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Vulvovaginitis in childhood

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Symptoms related to vulvitis and vulvovaginitis are a frequent complaint in the paediatric age. Knowledge of the risk factors and the pathogenetic mechanisms, combined with thorough clinical examination, helps to distinguish between dermatological diseases, non-specific vulvitis and vulvovaginitis proper. On the basis of microbiological data, the most common pathogens prove to be \textit{Streptococcus pyogenes}, \textit{Haemophilus influenzae} and \textit{Enterobius vermicularis}; fungal and viral infections are less frequent. The possibility of isolating opportunistic pathogens should also be considered. In rare situations, the isolation of a micro-organism normally transmitted by sexual contact should prompt a careful evaluation of possible sexual abuse. Current treatments for specific and non-specific forms are outlined, together with pointers for the evaluation of recurrence.

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Vulvitis, if associated with vaginitis, is one of the most common gynaecological complaints in prepubertal girls. Majority of cases are treated by paediatricians or general practitioners, but gynaecologists are often consulted in those cases in which the symptoms are particularly troublesome and recurrent or there is no response to standard treatments.

Risk factors and clinical work-up

Young girls are particularly susceptible to vulvovaginitis for both anatomical and behavioural reasons. The former comprise: the thinness of the vulvar skin and the physiological atrophy of the
vaginal epithelium, low in glycogen, with neutral pH and non-production of cervical mucus, the poor local immune system, the lack of protective labial fat pads and the closeness of the vulva to the anal region. The latter, albeit probably less important, are: inadequate hand washing, difficulties in cleansing after evacuation, contact with sand or, sometimes, soil, abuse of inappropriate intimate detergents and underwear.

Germs can reach the genital area as a result of contiguity from the rectum, urethra or the surrounding skin. A diffusion of bacteria from the upper airways is also possible through auto-inoculation or occasionally haematic spread.

The possibility that the vulvovaginitis may be secondary to intravaginal foreign bodies or to sexual abuse must also be borne in mind.

The core aspects of the medical history are summarised in Table 1.

The evaluation should include a general physical examination to seek evidence of dermatological problems, in particular, allergic reactions and dermatitis. In a set of 130 prepubertal girls with vulvar complaints, 33% had atopic or irritant dermatitis, 10% had authentic vulvovaginitis and the remainder various dermatological conditions (e.g., lichen sclerosus, psoriasis and hemangiomas).

The inspection of the ano-genital region should be made in the frog-leg position, evaluating the anal region, the perineum, the vulva and the vaginal introitus. The presence and the localisation of hyperemic areas, swelling, signs of scraping, vesicular lesions or ulcers, whitish patches, bleeding, vaginal discharge, labial adhesions as well as an evaluation of the status of oestrogenisation should be carefully considered. Anatomic anomalies (e.g., dislocation of urethral or anal openings or signs of suspected vesicovaginal or entero vaginal fistulae) and any abnormalities of the hymen should be documented. Perianal hyperaemia is particularly evident in case of streptococcal infection, but can also be related to the presence of candidiasis or intestinal parasites.

The main objective of the examination is to distinguish between non-specific vulvar and distal vaginal inflammation, not infectious in origin (Fig. 1), which accounts for the majority of cases, and deep vaginal involvement by specific pathogens (specific vulvovaginitis), marked by diffuse swelling and vaginal discharge.

A sample of the discharge should be obtained for a microbiological study – in peripubertal girls using a sterile saline-moistened urethral swab is recommended. In younger children, the use of a sterile newborn suction catheter carefully introduced through the vaginal introitus is recommended. The vaginal secretion can be collected by simple aspiration or obtained with a small amount of saline dropped within the vestibule and then removed using an attached syringe. A Gram stain is the most simple diagnostic technique but there is very little literature dealing with vaginal smears in children: the discovery of leucocytes in vaginal secretion as an indicator of the growth of bacterial pathogens revealed high sensitivity, but a specificity of only 59%. Consequently, the predominant growth of a pathogen in an appropriate culture on agar plates is considered the primary diagnostic tool.

If night-time itching suggests the presence of pinworms, the mother should be instructed to press the sticky side of a piece of adhesive tape onto the skin adjacent to the anus, at the child’s awakening, and then to stick it on a slide for microscopic examination for ova. If the child has a history of a diarrhoeal illness, it is appropriate to propose a faeces culture. Depending on the history, a urine sample for culture may also be useful.

Table 1
Points for the medical history.

- Atopy, allergies and contact sensitivities (also in parents)
- Hygiene habits
- Physical activities (cycling, horse-riding, swimming…)
- Voiding habits
- Previous or current urinary infections
- Bowel irregularities and recent gastroenteritis (the latter also in the family)
- Enuresis, encopresis
- Recent infectious diseases (chickenpox, glandular fever)
- Pharmacological treatments (antibiotics, corticosteroids)
- Symptoms (soreness, itching, burning, dysuria, discharge), their localisation, time of day when disturbance is worst
- Social setting (who are the caregivers? where is the child during the day?)
If bleeding or a recurrent malodorous discharge raises the suspicion of a foreign body, a vaginoscopy in sedation should be planned.

A competent clinical examination should also comprise diagnosis of genital lesions related to viral diseases: the wart-like lesions caused by Papilloma virus, the blisters and ulcers related to the Herpes virus and the pink dome-shaped growths of Molloscum contagiosum; in selected cases nucleic acid amplification tests may be needed to clarify the diagnosis.

In the differential diagnosis, the possibility that vulvodynia, as expression of a neuropathic pain disorder, can occur even in very young girls must be borne in mind. Sudden nocturnal vulvovaginal burning, sometimes associated with enuresis, appears from retrospective studies to be a marker of the tendency to chronic painful syndrome in the genital area, and is frequent in the history of women suffering from vulvar vestibulitis syndrome. The diagnosis is often made after exclusion of other causes: a mild vestibular erythema can sometimes be present: a gentle cotton swab testing for tenderness at the posterior introitus or in the surrounding area generally reveals discomfort.

**Causes of specific vulvovaginitis**

Knowledge of the normal vaginal microflora in prepubertal age is an essential prerequisite for definition of the pathogens of the lower genital tract. The results of studies on healthy children, using appropriate methods of specimen collection and encompassing the possibility of sexual abuse, are shown in Table 2.

The main causative agents of paediatric vulvovaginitis are represented by *S. pyogenes*, *H. influenzae* and *E. vermicularis*.

*S. pyogenes* (*Streptococcus β hemoliticus* A group) is a spherical Gram-positive bacterium present in the upper airways of 5–15% of asymptomatic individuals. It is a common cause of pharyngitis in school-age girls; a different serotype is involved in impetigo: various studies suggest that vaginal infections can arise from a previous respiratory or skin source. A family history of pharyngitis may also be present. The onset of symptoms is generally sudden with seropurulent and sometimes haematic discharge; an erythematous vulvitis with involvement of the perianal area is often present, together with dysuria related to the burning of skin at voiding.

The important role of *H. influenzae* and particularly but not exclusively of the unencapsulated strains of this Gram-negative coccobacillus as an agent of vaginal infection, as well as of otitis and conjunctivitis, has been documented for many years. The divergences between the various clinical reports are
probably related to the fact that this agent requires appropriate media for its culture, preferably chocolate agar.\textsuperscript{13} Most strains of \textit{H. influenzae} are opportunistic pathogens and cause an authentic infection only when other factors (such as a viral infection or reduced immune function) create an opportunity. In areas where the vaccination against encapsulated type b – as an agent of acute bacterial meningitis – is widespread, the isolation of all bacteria of the \textit{Haemophilus} genus can be partially reduced.

Another known cause of vulvovaginitis is pinworm infestation. The clinical history is generally more indicative than the search for eggs, and a negative test does not rule out this pathogenesis. Sometimes bowel flora are isolated in the vaginal cultures.

The isolation of yeasts is not frequent, but both \textit{Candida albicans} and \textit{C. glabrata} may be found in small children wearing diapers or in subjects with predisposing factors, such as recent courses of antibiotics or corticosteroid treatments or those suffering from diabetes. The recovery of yeasts in girls during pubertal maturation is more frequent, generally associated with the presence of vaginal \textit{Lactobacilli}.

Vaginal involvement during infections caused by \textit{Yersinia enterocolitica} or \textit{Shigella flexneri} is also reported, especially in communities where these pathogens are endemic. The first is a species of Gram-negative bacterium belonging to the family of \textit{Enterobacteriaceae}; the infection is acquired by consumption of undercooked pork, milk or contaminated water and produces severe diarrhoea, with fever and sometimes mesenteric adenitis and acute terminal ileitis. \textit{Shigella} are Gram-negative, highly infectious bacteria transmitted through the faecal–oral route, which can invade the epithelium of the colon, causing dysentery.

The predominant growth of \textit{Staphylococcus aureus} and \textit{Streptococcus agalactiae} (\textit{Streptococcus \textbeta \ hemolyticus \text{B group}}) in vaginal cultures from symptomatic girls is not rare, even if their role as pathogens is questionable. In fact, both are saprophytic bacteria, but the possibility that they act as opportunistic pathogens when the child has a temporary decrease in her immune defenses has been acknowledged. The first is present on the skin, particularly perineal, in the nose and the pharynx and can became infectious in association with certain risk factors, such as atopic dermatitis and low serum iron; the second colonises the bowel and the urinary tract.

Bowel flora (e.g., \textit{Escherichia coli}, \textit{Enterococcus foecalis} and \textit{Proteus mirabilis}) are frequently present in vaginal cultures, in addition to \textit{Streptococcus viridans}, a name covering a large group of commensal streptococcal bacteria, with low pathogenicity, especially abundant in the mouth. Other opportunistic bacteria that are occasionally involved are derived from the skin flora, such as \textit{Pseudomonas aeruginosa} and non-diphtherial \textit{Corynebacteria}.

In rare cases, a pathogen primarily transmitted through sexual contact may cause vulvovaginitis in a child: a repetition of the culture or of a specific nucleic acid amplification test is mandatory, together with an appraisal in very small children of the possibility of perinatal transmission.

\textbf{Table 2}

<table>
<thead>
<tr>
<th>Anaerobes</th>
<th>Aerobes</th>
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<tbody>
<tr>
<td>Gram positive:</td>
<td>Gram positive:</td>
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<tr>
<td>\textit{Actinomyces}</td>
<td>\textit{Staphylococcus aeruginosa}</td>
</tr>
<tr>
<td>\textit{Bifidobacteria}</td>
<td>\textit{Streptococcus viridans}</td>
</tr>
<tr>
<td>\textit{Peptococcus}</td>
<td>\textit{Enterococcus foecalis}</td>
</tr>
<tr>
<td>\textit{Peptostreptococcus}</td>
<td>\textit{Corynebacteria or Diphtheroids}</td>
</tr>
<tr>
<td>\textit{Propionibacterium}</td>
<td></td>
</tr>
<tr>
<td>Gram negative:</td>
<td></td>
</tr>
<tr>
<td>\textit{Veillonella}</td>
<td></td>
</tr>
<tr>
<td>\textit{Bacterioides}</td>
<td></td>
</tr>
<tr>
<td>\textit{Fusobacteria}</td>
<td></td>
</tr>
<tr>
<td>\textit{Gram negative cocci}</td>
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Neisseria gonorrhoeae can be present in vaginal purulent discharge, but is a multisite infection, so that cultures from the rectum and the oropharynx should also be obtained. The use of current nucleic acid amplification tests for this diagnosis gives less specific results. If we exclude a maternal infection at the time of delivery, the possibility of transmission of the bacterium through contact with contaminated objects or surfaces is extremely low and an evaluation of the child for possible sexual abuse, carried out by a specialised team, is called for.

Vulvovaginal infection with Chlamydia trachomatis may be both symptomatic and asymptomatic. The possibility of infection of this bacterium of the non-stratified vaginal epithelium of children has been demonstrated. The gold standard for diagnosis of chlamydial infection in children continues to be the culture of the vagina and rectum, but, recently, the available DNA probes have also been admitted, where cultures are not available, with the recommendation of a confirmatory test. In prepubertal children with C. trachomatis, penetrative sexual contact is the most likely mode of transmission. In very young children, the acquisition can occur through perinatal inoculation from infected cervical secretions during delivery or through caesarean section after rupture of infected membranes. Neonatally acquired disease has been associated with the co-existence of conjunctival or nasopharyngeal localisation. There are reports of perinatally transmitted Chlamydia infection persisting for up to 3 years.

Trichomonas vaginalis can be identified from vaginal discharge as mobile ciliated protozoan via wet-mount examination or culture: in children older than 1 year, this isolation raises serious suspicions about sexual abuse, but clear evidence of the age at which vertical transmission can be ruled out is lacking.

In relation to viral lesions, the presence of anogenital warts could be a marker of sexual abuse, especially in older prepubertal girls. However, the possibility of different modes of transmission (e.g., vertical, through inoculation from cutaneous warts of caregivers, through auto-inoculation from cutaneous warts and so on) has also been demonstrated. Human papillomavirus (HPV) typing could be helpful in the identification of genital types, but the data present in literature about suspected sexual abuse in children are limited. Moreover, considering that there is a lack of adequate studies about the incubation or latency period in this age group, we cannot assume a cut-off age above which vertical transmission can be ruled out.

Genital herpes lesions can be caused by both herpes simplex viruses (HSVs), types 1 and 2, with clinical presentation very similar to that in adult women, and comprising watery blisters or sores on the skin and mucous membranes. The virus is transmitted through close contact with lesions anywhere in the body, so that it can be acquired by sexual and non-sexual contact and through auto-inoculation. A confirmation of the diagnosis can be obtained through viral cultures or polymerase chain reaction (PCR). There are no major studies addressing the seroprevalence of HSV-1 or HSV-2 antibodies in abuse-suspected children. Generally, when a child has genital herpes lesions without any evidence of different transmission, the possibility of sexual abuse should be considered, but the infection itself is not seen as decisive evidence of abuse.

If the presence of a sexually transmitted disease arouses the suspicion of sexual abuse, the use of laboratory results in medico-legal proceedings demands a chain of evidence for the samples collected, so that treatment can be commenced without the need for the examination to be repeated.

Table 3 lists the pathogens more frequently responsible for vulvovaginal infections in children.

In older girls, when pubertal oestrogens alter the vaginal milieu, enabling the growth of lactobacilli, Gardnerella vaginalis, Mobilunculus, Mycoplasma hominis and Ureaplasma urealyticum, can also be isolated: there is no evidence regarding the probability of sexual transmission of these bacteria in this age group.

Management

If the history and the clinical examination suggest a nonspecific vulvitis, it is important to instruct the girl and her mother in a few basic rules of vulvar hygiene: avoid contact of the genital area with deodorants, perfumed soaps, bubble baths or shower gels and preferably choose oily detergents; dry the ano-genital region thoroughly after bathing or swimming; wipe the genital area from front to back after using the toilet; use plain white toilet paper; wash hands frequently, choose white cotton underwear washed with unscented and white detergents; void with the legs well open.
An emollient and protective cream may offer symptomatic relief. The use of topical antimicrobials should be restricted to situations where a bacterial superinfection is suspected. Low-dose hydrocortisone cream can be used for a limited period of time to break the itching–scratching–infection cycle.

If *S. pyogenes* is identified in culture, or even where the symptoms and the clinical history point significantly to this aetiology, an oral treatment with amoxicillin 50 mg kg\(^{-1}\) daily divided into three doses for 10 days is recommended. It has been demonstrated that recurrence, especially in younger girls, may be associated with asymptomatic pharyngeal carriage in the child or in a family member. The failure of penicillin derivatives to eradicate the bacterium can be related to pharyngeal colonization with beta-lactamase generating co-pathogens with *in vivo* inactivation of the drug, or to a capacity of the micro-organism to hide within the pharyngeal cells.\(^{19}\) A suggested option for the eradication of the *Streptococcus* carriage is the association of amoxicillin with rifampin 10 mg kg\(^{-1}\) every 12 h for 2 days.

Amoxicillin is also the first-line antibiotic for mucosal infection caused by *H. influenzae*; in several countries, strains of non-encapsulated *Haemophilus* producing beta-lactamase are described. In such cases, or where the treatment fails, the use of amoxicillin–clavulanate is recommended.

The standard treatment for pinworms is 100 mg of oral mebendazole, repeated 2 weeks later to kill the parasites that may have hatched before the initial dose. An alternative is pyrantel pamoate 10 mg kg\(^{-1}\) in a single administration. Underwear and bedding should be carefully laundered. This approach should be followed as empiric treatment in all cases where clinical features suggest infestation.

The first-line treatment for *C. albicans* infections is topical antifungal creams (e.g., clotrimazole and miconazole) for 6 days, combined with bathing in slightly alkaline solutions; in children with contact reactions to imidazole derivatives, boric acid preparation can be suggested. In immuno-suppressed subjects, in the case of relapse or of the need for drugs to facilitate yeasts, oral fluconazole 20 mg kg\(^{-1}\) in a single dose should be considered. *C. glabrata* is less sensitive to conventional antifungal creams, and longer periods of treatment with boric acid 1% cream are recommended.

The treatment of choice for extraintestinal focal *Yersinia* infection is trimethoprim and sulfamethoxazole at a dosage of trimethoprim 6 mg kg\(^{-1}\) daily for 3 days. The same drug is generally active against *Shigella*, but considering the frequency of antimicrobial resistant strains, a test of antibiotic susceptibility is generally indicated.

The decision for oral treatment of an opportunistic pathogen should be based on the severity of symptoms and an evaluation of the patient’s state of health. *Staphylococcus aureus* can be treated by applying topical mupirocin 2% 3 times daily to the affected skin; if a systemic therapy is required,

### Table 3

Agents of infective vulvovaginitis in childhood.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Opportunistic pathogens</th>
<th>Sexually transmitted pathogens</th>
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<tbody>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td><em>Staphylococcus aureus</em></td>
<td><em>Neisseria gonorrhoeae</em></td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td><em>Streptococcus agalactiae</em></td>
<td><em>Chlamydia trachomatis</em></td>
</tr>
<tr>
<td><em>Enterobius vermicularis</em></td>
<td><em>Streptococcus viridians</em></td>
<td><em>Trichomonas vaginalis</em></td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td><em>Escherichia coli</em></td>
<td><em>Papilloma virus, Herpes virus</em></td>
</tr>
<tr>
<td><em>Candida glabrata</em></td>
<td><em>Enterococcus faecalis</em></td>
<td>(sexual transmission not exclusive)</td>
</tr>
<tr>
<td><em>Yersinia enterocolitica</em></td>
<td><em>Proteus mirabilis</em></td>
<td></td>
</tr>
<tr>
<td><em>Shigella flexneri</em></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td><em>Corynebacteria</em></td>
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</tbody>
</table>
Amoxicillin + clavulanic acid (amoxicillin 45 mg kg\(^{-1}\) for 7 days) is the first choice, since this bacterium is typically penicillin resistant. The extensive resistance of S. aureus to many commonly used antibiotics has been reported in medical literature, and hence antibiotic susceptibility testing is called for.

Other opportunistic micro-organisms originating from the flora of the bowel or skin also frequently display the capacity to become resistant to various antimicrobials. This fact, together with the evidence of a link between extensive antibiotic use at both individual and hospital level and the risk of the emergence of multidrug-resistant bacteria,\(^{20}\) suggests that caution should be used in the prescription of general antibiotics as first-choice intervention. The first step of treatment should instead be the use of oral probiotics, sitz baths with soothing compounds and local application of antiseptic ointment.

The treatment of concomitant constipation through appropriate diet and, if necessary with lactulose or macrogol, can help to resolve vulvar symptoms related to intestinal pathogens.\(^{21}\)

Obviously, sexually transmitted infections require prompt and specific treatment, in line with the most recent guidelines.\(^{22}\)

Gonococcal infection can be treated in very young girls with an oral cephalosporin such as cefixime 10 mg kg\(^{-1}\) in a single dose, as an alternative to ceftriaxone 125 mg IM. A diagnostic re-evaluation is necessary because resistance to oral third-generation cephalosporins has emerged.\(^{23}\) The bacterium is also sensitive to azithromycin, 20 mg kg\(^{-1}\) (maximum 1 g) generally prescribed as a single dose, because of the extensive tissue penetration of the drug, its long half-life (\(>50\) h) and the capacity to concentrate in neutrophils and macrophages. Gastrointestinal side effects are not rare and allergic reactions are described.

This latter drug is also indicated for Chlamydia infection; but, in young children, the use of erythromycin ethylsuccinate 50 mg kg\(^{-1}\) day\(^{-1}\) orally divided into four doses for 14 days is recommended.

Trichomonas vaginalis is sensitive to nitroimidazoles: in paediatric age metronidazole is used primarily for oral treatment and the usual dosage is 15–25 mg kg\(^{-1}\) day\(^{-1}\) for 5 days.

If genital warts are asymptomatic, a clinical follow-up at 60 days has been proposed, to allow for a potential spontaneous clearance of the lesions. Otherwise, the recommended treatments are cryotherapy with liquid nitrogen or carbon-dioxide laser therapy. If laser therapy is not available, electrocautery in general anaesthesia should be restricted to young patients with a large number of genital warts. Imiquimod in 5% cream, a topical immunomodulator approved for genital wart treatment in adults, has also been proposed for off-label paediatric use in cutaneous warts\(^{24}\): it should be applied once daily at bedtime, 3 times a week for up to 16 weeks. The treatment area should be washed with soap and water 6–10 h after the application.

The first episode of genital herpes should be treated with antiviral therapy: acyclovir orally 3 times a day for 7–10 days, famciclovir orally 3 times a day for 7–10 days or valacyclovir 1 g orally twice a day for 7–10 days. Topical gentamicin can prevent superinfections.

Recurrent vulvovaginitis

If the symptoms of vaginal discharge and genital soreness do not resolve or appear again shortly after the end of the treatment, from a diagnostic point of view it is important to reappraise the history, to re-evaluate urinary and intestinal habits and disturbances, to consider the general status of the child (e.g., anaemia, viral diseases and chronic illnesses), to exclude the possibility of an allergic reaction to topical treatment or of a traumatic or abusive component and to appraise the option of a vaginal foreign body. The most common situation is the presence of wads of toilet paper, but all kinds of small objects can be recovered from the vagina during a vaginoscopic examination.

If the recurrences are related to S. pyogenes or to Haemophilus, the possibility of asymptomatic pharyngeal colonisation or of family carriers should be appraised, as well as the presence of co-pathogens.

In selected cases and in older girls, the possibility of a local treatment through a cut catheter, using clindamycin cream or metronidazole gel may be considered. The topical use of promestriene 1% cream for 10 days can be useful in promoting a transient increase in genital mucous that enhances the resistance to opportunistic or pathogenic micro-organisms.

Finally – especially in girls with traumatic life experiences – the possibility that vulvar pain may persist after the recovery from a local non-specific or specific inflammatory or dermatological disorder
has been demonstrated. Vulvar hypersensitivity or vulvodynia in childhood generally resolve after a limited period of treatment with low-dosage tricyclic antidepressants.5

References


