

Review

Pediatric and Adolescent Gynecology – a Current Overview

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Abstract

In pediatric and adolescent gynecology we encounter a number of diseases that occur solely during a specific phase of physical development. The diseases need some experience in the field as well as an accurate diagnosis and are therefore often diagnosed somewhat late.

The separation and traction technique is a painless method of inspecting the child's genitals. It is also effective and easy to perform. In contrast to a routine investigation in adults, very specific diagnostic questions require the insertion of a speculum, vaginoscopy, taking swabs for analysis, ultrasound investigations, or blood sampling in children.

A number of diseases that occur frequently in prepubertal girls are listed in the following.

The etiology, clinical characteristics, treatment and prognosis of the following diseases will be addressed in detail: vulvovaginitis, lichen sclerosus, labial adhesions, ovarian torsion, abnormal uterine bleeding, uterine fibroids, and hypertensive disorders of pregnancy.

Keywords: Methods of investigation, phases of development, vulvovaginitis, lichen sclerosus, labial adhesions

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Introduction

A number of diseases are encountered in pediatric and adolescent gynecology, depending on the child's stage of development and the level of estrogenization. A few specific gynecological diseases concern only children, whereas others occur in adults as well, but are subject to a different pathogenesis and treated differently in children. Thus, the treatment of gynecological diseases in children and adolescents requires specialized knowledge of the subject.

Depending on their age, children and adolescents present with a variety of problems and questions in a doctor's medical office. The reason for seeking medical advice for prepubertal children are findings or problems in the outer genitals (vulvovaginitis, labial adhesions, lichen sclerosus, unclear pruritus). In adolescents and pubescent individuals, the main focus of treatment is disorders of pubertal development, menstrual symptoms, menstrual disorders,

especially primary and secondary amenorrhea, contraception, sexual relationships, and sexuality.

Many children are anxious and withdrawn at their first visit, and even subsequent visits, to the gynecologist. It is extremely important to gain the child's trust.

The following should be kept in mind from the very start:

The waiting room should be provided with a play corner and aligned to the needs of children.

It would be advisable to keep the consultation hours for pediatric and adolescent gynecology at the start or the end of the regular consultation hours. Depending on the reason for the visit, the treatment of children and adolescents is much more time consuming than that of an adult.

About 30-60 minutes should be allocated for the treatment of a child or adolescent.

The pediatric gynecological investigation

Depending on the issue in question, the pediatric gynecological examination may be a whole-body investigation, as in cases of a suspected general disease or sexual violence. In the event of specific questions concerning the genitals alone, it may not be necessary to inspect the entire body. The child's medical checkup booklet should be reviewed. The patient's current height and weight should be noted on the percentile curve. A pleasant atmosphere should be created in the pediatric and adolescent gynecological consultation hours. The treatment should be provided in a calm environment and without haste. The procedure should be explained to the child before it is performed. The process, purpose, and potential limits of the investigation should be explained to the parents or the accompanying person. If the child is defensive or refuses to undergo the investigation, she should not be compelled or held forcibly. The doctor's assistant or (pediatric) nurse who accompanies the investigation may try to divert the child's attention with water-filled syringes or an inflated glove. If this is not successful, the investigation may either be deferred to a later point in time or, depending on the urgency of the question and the severity of symptoms (such as starting sepsis in case of a suspected foreign body in the vagina), one might consider short-acting anesthesia. Handing out a small gift to the child at the time of her departure or after the investigation has proved to be a useful measure. A treasure chest filled with soap bubbles or small toys could serve as a motivation for the upcoming investigation.

Three positions of examination may be used for the inspection of the external genitalia:

1. Supine with drawn legs; the "frog" position
2. In the mother's or caregiver's lap
3. On the gynecological chair in lithotomy position and/or knee-elbow position

Inspection of the external genitalia plays a key role in the gynecological investigation. The following entities must be evaluated: the labia majora and minora, clitoris, external urethral meatus, anus, perineum, posterior commissure, navicular fossa, the hymen and its margin, vaginal introitus, and the distal third of the vagina. While the speculum is mandatory for adequate evaluation of the vagina in adults, usually the so-called separation and traction technique is sufficient for prepubertal girls. The physician takes a light hold of the outer aspect of the labia majora or perianal region and exerts a slight pull in lateral-caudal direction. The genitals are thus unfolded. The above mentioned anatomical structures can be assessed without further aids (Figure 1).

Depending on the issue of investigation or symptoms, it may be meaningful to perform more detailed investigations; these are definitely not a part of the routine examination (1):

- Vaginal swab (bacteriology, virology)
- Microscopic investigation of vaginal secretion
- Vaginoscopy (foreign body, injuries, fistulae)
- Blood sampling (STD, inflammatory values, endocrinological diagnosis)
- Ultrasound of the abdomen (with a filled bladder)

Phases of development

Depending on estrogen levels, the development of a girl may be divided into various phases, each accompanied by specific pathologies (2). Table 1 shows the various phases of development, the corresponding age, hormonal characteristics, and respective disease syndromes.

A number of diseases that occur in girls of prepubertal age are listed in the following.

Vulvovaginitis

Vulvovaginitis is the most common disease in the non-estrogenized environment of the pediatric genitals. Inflammatory changes in the vulva are rather rare in puberty, but may occur in conjunction with a vaginal candida infection.

Etiology

Non-specific vulvovaginitis occurs in about 80% of cases. In other words, no specific pathogen is found. This condition is referred to as irritant contact dermatitis. In specific vulvovaginitis, on the other hand, one is able to isolate a specific pathogen. Quite often the patient undergoes a protracted period of unsuccessful treatment with local agents, especially antifungal substances. Vulvovaginitis is frequently aggravated by poor hygiene, especially at an age when girls start to go to the toilet independently. Bacteria such as *E. coli*, enterococci, staphylococci, *Proteus mirabilis* or *Pseudomonas aeruginosa* are found in many cases (3-5). The genitals of prepubertal girls have a predilection for vulvovaginitis due to the following reasons: the absence of a labial fat pad, the thin and sensitive skin of the vulva, proximity to the anus, and a wide introitus. The physiological estrogen deficiency and an alkaline intravaginal pH favor the emergence of vulvovaginitis. In some cases it may coincide with respiratory infections; the path of transmission is usually an oral-genital smear infection (6). Obesity, tight clothing, or underclothes made of synthetic fiber favor the emergence and persistence of vulvovaginitis.

Clinical symptoms

The labia majora and minora, and in some cases the perineum and the perianal region, are reddened to a greater or lesser degree in the presence of vulvovaginitis. The patients present with dried secretion known as smegma (desquamated cells, urine residues) in the interlabial aspect. Whitish or yellowish-green vaginal discharge is the most frequent symptom of vulvovaginitis. The condition may be divided into an acute and a chronic stage. In the *acute stage* the vulva and the vaginal introitus are inflamed and reddened; the redness is marked by blurred margins. The labia minora and hymen are swollen due to edema. Smegma or in some cases stool residues are found in the interlabial or in the perianal aspect. The *chronic stage* is marked by pink coloring with intermittent whitish zones and scratch marks. The vulva is significantly dry. The mildly reddened and dry, scaly region of the vulva usually includes the anus and has a rather clearly delineated margin.

Figure 2a shows the acute stage of vulvovaginitis while Figure 2b depicts chronic disease.

The patients complain of an itching and burning sensation in the external genitals, especially during micturition.

Diagnosis

The first step is an exact medical history about the duration of symptoms, followed by documentation of the following:

- Previous therapies, such as antifungal agents and/or creams containing cortisone
- Comorbidities such as dermatosis
- Hygiene habits
- Current use of external agents
- Possibility of trauma or insertion of a foreign body

The following should be given attention during the inspection:

- Tanner stages (signs of puberty)
- Signs of dermatosis
- Detailed local findings (redness, scratch marks, bloody or putrid vaginal discharge, level of hygiene)

A rectal palpation and a vaginoscopy should only be performed in case of a suspected foreign body, but should be a routine procedure in patients with a bloody vaginal discharge.

Microbiological investigation of a swab provides evidence of specific pathogens only in about 50% of cases (7). In case of clinical symptoms such as a white vaginal discharge or a distinct redness, a smear should be obtained. Care should be taken to ensure that the smear is taken from the vagina and not the introitus. Furthermore, as injury to the hymen would be very painful for a girl, the hymen should be left untouched as far as possible.

In terms of the differential diagnosis of unspecific vulvovaginitis, the following causes should be ruled out:

- Vulvovaginitis due to specific pathogens (group A streptococci, trichomonas, chlamydia, genital herpes, genital warts, gonorrhoea)
- Foreign body in the vagina (blood, putrid discharge)
- Dermatitis (lichen sclerosus, psoriasis, neurodermitis, Behçet's disease)

Pathogens are found in about a third of smears taken from symptomatic girls. The most common of these (about 60% of cases) are group A hemolytic streptococci (pyogenic streptococci or "anal scarlet fever" (4)). This germ is considered highly pathogenic and should be treated systemically with penicillin.

Further pathogens include Haemophilus influenzae, Klebsiella pneumoniae and Streptococcus pneumoniae (7). Depending on the severity of symptoms, the patient may be given specific (oral) systemic therapy after an antibiogram has been obtained.

A candida infection is observed exclusively in the estrogenized epithelium (i.e. during puberty) or at the age when diapers are used.

Candida albicans is rarely isolated as a pathogen (1 %) in girls with vulvovaginitis prior to puberty (3, 4, 8). 12.5% of 3- to 9-year-old girls are asymptomatic carriers of candida.

Pathological growth of candida with symptoms usually occurs only in cases of immunodeficiency, malignant disease, preterm birth, previous antibiotic treatment, or estrogenization. Nevertheless, at least one antifungal therapy had been administered in more than 80% of children with unspecific vulvovaginitis (8).

Antifungal agents and antibiotics (local or systemic) are not indicated in unspecific vulvovaginitis.

Therapy

- Omit all external irritants, such as bath additives or washing lotions; dispense with wet wipes, wear comfortable clothing; adhere to consistent and careful genital hygiene, wash only with plain water, appropriate voiding behavior.
- Sitz baths with sodium chloride; local application of a neutral lipid-containing cream.
- Oral antibiotic treatment after obtaining an antibiogram; only if there is evidence of pathogens (as detailed above).

Lichen sclerosus

Lichen sclerosus is a chronic inflammatory autoimmune dermatosis with a predilection for the skin in the anus and the genital tract. About one in every 900 girls is affected by this autoimmune disease (9). The mean age of disease onset is 5 years, but the mean age at diagnosis is about 7 years (9). The disease is marked by two peaks, namely before puberty and after menopause.

Etiology and Pathogenesis

The etiology of lichen sclerosus is largely unknown. A number of causes with an autoimmune component have been suggested. The autoimmune component induces a dysregulation of the immune system. In 4–14 % of cases, it is associated with other autoimmune diseases such as Hashimoto's thyroiditis, vitiligo, alopecia areata, pernicious anemia, rheumatoid arthritis, or diabetes mellitus. A family history of autoimmune disease in parents or grandparents has been observed in more than 50 % of cases (9, 10).

Clinical symptoms

The principal symptoms are pronounced itching, especially in the evening and at night before falling asleep, as well as pain and a burning sensation in the vulva. Secondary symptoms include constipation, perianal symptoms with painful fissures, dysuria, and superficial bleeding. The diagnosis is frequently delayed by several years because of inappropriate treatment due to a suspected candida or bacterial infection. In a large number of cases, the patient will have undergone various treatments with local and systemic antibiotics and antifungal agents. When a patient presents with lichen sclerosus, sexual abuse is suspected in more than 70% of cases (9).

The local appearance of lichen is the typical figure of eight (around the vulva and the anus). The skin is red, stretched, and has a porcelain-like shine. In the early stage one frequently finds perilabial and transverse grooves. Indurations/sclerosis and hyperkeratosis may also be observed. Patients in advanced stages may present with a whitish atrophy. Further characteristics include superficial ecchymosis (bleeding), hyperpigmentation or depigmentation, and rhagades. Figures 3a and b show the typical appearance of lichen sclerosus.

Complications occur especially in advanced stages or in cases of non-diagnosed or inappropriately treated disease. These include atrophy, scarring, destruction of vulvar architecture, and chronic pain/vulvodinia (9).

Diagnosis

The diagnosis is derived from typical clinical findings and the symptoms described by the patient. In contrast to adults, the physician should never perform a biopsy of the whitish vulva in children for confirming the diagnosis.

Therapy

The first step is to institute or follow so-called basic measures. These include the avoidance of local irritation, such as tight underclothes or underclothes made of synthetic fiber, careful genital hygiene, the use of non-perfumed, preservative-free detergents, and washing with plain water.

Specific *first-line therapy* consists of de-escalating treatment with ultrapotent topical corticosteroids (9, 11, 12), such as Clobetasol cream for 12 weeks. The following regimen proved to be effective:

Week 1–4: once daily

Week 5–8: every 2 days

Week 9–12: twice a week

Corticosteroid therapy may be administered in shorter intervals. Regardless of the duration of treatment, it should always be tapered off slowly.

Maintenance therapy with local agents (such as Linola fat cream or Deumavan cream) and the above mentioned basic measures should be used after, or even during, corticosteroid therapy.

Failure of corticosteroid therapy is extremely rare. If the symptoms do not improve despite cortisone treatment, the diagnosis should be reviewed first and possible differential diagnoses should be taken into account and/or ruled out, such as other types of dermatosis, atopic eczema, vitiligo, infection. Once the corresponding differential diagnoses have been ruled out, the physician should check the parents' compliance.

Second-line therapy consists of topical calcineurin inhibitors from the group of immunosuppressants or immunomodulators (12).

- Pimecrolimus 1% cream for a maximum of 12 weeks or
- Tacrolimus 0.03% ointment for 3 weeks

Both substances are for off-label use.

In the event of recurrence, corticosteroids should be used again for 7 days. The second treatment should be started no earlier than three months after conclusion of the last course. If the vulva is atrophic due to preceding corticosteroid therapy, it may be advisable to use calcineurin inhibitors instead.

Prognosis

Sustained complete remission is achieved in a mere 22% of children (13). Lichen sclerosus diagnosed before puberty reappears after puberty in 75% of cases (14, 15). Fortunately, in children this condition is not associated with squamous cell carcinoma or other neoplasms. In contrast, the risk of an adult developing a squamous cell carcinoma (SCC) on the basis of lichen sclerosus is <5% (16, 17).

Note: Delayed or inappropriate treatment of lichen sclerosus may destroy vulvar anatomy permanently.

Labial adhesions

Definition

Labial adhesion is defined as a fusion of the labia minora, which may be partial, subtotal, or complete. The adhesion forms a thin and partly translucent membrane that closes the vulva.

Etiology and Epidemiology

Labial adhesions are favored by the physiological estrogen deficiency in prepubertal girls.

Vulvitis, poor hygiene, or the use of wet wipes may also favor its emergence.

About 1.8 % of girls between the ages of 3 months and 4 years are affected by this condition.

The peak incidence is between the ages of 13 and 23 months (18).

Clinical symptoms

The disease is most frequently asymptomatic and is diagnosed in the course of a routine investigation. Depending on the severity of the adhesion, the labia will be adherent from the midline to the clitoris. Quite often, there is just a tiny opening above the urethra. The introitus and the hymen are covered by a parchment-like membrane. Figures 4a and 4b show the typical appearance of labial adhesions.

Complications

- Aberrant urinary stream
- Dribbling of urine after micturition; urine accumulates in the intravaginal aspect
- Asymptomatic bacteriuria (20%), urinary tract infection (20-40%)
- Very rare: obstruction with bladder distension and hydronephrosis

Therapy

Therapy recommendations are not based on randomized studies but only retrospective data.

Basic therapy consists of careful and consistent hygiene, washing the genitals only with warm water, and the omission of external irritants (perfumed wet wipes, washing lotions, creams).

Twice daily application of Linola fat cream or Deumavan cream is recommended.

Specific therapy consists of de-escalated application of an estriol cream (such as Oekolp or Ovestin) for 4 weeks, applied directly on the line of fusion with a cotton swab for 10 seconds under slight pressure. Care should be taken to ensure that the layer of cream is not too thin, as this may be ineffective. This should be followed by local application of a neutral lipid-containing cream.

Surgical or mechanical treatment, which would involve cleavage of the membrane, should be considered only when conservative treatment has failed and clinical symptoms persist, such as

dribbling of urine or recurrent urinary tract infection. After treatment with estriol and under local anesthesia with EMLA cream, the line of fusion is separated mechanically. Depending on the child's behavior, it may be necessary to administer brief anesthesia.

Progress and Prognosis

Spontaneous remissions within one year have been reported in 80% of cases (19).

If micturition is not hindered, one could dispense with treatment. The parents must be informed about the benign nature of labial adhesions and their self-limiting nature with the onset of endogenous estrogen production during puberty.

Success rates of 47-100% have been reported for estriol therapy (20, 21); most studies report success rates in excess of 90%.

A wide range of recurrence rates have also been mentioned for estriol therapy (0-40%) (20) (21). However, the majority of studies mention low recurrence rates (0-11%).

One alternative is a 0.05% betamethasone cream applied twice daily for two weeks. Similar results have been reported for this treatment (22), and in some cases even faster remissions, than those achieved with estriol (23). Betamethasone may be considered in cases of symptomatic recurrence or failure of estriol therapy.

In addition to the above-mentioned clinical pictures, which have been discussed in great detail, another four clinical pictures will be presented in the following. They are as well important in pediatric and adolescent gynecology and their diagnosis and treatment should be known.

Ovarian torsion represents a surgical emergency and occurs in 2.7% of all pediatric/adolescent patients (24). The vague clinical presentation and variable imaging findings make this diagnosis difficult. The patient suffers from acute abdominal pain which leads to an urgent investigation and often consecutive operative management with laparoscopic adnexal detorsion. The ovary should be preserved even in case of a necrotic-appearing ovary because studies persistently show follicular development and ovarian function after a short time period after detorsion and no increased patient morbidity. Furthermore, oophoropexy may be considered in case of severe necrosis (24, 25). The appearance of the ovary does not correlate with long-term ovarian viability or function. The consensus recommendation for imaging surveillance following ovarian detorsion is an ultrasound at three months postprocedure but sooner if there is a concern for malignancy (26).

Abnormal uterine bleeding (AUB) is defined as any atypical genital bleeding originating from the uterine cavity, but without the characteristics of a normal menstrual period. This bleeding disorder can appear equally in adolescents and adults. AUB is a common problem which has significantly adverse effects on an affected adolescent's quality of life (27). The most common underlying condition in AUB in adolescence is anovulation. Although about 95% of abnormal uterine bleeding could be considered as a dysfunctional disorder, this clinical picture requires well-defined diagnostic procedures in order to detect a possible physical cause or ruling out complex or systemic diseases, including oncological ones (28). A complete gynecological evaluation (if possible) and a full physical examination are useful to detect any kind of general disease which can compromise the hormonal reproductive system. Auxiliary tools such as gynecological ultrasonography for pelvic examination are allowed in sexually-active women, otherwise abdominal or transrectal ultrasonography could be considered, if needed. Although observation is sufficient in the mild form of AUB, the first-line treatment consists of combined oral contraceptives and, when they are contraindicated, progesterone alone, medicated intrauterine devices, GnRH-analogues, or desmopressin are the most common second-line treatments (27, 28).

Uterine fibroids are benign tumors originating from the smooth muscle of the myometrium and affect women mainly during their reproductive years. The symptoms and their severity

may differ, depending on the size and location of the fibroids. The most common presenting symptom is heavy menstrual bleeding, which may lead to anemia, fatigue, or painful periods. Other possible symptoms include lower back pain, pelvic pressure or pain, and pain during intercourse (29). Fibroids are diagnosed in up to 70% of white women, whereas increased age among premenopausal women is a risk factor for fibroids (29, 30). Conversely, this means that fibroids exist, but are relative rare in adolescence. Vitale et al. wrote an interesting comment on "Laparoscopic Myomectomy of a Symptomatic Uterine Leiomyoma in a 15-Year-Old Adolescent" (31). The authors support the use of robotic-assisted laparoscopic myomectomy even in young patients for better results in wound healing, anatomical reconstruction and fertility outcome later in life (31). Consequently, even in the rare case of symptomatic fibroids in adolescents, the treatment strategies are analogous to that of adults. Another topic that should be discussed and should be kept in mind is the association between adolescent pregnancy and severe outcome, like preeclampsia, preterm premature rupture of the membrane, maternal anemia, sexually transmitted diseases, postpartum depression, and maternal deaths, and adverse neonatal outcomes, including low birth weight, prematurity, stillbirths, early neonatal demise, and low Apgar score (32). Rates of adolescent pregnancy are increasing in developing countries, with higher occurrences of adverse maternal and perinatal outcomes (33). Especially the prevalence of preeclampsia and eclampsia has to be mentioned. Macedo et al. performed a systematic review and meta-analysis concerning this topic and included 30 countries and 291,247 adolescents between 1969 and 2019 (34). The authors showed an overall prevalence rate of preeclampsia and eclampsia in adolescents of 6.7 % (95 % CI = 5.8-7.6). Subgroup analysis revealed association of preeclampsia and eclampsia ($P = 0.050$) and eclampsia ($P = 0.0113$) with country income, and the highest prevalences were found in low-and medium-income country groups (11.5 %, 95 % CI=7.8-15.8 and 10.6 %, 95 % CI=6.05-16.2) (34). Consequently, a close-meshed care and precaution is indispensable in case of adolescent pregnancy.

Conclusion

- The investigation should be explained calmly to the child and/or the accompanying person. The examination should be conducted in a quiet atmosphere with no exertion of force or compulsion on the patient. If necessary, another appointment could be fixed for a later point in time.
- Antifungal agents or antibiotics (local or systemic) should not be used in cases of unspecific vulvovaginitis.
- Lichen sclerosus as such, its delayed diagnosis or inappropriate treatment may destroy vulvar anatomy permanently (note: mean age at disease onset 5 years, mean age at diagnosis 7 years).
- Labial adhesions are a benign self-limiting disease. In cases of undisturbed micturition, one may dispense with treatment altogether.
- Ovarian torsion represents a surgical emergency and should be treated with laparoscopic adnexal detorsion and, if necessary, oophorectomy.
- Abnormal uterine bleeding (AUB) is defined as any atypical genital bleeding originating from the uterine cavity. The most common underlying condition in AUB in adolescence is anovulation.
- Adolescent pregnancies are associated with severe outcome, like preeclampsia and eclampsia.
- Uterine fibroids are quite rare in adolescents but may lead to the same symptoms as adults suffer from. Laparoscopic myomectomy or even robotic-assisted laparoscopic myomectomy are advisable therapy options.

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Table 1. Phases of development and typical diseases associated with different levels of estrogenization

Phase	Characteristics	Diseases
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Neonates/infants	Active hypothalamic-pituitary-adrenal (so-called mini-puberty); elevated E2; elevated androgens	Labial adhesions, malformations, ovarian cysts
Pre-pubertal phase	The hypothalamic-pituitary-adrenal axis is subject to inhibitory influences → estrogen deficiency, alkaline vaginal pH, genital atrophy; activation of NNR from the age of 5 years → rise in DHEAS	Vulvovaginitis, lichen sclerosus, including dermatosis, labial adhesions, premature (partial) development: growth disorders;
Onset of puberty	Activation of the hypothalamic-pituitary-adrenal axis	Premature onset of puberty, pain in the lower abdomen; vulvovaginitis
E2: Estradiol, NNR: Adrenal cortex; DHEAS: Dehydroepiandrosterone sulfate		



Figure 1. The normal vulva. The separation and traction technique serves to view and inspect the external genitals



a



b

Figure 2. (a) Acute vulvovaginitis with marked reddening of the genitals. (b) Chronic vulvovaginitis with moderately reddened and dry, scaly areas



a



b

Figure 3. (a, b) Lichen sclerosus with the white discoloration characteristic of the disease, in a figure of eight around the vulva and anus



a



b

Figure 4. (a, b) Labial adhesions. Fusion of the labia minora, which form a thin membrane covering the introitus and the hymen