH ↓, Androgens ↓</td>
</tr>
<tr>
<td>Childhood (resting stage) up to 8th year of life</td>
<td>Hymen smooth, sharp-edged, B1, P1 = no secondary sexual characteristics</td>
<td>Estrogens ↓, FSH up to the 3rd month ↑, Androgens ↓</td>
</tr>
<tr>
<td>Prepuberty ca. 8th to 10th/11th year of life</td>
<td>Hymen becomes edematous, Thelarche and pubarche commence</td>
<td>Low estrogens ↑, FSH gradual ↑, LH constant ↓, Adrenal androgens ↑</td>
</tr>
<tr>
<td>Puberty ca. 10th to 15th year of life</td>
<td>Hymen is swollen, edematous folds, Breasts up to stage B4, Pubes up to stage P4, Menarche up to 2.5 years after the thelarche, Cycles are normally anovulatory</td>
<td>Estrogens ↑, FSH &gt; LH basal ↑, Androgens ↑</td>
</tr>
<tr>
<td>Adolescence ca. 15th to 18th year of life</td>
<td>Complete sexual maturity, Cessation of growth, Ovulatory cycle</td>
<td>GnRH episodes ↑↑, Estrogens/gestagens are balanced</td>
</tr>
</tbody>
</table>

An excellent way of measuring the presence or lack of estrogen stimulation is exact inspection of the outer genitals, with special consideration given to the structure of the hymen (Fig. 1).
Figure 1: Estrogenization and hymen  
a: hymen during the hormonal resting phase: smooth-walled, sharp-edged, atrophic,  
b: hymen during prepuberty: beginning of edematous swelling,  
c: hymen during puberty: fimbriae, succulent, flor pubertalis

Anamnesis in Pediatric and Adolescent Gynecology
From prepuberty, at the latest, girl patients should be actively involved in a comprehensive anamnesis (the patient’s, familial, social and current). The value of the information gained in this manner is greater than by just questioning the mother, particularly on the subject of general and »intimate« hygiene. Depending on the reason for the consultation, the physician should give a detailed explanation of the expected procedure of the examination. An examination should never be performed, even on small girls, against their will. The problems of all those involved should be taken seriously and looked at from their point of view, as it is very important to win the trust of the child.

General Clinical and Gynecologic Examination
This examination includes:
• A full physical examination: sexual maturation (Tanner stages), height, and weight (auxologic documentation if there are any deviations!)
• Gynecologic examination: should be specific, corresponding to the reason for consultation, and is best carried out in a gynecological chair (position, light, colposcope). Before the examination the use of the “chair” should be explained to the child in language suited to her age. Alternatively, small, fearful children can be examined in their mother’s lap.
• Inspection of the outer genitals: the colposcope should be used if possible.
• Palpation of the inner genitals: (normally rectal, but often virgins who use tampons prefer vaginal palpation); this examination can provide valuable information, apart from that gained by the obligatory sonography, on, for example, suspected malformations or non-specific abdominal pain.

Some pediatric gynecologists do without palpation of the inner genitals in children under the age of 14 years, as “the results are not yielding and for most children it is a great strain”. The children undergo vaginoscopy and then abdominal and perineal sonography. The indications for gynecologic examination are listed in Table 3.

Table 3: Indications for gynecologic examination
- Vulvovaginitis and discharge
- Abnormalities of the outer genitals
- Menstrual disorders
- Unclarified pain in the lower abdomen
- Genital bleeding during childhood
- Injuries
- Developmental disorders: premature partial development, pubertas praecox, pubertas tarda, menstrual disorders
- Suspected malformation
- Suspected tumor
- Masturbation
- Suspected sexual abuse
Other methods of examination, depending on the indication, are summarized in Table 4.

### Table 4: Indication-dependent methods of examination

<table>
<thead>
<tr>
<th>Examination method</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginoscopy</td>
<td>• Genital bleeding during childhood: exclusion of tumor (sarcoma botryoides) • Intravaginal foreign body • Therapy-resistant discharge</td>
</tr>
<tr>
<td>Tests on vaginal secretion and urine</td>
<td>• Microscopic and microbiologic in the case of fluor vaginalis: native, gram, aerobic and anaerobic culture with determination of resistance, smear from the the back of the vaginal vault, not from the vulva or introit! • PCR to exclude specific vulvovaginitis: chlamydia(!) gonorrhea • Vaginal maturity in pubertas praecox or tarda, smear from the side of the vaginal vault, coloring according to Papanicolaou</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>• In all developmental disorders such as pubertas praecox and tarda and in the case of androgenization. Extent of tests depends on the symptom!</td>
</tr>
<tr>
<td>Chromosome analysis</td>
<td>• Indispensable in suspected gonadal dysgenesis, DD: Mayer-Rokitansky-Küster-Hauser syndrome (MRKH), testicular feminization = androgen insensitivity syndrome (AIS)</td>
</tr>
<tr>
<td>Imaging methods</td>
<td>• Obligatory in all developmental and menstruational disorders, suspected tumor, unclarified abdominal pain, suspected malformation of the genitals • Transabdominal or transrectal, depending on the visibility and on how full the bladder is (important as an anatomical landmark); a transvaginal sonography is sometimes possible during puberty if the hymen is distendable</td>
</tr>
<tr>
<td>• Sonography of the inner genitals</td>
<td></td>
</tr>
<tr>
<td>• X-ray diagnostic</td>
<td>• Bone age: imperative in pubertas praecox and tarda, and growth disorders • i.v. urogram: if the sonography provides grounds for suspected malformation of the urinary tract in the context of genital malformation</td>
</tr>
<tr>
<td>• CT and MRI</td>
<td>• Suspected tumor in the cranial area and unclear abdominal sonographic findings</td>
</tr>
<tr>
<td>Invasive diagnostic methods</td>
<td>• Recurrent unclarified lower abdominal pain, suspected endometriosis, unclarified tumors or malformation • Strict indication; generous excision in the case of unclarified neoplasms!</td>
</tr>
<tr>
<td>• Diagnostic laparoscopy</td>
<td></td>
</tr>
<tr>
<td>• Exploratory excision</td>
<td>• Cave: Unilateral thelarche! Exploratory excision is contraindicated! Wait!</td>
</tr>
</tbody>
</table>
Infections of the outer genitals

During childhood, only the vulva and vagina are affected by infections. Ascending infections that pass the cervical barrier only occur after the menarche and the number escalates rapidly after sexual relationships commence.

Inflammatory alterations of the vulva

Vulvitis and vulvovaginitis (40% to 60%) are the most frequent illnesses found in pediatric gynecology. Depending on the clientele, the percentage may be over 80%. During the resting stage, when estrogen levels are low (1st to 8th year of life), such inflammations are particularly common. During the anamnesis, attention should be paid to hygiene habits and possible connections to recent infections of the upper respiratory tract or children’s illnesses!

Symptoms include burning and painful micturition, redness, and swelling of the vulva, itching, scratches, and vaginal discharge of varying consistency. In small girls, this is caused (Table 5) particularly by nonspecific germs from the intestines such as enterococci and *E. coli*, and recently hemolysing A-streptococci, have frequently been observed to be the cause; Proteus and Klebsiella are less frequent. Smear infections often develop after infections of the respiratory tract, ears and eyes.

If recurrent, the possibility of anaerobes should be considered!

If the discharge is bloody and fetid, the possibility of an intravaginal foreign body should always be excluded. Perianal scratches: an indication of pinworms? *Candida albicans* is rare in small girls.

Table 5: Causes of vulvovaginitis

<table>
<thead>
<tr>
<th>Causes</th>
<th>Childhood</th>
<th>Puberty</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Nonspecific</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>• Specific (STD)</td>
<td>(+)</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Viruses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Herpes simplex</td>
<td>(+)</td>
<td>(+)</td>
<td>++</td>
</tr>
<tr>
<td>• Varicella</td>
<td>+</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>• Condylomata acuminata</td>
<td>(+)</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>• Molluscum contagiosa</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Secondary causes</td>
<td>+++</td>
<td>+</td>
<td>(+)</td>
</tr>
<tr>
<td>Dysfunctional</td>
<td>−</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>External noxa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intestinal parasites</td>
<td>+++</td>
<td>+</td>
<td>(+)</td>
</tr>
<tr>
<td>• Foreign bodies</td>
<td>+++</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>• Chemical/mechanical irritant</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>• Allergic</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Dysfunctional discharge is common in young girls due to developmental processes during prepuberty and puberty, and it is not pathologic. Diagnosis of exclusion!

When girls commence sexual relationships specific infections (primarily "sexually transmitted disease", STD) increase, in particular chlamydia, Gardnerella, and less frequently trichomonads and gonococci.

Diagnostics: In the case of a suspected bacterial infection, the pathogen should always be qualitatively (and quantitatively) determined, as well as the resistance. A smear should be taken, using a moistened narrow swab or suction catheter, from the back of the vaginal vault without touching the outer genitals. A vaginoscopy should always be performed if the discharge contains blood, if the discharge is therapy-resistant and recurrent, or if there is suspicion of an intravaginal foreign body.

Treatment of nonspecific vulvovaginitis: 90% of the cases are caused by mistakes in hygiene and the complaints cease stop when hygiene is improved. Only water should be used for daily intimate hygiene. Principally, the genitals should be clean, dry, and well aired. Less than 10% of the girls with nonspecific vulvovaginitis require treatment with antibiotics (Table 6).

Table 6: Treatment of nonspecific vulvovaginitis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most of the pathogens</td>
<td>• Medication is only necessary in &lt; 10%</td>
</tr>
<tr>
<td>• Ask for intimate hygiene!</td>
<td></td>
</tr>
<tr>
<td>• Note secondary vulvovaginitis!</td>
<td></td>
</tr>
<tr>
<td>Pathogens such as Proteus and Klebsiella</td>
<td>• Note urologic symptoms!</td>
</tr>
<tr>
<td>• Intraginal antibiotics according to the resistogram</td>
<td></td>
</tr>
<tr>
<td>Hemolysing A-streptococci</td>
<td>• Systemic antibiotics</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>• Children: metronidazole oral 10 mg to 20 mg/kg BW 5 days</td>
</tr>
<tr>
<td></td>
<td>• Adolescents: metronidazole oral 2x500 mg 5 days</td>
</tr>
</tbody>
</table>

If inflammation is recurrent, the possibility of specific antibiotic intravaginal therapy should be considered, e. g. antibiotic solutions from the field of ear, nose and throat (ENT).

Specific vulvovaginitis should be treated according to the respective pathogen (Table 7). Unfortunately, in children inflammation of the outer genitals is all too frequently
treated with “antifungicidal creams”. Vulvovaginal candidiasis during the hormonal resting phase is, however, very rare. Candida infections are normally found in the estrogenized surroundings of the neonatal phase or during puberty.

Table 7: Treatment of specific vulvovaginitis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida vulvitis</td>
<td>Children: clotrimazole cream/solution 6 to 10 days</td>
</tr>
<tr>
<td></td>
<td>Adolescents: clotrimazole intravaginal 3 to 6 days</td>
</tr>
<tr>
<td></td>
<td>Fluconazole 150 mg single oral dose</td>
</tr>
<tr>
<td></td>
<td>Recurrence: bear in mind the non-candida types!</td>
</tr>
<tr>
<td>Gardnerella</td>
<td>Metronidazole oral, as for anerobes (see Table 6)</td>
</tr>
<tr>
<td>Trichomonads</td>
<td>Metronidazole oral, 1 to 2 g single dose</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Children: erythromycin kg/BW 7 days</td>
</tr>
<tr>
<td></td>
<td>Adolescents: doxycycline 200 to 100 mg/7 to 14 days. Simultaneous treatment of partner, if possible!</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>Determine resistance!</td>
</tr>
<tr>
<td></td>
<td>Children: decision on individual dosage</td>
</tr>
<tr>
<td></td>
<td>Adolescents: spectinomycine oral 2 000 mg single dose</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone 250 mg single oral dose</td>
</tr>
</tbody>
</table>

**Non-inflammatory Alterations of the Vulva**

**Synechia of the Vulva (Synechia of the Labia Minora)**

Vulva synechia is a postnatal acquired adhesion of the small labia or of the whole of the entrance to the vagina, which affects small girls during the so-called hormonal resting phase, particularly between the 2nd and 4th year of life (Fig. 2). It is normally caused by clinically latent, inflammatory alterations that lead to adhesion of the labia.

Local application of an ointment containing 0.1% estriol is the method of choice. Operative separation of the synechia is obsolete, irrespective of the method, and is an unnecessary burden for the small girl. An operation does not reduce the rate of recurrence, which is between 2% to 3%.

**Lichen sclerosus**

Genitally located lichen sclerosus particularly affects girls from three to six years of age and is identified by visual diagnosis.

In the acute phase, the symptoms include reddening of the vulva, which has a pergament-like surface with a dull shine; later the skin of the vulva has a dry appearance and is partly white in color with sharply delimited edges. Normally, the hyperkeratotic skin is torn above the clitoris and from the back of the commissure to perianal. During all phases, small transient subepithelial hemorrhagic blisters, similar to petechiae, are found on the vulva. Due to the extreme itchiness and scratching, further bleeding, ulceration, and superinfections may develop (Fig. 3).

![Figure 2: Subtotal synechia of the labia (vulva)](image1)

- a: Urethral opening is displaced, urethrovaginal reflux
- b: Loosening of the adhesion after 6-day local treatment with estriol

![Figure 3: Lichen sclerosus](image2)

- a: Acute phase, 8 years of age
- b: Chronification, 5 years of age
The causes of the disease are still unknown. A lack of estrogen or a predisposition to neurodermatitis are considered to be possible causes.

Causal therapy is not possible! The primary aim is to relieve the pruritus to alleviate the girl’s suffering and to avoid additional skin lesions and superinfections caused by scratching. Apart from gentle intimate hygiene (only water on a daily basis), a corticoid ointment (e. g. triamcinolone such as Volon® A cream without antibiotics or clobetasol such as Dermoxin® ointment) can be applied for two (to four) weeks at the most, in one treatment cycle. In the case of superinfections, local bacteriostatic ointments are the treatment of choice. There is usually spontaneous healing as puberty advances, or the condition improves sustainably.

It is not rare for traces of blood in the girl’s underwear, caused by lichen sclerosus, to be interpreted as a sign of sexual abuse!

Infections of the Inner Genitals
Adnexitis (“pelvic inflammatory disease”, PID) is always caused by ascending infections in sexually active adolescents.

The most common complaints are dysuria, pollakisuria, or symptoms of a gastroenterologic disorder. Acute abdominal symptoms such as pressure pain, the Blumberg sign, and abdominal guarding may occur.

Germs ascending from the infected cervix are the predominant cause of adnexitis. When sexual relations commence, pathogens such as chlamydia and gonococci (the latter are again on the increase) are possible causes. Diagnostics are the same as in adult women. In adolescents, there should be generous indication for laparoscopy.

Treatment of confirmed adnexitis consists of targeted administration of antibiotics according to the microbial genesis; in young girls, this is best performed under inpatient conditions (compliance!). If possible, particularly in the case of chlamydia and gonococci, it is imperative that the partner is treated simultaneously.

In order to prevent such infections, counseling on sexually transmitted diseases is indispensable! In this context, information should always be provided on the use of condoms!

Genital Bleeding in Childhood
“Menstruation” never occurs during childhood without the development of secondary sexual characteristics!

The rate of genital bleeding in pediatric gynecological diseases is about 1%. Principally, three questions must be answered if genital bleeding is found in girls up to the age of 8:

• Are there also signs of premature maturity such as breast development, pubic hair, and accelerated bone age? Pubertas praecox must then be excluded.
• Did the bleeding occur in a girl appropriately developed for her age?
• Is the bleeding actually vaginal or could it have an extragenital cause?

In newborn girls vaginal bleeding that occurs during the first four to six weeks of life is physiologic uterine withdrawal bleeding, caused by the reduction of the effects of maternal estrogen and a progressive reduction in fetal hormone production (so-called Halban reaction). Treatment is therefore unnecessary.

The following questions should be asked during the anamnesis:

• Could the girl have injured herself? Artificial injury or sexual delict?
• Was there any discharge before the bleeding began?
• Before the bleeding developed, was there any infectious disease, infection of the upper respiratory tract, the ears, eyes or nose, or is there any current infection?
• Does the girl have worms?
• Are there any micturitional complaints?
• Has the child had access to drugs, in particular to the mother’s contraceptive pill?
• Is there the possibility of a coagulation disorder?

More than 60% of all childhood vaginal bleeding is caused by primary or secondary vulvovaginitis, particularly by hemolyzing streptococci of group A, but also by aerobic mixed flora (E. coli, enterococci, Proteus) with anaerobic participation. Injuries to the outer genitals are often characterized by strong bleeding that is disproportional to the size of the wound. Sexual delicts should also be excluded in such cases, as well as STD pathogens. Intravaginal foreign bodies usually cause a fetid smell, which accompanies the vaginal spotting.

Tumors of the outer and inner genitals are rarely the cause of genital bleeding in children (1% to 2%) (sarcoma botryoides = embryonic rhabdomyosarcoma, usually between the 2nd and 5th year of life). The transient estrogenization of the vaginal epithelium is a diagnosis of exclusion, i. e. there must be definitive exclusion of all other
possible causes of genital bleeding. The temporary effect of estrogen disappears without treatment and the bleeding does not reoccur.

Extragenital bleeding from the urethra or rectum may be mistaken for genital bleeding!

The disease is diagnosed by a complete physical appraisal: if the size of the body and stage of development according to Tanner are normal for the age of the child, pubertas praecox is unlikely. The outer genitals are then examined by colposcopy for possible sources of bleeding.

Vaginoscopy is imperative in all cases of genital bleeding or suspected bleeding in small girls!

General anesthesia is normally rarely necessary. The examination of the inner genitals should be objectified by sonography to assess the size of the uterus, the endometrium, the ovaries, and possibly the kidneys.

The disease is treated according to its cause.

Developmental Disorders in Childhood
Disorders of general physical and sexual development are caused by anatomic and endocrinologic or genetic malformations. Evidence of such malformations may already be found in newborns (e.g. AGS, hymenal atresia, Turner syndrome), others develop during childhood (e.g. premature partial development and pubertas praecox, gonadal dysgenesis), and many do not become manifest until puberty (e.g. primary amenorrhea, aplasia of the uterovaginal canal, amongst others).

Premature partial development and pubertas praecox affect girls during the so-called hormonal resting phase, during which isolated development of the breasts, isolated growth of the pubic hair (= premature partial development) or the progressive development of secondary sexual characteristics, including physical acceleration, and finally menstruation (= pubertas praecox) occur before eight years of age.

Isolated Premature Thelarche
Isolated premature telarche is usually characterized by unilateral or sometimes bilateral development of the breasts before the 8th birthday, without additional criteria, and is most frequent between two and four years of age.

Diagnostics: In this case one should wait, as more than 95% of the children affected experience spontaneous remission. During the first examination, therefore, no superfluous endocrinologic or sonographic examinations should be performed. The patient should undergo quarterly clinical monitoring. When inspecting the hymen, the question of estrogenization should always be kept in mind.

Treatment is not indicated. However, advisory consultation and regular check-ups should take place. If the development of the breasts continues and the hymen shows signs of estrogenization, pubertas praecox should be excluded (Table 8).

Table 8: Differential diagnostics for premature thelarche and pubertas praecox

<table>
<thead>
<tr>
<th>Physical development</th>
<th>Premature thelarche</th>
<th>Pubertas praecox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other secondary sexual characteristics</td>
<td>Age-appropriate</td>
<td>Accelerated</td>
</tr>
<tr>
<td>Body size</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Hymen</td>
<td>Age-appropriate</td>
<td>Accelerated</td>
</tr>
<tr>
<td>None or slight</td>
<td>Estrogenized</td>
<td></td>
</tr>
<tr>
<td>Estrogenized</td>
<td>Age-appropriate</td>
<td>Accelerated</td>
</tr>
<tr>
<td>Uterine-ovarian volume</td>
<td>Estrogenized</td>
<td></td>
</tr>
<tr>
<td>Vaginal smear</td>
<td>Atrophic to slight</td>
<td></td>
</tr>
<tr>
<td>LH-RH stress test</td>
<td>LH: FSH &lt;1</td>
<td></td>
</tr>
<tr>
<td>X-ray bone age</td>
<td>LH: FSH &gt;1</td>
<td></td>
</tr>
<tr>
<td>Age-appropriate</td>
<td>Accelerated</td>
<td></td>
</tr>
</tbody>
</table>

Isolated Premature Pubarche
Isolated appearance of pubic hair before the 8th birthday, without additional criteria. The peak frequency is between five and seven years of age.

Diagnostics: exclusion of possible disorders of the androgen biosynthesis.

Treatment is not indicated. However, the patient should receive psychological counseling. Yearly clinical check-ups; sonography of the inner genitals and possibly endocrinologic examinations are also recommended at the onset of puberty, as polycystic ovary syndrome (PCOS) is significantly more frequent in the adolescence of pubertal girls with isolated premature pubarche.

Pubertas praecox
Central or gonadotropin-dependent pubertas praecox is characterized by a premature activation of the axis hypothalamus-pituitary-ovary. It is to > 90% idiopathic or may be induced by brain tumors such as hamartomas, astrocytomas, optic gliomas, ependymomas, pineal tumors, amongst others, or by non-tumorous diseases of the central nervous system, such as inflammation, malformations and trauma as a result of the activation of the GnRH pulse generator.
The symptoms are secondary sexual characteristics, including menarche before the 8th year of life and accelerated upward growth due to increased estrogen production. Ultimately, girls with central pubertas praecox are growth-restricted due to premature epiphyseal arrest.

Idiopathic pubertas praecox is a diagnosis of exclusion that should exhaust all endocrinologic and imaging procedures, without pathologic causes: “The patient’s intrinsic clock is fast”. This is true of 70% of the girls with pubertas praecox. In the GnRH stimulation test, the gonadotropins increase and the LH/FSH quotient is > 1. Sonography shows the uterine and ovarian volumes to be above the normal range for the child’s age. A cranial CT or MRI can exclude a brain tumor! Other central causes can be excluded by ophthalmologic examination to test the field of vision and a neurological examination that includes an ECG. At present, idiopathic pubertas praecox is best treated with depot GnRH analogues (triptorelin, leucoprelin). As in almost all cases the disease is self-limiting, the indication for medicative treatment should be critically evaluated. Such treatment is indicated if the menarche commences before the age of 8 or if development continues rapidly. Tumors should be removed surgically.

Peripheral pubertas praecox is gonadotropin-independent and is caused by hormonally active ovarian tumors or by exogenous hormone supply. In girls, the possibility of the McCune-Albright syndrome should be considered. Peripheral pubertas praecox is diagnosed using sonography. In the GnRH stimulation test, gonadotropin levels do not increase.

Disorders of sex development (DSD)

Definition: a congenital condition in which the sexual chromosomes, the development of the gonads, or the anatomic sex are atypical. Terms such as intersexuality, pseudo-hermaphroditism and hermaphroditism should no longer be used, as they do not correspond to present-day knowledge and do not do fulfill the requirements of those affected. Chromosomal and gonadal anomalies, gene and receptor defects, or more rarely, exogenous factors may be responsible for the absence or interruption of pubertal development, or for discrepancies between chromosomal, gonadal, and genital sex. Sexual development disorders may, to a certain extent, already be diagnosed in newborns, babies and in small children. The symptoms very often do not develop until puberty and adolescence.

Gonadal Dysgenesis

The symptoms of gonadal dysgenesis often include growth-restriction as early as childhood, usually a lack of sexual development in prepuberty and primary amenorrhea during puberty.

Due to the lack of chromosomal separation (“non-disjunction”) or to structural alterations (translocation, deletion, crossing-over, inversion), a sexual chromosome may be absent or surplus sexual chromosomes and diverse mosaic forms may develop. Instead of functional ovaries, “streak gonads” are found, which neither contain a follicle, nor do they produce hormones. These functionless gonads may also be found in normal sets of female or male chromosomes.

Diagnostics: high FSH and possibly LH values, with a very low estradiol level and hypergonadotropic hypogonadism. The bone age is retarded. Chromosome analysis: 45,X0, mosaics, more rarely 46,XX and 46,XY. Body size: usually microplasia, less frequently macrosomia. Gonadal dysgenesis is often combined with malformation of the skeleton, the cardiovascular system, and the urinary tract.

Treatment: Substitution of the missing ovarian hormones with so-called natural estrogens.

Maturity induction: From a bone age of about 11 to 12 years onwards, slow introduction of 0.2 mg estradiol valerate per day for six months, and for a further six months 0.5 mg as monotherapy until Tanner Stage B3/P3. For example, full substitution therapy from the 2nd year of treatment, at the earliest, with 2 mg estradiol valerate in combination with a progestagen.

Ullrich-Turner Syndrome

With a rate of 1 in 2,000 to 1 in 2,500 the Ullrich-Turner syndrome is the most common form of gonadal dysgenesis with the typical karyotype 45,X0. Mosaic forms are found in more than 50%, so that these girls may even develop normally during puberty. In the classical Turner syndrome 45,X0, sexual development and the menarche are absent and the girls are usually already too small during childhood. Treatment with growth hormones is therefore indicated before treatment with estrogens.
The Turner syndrome should be diagnosed during childhood, at the latest, in order to begin treatment with growth hormones early enough, before estrogen substitution is commenced.

In the case of XY mosaics, the partially functional gonads should be surgically removed after diagnosis due to the potential risk of malignancy, and the patient should subsequently receive hormonal substitution.

Swyer Syndrome (Pure Gonadal Dysgenesis)
This disorder, characterized by the male karyotype 46,XY is much rarer. “Girls” with XY gonadal dysgenesis are more likely to be very tall, boyishly slim and, if untreated, without secondary sexual characteristics. The outer and inner genitals are female. Operative removal of the functionless gonads is imperative on diagnosis – independent of the child’s age – as gonadoblastomas and dysgerminomas may develop in ca. 30% of the patients.

Androgen Insensitivity Syndrome (AIS)
Out-dated: Testicular feminization, obsolete: pseudohermaphroditism
Masculinus (= intersexuality if the testicles are normal)

Causes: Androgen resistance develops due to an androgen receptor defect due to genetical or enzymatic causes. Differentiation of the Wolffian ducts does not take place; the Müllerian ducts regress due to the Anti-Müller hormone (AMH) produced in the embryonic testicles.

Anamnesis: Hernia in babies or small children.

Symptoms: Complete AIS phenotype female: normal female outer genitals; during puberty the breasts are well developed; axillary and pubic hair is either lacking or is thin (“hairless women”). The patients are tall, slim girls with primary amenorrhea. In the incomplete type with a partial androgenetic effect, virilized outer genitals with a hypertrrophic clitoris may already be observed during childhood.

Diagnostics: The uterus and tubes do not develop; there is partial vaginal aplasia. Sonography shows no typical ovarian structure; the testicles are intra-abdominal or inguinal; karyotype 46,XY.

Treatment: When physical development is complete, extirpation of the testicles is still standard practice, as there is the possibility of malignancy, despite the discussion surrounding this method. The subsequent mono-estrogen substitution is obligatory. In the case of incomplete AIS and increasing virilization, extirpation of the testicles should be considered during childhood, with the slow introduction of monoestrogen therapy from prepuberty onwards.

Adrenogenital Syndrome (AGS)
Obsolete: Feminine pseudo-hermaphroditism (= intersexuality if the ovaries are normal)

Cause: If the karyotype is female and the girl has ovaries, the outer genitals may become virilized to different degrees because of enzymal disorders of the steroid hormone synthesis (21-hydroxylase-mutation). This is best documented according to the Prader classification.

The disease is usually diagnosed in newborns or, at the latest, during childhood.

Operative correction of the outer genitals during childhood should be of a conservative nature and ethical principals should be taken into consideration!

Late-onset AGS plays an important role in pediatric and adolescent gynecology. Anamnesis: premature adrenarche, bone age acceleration. Following normal sexual development, during puberty or adolescence signs of androgenization develop such as hirsutism, hypertrophy of the clitoris, and a deep voice. The menstrual cycle progresses from oligomenorrhea to amenorrhea.

Diagnostics: Testosterone, DHEA-S, and 17-hydroxyprogesterone values are slightly increased. The ACTH short test is decisive: after 60 minutes, there is a significant increase in 17-OHCS. The diagnosis is confirmed by molecular genetics of the 21-hydroxylase-mutation.

Differential diagnosis: PCOS; in rare cases an androgen-producing tumor.

Treatment: Dexamethasone

Developmental Disorders in Puberty
These disorders predominantly consist of disruptions in the maturation of the neuroendocrinologic axis. A disruption in GnRH activity during the process of pubertal maturation leads to impairment of the ovarian function. This may be responsible for primary and secondary amenorrhea, cycle interval disturbances (oligo-, polymenorrhea), disturbances in the type of menstrual cycle (hyper-, hypomenorrhea), as well as for dysfunctional juvenile bleeding.

Menstrual Disorders
After the age of 12, menstrual disorders are the most frequent reason for consulting a physician (40%). The anamnesis should include questions on the start of the menarche, the type of complaints, and the date they began, the severity, duration, and intervals of the bleeding, as well as the maternal anamnesis, particularly in the case of dys- and amenorrhea.
Basic diagnostics: valid for all girls with cycle disorders:
• Full-body appraisal: does the stage of development correspond to the age of the child (Tanner stages)?
• Somatogram to monitor physical growth and weight, BMI
• Gynecological examination: discharge? Is there a hymenal opening? Vaginal structures? Palpation and sonography of the inner genitals

Additional diagnostic procedures depend on the type of menstrual disorder.

Primary Amenorrhea

Definition: The first menstruation (menarche) has not begun by the 16th birthday.

Causes: Congenital anatomic malformations are usually the cause in the case of a normal pubertal development and primary amenorrhea. Additional cardinal symptoms include delayed onset of puberty, infantilism, and microplasia or virilism.

<table>
<thead>
<tr>
<th>Cardinal Symptom</th>
<th>Cause</th>
<th>Additional diagnostics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pubertal development</td>
<td>Hymenal atresia</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Proximal vaginal and cervical atresia</td>
<td>Vaginoscopy</td>
</tr>
<tr>
<td></td>
<td>Utero-vaginal atresia (Mayer-Rokitansky-Küster-Hauser syndrome, MRKH)</td>
<td>Sonography of the kidneys, i.v. urogram, possibly chromosome analysis (DD: testicular feminization)</td>
</tr>
<tr>
<td></td>
<td>Androgen insensitivity syndrome, AIS (testicular feminization)</td>
<td>Anamnesis: “hernias”? Chromosome analysis</td>
</tr>
<tr>
<td>Delayed onset of puberty without additional criteria</td>
<td>Constitutional or idiopathic</td>
<td>Anamnesis: when did maternal puberty commence? High-performance sport? Bone age X-ray, possibly estrogens, LH/FSH and LH-RH tests</td>
</tr>
<tr>
<td>Infantilism/microplasia</td>
<td>Gonadal dysgenesis (45,XX = Turner syndrome or mosaics, also 46,XX)</td>
<td>Somatogram, LH/FSH, bone age x-ray, chromosome analysis</td>
</tr>
<tr>
<td></td>
<td>Ovarian dysgenesis 46,XY (Swyer syndrome)</td>
<td>LH/FSH, chromosome analysis</td>
</tr>
<tr>
<td></td>
<td>Hypothalamic (anorexia nervosa)</td>
<td>BMI (&lt;17), estrogens, LH/FSH, possibly LH-RH test</td>
</tr>
<tr>
<td></td>
<td>CNS tumor (craniopharyngioma)</td>
<td>Cerebral CT, MRI, bone age X-ray</td>
</tr>
<tr>
<td></td>
<td>STH deficiency</td>
<td>Bone age X-ray, STH</td>
</tr>
<tr>
<td>Hirsutism, virilism</td>
<td>Idiopathic (familial) PCOS</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Late-onset type, AGS</td>
<td>Testosterone, DHEA-S, SHBG, LH/FSH, possibly insulin values and glucose tolerance test, possibly cholesterol, HDL/LDL</td>
</tr>
<tr>
<td></td>
<td>androgen-producing tumor (ovary, adrenal cortex)</td>
<td>Testosterone, DHEA-S, androstendione, 17-hydroxyprogesterone, ACTH short test</td>
</tr>
</tbody>
</table>

Table 9: Cardinal symptoms and additional diagnostics in primary amenorrhea
If the estrogen deficiency is absolute or relative (gonadal dysgenesis, pubertas tarda, hypothalamic amenorrhea), hormones should be substituted to induce or promote pubertal development, which is the equivalent of hormonal development therapy.

Treatment according to the cause of the amenorrhea (Table 10).

<table>
<thead>
<tr>
<th>Cause</th>
<th>Timing and type of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atresia if the girl has a uterus</td>
<td>Hymenal atresia</td>
</tr>
<tr>
<td></td>
<td>Hymenal resection before puberty begins, if there is suspected hematosalpinx, possibly laparoscopy, broadband antibiotic</td>
</tr>
<tr>
<td>Uterovaginal agenesis</td>
<td>Proximal vaginal atresia and cervical atresia</td>
</tr>
<tr>
<td></td>
<td>Surgical removal of the atresia</td>
</tr>
<tr>
<td>Mayer-Rokitansky-Küster-Hauser syndrome (MRKH)</td>
<td>First choice: If there is a vaginal recess, the initial therapy is conservative; the patient should be motivated to stretch the recessus herself and to have vaginal sexual intercourse. Second choice: Surgery to construct a neovagina; inform patient of the protracted follow-up treatment of the prosthesis; not before 16 years of age.</td>
</tr>
<tr>
<td>Androgen insensitivity syndrome (AIS)</td>
<td>Androgen insensitivity syndrome (AIS)</td>
</tr>
<tr>
<td></td>
<td>Gonadal extirpation followed by estrogen monotherapy, in the case of rare vaginal atresia (see MRKH)</td>
</tr>
<tr>
<td>Pubertas tarda</td>
<td>Pubertas tarda</td>
</tr>
<tr>
<td></td>
<td>At the age of 16 at the latest, therapy with combined estrogen-gestagen preparations</td>
</tr>
<tr>
<td>Gonadal dysgenesis</td>
<td>45, Xo (Turner syndrome) and mosaics</td>
</tr>
<tr>
<td></td>
<td>Depending on the microplasia: growth hormone, gradual substitution with estrogen mono-therapy from the age of 11 to 12; from the B3 stage, combined estrogen-gestagen preparations</td>
</tr>
<tr>
<td>46, XY (Swyer syndrome)</td>
<td>46, XY (Swyer syndrome)</td>
</tr>
<tr>
<td></td>
<td>Gonadal extirpation immediately after diagnosis, hormone substitution as with the Turner syndrome</td>
</tr>
<tr>
<td>46, XX</td>
<td>46, XX</td>
</tr>
<tr>
<td></td>
<td>Hormone substitution as in the Turner syndrome</td>
</tr>
<tr>
<td>Hypothalamic</td>
<td>Hypothalamic</td>
</tr>
<tr>
<td></td>
<td>Immediate: treatment ranging from psychotherapeutic to psychiatric counseling; treatment with combined estrogen-gestagen preparations from the age of 16, at the latest</td>
</tr>
<tr>
<td>CNS tumor</td>
<td>CNS tumor</td>
</tr>
<tr>
<td></td>
<td>Immediate: operative treatment, possibly growth hormone, hormone therapy as in the Turner syndrome</td>
</tr>
<tr>
<td>STH deficiency</td>
<td>STH deficiency</td>
</tr>
<tr>
<td></td>
<td>Immediate: growth hormone; after growth is completed, possibly combined estrogen-gestagen treatment</td>
</tr>
<tr>
<td>PCO syndrome</td>
<td>PCO syndrome</td>
</tr>
<tr>
<td></td>
<td>Immediate: regulation of body weight; treatment with combined estrogen-antiandrogen preparations, possibly metformine, from the onset of adolescence, at the latest</td>
</tr>
<tr>
<td>Late-onset AGS</td>
<td>Late-onset AGS</td>
</tr>
<tr>
<td></td>
<td>Immediate: gluocorticoids</td>
</tr>
<tr>
<td>Androgen-producing tumor</td>
<td>Androgen-producing tumor</td>
</tr>
<tr>
<td></td>
<td>Immediate: surgery</td>
</tr>
</tbody>
</table>
Combined micropills can be prescribed for hormone substitution if simultaneous contraception is necessary. If there is no uterus (testicular feminization after testicular extirpation) substitution is administered in the form of a monotherapy with 2 mg of estradiol valerate.

Secondary Amenorrhea
Definition: Absence of menstration for more than four months after commencement of the menarche.

Causes: during adolescence, > 40% of the cases have metabolic-endocrinologic causes, in particular eating disorders, over- and underweight, but also hypothyreosis and diabetes mellitus. In 50% of the patients, the cause is either PCOS or hypothalmic (eating disorders! loss of weight!); hyperprolactinemia is relatively uncommon.

The disease is diagnosed according to the suspected clinical cause. Determination of prolactin, LH/FSH, FT3/4 and TSH are obligatory, and if there should be suspicion of hyperandrogenemia, testosterone, androstendione, DHEAS and SHBG should also be determined.

The treatment depends on the respective endocrinologic disorder.

Dysfunctional Uterine Bleeding (DUB)
DUB accounts for more than 60% of all menstruational disorders.

Juvenile Bleeding
Definition: Persistent dysfunctional uterine bleeding that lasts from over ten days to several weeks, followed by long pauses without any recognizable regular cycle.

Causes: Estrogen-induced over-proliferation of the endometrium develops due to existing follicle persistence and anovulation that result from developmental processes. If there is also a lack of progesterone, secretory transformation of the endometrium does not take place and irregular periods of continuous bleeding occur. The possibility of a coagulation disorder must be excluded.

Treatment: The initial treatment consists of administration of additional estrogen to still the bleeding. This can be achieved within 48 to 72 hours by oral administration of a contraceptive sequential or combined preparation containing 50 μg of ethinylestradiol/d for 21 days.

Prevention: From the next cycle, an antiandrogenic gestagen is prescribed from the 13th to 24th day of the cycle, over a period of three months, to ensure the secretory transformation of the endometrium.

Hyper- and Hypomenorrhea
Hypermenorrhea is characterized by severe menstrual bleeding.

Exclude coagulation disorders!

Treatment: Gestagens from the 13th to 24th day of the cycle; contraceptive micropill; in exceptional cases, long-term contraception. When therapy does not succeed, at the latest, the possibility of a coagulation disorder should be considered (Jürgen-Willebrand syndrome!).

It is unnecessary to treat menstrual bleeding that is too weak (hypomenorrhea).

Poly- and Oligomenorrhea
Polymenorrhea is characterized by too frequent bleeding with cycle intervals of less than 25 days. Treatment is the same as for hypermenorrhea.

In oligomenorrhea, menstrual bleeding is too infrequent, with cycle intervals of more than 35 days. Treatment with an estrogen-gestagen combination should be considered if there is a simultaneous estrogen deficiency.

Dysmenorrhea
Definition: Severe or less severe lower abdominal pain in connection with menstruation, sometimes accompanied by nausea, vomiting, and a tendency to collapse.

Causes: Usually, during puberty the condition is primary dysmenorrhea without a pathologic correlate, caused by hormonal factors due to estrogen-gestagen imbalance and the increased effect of prostaglandin on the endometrium. A familial maternal disposition is often found.

Secondary dysmenorrhea with organ-pathologic findings is much more infrequent in young girls than in adult women.

Differential diagnosis: Should be performed in cases of therapy-resistant endometriosis or uterine malformations causing impeded outflow, such as a rudimentary double uterus.

Treatment: Primary dysmenorrhea should be treated with prostaglandin synthesis inhibitors (ibuprofen, naproxen). If the complaints continue, treatment with gestagen is indicated in the second half of the cycle as well as combined contraceptive micropills, possibly as long-cycle therapy. Secondary dysmenorrhea is treated according to its cause.

Anatomic malformations
Cause: Lack of or disrupted differentiation of the Müllerian ducts between the 6th and 9th week of pregnancy leads to uterine/vaginal aplasia, between the 10th and 12th week of pregnancy to a double uterus, and up to the 20th week, to hymenal and superhymenal atresia. Due to the close
connection between the embryonic development of the Wolffian and Müllerian duct system, malformations of the urinary tract are often found.

If there is a uterus, symptoms do not develop until puberty, when there is no outflow for the menstrual blood. If there is no uterus, it is initially assumed that there are no disorders due to the normal female development. The girls do not visit a physician until the menarche does not begin when expected. The less frequent asymmetric double uterus with one-sided normal development of the uterus and vagina and contralateral incomplete aplasia of the uterus and/or vagina can present considerable diagnostic difficulties, as if the menarche has commenced, with acute abdomen, the possibility of an atretic double uterus is not anticipated.

Aplasia

The rare aplasia of the vagina with a uterus is normally first diagnosed after the menarche due to increasing abdominal pain.

Aplasia of the vagina with dysfunctional uterus is more common (Mayer-Rokitansky-Küster-Hauser syndrome, MRKH) with a rate of 1 in 5,000 in newborn girls. A normally developed girl usually initially visits a physician due to primary amenorrhea, but sometimes as the result of an unsuccessful attempt at sexual intercourse.

Diagnosis: Inspection: A hollowed introitus is located behind the hymenal seam with a recess that can nearly always be stretched to at least 2 cm.

Sonography: There is no uterus, but possibly a solid rudimentary structure; the ovaries and tubes are normal; there is no vaginal echo. Karyotype: 46,XX. Often found in combination with malformations of the urinary tract.

Differential diagnostics: Distinguish from complete androgen insensitivity syndrome CAIS (previously termed testicular feminization (karyotype 46,XY).

Treatment is conservative: if there is a vaginal hollow, digital stretching of the tissue by the patient herself should be recommended, explained, and demonstrated. If the girl is motivated, the method is often very successful. In the case of the surgical construction of a neovagina, the girls (particularly those without a partner) should be thoroughly informed on the lengthy follow-up treatment of the vaginal prosthesis as adhesions will otherwise develop in the neovagina and it will shrink. Girls with MRKH require expert and sensitive guidance, initially to help them overcome the prospect of childlessness and then to help them decide on suitable treatment to create a vaginal structure that enables cohabitation. Digital stretching by the patient herself should be recommended as the therapy of choice, with surgery as an alternative possibility.

Atresia

Knowledge of the many variations of the normal hymen is important such as hymen bifenestratus, h. cribriformis, h. altus, amongst others. These types are in fact harmless, but they may make the desired tampon hygiene impossible or hinder cohabitation.

Hymenal atresia is probably the result of a persisting membrane at the site of the Müllerian tubercle. This disease should be diagnosed in the newborn girl or during the regular pediatric check-ups. If the hymenal closure still persists after the menarche, the inevitable hematocolpos, -metra and -salpinx, and all the consequences of tubular sterility develop, which can be avoided if the disease is recognized at an early stage.

Treatment consists of partial resection of the hymen.

\[\text{No incision due to the risk of adhesion!}\]

Suprahymenal atresia and the very rare cervical atresia are not usually diagnosed until after the menarche. The higher the location of the atresia, the more difficult it is to perform successful surgical treatment.

Uterine duplication

Asymmetric duplicate structures with one-sided out-flow impediment are relevant in pediatric and adolescent gynecology. The indication for surgical treatment is decided individually, taking fertility preserving measures into consideration.

Androgenization

- Hypertrichosis: Strong growth of fine velus hair, in particular in locations where the hair follicle is not androgen-dependent (lower leg, forearm, sacral region)
- Hirsutism: Appearance of terminal hair in androgen-dependent hair follicles (upper lip, chin, cheek, front of the neck, chest and sternal or pubic region).

Hirsutism and hypertrichosis are two different diseases that cause severe cosmetic impairments. The exact cause of the hirsutism should be sought (Table 11). Hirsutism is treated according to its cause.
Polycystic Ovary Syndrome (PCOS)
PCOS is the most common cause of hirsutism during adolescence: up to 30% of young girls are affected.

The symptoms are hirsutism, acne, seborrhea, oligomenorrhea, amenorrhea and in 50% to 70%, adipositas.

PCOS can be caused by chronic-excessive exposition to LH and estrogen, chronic androgen exposition, insulin resistance, and hyperinsulinemia.

Diagnosis: Sonography (peripheral follicle > 10, ovarian volume ↑); endocrinology: LH ↑, FSH ↓; ↑: DHEAS, testosterone, androstendione, free androgen index; SHBG ↓; ↑: triglycerides, cholesterol, insulin, IgF-1.

The aim of therapy is to eliminate the hyperandrogenemia and hyperinsulinemia as well as to normalize lipid metabolism, thereby preventing the long-term consequences such as metabolic syndrome, type 2 diabetes and cardiovascular disease, breast and endometrial carcinoma, as well as infertility. Oral contraceptives with antiandrogenetic effects are used to relieve the hyperandrogenemia, also as a long cycle. Effective combined preparations contain the gestagens cyproterone acetate, dienogest, chlormadinone acetate or drospirenone. If the adrenals glands are involved, dexamethasone should be given additionally. Weight-loss plays the main role in treating hyperinsulinemia. Reducing calorie intake and doing sport can simultaneously normalize lipid metabolism. Serum insulin and ovarian androgen production can be significantly reduced by administration of the insulin sensitiser metformine (off-label use!).

Differential diagnostics: in particular, adrenal cause or involvement!

Genital and Pseudotumors
Almost all types of benign and malignant genital tumors may already be found in small and adolescent girls; sometimes, only one or two cases are described in international scientific literature. In children, the ovaries are particularly affected; germ cell tumors are the most the common type (60% to 90%).

Treatment of genital tumors in small and developing girls should take into consideration that in the case of malignoma, saving the life of the patient is the topmost priority, but at the same time, attempts should be made to preserve, as far as possible, endocrine functions, fertility, and the capacity to experience sexuality. Individual therapy concepts are required and these can only be developed through interdisciplinary cooperation, in order to avoid over or under therapy or even superfluous treatment due to a lack of experience. The prognosis of malignant genital tumors has improved significantly in recent years.

Tumors of the Vulva
Tumors of the vulva are easily visible due to their outer location and are therefore often the reason for consulting a physician.

- Benign tumors are pseudotumors such as the hymenal polyp, atheroma, lymphangioma, hemangioma, urethral caruncle and during puberty, hyperplasia of the small labia. Usually visual diagnosis is sufficient for correct classification.
- Real benign tumors of the vulva are rare. Dysontogenetic cysts consisting of the remains of the sinus urogenitalis or of the parareural ducts may be localized on the perineum, the small labia, the vestibule or the hymen.
- Malignant tumors of the vulva are very rare and are predominantly sarcoma or embryonic tumors. Of the sarcoma, the rhabdomyosarcoma (sarcoma botryoides) is the most frequent type found in early childhood, but this more often affects the vagina.

Tumors of the Vagina
Vaginal tumors are often coincidental findings as they are difficult to see and lack symptoms.

Benign tumors are pseudotumors such as hymenal atresia with mucoceles in newborns and hematocites during puberty. Real benign tumors are usually dysontogenetic cysts consisting of the remains of the Wolffian ducts (Gartner’s duct) or the remains of the Müllerian ducts. Treatment consists of marsupialization.

Adenosis vaginae is primarily a benign alteration in the vaginal epithelium, whereby, the remaining glandular structures of the Müllerian duct persist as islands amidst the squamous epithelium. The main symptom is an annoying, slimy discharge.

Malignant tumors are mainly rhabdomyosarcoma, the frequency of which peaks between the age of 2 to 4 years. The cardinal symptom of malignant vaginal tumors is genital bleeding. The cause of any vaginal bleeding in childhood, which is always pathological, should be clarified by vaginoscopy, and possibly by biopsy and imaging.
rupture. An increase in body circumference may be caused by tumors. Sudden pain is characteristic of volvulus or disorders may also, in rare cases, be caused by ovarian signs of early maturity. During puberty, menstrual girls, vaginal bleeding may occur, usually accompanied by or abdominal pain may be a sign in all age groups. In small The symptoms are often completely uncharacteristic: fever or by germ cell tumors predominate. Tumors of the Ovary tumors are also rare. Sarcomas, mesodermal mixed tumors and carcinomas have been observed on a few occasions. Tumors of the Cervix Uteri Benign neoplasms are rare in children and are of little importance due to the lack of symptoms. Dysplasias of the cervix are being increasingly observed in young girls. Although the rate of spontaneous remission is high, young girls who have sexual contacts and who consult a gynecologist for a prescription for the «pill» should undergo regular colposcopy, cytological tests, and if necessary, an HPV test. They should definitely be encouraged to have a preventative vaccination against HPV.

Malignant tumors of the cervix uteri are very rare in children and adolescents. There are hardly any cases of squamous epithelial carcinoma. The similarly rare adenocarcinomas are of mesonephrogenic or paramesonephrogenic origin. At this age, the major symptom of the mostly advanced carcinoma is a fetid, sanguinous discharge or irregular bleeding. If these symptoms occur during childhood, vaginoscopy, and in girls who have attained menarche, speculum insertion with colposcopy and cytological tests are indicated. The treatment guidelines that apply to adult women also apply to children and adolescents with invasive cervical carcinomas. As with the vulva and vagina, the main type of sarcoma found in small girls is the rhabdomyosarcoma.

Tumors of the Corpus Uteri
Of the benign neoplasms, leiomyomas are very occasionally found between the 9th and 16th year of age. Malignant tumors are also rare. Sarcomas, mesodermal mixed tumors and carcinomas have been observed on a few occasions.

Tumors of the Ovary
Ovarian tumors are the most common type of genital tumor in small and young girls. Up to 30% of all ovarian tumors in children and adolescents are malignant, whereby germ cell tumors predominate.

The symptoms are often completely uncharacteristic: fever or abdominal pain may be a sign in all age groups. In small girls, vaginal bleeding may occur, usually accompanied by signs of early maturity. During puberty, menstrual disorders may also, in rare cases, be caused by ovarian tumors. Sudden pain is characteristic of volvulus or rupture. An increase in body circumference may be caused by a large benign tumor or by an advanced malignoma. Cystic ovaries in small girls are within the normal range of findings. During the so-called hormonal resting phase, sonographic imaging of the small, solid ovaries is only possible if they are cystic.

Diagnostics: All the clinical, endocrinologic, and imaging procedures available should be exhausted.

If the findings are not conclusive or if there is a tendency to growth, diagnostic laparoscopy and histological clarification!

Treatment: If there is a suspicion of a rupture or volvulus (usually an emergency operation), an experienced gynecologist should be consulted, and surgery with preservation of the ovaries and possibly subsequent ovaropexy should be attempted. If the sonographic findings show criteria of malignancy, the procedure should be according to the treatment guidelines for carcinoma surgery in adult women. In children and adolescents, individualized therapy concepts are needed: as much radicality as necessary, as much organ preservation as possible. The precondition is that the patient is provided with detailed and frank information on the advantages and disadvantages of fertility preserving surgery as well as on the possibility of cryopreservation of ovarian tissue. Chemotherapy should also be planned individually.

No precipitant surgical intervention in the case of functional cysts!

Apart from the necessary medical check-ups, the follow-up care of tumors includes psychological guidance of the parents and, depending on the age of the patient, sensitive care. The young patient requires both expertise and empathy.

Symptoms and Diseases of the Breasts
Abnormalities in the development of the breasts of young girls and adolescents are noticed exactly by both the parents and the young girl herself, and at the slightest sign of any abnormality a physician should be consulted. In contrast to the adult woman, pathologic-anatomic alterations in mammary gland tissue are rare in young girls and adolescents. The symptoms and diseases are normally caused by genetic and constitutional disorders, and endocrinopathies, or they are due to developmental, partially temporary abnormalities. Individual variations in the size, shape and consistence of the breasts, also with regard to the formation of the nipples and the areola mammae, are within the normal developmental range.
Malformations and Constitutional Developmental Disorders

Congenital malformations are altogether relatively rare and vary greatly in appearance (Table 12). They may also be associated with malformation of the kidneys.

Table 12: Malformations of the breasts

- Amastia and athelia
- Polymastia and polythelia
- Tubular breast
- Mammary asymmetry
- Poland’s syndrome
- Inverted nipples
- Mammary dysplasia
- Hyperplasia of the Montgomery glands

Constitutional developmental disorders such as mammary asymmetry, hypoplasia, and hyperplasia are to a great extent based on subjective evaluation and must be assessed in relation to the overall physical stature. In extreme cases, surgical correction cannot be avoided. Attempts at medicamentous treatment are obsolete.

Juvenile striae in adipose girls or as the result of an excessive reduction diet are caused by stretching and tears in the elastic fibers. They are irreversible and cannot be treated satisfactorily. Juvenile ptosis mammae is caused by the early onset of local aging processes. In extreme cases, a lifting operation may be indicated, but not, however, under the age of 20. Subsequent operations are often necessary.

Endocrinopathies as a Cause of Developmental Disorders

The absence or delayed development of the breasts is caused by primary ovarian insufficiency in the case of gonadal dysgenesis (see above), ovarian insufficiency as a result of chemo- or radiotherapy, the delayed induction of maturity in pubertas tarda, isolated gonadotropin deficiency (Kallmann syndrome) from the 12th year of life, and AGS.

Premature development of the breasts before the 8th year of life occurs either as an isolated premature thelarche (see above) or in connection with central (idiopathic) or peripheral pubertas praecox (see above). Neonatal macromastia is a normal variant caused by the affects of maternal estrogen and/or as a result of the normal increase in the neonatal prostaglandin level.

Functional Symptoms

Mastodynia is accompanied by varying and often cycle-independent pain (pressure pain), and is sometimes caused by oral contraceptives or familial carcinophobia. It is temporary and harmless, but is often accompanied by a great degree of suffering. A well-fitted brassiere may ease the situation or the oral contraceptive should be altered to a preparation with lower estrogen content.

Mastopathy is characterized by painful swelling of the breasts in the 2nd half of the cycle. If cysts develop, they should be sonographically monitored on a regular basis.

Mastitis nonpuerperalis: This condition should be specifically treated with antibiotics. Combined treatment with a prolactin inhibitor is recommended as a prophylactic against abscess formation.

Tumors

Malignant mammary gland tumors are very rare in childhood and adolescence. However, recently an increase in mammary carcinoma has been observed in women under the age of 25.

The fibroadenoma is the most frequent type of benign tumor, which grows to a maximum size of 5 cm in young girls. If the sonographic and palpatory diagnosis is conclusive, an operative intervention is unnecessary in the case of smaller fibroadenomas. These tumors regress spontaneously. If cystosarcoma phylloides is suspected (rapid growth, tuberous deformation of the breast), which is usually benign in adolescents, the tumor should be removed with a surrounding margin of healthy tissue. Punch biopsy is now obsolete.

Trauma of the breasts may appear to be a tumor due to an intramammary hemangioma. Treatment is conservative.

Contraception

Contraceptives recommended for use by adolescents must
- be very reliable,
- be easy to use,
- be acceptable to adolescents and must therefore have few side effects,
- be easily available and preferably, free of charge.

Otherwise, the aim of avoiding unwanted pregnancies in this age group will not be achieved. Girls that use oral contraceptives should be informed of the risk of STD.

Methods of contraception and recommendations for adolescents can be found in Table 13.
<table>
<thead>
<tr>
<th>Contraceptive</th>
<th>Recommendation</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal oral preparations</td>
<td>Preparation of choice</td>
<td>Advantages: highly reliable, therapeutic indications, slight side effects. Disadvantage: must be taken regularly.</td>
</tr>
<tr>
<td>Hormonal local preparations (the same effect as oral preparations)</td>
<td>Only gestagens (&quot;mini-pill&quot;)</td>
<td>Only if estrogen is contraindicated. Disadvantages: limited reliability, high compliance is required, bad control of the cycle.</td>
</tr>
<tr>
<td>Transdermal: &quot;hormone patch&quot;</td>
<td>Alternative!</td>
<td></td>
</tr>
<tr>
<td>Intravaginal: &quot;hormone ring&quot;</td>
<td>Only suitable to a limited extent</td>
<td>Disadvantage: lack of compliance.</td>
</tr>
<tr>
<td>Gestagen IUD</td>
<td>Only suitable to a limited extent</td>
<td>There is no experience in girls. Disadvantages: painful insertion, the coils are too large, bleeding disorders. Advantages: highly reliable for five years, no compliance necessary.</td>
</tr>
<tr>
<td>Injection of 150 mg DMPA (&quot;3-month injection&quot;)</td>
<td>Unsuitable</td>
<td>Disadvantages: cycle disorders, great increase in weight, bone density decreases, fertility is reduced for up to one year.</td>
</tr>
<tr>
<td>Subdermal implant</td>
<td>Only suitable to a limited extent</td>
<td>No experience in girls. Advantages: high reliability for three years, no compliance necessary.</td>
</tr>
<tr>
<td>Barrier methods</td>
<td>Unsuitable</td>
<td>Disadvantages: high failure rate, no acceptance.</td>
</tr>
<tr>
<td>Cup pessary, vaginal diaphragm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condom</td>
<td>Additional contraceptive with protection against STD</td>
<td>Disadvantage: unreliable as a contraceptive if used as the only method.</td>
</tr>
<tr>
<td>Temperature measurement, Knaus-Ogino, amongst others</td>
<td>Unsuitable</td>
<td>Disadvantage: unreliable due to the as yet, unstable cycle.</td>
</tr>
<tr>
<td>Emergency contraception</td>
<td>No routine contraception</td>
<td>Advantage: high reliability. For use in an emergency! Is it easily available?!</td>
</tr>
<tr>
<td>The &quot;morning-after&quot; pill</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Legal Questions Regarding the Prescription of Hormonal Contraceptives

Adolescent girls over the age of 14 may be prescribed hormonal contraceptives without the consent of their parents and without legal consequences, in so far as the physician has gained the impression after discussion with the girl, that without reliable contraception she may become pregnant. An exact documentation of the girl’s personality and her “insight and critical abilities” is urgently recommended.

The consent of the parents is necessary for girls under 14 years of age.

Sexual Abuse

The terms “sexual abuse”, “sexual seduction”, “sexual violence” and “sexual exploitation” of children are used synonymously. The comprehensive definition is: “Sexual abuse of children is the exploitation of a child by an adult or clearly older person with the aim of sexual gratification”.

Both the comprehensive and the legal definition make it clear that sexual exploitation of a child need not necessarily be accompanied by evidence of general physical or genital injuries!

Due to the overestimation of and unjustified expectations placed in the significance of gynecological examination, small and adolescent girls who are suspected victims of sexual abuse are brought or referred to a pediatric gynecologist by the parents, in particular by the mother, or to pediatricians, children’s facilities, the youth welfare office or the police. The pediatrician charged with the task should not only be capable of carrying out an age-appropriate gentle examination of the genital-anal region but should also have knowledge of the age-dependent anatomy, the normal variants and the correct interpretation of pathological findings.

With regard to the question: “Has the girl been sexually abused?”, the gynecological examination is only conclusive if sperm is found: either in the vagina (also without injury to the hymen), or in an anal or oral location, on the body, or in the child’s worn underwear. This is true in less than 1% of the cases. Acute tears or genital bleeding are not necessarily evidence of abuse. A report by a qualified expert on the credibility of the girl, which describes the connection between the symptom and the cause, is decisive in such cases.

In more than 90% of the cases, girls are brought for consultation due to suspected chronic sexual exploitation, or due to abuse that may have occurred once or repeatedly, which occurred months or years beforehand. In these cases it must be noted, particularly in small girls, that the repair processes after acute injury, e.g. tears in the hymen, may already have been completed after about 14 days and that no traces remain. Shortly before or after the menarche the hymen may have such a physiological width that even penetration leaves no injuries. Finally, girls are brought to the physician with various symptoms, such as reddening of the vulva, discharge, abdominal pain, enuresis nocturna, and masturbation without there being any ostensible question of sexual abuse.

Interpretation of the findings is exceptionally difficult!

The estimated number of unreported cases of sexual exploitation of children is high, as more than 70% of the offenders are found within the child’s intimate surroundings.

The care of sexually exploited children is an interdisciplinary task in which general practitioners and pediatricians, gynecologists, pediatric and adolescent psychologists, dermatovenerologists and social workers are involved. Gynecological examinations should only be performed by physicians with experience in pediatric and adolescent gynecology in order to avoid misinterpretation, and so that other warning signs may be correctly construed by way of specific and objective examination. Renewed trauma due to repeated physical examination of the child, particularly by an inexperienced colleague, should be avoided at all costs.
Keywords
Pediatric and Adolescent Gynaecology (PAG), surgery hours, peculiarities in childhood and adolescence, common symptoms and diseases

References

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Dr. Marlene Heinz has been a specialist for gynecology and obstetrics since 1968. Until 2001, she worked as a specialist at the Women’s Hospital in Berlin Lichtenberg. From 1968 until 2007, besides her clinical work, she also offered consultation in pediatric and adolescent gynecology.

In 1972, Dr. Heinz was a founding member and member of the Board of the Working Group Children and Adolescent Gynecology in the former GDR. Since 1992, she has been a member of the board of the Working Group Pediatric and Adolescent Gynecology in Germany and since 1998, the president. Dr. Heinz was a member of the “Executive Board of the FIGIJ” (International Federation Pediatric and Adolescent Gynecology) from 1998 until 2004, and took up the post again in 2007. She was one of the founding members of the Executive Board of the EURAPAG (European Association of Pediatric and Adolescent Gynaecology) and has been a permanent member since its establishment in 2008.

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**Question 1**

Exact examination of the outer genitals, paying attention particularly to the condition of the hymen,

a. is best performed under anesthesia in small children,

b. can always definitively confirm or exclude suspected sexual abuse,

c. is an excellent indicator of the presence or lack of estrogen stimulation,

d. is best performed without use of the colposcope,

e. is not possible in small girls.

**Question 2**

Which of the following statements is correct with regard to the most frequent symptoms and diseases in pediatric gynecological consultation?

a. The vulva and vagina are less frequently affected during childhood; it is above all, ascending infections that play a great role.

b. Labial synechia is a congenital malformation that is characterized by adhesion of the small labia or of the whole of the entrance to the vagina.

c. Lichen sclerosus is very rare in small children as it is almost always exclusively a disease found in the senium.

d. Genital bleeding during the so-called hormonal resting phase is rarely pathologic.

e. Vulvitis and vulvovaginitis are the most frequent diseases encountered in pediatric gynecology (40% to 60%).

**Question 3**

Which of the following applies to genital bleeding during childhood?

a. It is a frequent reason for mothers to take their child to see a pediatric gynecologist.

b. Genital bleeding during childhood is easy to diagnose.

c. Vaginal bleeding that may occur in newborn girls within the first four to six weeks of life is always pathological.

d. More than 60% of all vaginal bleeding during childhood is caused by primary or secondary vulvovaginitis.

e. Genital bleeding is always a sign of premature maturity.

**Question 4**

Which statement is correct with regard to disorders of the neuroendocrinologic axis?

a. Isolated disorders such as premature thelarche or pubarche should always be treated with drugs at an early stage.

b. Central or gonadotropin-dependent pubertas praecox is a premature activation of the hypothalamus–pituitary–ovarian axis.

c. In peripheral pubertas praecox, the gonadotropins increase in the GnRH test.

d. In central pubertas praecox, the gonadotropins decrease in the GnRH stimulation test; the LH/FSH-quotient is less than 1.

e. At present, idiopathic pubertas praecox is best treated with estradiol valerate monopreparations.

**Question 5**

Which statement is correct with regard to gonadal dysgenesis?

a. The most common symptoms are somatomegaly, early thelarche, and secondary amenorrhea.

b. With a rate of 1 in 2,000 to 1 in 2,500, the Ullrich-Turner syndrome is the most frequent type of gonadal dysgenesis.

c. It is best if the Turner syndrome is diagnosed at puberty, at the latest.

d. Treatment is not necessary until puberty.

e. Girls with the Turner syndrome cannot become pregnant.

**Question 6**

Which statement is incorrect?

Girls with androgen-insensitivity syndrome (AIS) suffer from which of the following symptoms?

a. They suffer from amenorrhea.

b. The major symptom may be hernias that occur in infancy and childhood.

c. They have no uterus.

d. They always suffer from hirsutism.

e. They develop normal breasts.
Question 7
Menstrual disorders are the most common reason for consultation (40%) in girls under the age of 12. Which statement is incorrect?
a. If a girl’s pubertal development is age-appropriate and she suffers from primary amenorrhea, the cause is usually an endocrinologic disorder.
b. Secondary amenorrhea in adolescence is caused by metabolic-endocrinologic disorders in > 40% of the cases.
c. Serious coagulations disorders should be excluded in cases of hypermenorrhea.
d. Primary dysmenorrhea causes great strain during puberty.
e. More than 60% of all menstrual disorders during puberty are cases of dysfunctional uterine bleeding (DUB).

Question 8
Which statement is correct with regard to anatomical malformations of the genital area?
a. Lack of or disrupted differentiation of the Müllern ducts between the 10th and 12th week of pregnancy leads to utero-/vaginal aplasia.
b. They are often associated with malformation of the upper gastrointestinal tract.
c. The uterus, ovaries, and the vagina are lacking in the Mayer-Rokitansky-Küster-Hauser syndrome.
d. The Mayer-Rokitansky-Küster-Hauser syndrome should always be treated by surgical construction of a neovagina.
e. Operative partial resection is required when treating hymenal atresia, not only an incision.

Question 9
Which statement is correct with regard to genital tumors in children?
a. Malignant tumors usually affect the corpus uteri.
b. The prognosis for malignant genital tumors has greatly improved in the last decade.
c. Up to 60% of all ovarian tumors in children and adolescents are malignant.
d. In childhood, every ovarian cyst is pathologic and should be removed operatively.
e. Carcinomas of the squamous epithelium of the cervix uteri are common in children and adolescents.

Question 10
Which statement is correct with regard to sexual abuse in childhood?
a. Sexual exploitation of a child is not necessarily associated with detectable general physical or genital injuries.
b. Sexual abuse of children always leaves physical traces.
c. Gynecologic examination can always provide a definitive answer on suspected sexual abuse.
d. The possibility of a sexual delict should always be considered if symptoms include reddening of the vulva, discharge, abdominal pain, and enuresis nocturna.
e. The findings of the medical physical examination are decisive evidence in cases of sexual abuse of children.