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Colposcopy of the Vulva and Perineum

Marta García-Yuste González,
Ana Maria Muñoz Ledesma,
Mayte Navarro Monge and José Schneider Fontán

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Abstract

Due to the normal histology of this area and the multifocal nature of vulvar intraepithelial disease, vulvoscopy is more difficult and less objective than the cervix examination. Basis of vulvar colposcopy as well as benign vulvar skin disorders that are usually found in a routine gynecology examination will be reviewed.

Keywords: colposcopy, vulvar, infections, trauma, Liquen esclerosus, HPV, VIN

1. Introduction

Colposcopy of the vulva—vulvoscopy—is an essential step in gynecology examination. However, it is not as systematic as colposcopic of the cervix examination due to the normal histology as this area and the multifocal nature of vulvar intraepithelial disease makes the examination more difficult and less objective than the cervix examination.

In this chapter, we will focus on the non-neoplastic disorders of vulvar skin disorders that we could usually find in a routine gynecology examination. Neoplastic vulvar disorders should need revised review in another chapter.

2. Tissue basis of colposcopy of the vulva

Presently, acetic acid is universally used as an adjunct to colposcopic examination [1]. As a tool for examination of the cervix and vagina, colposcopy is based on the variable absorption

and reflection of white light off different tissue interfaces [2]. Mucosal tissue color depends on the amount of hemoglobin viewed at the tissue surface, which gives the tissue different degrees of redness. The degree of redness depends on the distance between the underlying vasculature and the surface, which indirectly implies the amount of cellular material (stroma and epithelium) between the vessels and surface.

How acetic acid works as a contrast agent is unclear. Although acetic acid can improve the surface light reflection by dissolving mucus, it can also modify cellular proteins, including cytokeratins and nuclear proteins. Lastly, it is believed (but not yet proved) that acetic acid dehydrates the cell, which removes most of the cytoplasm. After dehydration, the cell is left with organelles, cytoskeleton filaments, and nuclear proteins. The effects of acetic acid are transitory: when rehydration of the cell cytoplasm occurs, any protein alterations revert to their normal state [3].

Because acetic acid specifically modifies cell cytoplasm and nuclear proteins, the contrast created by its application to the cervical and vaginal mucosa depends on the number of surface epithelial cells, the amount of cytoplasm in these cells, and the amount of nuclear material in each cell. It would follow that more light would be absorbed and little light would be reflected if there were few surface cells with small nuclei and large amounts of cytoplasm. The effects of acetic acid on these cells would require frequent reapplications to maintain the dehydrated state. The opposite (more light reflection) would occur if the surface interface were to consist of numerous cells with large nuclei and small amounts of cytoplasm. The effects of acetic acid would last longer because these cells would have little cytoplasmic fluid to rehydrate.

Thickness of the skin affects the opacity, and it varies from different areas of the vulva. Skin of hair-bearing areas is thicker than the skin of other areas of the vulva. This is why histologically identical lesions may have different appearance when present on different parts of the vulva. Its prominent surface keratin layer does not provide a clear view of the underlying blood vessels. Pigmentation can also obscure blood vessels. Therefore, vascular patterns are less marked and less reliable than with colposcopy of the cervix. Vascular aberrations such as punctuations and mosaic patterns do not easily develop on vulvar skin. They are less common and can be practically seen only on the non-bearing areas. Thus, leucoplasia and acetowhite epithelium are the most frequent colposcopic manifestations of vulvar pathology.

3. Technique of vulvoscopy

3.1. Inspection

The clinical examination of the vulva should form part of the routine gynecological examination, thus enabling both the correct diagnosis and treatment of numerous alterations and the prevention and early diagnosis of vulvar intraepithelial neoplasia (VIN) and invasive neoplasias. A correct evaluation should include basic anamnestic data, a list of symptoms localized in the vulva region, and a careful inspection and palpation. The vulva should be examined in a systematic fashion to include the mons pubis and labia majora, the labia minora, clitoral prepuce, clitoris, perineum, and anal areas. Attention should be given in the examination of the

vestibule to the hymeneal ring or remnants, to the gland openings (Bartholin's and Skene's), and to the urinary meatus.

The successive aim is to identify the main clinical aspects of the lesion which can be summarized as changes of color, presence of swellings on surface, and loss of substance. The critical evaluation of lesions should allow critical evaluation of lesions and also allow the gynecologist to formulate a diagnosis to propose to the pathologist. In this way, the collaboration between clinician and pathologist can contribute to progress in the diagnosis and treatment of vulvar diseases.

3.2. Application of acetic acid

It should be performed after applying 3–5% acetic acid to the vulva for several minutes using soaked gauze pads. Keratinization requires longer acetic acid application for effect and often renders typical colposcopic grading criteria useless. Colposcopy should begin by using the lowest magnification (6×) to quickly scan the vulva. Later, it can be proceeded to higher magnifications, as necessary, to examine smaller satellite lesions.

Acetic acid can cause acetowhitening of normal skin at the vestibule, normal variant of skin at the vestibule, and the normal variant of vestibular papillomatosis, which can limit its usefulness in practice. Any inflammatory condition of the vulva, including infection and trauma from intercourse, can cause acetowhitening (**Figure 1**).

3.3. Collins test

The test that uses a solution of toluidine blue to mark vulvar lesions is known as the Colling test. All foci of nuclear activity will keep the color and become stained. This may happen not only in neoplasias but also in the presence of ulcerations, lacetations, reparative changes, and



Figure 1. Normal acetowhitening of the vulvar skin.

parakeratosis. Historically, toluidine blue and Lugol's iodine solutions were used to stain the vulva and aid in identifying abnormal areas, but this practice has largely fallen out of favor because of high false-positive and false-negative rates [5].

3.4. Biopsy

Vulvoscopy can localize the lesion exactly. It usually cannot predict the histological nature of the lesion. Biopsy is indicated for visible lesions for which definitive diagnosis cannot be made on clinical grounds, possible malignancy, visible lesions with presumed clinical diagnosis that is not responding to usual therapy, lesions with atypical vascular patterns, or stable lesions that rapidly change in color, border, or size. Expert opinion is divided regarding the need for biopsy of all warty lesions, but biopsy should be performed in postmenopausal women with apparent genital warts and in women of all ages with suspected condyloma in whom topical therapies have failed.

Although information regarding the evaluation of women with immunocompromised conditions and human papilloma virus (HPV)-related disease is limited, human immunodeficiency virus (HIV)-seropositive patients and patients on immunosuppression after organ transplant may need biopsy of lesions when the level of suspicion is lower [6].

The area to be biopsied should be infiltrated with 1–2% lidocaine using a fine-gauge needle [7]. Epinephrine with the lidocaine can help with hemostasis but can make the injection burn.

After a test to ensure adequate anesthetic effect using fine-tipped forceps, a biopsy can be obtained using a cervical biopsy forceps, a keys punch 3–5 mm, or a small scalpel blade, depending on the size and nature of the lesion. Small biopsy sites can be treated with Monsel's solution or silver nitrate to achieve hemostasis. Only rarely absorbable sutures are needed. Location of biopsies should be indicated on a vulvar diagram or photograph, and multiple biopsies should be sent separately for pathologic evaluation (**Figures 2 and 3**).



Figure 2. Vulvar biopsy with cervical forceps.



Figure 3. Vulvar biopsy with keys punch.

The simplest method is biopsy with cervical biopsy forceps, but an attempt should be made to get a specimen, at least 5 mm thick. Ulcerative lesions and very thick lesions should be completely excised to rule out focal invasion (excision biopsy).

4. Physiological hyperplasia (vestibular papillomatosis)

The etiology and clinical significance of vulvar vestibular papillomatosis (VVP) are still controversial; in the past, it was considered to be a result of human papilloma virus (HPV) infection, but actually, there are many studies that show only a rare relationship between VVP and HPV. Currently, VVP is considered as an anatomical variant of the vulva [8].

VVP was first recognized in 1981. A few years later, in 1991, the report by the International Society for the Study of Vulvar Diseases (ISSVD) described papillomatosis of the vulvar vestibule as the presence of multiple papillae that may cover the mucosal surface of the labia minora. Since then, VVP has been reported under a variety of names: vestibular papillae, hirsutoid papillomas of vulvae, vulvar squamous papillomatosis, micropapillomatosis labialis, and many others [8]. VVP has been seen with HPV infection, but a consistent association has not been proven. Therefore, most recent studies consider VVP as a normal variant in the vulvar vestibule architecture, not directly related to infection by HPV [9]. It is likely that this finding is a female counterpart of male pearly penile papules [10] (**Figure 4**).

Vestibular papillomatosis has been recorded in healthy young women in the range of 1–33%. The papillae of 1–2 mm diameter have the same color as the adjacent mucosa. The lesions are soft and are symmetrical or may be linear. They may cover labia minora and the introitus vaginae to a variable extent. They may resemble warts but are distinguished by the fact that the bases of individual papules remain separate unlike in warts where filiform projections tend to fuse at the base and lesions are not confined to the vestibule or the inner aspects of labia minora. In addition, application of 5% acetic acid causes whitening of the lesions in warts, whereas vestibular papillae remain unchanged.



Figure 4. Vestibular papillomatosis.

5. Vulvar infections

Vulvar infections can be of variable location and multiple etiologies. Infections of the lower genital tract may be both specific and nonspecific, and affect the vulva more or less intensely. Some vulvar infections begin in the vulva and others in the vagina or nearby organs [11].

The external organs of the vulva include the labia majora and minora (folds of skin), the clitoris, and the vestibular glands. The basic symptoms of vulvitis are superficial red, swollen, and moisture-laden lesions on the skin of the vulva.

The characteristic symptoms are erythema, edema, pruritus, excoriation, and ulcers.

During vulvoscopy, color changes, topography, surface contour, and angioarchitecture of all parts of vulva should be noted. There are some vulvoscopic images characteristic of vulvar infections.

1. In skin, areas acetowhite and raised on skin, or areas with high yellow-white spots. If there is a predominance of reddish lesions, we may suspect infection by candida, dermatofitides, syphilis, erysipelas, or simply subcutaneous cellulitis.
2. In the mucosa, the infections produce an image of the mucosa acetoblanca and without being elevated.
3. We can visualize in the whole vulva injuries of the type of fissures, erosions, and ulcers of different characteristics.

4. The presence of tumors of infectious component makes one think of infection in sweat glands, sebaceous glands of the vulva or even in follicles, or Bartholin's glands.

6. Bacterial infections

6.1. Folliculitis

Local infection of the hair follicle of vulvar hair by germs of the type *Staphylococcus aureus* or *Streptococcus*. This can happen because of shaving, waxing, or even friction.

It is described as an inflammation of the skin surrounding the follicle and erythema with elevation, small painful erythematous plaques, or palpation with punctate pustule. The treatment is usually local topical antibiotic, and in cases of increased dissemination systemic antibiotic treatment, penicillin derivatives such as clavulanic amoxicillin or minocycline and in topical treatment mupirocin.

6.2. Cellulitis

Infection of the subcutaneous cellular connective tissues was found below the skin in the vulvar area, and with easy extension to other areas through the subcutaneous tissue. The entrance of the bacteria can be from a wound or erosion or a frequent boil on the vulva.

It is described as an erythematous zone, warm and with a slight edema that affects the subcutaneous tissue.

The most frequent germs in cellulitis are *Staphylococcus* and *Streptococcus*. Group A strep (*Streptococcus*) bacteria are the most common cause. The bacteria enter your body when you get an injury such as a bruise, burn, surgical cut, or wound.

Their treatment must be with systemic antibiotic, clavulanic amoxicillin, or ampicillin (Figure 5).

6.3. Necrotizing fasciitis

It is a severe acute bacterial infection that spreads tissue through subcutaneous cells and fascia resulting in tissue necrosis. One-third of patients end up in septic shock with multiorgan failure. Treatment should be rapid with hemodynamic support, extensive surgical treatment, and systemic antibiotic therapy.

In the case of the vulvar region may be associated secondarily to surgical processes, such as partial vulvectomies, episiotomies of labor, or vulvar tears due to trauma.

6.4. Hidradenitis suppurativa

Hidradenitis suppurativa (HS) [12] is an uncommon skin condition that affects the vulva and other parts of the skin. The pimple-like bumps tend to develop in places where everyday

pimples do not appear. Chronic inflammatory diseases of apocrine sebaceous glands are subsequently infected by bacteria such as *Proteus*, *Escherichia coli*, *Klebsiella*, *Pseudomonas*, *Streptococcus*, or *Staphylococcus*.

Initially, they are subcutaneous nodules that evolve occasionally to the formation of abscess due to bacterial superinfection and rupture. It can affect the skin of the vulvar region and fistulize later.

Early diagnosis and treatment can prevent HS from worsening. Early and long-term treatment may help control pain, promote wound healing, keep new lumps from forming, and prevent



Figure 5. Vulvar cellulitis.



Figure 6. Pimple-like bumps in hidradenitis suppurativa.

complications. The treatment is surgical with drainage and associated antibiotic treatment, sometimes systemic, depending on the dissemination and severity of infection (**Figure 6**).

7. Bartholin's abscess

The Bartholin glands are located under the skin on either side of the opening of the vagina. It is an infectious process secondary to the obstruction of the duct of the Bartholin's gland that favors bacterial overinfection. Generally, the germs that produce the infection are mixed bacterial flora.

Clinically, it manifests as a tumor, with pain, blushing, and local heat.

Generally, in the acute process with surgical drainage with marsupialization of the gland or spontaneous drainage is sufficient associated with the use of oral antibiotics (cephalosporins, amoxicillin, and doxycycline).

7.1. Syphilis

It is a sexually transmitted infection caused by the mildly contagious *Treponema pallidum*.

The initial lesion is called primary syphilis. It is defined as the primary chancre being the inoculation site of the treponema, and after a macula appear initial papules that end in an indurated and painless ulcer, this ulcer is usually accompanied by an inguinal adenopathy. This lesion is called chancre and is defined as a firm, painless, and non-irritating skin ulcer, but there may be multiple sores. The initial lesion may appear on the vulva, vagina, or cervix. It can be kept up to 2–8 weeks and then cure spontaneously.

Secondary syphilis can manifest at 6 weeks or 6 months later by hematopoietic dissemination of the treponema. At this time, the characteristic lesions of the vulva are flat condylomas and erosive macular exanthema (**Figure 7**).



Figure 7. Syphilis lesions.

Tertiary syphilis occurs in cases that have not been treated. After a few years after the first infection, it is characterized because it has no characteristic vulvar lesions.

The diagnosis of primary and secondary syphilis can be performed with a microscopic examination in dark background, in which the spirochete can be visualized, and another diagnostic method is the serological tests, although these become positive in the late primary phase (VDRL and RPR or specific TPPA and FTA-ABS).

The treatment in any stage is with benzathine penicillin G injected into a muscle 2.4 million. In tertiary syphilis, we should use benzathine penicillin G intravenous.

7.2. Chancroid

Sexually transmitted disease is caused by *Haemophilus ducreyi*. *H. ducreyi* is a fastidious gram-negative coccobacillus bacteria frequent in the third world.

After a period of incubation of 5–7 days, lesions develop in the vulvar area, clitoris, or lips. With multiple painful papules surrounded by erythema, these lesions end up overinfecting and end up ulcerating. The chancre is soft superficial and surrounded inflammatory erythema with necrotic background. Not all patients are presented with this chancre, one-third presents multiple ulcerations that tend to unite and are accompanied by the presence of inflammatory and painful inguinal adenopathy.

The diagnosis is made by staining gram. *H. ducreyi* can be cultured on chocolate agar. The treatment is a single dose of azithromycin or ceftriaxone.

7.3. Lymphogranuloma venereum

Lymphogranuloma venereum is an uncommon sexually transmitted disease caused by *Chlamydia trachomatis*. The *lymphogranuloma venereum* is endemic in certain areas of Africa, Southeast Asia, India, the Caribbean, and South America. It is rare in industrialized countries.

It is characterized by a painless ulcerated lesion in the vulvar or vulva fork, which at 15 days is associated with multiple and acute regional lymphadenitis. In vulvar lesions, the most affected nodes are the obturators.

Diagnosis is by culture or arrest of antibodies.

The treatment is oral doxycycline or erythromycin.

8. Fungus infection

8.1. Candidiasis

It is the most frequent vulvar infection and is usually associated with vulvovaginitis. Produced by candida fungus, saprophytic fungus is usually found in the genital and intestinal tract.

In our environment, the most frequent is *Candida albicans* and is estimated to produce 90% of vulvovaginal infections. Other less frequent but more resistant to treatment candida may be *Candida krusei*, *Candida glabrata*, or *Candida tropicalis*.

The clinic is variable and more in vulvar involvement, it may be asymptomatic, or produce pruritus attempt with erythema and vulvar edema. If accompanied by vaginitis, there will also be whitish leucorrhoea. In advanced cases, we can see papules and pustules with ulcerations and fissures.

Treatment is with local or systemic imidazoles. One should always think about discarding states of immunosuppression (**Figure 8**).

8.2. Dermatophytosis (Tinea infections)

Dermatophytosis (tinea) infections are fungal infections caused by dermatophytes—a group of fungi that invade and grow in dead keratin. Several species commonly invade human keratin, and these belong to the epidermophyton, microsporum, and trichophyton genera. They tend to grow outward on skin, producing a ring-like pattern, which coined the term “ring-worm.” The lesion is erythematous and itchy and extends through the folds and inner side of



Figure 8. *Candida albicans* vulvovaginal infection.

thighs, also called margin eczema of Hebra. The treatment is with antifungals agents, either topically or systemically (through the blood).

9. Parasites infection

9.1. Scabies

It is an infection produced by the *Sarcoptes scabiei* or the itching mite that is a parasitic arthropod that penetrates the skin and causes scabies. Lesions are considered to be a skin hypersensitivity reaction to the parasite.

The lesions are lines or grooves that have a small papule at the end. It is very pruriginous and is accompanied by scratching injuries. The diagnosis is made by visualizing the parasite in lesions.

The treatment is with 5% permethrin.

9.2. Pediculosis pubis

Pediculosis pubis is a human ectoparasitosis caused by *Phthirus pubis*, this is generally consider of sexual transmission and variable percentages is associated with other diseases of this kind.

It is an infection caused by lice, *P. pubis*, in vulvar hair. Pediculosis is a very contagious sexually transmitted disease. The parasite can survive up to 24 hours outside the host.

The primary clinic is pruritus, and as a consequence, the visible lesions are scratch lesions.

Diagnosis is the visualization of the insect or nits.

Treatment also was with 1% permethrin.

10. Virus infections

10.1. Molluscum contagiosum

It is an infection produced by a Poxvirus. The transmission is by direct contact and it is frequent in children. In adults, it can be considered sexually transmitted by contact. The lesion is characterized as a pink papular elevation, that then becomes more blauecina, is accompanied by an erythematous halo, the lesion is very pruriginous and is usually umbilicated.

They are multiple and of small sizes.

The treatment is with surgical or medical curettage.

10.2. Herpes virus

A total of 80% of vulvar and genital herpes virus lesions are produced by HSV-2 and estimated to be 15% HSV-1. Its prevalence has been increasing in recent years. Transmission may be by direct contact with ulcerated lesions or by relation to an asymptomatic person.

Vulvar lesions are vesicles in a different location with ulcers and erythema around them, characterized by being very painful. If it affects the urethra, it can lead to dysuria.

The diagnosis is clinical and confirmed by viral culture. Treatment is with Acyclovir, guanosine analog, or famciclovir or valaciclovir (**Figure 9**).



Figure 9. Vulvar herpes lesions are vesicles.

11. Human papilloma virus (HPV) infection

Papillomaviruses are a large and diverse group of viruses. It includes approximately 200 fully described types that have been detected in humans. Human papilloma viruses (HPV) are etiologic agents during various benign and malignant lesions of mucous membrane and skin epithelium. HPV is transmitted through contact with infected skin or mucosa. Very importantly, persistent HPV infection of certain types is a leading cause of carcinoma of uterine cervix, penis, vulva, vagina, anal canal, and fauces (including tongue base and tonsils). HPV infection prophylaxis is the best means to control HPV-conditioned diseases, and vaccination, as had been demonstrated, is the most effective method of its prophylaxis (**Table 1**).

A. Clinical: evident without magnification or acetic acid
1. Acuminate
2. Papular
3. Pamilomatosus
B. Subclinical: better assessed by magnification and acetic acid
1. Micropapillary
2. Flat
C. Non-clinical: evident by laboratory techniques

Table 1. Human papillomavirus (HPV) nomenclature.

HPV types are divided into low-risk and high-risk types based upon associated risk for cancer. The low-risk types HPV 6 and/or HPV 11 are detected in around 90% of anogenital warts, although coinfection with other low-risk or high-risk types of HPV is common.

Principle characteristics and clinical manifestations of papillomavirus infection are examined as follows:

11.1. Clinical HPV infection

HPV infection is the most common sexually transmitted disease in the world. At least 75% of sexually active adults in the USA have been infected with at least one genital HPV type at some time [13]. The estimated prevalence rate of HPV anogenital infection in the US adult population is 10–20% among unvaccinated individuals. HPV infection rates are trending downward in countries where HPV vaccination has been implemented.

Condylomata are relatively common. Reported prevalence rates based upon reviews of administrative databases or medical charts and prospective physician reports ranged from 0.13 to 0.56%, and reported prevalence rates based upon genital examinations ranged from 0.2 to 5.1%. Condylomata acuminate (CA) is the most common in young adults [15].

Sexual activity is the primary risk factor for anogenital human papillomavirus (HPV) infection. Once acquired, HPV infection can enter a latent phase without signs or symptoms.

However, only a small proportion of patients infected by this virus will express the disease. Nevertheless, this dermatitis remains one of the most prevalent of sexually transmitted diseases and poses problems in its management. These problems are centered on phenomena of viral latency, which do not permit one to guarantee the cure of the patient, and the absence of specific anti-viral treatment.

Immunosuppression is associated with the development of larger and more treatment-resistant condylomata, higher rates of recurrence, and malignant transformation of anogenital warts. As examples, condylomata in patients with human immunodeficiency virus (HIV) infection, receiving immunosuppressive therapy, or with diabetes [16] can be challenging to

treat. Extensive anogenital warts have been reported in patients with human T-lymphotropic virus type I (HTLV-I) infection, and in association with the immune reconstitution inflammatory syndrome [14, 17].

Smoking has been associated with increased risk for condylomata. Risk for condylomata may increase as the number of cigarettes smoked per day and number of pack-years increase.

Male circumcision may reduce risk for HPV infection.

HPV may infect any part of the vulva, but initial changes most often appear on the areas traumatized during sexual intercourse. External anogenital warts are typically found on the vulva and groin. They often extend to the lower vagina, and sometimes the entire vagina is affected. Posteriorly infection might extend to the perineum, perianal skin, and/or suprapubic skin. During the examination, acetic acid is applied and the field is colposcopically examined.

11.1.1. *Condyloma acuminata*

Although human papillomavirus (HPV) 6 and HPV 11, low-risk HPV types, are responsible for most cases of CA, coinfection with high-risk HPV genotypes linked to anogenital and head and neck cancers is common.

In patients who develop CA, the usual incubation period is three weeks to eight months.

In most cases, clinicians familiar with the clinical manifestations of CA can diagnose CA based upon the physical examination. Findings that suggest CA are single or multiple soft, smooth, or papillated papules or plaques are limited to the anogenital area. The color varies: warts may be white, skin-colored, erythematous (pink or red), violaceous, brown, or hyperpigmented. Anogenital warts are usually soft to palpation and can range from 1 mm to more than several centimeters in diameter. The warts are typically asymptomatic but may be pruritic.

Patients may have simultaneous infection of the genital area and perianal skin. Therefore, all areas of predilection for CA (vulva, penis, perineum, perianal skin, mons pubis, and crural folds) should be examined. Of note, uncircumcised foreskin or hair can obscure warts, warranting careful examination.

The physical examination should also include an assessment for other clinical signs that may suggest coexisting sexually transmitted diseases, such as ulcerations, adenopathy, vesicles, or discharge.

If there is uncertainty about the diagnosis, a biopsy should be performed. A shave procedure to remove a suspected wart or sample a large suspected wart is usually sufficient.

In addition, a biopsy to confirm the diagnosis and rule out malignancy is beneficial for CA that appear refractory to treatment, especially in immunosuppressed patients. Other indications for biopsy include atypical features (e.g., induration, fixation to underlying structures, bleeding, atypical pigmentation, or ulceration).

Human papillomavirus (HPV) testing of warts is not routinely indicated for diagnosis. Testing does not confirm the diagnosis and does not influence management of CA [18].

Application of acetic acid has a low positive predictive value for diagnosing external anogenital warts. Therefore, use cannot be advocated for diagnosis [19]. False-positive results commonly occur, resulting from parakeratosis in other pathologic processes (e.g., psoriasis, candidiasis, healing epithelium, and lichen planus). The pain associated with acetic acid examination is another reason to avoid its use.

The evaluation of patients with CA should include a review of the need for testing for other sexually transmitted diseases and concomitant internal involvement.

Patients with external anogenital warts may have concomitant involvement of the urethra, vagina, cervix, or rectum.

Giant condyloma acuminatum is a rare tumor first described as Buschke-Löwenstein tumor. The disease begins as an apparently straightforward viral wart, but relentlessly enlarges destruction to surrounding tissue. It is a low-grade form of squamous cell carcinoma associated with HPV 6 and 11 that most commonly manifests on the glans penis, foreskin, and perianal regions. Giant condyloma acuminatum can manifest in large cauliflower shapes and can form fistulas and/or abscesses with local neoplastic invasion. Clinically, the tumor looks malignant, but in contrast to cancer, it does not metastasize. It tends to infiltrate underlying tissues and cause local destruction.

For women with limited vulvar disease who can comply with self-therapy at home, we suggest imiquimod over podophyllotoxin as initial medical treatment. For those who cannot comply with self-therapy or fail self-therapy, we suggest treatment with trichloroacetic acid (TCA) rather than cryotherapy.

Laser ablation is our preferred surgical approach as it is possible to reach into the vagina and the depth of treatment can be controlled (**Figure 10**).

11.2. Subclinical infections

Subclinical infections may be visualized through the colposcope after the application of 3–5% acetic acid. They are associated with intraepithelial disease (VIN) in 10–20% of cases. These lesions are distributed around the vaginal introitus, on the perineum and perianal areas. They can be asymptomatic, but in many women, they can cause pruritus and dyspareunia. Vulvar inspection will be normal skin, and colposcopically subclinical HPV infection cannot be distinguished from VIN, making biopsy necessary. Conservative treatment is recommended (**Figure 11** and **Table 2**).

11.2.1. Vulvar trauma

The etiological factors that can damage the genital tract are multiple and varied and range from births, coitus, foreign bodies, thermal stimuli, chemical, accidents, surgical acts and in another dimension, injuries or caused by sexual aggression.

The most severe forms that significantly compromise the anatomy or physiology of the genitals.



Figure 10. Vulvar condylomata.

The most frequent injuries are the direct ones and according to where they are located, we can speak of:

1. Hymen trauma: The hymen is a rudimentary membrane that is not very vascularized and can rupture with first relation or with the penetration of other objects such as tampons.
2. Vulvar tear: They can be secondary to sudden sexual intercourse or penetration of foreign bodies and usually have continuity with the vagina. Here, we could also describe the episiotomy or tear due to vaginal delivery.
3. Accident wounds are the most common vulvar trauma, as we have described before may be direct or indirect.

The direct ones are by falls, blows, or impalamientos with other objects. They are frequent in girls due to injuries with bicycles or blows when leaving the bath or pool.

The indirect ones we see them in great traffic accidents or collapses.

Treatment of injuries and injuries of the genital tract: It is designed to contain bleeding and plastic reconstruction of the injured organ if appropriate. The first will be done by ligating the



Figure 11. Acetowhite mosaic changes.

Feature	Low-grade lesion	High-grade lesions
Color	Snow white to bright white	Bright white to dull (oyster) gray
Lesion size and shape	Relatively large and geographic; raised and papillary	Relatively small; smooth and flat
Location	Throughout the ectocervix	In the upper transformation zone at or near the new squamocolumnar junction
Time interval to color change; number of reapplications	Slow to change; requires numerous reapplications to maintain color differential	Rapid change; requires few reapplications to maintain color differential
Border	Irregular; relatively indistinct	Straight, raised or rolled; prominent

Table 2. Acetowhite changes in low- and high-grade colposcopic lesions.

bleeding vessels that are identified or by hemostatic points. The wound will be sutured with loose stitches. There will then be a plugging in the area of the wound.

In the case of bruises, most cases require drainage to prevent the hematoma from dissecting the adjacent tissues by the tension they generate.

In all injuries, it must be ruled out that there has been no injury to internal organs either directly or indirectly.

The most common vulvar trauma is that produced by labor, vulvovaginal tear that may require subsequent suturing (**Figure 12**).

11.2.2. *Liquen esclerosus (LS)*

LS is a non-neoplastic chronic lymphocyte-mediated inflammatory dermatosis with distinctive dermal sclerosis and with a predilection for the anogenital skin in women. The true prevalence is not known.



Figure 12. Vulvar trauma.

It usually occurs in the anogenital region (85–98% of cases), but can develop on any skin surface. Extragenital lesions are present in up to 15% of patients, although this may be an underestimation. Vulvar LS can occur at any age but tends to have two peaks of onset: prepubertal girls and perimenopausal or postmenopausal women [4]. It is one of the most common conditions treated in vulvar clinics. The true prevalence is not known; estimates range from 1 in 30 older adult women to 1 in 59 women in a general gynecology practice to 1 in 300 to 1000 patients referred to dermatologists.

Pruritus and soreness or irritation are the most common symptoms of vulvar LS.

Other women are asymptomatic; in these patients, LS is detected by careful inspection of the vulva for the characteristic thin, white, wrinkled skin, and changes in vulvar architecture. For example, there may be loss of portions or all of the labia minora, and the clitoris may become buried under the fused prepuce. Although uncommon, active disease may be asymptomatic.

Classic vulvar LS is expressed as white, atrophic papules that may coalesce into plaques, and follicular plugging may be observed in early lesions. LS can also be hemorrhagic, purpuric, hyperkeratotic, bullous, eroded, or ulcerated. The lesions most frequently affect the labia minora and/or labia majora, although the whitening may extend over the perineum and around the anus in a keyhole fashion. Extension onto the genitocrural folds or buttocks also may occur. Fissuring is frequently seen at the posterior fourchette, perianally, in the interlabial folds, or around the clitoris. The introitus may have a yellow, waxy appearance. Fordyce spots (small raised papules along the inner aspect of the labia minora, which represent normal sebaceous glands) disappear.

Scratching may result in excoriations and secondary mild lichenification (thickening of the epidermis with exaggeration of normal skin lines), often associated with edema of the labia minora and the prepuce.

The vulvar architecture remains intact early in the course of the disease. As the disease progresses, the distinction between the labia majora and minora is lost, and the clitoris becomes buried under the fused prepuce. Shrinkage of the introitus and perineum causes dyspareunia and more fissuring upon intercourse or insertion of a speculum. At the end stages of LS, the vulva is pallid and featureless due to midline fusion, which leaves only a posterior pinhole orifice.

The diagnosis of vulvar LS is based upon the presence of characteristic clinical manifestations, ideally with histologic confirmation.

Evidence-based guidelines from the European Academy of Dermatology and Venereology state that not all cases of adult-onset vulvar LS require a confirmatory biopsy. However, a biopsy may be helpful to confirm the diagnosis or to reevaluate the diagnosis if initial treatment fails or if malignancy is suspected.

An association between LS and squamous cell cancer of the vulva (SCCV) has long been recognized and thought to be the result of chronic inflammation and scarring. Much of the available evidence of the relationship between LS and SCCV is based on historical studies and retrospective case series. Risk has never been defined in terms of treated versus non-treated or unrecognized disease, or to the length of time the disease has been present. A 4.5% frequency of SCCV arising in LS has been estimated, with an average duration of antecedent LS of 10 years. This frequency is probably an overestimate. Earlier detection, the introduction of potent topical corticosteroids, the more liberal use of outpatient biopsy, excision of abnormally thickened skin resistant to medical treatment, and an increased appreciation of the nature and management of the condition hopefully will contribute to a reduction in the risk of vulvar cancer in women diagnosed with LS today. Those women who are not treated or have irregular treatment for their LS seem to be at a greater risk of developing cancer, although the figures are too small to be statistically significant.

Therefore, we recommend treatment of all women with vulvar LS, including those who are asymptomatic, to try to prevent progression of the disease. The goals of therapy should be resolution of the symptoms (pruritus and pain) and signs of disease, including hyperkeratosis, fissuring, and ecchymoses [20]. Atrophy and depigmentation may sometimes improve with therapy; however, scarring, if present, will remain. Clinical photography may assist in monitoring of the disease and can be helpful when showing patients where to apply topical therapy.

We recommend initial treatment of vulvar lichen sclerosus with a superpotent topical corticosteroid ointment. We typically administer clobetasol propionate 0.05% ointment or halobetasol propionate 0.05% ointment daily at night for 6–12 weeks, followed by maintenance therapy two to three times per week if symptoms improve. Thickened hypertrophic plaques may respond best to intralesional corticosteroid therapy.

In patients with persistent symptoms, we suggest a careful evaluation for causes of treatment failure (**Figure 13**).

11.2.3. Vulvar intraepithelial neoplasia (VIN)

Traditionally, squamous VIN was classified into three grades, analogous to the three-grade cervical intraepithelial neoplasia classification. In 2004, ISSVD replaced the previous three-grade



Figure 13. Vulvar lichen sclerosus.

classification system with a single-grade system, in which only high-grade disease is classified as VIN [21]. In that system, VIN is subdivided into

1. Usual type VIN (including warty, basaloid, and mixed VIN)

Commonly, it is associated with carcinogenic genotypes of HPV and other HPV persistence risk factors, such as cigarette smoking and immunocompromised status.

2. Differentiated VIN: It is associated with lichen sclerosus and a squamous cell carcinoma of the vulva than usual type VIN. Furthermore, it has a higher recurrence rate [22] and decreased disease-specific survival from invasive squamous cell carcinoma [23].

Based on the 2015 ISSVD terminology of vulvar squamous intraepithelial lesions, usual type of VIN is now classified as vulvar HSIL, and differentiated VIN remains the same. Flat lesions associated with basal atypia and koilocytic changes (formerly termed VIN 1) are considered LSIL (condyloma or HPV effect) in the current 2015 ISSVD classification system.

11.2.3.1. Usual vulvar intraepithelial neoplasia (classic VIN, uVIN)

Basaloid/warty SCCs develop from classic or usual VIN (uVIN) which occurs more commonly, but not solely, in relatively young women between the ages of 40 and 50 years and is associated with high-risk HPV infection, most often HPV 16 and less commonly HPV 18 or HPV 33. In addition, uVIN is usually multifocal, multicentric, and therefore associated with other lower anogenital intraepithelial neoplasia including cervical, vaginal, and anal.

There has been an increase in the incidence of uVIN, and in some countries, the incidence has doubled in the past 10 years.

11.2.3.1.1. Gross findings

Low-grade uVIN presents usually as single or multiple pale-whitish areas, whereas high-grade uVIN presents as multifocal raised plaques or papules that tend to coalesce. A small percentage of the lesions (10%) may be hyperpigmented. There is a high frequency of multifocality in patients presenting with multiple lesions within the lower female anogenital tract [24].

Evidence exists that VIN III may progress to invasive vulvar carcinoma. However, the available literature suggests that the progression rate to invasive vulvar carcinoma is low (**Figure 14**).

11.2.3.2. Differentiated or simplex-type vulvar intraepithelial neoplasia

Although dVIN can occur in young patients, this type of VIN is usually found in postmenopausal women and tends to be unifocal and unicentric. Frequently, dVIN develops in women with chronic dermatological diseases such as squamous cell hyperplasia, lichen sclerosus (LS), and lichen simplex chronicus. In addition, mutation of the p53 gene seems to be an early event in the development of dVIN [25] with studies showing identical p53 mutations in LS and adjacent SCC.



Figure 14. VIN: hyperpigmented multifocal raised plaques.

11.2.3.2.1. Gross findings

dVIN is found in patients with chronic skin conditions related to LS, squamous cell hyperplasia, and lichen simplex chronicus. However, clinical presentation is nonspecific with patients often being asymptomatic. They may present with focal discoloration, ill-defined white plaques as well as red hyperkeratotic lesions. Pruritus and pain are the most frequent symptoms.

dVIN has a higher risk of progression to invasive SCC than uVIN, and time of progression to SCC is significantly shorter in dVIN cases when compared with uVIN.

Author details

Marta García-Yuste González*, Ana Maria Muñoz Ledesma, Mayte Navarro Monge and José Schneider Fontán

*Address all correspondence to: martagyuste@hotmail.com

1 Department of Obstetrics and Gynecology, Hospital Universitario Río Hortega, Valladolid, Spain

2 Faculty of Medicine, Valladolid, Spain

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