CHAPTER 1
Vulvar Dystrophies

Denniz Zolnoun, MD
Department of Obstetrics and Gynecology,
University of North Carolina School of Medicine, Chapel Hill, NC, USA

Pathology Notes: Chad Livasy, MD
Associate Professor, Department of Pathology and Laboratory Medicine, University of North Carolina School of Medicine,
Chapel Hill, NC, USA

Background

Vulvo-vaginal symptoms are among the most common reasons that women seek health care; upward of 6 million physician office visits are made by women of all age ranges for vulvo-vaginal symptoms.\(^1\) Despite such staggering statistics, most clinicians are not adequately prepared to diagnose and treat chronic vulvo-vaginal symptoms. Overlapping clinical appearance, symptoms, and pathophysiology, compounded by nonspecific histology on biopsy, are the main causes for confusion.

This chapter will focus on the following six non-malignant vulvo-vaginal conditions that clinically may raise concern about premalignant processes:

- Lichen sclerosis
- Contact dermatitis
- Lichen simplex chronicus
- Lichen planus
- Plasma cell vulvitis
- Desquamative inflammatory vaginitis

These conditions share overlapping symptoms of itching and burning to variable degrees. Collectively, these conditions are challenging to care for due to lack of consensus on diagnosis and treatment, intractable and fluctuating clinical course, overlapping morphology and histology, and significant individual variation in treatment response. Additionally, many of these conditions often coexist, posing yet another layer of complexity in deciphering the cause of a patient’s chief complaint. Given the intertwined pathophysiology, it is no wonder that the care of these patients seems more a proverbial shot in the dark than a stepwise methodical process.

The diagnostic definition of these six conditions is based on a constellation of symptoms, morphology, and histopathology. As noted in Table 1.1, the primary complaint of the first three conditions is itching, while the primary complaints of the last three are burning, rawness, and pain with intercourse. Thus, using a symptom-based approach, the discussion of these disorders is divided into two parts: conditions with primary complaints of itching (lichen sclerosis, contact dermatitis, and lichen simplex chronicus), and those with primary complaints of burning/rawness sensation (lichen planus, plasma cell vulvitis, and desquamative inflammatory vaginitis). Vulvar intraepithelial dysplasia (VIN), which is often associated with unilateral and focal itching, will be discussed in Chapter 2.
### Chapter 1

#### Table 1.1 Overview of vulvar dermatoses

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Morphology &amp; exam</th>
<th>Histopathology</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presenting Chief Complaint: Itching and Secondary Burning</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Lichen sclerosis (LS)</strong></td>
<td>Itching; secondary symptoms of dysparunia, dysuria, and burning develop from trauma and agglutination.</td>
<td>Thin, atrophic, wrinkled skin. Agglutination with loss of architectures. In addition may have superimposed features described under contact dermatitis and LSC.</td>
<td>Epidermal atrophy with loss of rete ridges. Upper dermis shows band-like infiltrate and homogenization of collagen. Squamous hyperplasia often present from chronic itching.</td>
</tr>
<tr>
<td><strong>Contact dermatitis</strong></td>
<td>Itching, burning and “dryness” sensation. Can be acute (allergic) vs. chronic (irritant). Washing with cold water suits symptoms.</td>
<td>Red, classic “diaper rash,” with variable excoriations in acute presentation. With chronicity appearance similar to LSC.</td>
<td>Dermal chronic infiltrate, spongiosis, acanthosis, parakeratosis. Similar to atopic/allergic dermatitis.</td>
</tr>
<tr>
<td><strong>Lichen simplex chronicus (LSC)</strong></td>
<td>Prolonged bouts of itching and scratching. Itching intensifies a night with scratching during sleep. Warm water/sitz bath provokes itch–scratch cycle.</td>
<td>Thick, pale orange-peel appearing labia majora and minora. Progressively ashy scaly vulva with exposure to air during exam. Otherwise similar to contact dermatitis with change in pigment</td>
<td>Lichenification: thickening in epidermus (acanthosis) AND stratum corneum (hyperkeratosis); additional findings similar to contact dermatitis.</td>
</tr>
<tr>
<td><strong>Presenting Chief Complaint: Burning &amp; Rawness</strong></td>
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<tr>
<td><strong>Lichen planus (LP)</strong></td>
<td>Burning pain, rawness, postcoital bleeding.</td>
<td>Red, well-demarcated lesions in vulva, vagina, and gingiva. On keratinized skin, flat-topped papules with lacy white dome; lesion-specific punctuate allodynia.</td>
<td>Lichenoid pattern: band-like lymphocytic infiltrate in the upper dermis with basal cell damage, cell death, or vacuolar alteration.</td>
</tr>
<tr>
<td><strong>Plasma cell vulvitis</strong></td>
<td>Burning sunburn-type pain and dryness, variable dysparunia.</td>
<td>Normal vagina. Irregular heart’s line with glossy moist well-demarcated red inner labial fold. Greater mechanical than punctuate allodynia.</td>
<td>Lichenoid vasculopathic pattern with band-like infiltrate of mainly plasma cells in the superficial dermis and extravasated RBCs.</td>
</tr>
</tbody>
</table>
Table 1.1 (Continued)

<table>
<thead>
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<th>Histopathology</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Desquamative inflammatory vaginitis (VIN)</td>
<td>Discharge, vulvar burning, irritation, and dyspareunia.</td>
<td>Normal vulva (mucosa and skin), dripping thin yellowish discharge at introitus; petechial redness on vaginal walls. Greater mechanical than punctate allodynia.</td>
<td>Biopsy non-specific; clinically similar to LP confined to vagina with excessive discharge.</td>
</tr>
</tbody>
</table>

Lichen sclerosis, contact dermatitis, and lichen simplex chronicus

Lichen sclerosis

Generally, lichen sclerosis (LS), also known as lichen sclerosis et atrophicus, affects women in two extremes of reproductive life: pre-puberty and menopause. While the prevalence of LS is unknown in the general population, it is estimated to be as high as 1% and constitutes the most common anogenital dermatitis. While most cases of LS appear de novo, LS lesions may develop at a site of injury and traumatized skin (Kobner phenomenon). The most common symptom of LS is intractable itching with secondary burning and rawness from self-inflicted trauma (scratching and rubbing). In addition, it is common for chronic sufferers to develop superimposed contact dermatitis. Characteristic findings on physical examination are hypopigmentation and thin wrinkled skin with atrophy of subcutaneous tissue. In addition, there is loss of vulvar topography caused by agglutination of the clitoral hood, with the clitoral glans “buried” under the fused tissue, and flattening of the labia minora. Age distribution and posttraumatic development of LS suggests a hormonal etiology, but to date no association between estrogen metabolism and LS has been identified. Nevertheless, estrogen therapy for associated atrophy is a common practice.

LS is one of the few dermatoses with specific histopathology. Lichenoid inflammation (a band-like upper dermal lymphocytic infiltrate) and dermal homogenization (loss of collagen) together are classic findings in LS. Although the presence of lichenoid inflammation and epidermal basal layer damage is not itself pathognomonic of LS, this finding in association with dermal homogenization is used by dermatopathologists to render a diagnosis of LS.

Complications associated with lichen sclerosis

Due to the severe itching associated with lichen sclerosis and the subsequent itch–scratch cycle, patients may develop superimposed contact dermatitis either caused by allergic reaction to a variety of topical agents or by irritation from rubbing. Intractable itching and scratching (the itch–scratch cycle) in turn gives rise to the characteristic skin changes seen with lichen simplex chronicus, namely a thick, leathery, excoriated skin. Comorbid lichen plans and malignancy has also been described in long-standing lichen sclerosis (see Clinical Scenario 1).

Contact dermatitis

Vulvar contact dermatitis is the most commonly overlooked vulvar condition, with a reported incidence of 20% to 30% in specialty vulvar clinics. Although it is usually not the primary cause of vulvar symptoms, it is often a compounding factor in patients complaining of persistent vulvar pruritus (eg, primary lichen simplex chronicus), irritation (eg, plasma cell vulvitis), or burning (eg,
generalized vulvodynia). This is not surprising considering the host of behavioral factors (eg, overzealous hygienic practices and self-medication) and clinical factors (eg, chronic use of high-potency steroids and polypharmacy) that are both associated with intractable vulvo-vaginal symptoms.\textsuperscript{7,8}

Similar to lichen sclerosis, the primary complaint of contact dermatitis is itching.\textsuperscript{7,9} An associated stinging sensation is common with allergic contact dermatitis, while an associated raw or chafing sensation is suggestive of irritant contact dermatitis (eg, diaper rash). The physical exam findings of contact dermatitis demonstrate varying degrees of redness interposed with normal skin. Although scaly skin is common with contact dermatitis in other areas of the body, it is not usually seen on the vulva.\textsuperscript{10} The moist and warm environment of the vulvar region does not readily reveal scaly dermatosis; however, with progressive airing one begins to see a scaly dusky hue over the labia, which is suggestive of atopic dry skin.

A cotton swab test is a useful tool for the differential diagnoses of vulvovaginal conditions such as contact dermatitis. The cotton swab test is conducted by applying the tip of the cotton swab perpendicular to the vulvar skin and asking the patient to rate the sensation as “a cotton swab sensation” versus “a pinprick sensation.” If the application of the cotton swab is perceived as a pinprick, then the test is abnormal (punctuate allodynia), which is indicative of an intrinsic inflammatory process of the skin, such as lichen planus. Patients with contact dermatitis, however, have a normal cotton swab test but demonstrate hypersensitivity to gentle stroking (mechanical allodynia).

Vulvar contact dermatitis can be broadly subclassified into two categories: irritant and allergic.\textsuperscript{7} Both variants of contact dermatitis have similar clinical appearances and often coexist. However, it is the nuances of the clinical presentation that favor one subtype over the other. The hallmark of allergic contact dermatitis in the acute phase is severe pruritus, vesiculation, and most importantly, a tendency to spread beyond the initial site of contact. Biopsy is only of value in ruling out malignant processes (squamous cell carcinoma)\textsuperscript{5} or premalignant processes (VIN lesions). More often than not, the biopsy results from cases of contact dermatitis are clinically vague, with descriptions such as “chronic inflammation with neuropil infiltrate,” “spongiosis,” “acanthosis,” and “parakeratosis.” These descriptors are simply histopathologic correlates of what is observed by the clinician. For example, the clinical correlates of acanthosis are an orange peel-appearing, thick skin, while the correlates of parakeratosis are scaliness and an ashy appearance following exposure to air.

**Lichen simplex chronicus**

Lichen simplex chronicus (LSC) is divided into two clinical subtypes: primary and secondary.\textsuperscript{11} Primary LSC refers to a condition that arises de novo on “normal” skin. As suggested by its alternate name, neurodermatitis,\textsuperscript{11} primary LCS is commonly associated with anxiety disorders. In contrast, secondary LCS develops because of a preexisting dermatologic disorder such as lichen sclerosis. Although the exact prevalence of LCS is unknown, it is estimated to affect up to 0.5% of the general population in western countries.\textsuperscript{11} In response to chronic excoriation associated with LCS, the vulvar skin thickens. It can be likened to a callous, similar to what is observed in the extremities. Histologic correlates of this thickening are described in terms of dermal (acanthosis) and epidermal (hyperkeratosis) thickening; otherwise, histologic findings in LSC are nonspecific (Table 1.1).\textsuperscript{11} In the presence of moisture, the skin assumes a wrinkly, white appearance, similar to how fingertips will wrinkle and whiten in a long hot bath. Thus, the term lichenification is used to describe the pale, orange-peel appearing, thick skin of the vulva that is seen in LSC. Other associated findings are decreased sensation on the affected skin and a change in skin pigmentation (hypopigmentation or hyperpigmentation).

**Summary**

Chronic diffuse itching is rarely caused by infectious conditions (eg, yeast infection) or premalignant processes such as VIN, which tend to cause focal, unilateral symptoms (Chapter 2). Many overlapping dermatoses are often present in a given patient. The key in deciphering the cause of a patient’s
Table 1.2 General vulvar care

**Minimizing Daytime Friction**
- Liberal use of oil-based creams such as Gene’s Vitamin E Cream.\(^a\) For patients with excessivesensitivity, use Crisco shortening or shay butter.\(^b\) Reapply throughout the day.
- Use cold water after using the bathroom to rinse the area. Ask patients to carry a water bottle for this purpose. Cold water (unlike warm water) stops itching.
- Instruct patients to not wipe but pad dry their perineum after washing with cold water.

**Abortng Bouts of Intense Itching Sensation**
- Apply deep pressure when faced with an itching sensation rather than rubbing of any kind.
- Reapply copious amounts of creams (as above).
- Place a bag of frozen peas wrapped in a thin towel over the labial folds and perineum.

**Abortng Nighttime Scratching During Sleep**
- Use a sedating agent (titrate slowly to maximal tolerance):
  - Doxepin 10–50 mg 1–2 h before bedtime
  - Diphenhydramine 25–50 mg 30 min before bedtime
  - Hydroxyzine 10–50 mg 2 h before bedtime
- Keep nails short and wear white cotton gloves at night.

\(^a\) Can be purchased from Sam’s Club or http://www.genesvitamine.com

\(^b\) Compounding pharmacy; for assessment of qualifications please refer to http://www.pcab.info/

Vulvar Dystrophies

Symptoms is to use a symptoms-based approach in alleviating symptoms, aborting the itch–scratch cycle, and ultimately promoting the skin’s health (Table 1.2). Targeted biopsy can then be used to rule out premalignant processes and to guide additional therapy. The case studies at the end of this chapter will provide a guide to differential diagnosis, relief of symptoms, and treatment approach for patients with LS and contact dermatitis.

**Lichen planus, plasma cell vulvitis, and desquamative inflammatory vaginitis**

Whereas lichen sclerosis, contact dermatitis, and lichen simplex chronicus are characterized by a chief complaint of itching, lichen planus, plasma cell vulvitis, and desquamative inflammatory vaginitis are primarily associated with symptoms of burning, pain with intercourse, and discharge (Table 1.1).

**Lichen planus**

Classical lichen planus (LP) is characterized by shiny, flat-topped, firm papules (bumps) on the extremities, trunk, and mucosa. The most common form of this mucocutaneous dermatosis that is seen in gynecology is known as vulvo-vaginal-gingival syndrome. Vulvo-vaginal-gingival syndrome typically presents as a single or multiple well-demarcated, intensely red lesions with a reticular appearance.\(^*\) In cases with extensive vaginal involvement, synechiae and varying degrees of vaginal obliteration are common. While oral lesions can vary from painless white lacy streaks to desquamative gingivitis, vulvo-vaginal lesions tend to consistently show lichenoid inflammation.

While lesions of LP on the mucosal surface are tender, lesions on the extremities (eg, wrist or ankles) are typically nontender. LP is a relatively rare condition (1–2% of the U.S. population); nevertheless the prevalence of LP is reported to be as high as 8% in the referral setting.\(^13,14\) Histolopathology in LP is characterized by lichenoid inflammation with basal layer damage (Table 1.1). As described earlier, lichenoid inflammation is also seen with lichen sclerosis. What sets LP apart from LS,  

\(^*\) Photo discussion of LP and other dermatologic lesions in differential diagnosis can be found at http://dermnetnz.org/scaly/lichen-planus
however, is the histologic absence of dermal homogenization (loss of collagen and sclerosis). Interestingly, the histopathology and morphology of LS and LP may converge over time. For example, it is common for patients with long-standing lichen sclerosis to develop clinical and histologic features of erosive LP. Similar to other inflammatory vulvo-vaginal conditions, the etiology of LP remains elusive. Similar to many such ulcerative lesions, LP is highly responsive to steroids and therapy with immunomodulators. Mucosal responsiveness to treatment varies depending on anatomic location. While oral mucosal lesions are highly responsive to treatment with steroids, vulvo-vaginal lesions tend to be more resistant and in fact more painful.14

Plasma cell vulvitis
Plasma cell vulvitis, or Zoon balanitis (the common term for the condition in men), is a benign but chronic and erosive inflammatory condition of the genital skin. While this condition is most often reported in uncircumcised men, its manifestation and prevalence in women is not well described. In either gender, however, plasma cell balanitis and vulvitis are often difficult diagnoses to make histologically and need to be correlated with clinical presentation. Histologic and clinical similarity between plasma cell vulvitis and LP has raised debate as to whether this is a distinct entity or a disorder within the spectrum of LP.15

The most common compliant is persistent rawness and sunburn sensation, painful intercourse, and pruritus. The diagnosis is rendered after excluding infectious conditions, specifically fungal infection. It is not uncommon for patients to have been treated with a variety of antifungal and/or antibacterial therapy before receiving the definitive diagnosis. Extensive and well-demarcated moist erythema in plasma cell vulvitis is confined to the vulvar mucosa, especially in the inner labial folds. Speculum examination is otherwise normal. Excessive discharge, loss of architecture, and agglutination are not characteristically observed. The clinical diagnosis can be confirmed by a biopsy showing a band-like infiltrate of plasma cells in the superficial dermis. The most effective treatment in men is circumcision when possible; otherwise, use of topical corticosteroids and immunomodulators such as tacrolimus is the mainstay of therapy. Because the pathogenesis of this condition remains unclear, variable response to treatment is common in clinical practice. Thus, trial and error using a variety of medications alone or in combination is a mainstay of practice.

Desquamative inflammatory vaginitis
Desquamative inflammatory vaginitis (DIV) is a specific inflammatory condition of the vagina and the subject of much controversy. The etiology and the population prevalence of DIV are unknown. While some authorities view DIV as an independent entity, others view it along the continuum of inflammatory conditions of the vulvo-vaginal region. Clinically, the diagnosis of DIV is rendered in patients who complain of increased vaginal discharge and pain with intercourse when no identifiable cause of vaginitis can be identified. Because postmenopausal atrophic vaginitis may have similar presentations, empiric therapy with topical estrogen should be considered as first-line therapy. Failure to respond after 3 to 6 months of estrogen therapy supports the diagnosis of inflammatory vaginitis such as DIV when all known etiologies been eliminated. Unlike LP and plasma cell vulvitis, however, the vulvar region in a DIV case is normal in appearance. DIV is characterized primarily by a sterile discharge that is a watery and yellow, and by painful intercourse. Examination of the vulva is often normal, although discharge of variable consistency may be present. Speculum examination may reveal synechiae, vaginal stenosis, and most commonly, erythema. Stroking the vaginal walls with a cotton swab is commonly associated with an intense burning sensation. Generally, histology shows nonspecific inflammation. Because DIV patients present with nonspecific symptoms of burning and pain, and because cursory examinations reveal limited clinical findings, it is important to conduct a detailed assessment of the vaginal wall and to specifically look for erythema and mechanical allodynia (burning sensation on stroking of the vaginal wall with a q-tip).
Summary

It is apparent from the above description of these six vulvo-vaginal conditions that there is much overlapping morphology and pathophysiology. Diagnosis of any these conditions can be confusing and is further complicated by the fact that there are three embryologically distinct skin types (juxtaposed on the labia) unlike any other area of body. Consider, for example, how dermatitis is a scaly disease in other parts of the body, yet the scales are typically absent in the vulvar region and even a sophisticated observer is likely to see only shiny, glazed skin.

Clearly, the treatment approach in clinical practice is symptoms-based in that it is more guided by ameliorating the symptoms than untangling key driving factors. For example, as will be demonstrated in the upcoming case discussions, overlapping histopathologic and clinical presentation are common in seemingly diverse pathophysiologic processes such as lichen simplex chronicus, contact dermatitis, and lichen sclerosis. Dermatologic responses to irritant and/or chronic inflammation, regardless of the triggering event, have a similar appearance. Hypopigmentation and/or hyperpigmentation, atrophy, excoriation, and leather-like thickening of the skin are the end result of a number of interrelated or superimposed pathophysiologic processes. A prototypical patient with itching from lichen sclerosis may develop irritant dermatitis (chafing) from frictional forces. Chronic use of corticosteroids may in turn exacerbate the associated atrophy. Atrophy and the loss of protective layers then intensifies the symptoms of contact dermatitis. Lastly, use of topical anesthetics in an attempt to bring about relief may backfire and lead to an allergic response, resulting in a new onset of itching and burning suggestive of allergic contact dermatitis. Thus, unlike many medical conditions in which treatment follows a stepwise approach, it is not surprising that the care of these patients is complex, often involving diverse treatment approaches tailored to the individual’s needs.

The following section presents representative case studies of each of these six vulvo-vaginal conditions. The cases are structured in order to demonstrate the overlap between conditions and to detail the means by which clinicians can determine the primary diagnosis and treatment approach.

Clinical Scenario 1

A 55-year-old woman presents with lichen sclerosis that was first diagnosed 15 years earlier. She reports a worsening of her symptoms over the past 3 years since menopause. She readily admits a chronic itch–scratch cycle, especially after taking a warm bath or shower. Recently, she has noticed postcoital bleeding. She has been using a high-potency steroid (clobetasol propionate cream 0.05%). While the steroid initially helped, with progressive use she experienced worsening symptoms after 6 months of daily treatment. She then tried tacrolimus (Protopic) and pimecrolimus (Eliidel) without any improvement in symptoms.

How should this patient be evaluated?

When presented with steroid-resistant dermatoses and exacerbation after a long hiatus, superimposed malignancy should be excluded, because it is identified in 4% to 6% of patients with lichen sclerosus. In chronic sufferers, comorbidity with other dermatoses is the rule rather than the exception. In addition to malignancy, superimposed infection and cellulitis from chronic itching should be ruled out. Lastly, it is common for lichen sclerosis and lichen planus to coexist, and their histopathology would reflect this overlap. For this reason, several biopsies representative of the different abnormal areas observed on the individual patient’s vulva should be obtained.

Consistent with acute exacerbation, there is redness extending to the thighs (Plate 1.1). The labial skin is otherwise thick and pale, with superficial excoriation from itching. Bilateral fissuring is present in the lower labia majora (Plate 1.1), where none had been evident in the preceding visit. Two representative biopsies were y
obtained, which showed two different histologies: lichen simplex chronicus and lichenoid dermatitis favoring lichen planus. The following excerpt is directly taken from the patient’s pathology report:

The lesions near lateral thigh are similar to previous biopsies. Epidermal hyperplasia is more marked than previous biopsy [consistent with clinical and histologic diagnosis of LSC, and clinical exacerbation]. The features in LSC are all secondary to rub or scratch and are not specific to the etiology (Plate 1.2A).

The medial labial lesions have different features with sparse to moderate lichenoid inflammatory infiltrate in addition to hyperkeratosis [consistent with LSC] and epidermal hyperplasia [another feature of LSC]. [Previous biopsies] do not exhibit any evidence of lichenoid inflammation favoring lichen planus (Plate 1.2B).

How should you treat this complex case?

The pathologist has rendered the diagnoses of lichen sclerosis, lichen planus, and lichen simplex chronicus. It is recognized that these conditions can coexist (sometimes referred to as “the three lichens”16), and a targeted biopsy based on the patient’s localization and topography is most useful in finding the cause of new-onset symptoms or symptom exacerbation.

Reviewing and re-reviewing skin care is a must in patients with chronic vulvar dermatoses. It is common for patients to try a number of over-the-counter or “girlfriend-endorsed” remedies in an attempt to find relief. Overzealous hygiene from fear of infection is common in this population of patients. In this particular case, the patient was asked to stop using all of her medications, including any self-medication. The patient should be instructed as to the importance and rational for NOT using soap in the vulvar region; the vulva needs its natural oil to maintain its barrier mechanisms against constant contact, moisture, and irritants.10 The patient should be further advised to avoid lukewarm water. While the sitz bath is a common practice in obstetrics, exposure to heat may precipitate intense itching and should be avoided in patients with an itch–scratch cycle.

Lastly, copious use of vitamin E cream or other nonirritating thick petroleum-based compounds should be recommended since these medications make a barrier between the vulvar surface and clothing. In cases like this, patients in our practice are also instructed to apply a “Press’n Seal” barrier similar to plastic wrap, to the crotch of their underwear, in order to keep the maximum amount of cream on the vulva. Again, the overarching objective in these measures is to avoid contact to the irritated skin while aggressively controlling bouts of the itch–scratch cycle.

In this situation we also prescribed Doxepine, titrated up by 10 mg every 3 to 5 days to a total of 50 mg nightly, in order to decrease the likelihood of nighttime scratching. In addition, we prescribed our “plan B topical regimen† as a last resort. Our Plan B topical regimen consists of a combination of topical 5% lidocaine and 0.05% estradiol compounded in hydrophilic petrolatum.

While the exact mechanism by which this cream brings about relief is unknown, a higher dose of topical estrogen in combination with a topical anesthetic decreases the skin’s propensity toward itching and promotes estrogen-mediated “thickening” of the skin. Due to severity of this case, a nighttime sedative, reestablishment of dermatologic health, and the plan B regimen were instituted concurrently. But typically we reserve our plan B regimen for patients who have failed to respond to our standard skin care (Table 1.1) while being off of any topical agents. The plan B regimen is typically used for a short duration (8–12 weeks), in order to abort the itch–scratch cycle and restore vulvar skin health in patients with long-standing dermatoses and polypharmacy. Caution should be exercised in that application of this compound on the mucosal surface is associated with systemic absorption to varying degrees. At the end of the 8 to 12 weeks of therapy with this regimen and concurrent skin

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† Lidocaine 5% and estradiol 0.5 mg/g in hydrophilic petrolatum, 60-g tube formulated by Triangle Compounding Pharmacy, Cary, NC. Note: It is best to use high-volume pharmacies that are registered by the board. For further information on compounding pharmacies visit http://www.pcab.info/ and http://www.pcab.org/
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care, we prescribe a progestational agent in menopausal patients with an intact uterus, and switch patients back to their mainstay therapy for lichenoid conditions. In our experience, most patients can be maintained using a multitier therapy using intermittent topical anti-inflammatory medications (eg, every month), topical estrogen, and attention to skin care.

Clinical Scenario 2

A 36-year-old who reports being in good health until a year ago presents with a chief complaint of a “burning sensation” in the vulvar region. On initial evaluation, she had been empirically treated with topical antifungal creams. With persistent symptoms, she had been offered various topical treatments including topical steroids. After a week of using topical steroids, she noticed a burning sensation that became progressively worse. When she called her physician’s office, she was reassured that her symptoms would improve with ongoing steroid use. She finally discontinued the treatment after 3 to 4 weeks. Since then, she experienced worsening of her symptoms to the point where she is no longer able to wear fitted pants. She also has developed an itching sensation in addition to burning. She denies having an itch–scratch cycle and has no exacerbation of her symptoms with intercourse. The generalized vulvar discomfort and rawness, nevertheless, has affected her interest in intimacy.

Based on the historical information, what is the differential diagnosis?

Based on her history and her presentation, the top two differential diagnoses in most clinicians’ minds would be an infectious etiology (eg. yeast or bacterial vaginosis) or an idiopathic pain disorder (eg. vulvar vestibulitis syndrome). When faced with persistent vulvo-vaginal symptoms, empiric treatment with a host of antibacterial and antifungal creams is not only ineffective but in most cases counterproductive and even harmful. While the discussion and management of idiopathic pain disorders is beyond the scope of this chapter, this diagnosis is considered when no dermatologic and pathologic explanation can be identified. In this case, the best course of action would be to obtain a vaginal and vulvar culture prior to empiric treatment.

Non-judicious use of over-the-counter medications, steroids, and prescription medications may trigger an allergic reaction. Regardless of her initial diagnosis, because the likely trigger of her symptoms was steroid use, she was likely to have superimposed allergic dermatitis.

On physical examination, the labia majora are diffusely red without visible scaling (Plate 1.3), but the vulvar surface is progressively dry and dusky with air exposure. There is tenderness to a cotton swab test, a glossy appearance, and small fissures in the folds of both the labia majora and minora. Although minimal punctuate allodynia (pinprick sensation with a cotton swab) is observed during the examination, significant mechanical allodynia (hypersensitivity on gentle stroking of vulvar surface) is observed. The vestibular mucosa is pale and atrophic with mild tenderness (Fig. 1.1). What is the most likely diagnosis?

The examination confirms the likely diagnosis of allergic dermatitis as noted by the expansion of a rash beyond the affected region of the labia. In addition to allergic dermatitis, she is likely to have a component of irritant dermatitis due to dryness, superimposed irritation, and friction from clothing on the irritated skin. The cause of her initial presentation cannot be evaluated at this time because of her superimposed dermatologic condition. Thus, the initial goal of the treatment should be to address her symptoms and restore her dermatologic health.

What additional diagnostic and treatment approaches should be considered?

Cultures from labial folds for yeast were obtained and returned negative. The treatment approach was aimed at (1) aborting the cycle of irritation and rawness, (2) minimizing the sensation of itching, and (3) promoting general vulvar health. The patient was instructed to discontinue the use
Chapter 1

Swab visible through thin skin

Contact dermatitis and atrophy

Figure 1.1 Pale atrophic thinning of the skin in context of contact dermatitis.

of topical agents and was started on vitamin E cream and general vulvar skin care (Table 1.2). After 4 to 6 weeks of topical vulvar skin care and nightly application of Estrace cream, her dermatologic symptoms resolved.

On repeat examination 3 months to the date of her initial visit, she had no abnormal dermatologic findings. Her labia exhibited no tenderness to a point palpation with a cotton swab (punctate allodynia). Although her labia were normal, they were sensitive to a gentle stroke of a cotton swab (mechanical allodynia), as it caused a sensation of rawness and burning.

What could be causing these symptoms?
She was diagnosed with generalized vulvodynia and started on slowly accelerating doses of amitriptyline (10 mg at bedtime, increasing by 10-mg increments every 3–5 days to a total daily dose of 75–100 mg). She reported an 80% improvement in symptoms with 75 mg of nightly amitriptyline. A detailed discussion on the management of idiopathic vulvo-vaginal pain disorders (eg, vulvar vestibulitis syndrome) can be found in Consensus Statement 2005.\textsuperscript{18}

Clinical Scenario 3

A 37-year-old woman presents with a chief complaint of intractable pain with intercourse that started 5 years ago. Up until then, she had no history of pain with intercourse. Over the years, her symptoms have progressively worsened to a point where she now reports daily unprovoked pain. Her last attempt at intercourse was 2 years earlier, during which she experienced bleeding. She also has noted a progressive increase in vaginal discharge, especially during menses, which tends to linger on as ongoing spotting. She denies an itch–scratch cycle but does report an “itchy-burning sensation” of her vulva.

Previously, she had undergone a laparoscopy where a diagnosis of endometriosis was rendered. She was given a trial of Lupron, which coincided with the exacerbation of her symptoms, including a progressive increase in dryness and burning. Otherwise, she has not sought care for this condition for the past 2 years.

What is her differential diagnosis based on history?
In the absence of an acute infectious process, as in this case, the likely differential diagnosis is a chronic inflammatory vulvo-vaginal process. The age of this patient, however, warrants a careful assessment of the vulvo-vaginal region. A simple magnifying glass will provide sufficient power to rule out any raised, atypical lesions suggestive of VIN. Also, it is unlikely that her condition could be explained by endometriosis alone. Histologic findings suggestive of endometriosis during laparoscopy may be an incidental
finding and not the cause of dysparunia. Administration of Lupron for treatment of endometriosis not surprisingly exacerbated her condition by causing a hypoestrogenic state with worsening atrophy and dryness sensation.

Exam findings included tender, well-circumscribed mucocutaneous lesions of the vulva (Plate 1.4). While the vaginal lesions were not distinct enough to be seen with a speculum exam, the posterior cervix was agglutinated to the posterior vaginal wall, which could be “softened” and separated with gradual genital digital pressure application.

**What physical exam findings confirm your diagnosis?**

It is imperative that the physical exam include a full dermatologic assessment. In the author’s experience, patients rarely voluntarily disclose symptoms related to the oral cavity or other “unrelated” parts of the body. On exam and subsequent questioning, this patient reported a longstanding problem of recurrent oral burning and a previous diagnosis of oral lichen planus (Plate 1.5). Due to financial reasons, she has not had an additional workup and evaluation for her erosive oral lesion. Incidentally, on further query, it was found that the fluctuation in oral lesions closely mirrored that of the vulvo-vaginal regions. A prototypical fluctuation consisted of a worsening of burning in the mouth followed by an immediate increase in oral cavity redness. Even though the appearance of the vulvar lesions took an average of 3 weeks to develop, they rapidly became painful and more resistant to healing. Unlike oral lesion, the vulvar lesion showed nonspecific inflammation. However, clinopathologic diagnosis of lichen planus was rendered based on history and exam findings. While it is true that many women with vulvar lesions seem to also suffer from oral lesions, the converse is not true in the author’s experience. And in this case, history and biopsy findings would have been sufficient in making the diagnosis once other known etiologies had been ruled out (eg, infectious, atrophy).

**What is the appropriate treatment?**

A three-pronged treatment approach should be used in order to (1) promote healing of the current ulcer, (2) reduce pain and suffering, and (3) induce long-term remission. In general, when faced with extensive systemic lesions or resistant/intractable local lesions, oral steroids and steroid-sparing adjunct treatments such as methotrexate should be used in combination. Thus, consultation with a dermatologist with experience in the treatment of ulcerative mucocutaneous lesions should be initiated in the first visit. Treatment with topical anti-inflammatory agents and local anesthetics can then be used to treat the inflammation and pain associated with active lesions. In this case, a pulse oral steroid regimen was used starting with a 40-mg dose, tapered very slowly over 4 months to 2.5 mg/day. In addition, in order to decrease the probability of flares, she was started on weekly intramuscular methotrexate.

While her oral lesions rapidly responded to steroids (within 2 weeks), her vulvo-vaginal lesions were more resistant (4–6 weeks), necessitating a concurrent use of vaginal hydrocortisone suppositories. In our experience, a prolonged titration regimen (up to 3–4 months) is required with vulvar lesions. This patient was co-managed by our colleagues in dermatology. Please note the discussion below about the role of topical agents in treating inflammation localized to the vulva (plasma cell vulvitis) and vagina (DIV).

In our experience, commercially available topical anesthetic agents (especially Benzocaine) are allergenic and are not well tolerated. Thus, we often use a compounding pharmacy in order to develop individualized treatment. While a detailed discussion of compounding medications, including the pros and cons, are beyond the scope of this chapter, most specialized compounding pharmacies with a focus on women’s health can serve as a valuable resource for busy clinicians (http://www.pcab.info/). Our typical regimen for the management of pain with active ulcers is as follows: 5% lidocaine and 10% benzocaine compounded in hydrophilic petrolatum. For oral
lesions or excessively moist vulvar lesions, we change the formulation to an Orogel base, which is more paste-like and adheres better to a moist surface.

Clinical Scenario 4

A 52-year-old presents with a chief complaint of vulvo-vaginal pain, specifically a burning and raw sensation, which began around the time of menopause at age 48. After a year of monthly treatment with a variety of antifungal and antibacterial medications for presumed yeast and bacterial vaginosis, she was treated with boric acid for an intractable vulvo-vaginal yeast infection. Application of boric acid precipitated severe burning and a diffuse rash, for which she was treated with daily steroids. After 3 months of steroid therapy, her symptoms improved, but her burning persisted and progressively became worse. At this point, the diagnosis of generalized vulvodynia was made by the third clinician who had examined her, and she was started on amitriptyline about 6 months prior to this clinic visit. She reports that she is “over the acute flare caused by medication” and her symptoms are back to the baseline of “sunburn-type rawness and burning in her inner labial lips,” pain with intercourse, and a general sensation of dryness. Her previous two biopsies indicated “chronic nonspecific inflammation and epithelial atrophy” and “no malignant or premalignant lesions were identified.” Thus she was told that her biopsies were “normal” and was left with the perception that nothing was wrong with her.

What is her differential diagnosis based on history?

Based on her history, iatrogenic allergic dermatitis caused by boric acid is the likely cause of her initial flare. Because it is extremely unlikely that infectious processes are the cause of her persistent symptoms, this case emphasizes the importance of confirming the diagnosis of infectious processes prior to embarking on empirical treatment. Whereas the itch–scratch cycle is an unlikely cause of her symptoms, the presence of atrophy and chronic inflammation favors dermatopathology. The least likely cause of her symptoms based on her history and workup to date is an idiopathic pain disorder such as generalized vulvodynia.

On physical exam, no abnormality on the labia major and external surface of labia minora was noted. With the patient’s guidance the “irritation” was localized to the inner lips of the labia minora. On close inspection, glossy “wet” redness was noted in the inner folds of the labia minora with irregular and asymmetric margins of “heart’s line” (Plate 1.6). Both tactile and mechanical allodynia were present on sensory examination. Gental stroking with a cotton swab (mechanical allodynia), however, reproduced over 80% of her chief complaint of “rawness and sunburn type irritation.”

Given these findings, what is your presumed diagnosis and what other evaluation is appropriate?

This case clearly illustrates the diagnostic conundrum that gynecologists encounter. Faced with clinical signs of inflammation, our immediate instinct is to perform a biopsy from representative areas in order to appropriately rule out premalignant and malignant processes. In evaluation of vulvar dermatoses, biopsies serves not only to eliminate the possibility of premalignant processes, but the “histologic features” of the biopsies are useful in arriving at a clinicopathologic diagnosis. Unfortunately, most of us (as gynecologists) are not trained in dermatopathology and in fact have limited knowledge of how to go about arriving at a clinicopathologic interpretation of the histology and the presenting signs and symptoms. In this case, biopsy showed band-like plasma cell infiltrate in the upper dermis, and in conjunction with findings of moist erythema confined to the inner labial fold, the diagnosis of plasma cell vulvitis was rendered.

Close collaboration and guidance from our colleagues in dermatopathology (pathologists with specialized training in dermatoses) are
imperative in arriving at a diagnosis and tailoring an individualized treatment plan. In this case, the biopsies were mailed to our institution and read by dermatopathologists. Based on the histologic feature and clinical presentation, this patient was diagnosed with Zoon balinitis or plasma cell vulvitis.

**What is your treatment approach?**

As in earlier cases, the general approach for treatment is to (1) eliminate irritation and restore dermatologic health (Table 1.2), (2) reduce pain and suffering, and (3) induce remission. The cardinal rule of therapy is to find the right combinations of dose, frequency, and intervals that give maximal benefit with limited side effects. To this end, some general guidelines are noteworthy. First, higher frequency and potency of anti-inflammatory agents are most effective in inducing remission but should only be used for a brief period of 3 to 4 weeks. Second, titration should be done slowly, expanding each step over a period of 2 weeks in order to assess the consequence of tapering. Third, the order of tapering should be that of decreasing frequency first, followed by decreasing the potency. Further decrease in the frequency (eg, from once a day to once every other day) should be the last step before final titration. This less-frequent, lower-potency dosage should be maintained for 4 weeks before final titration. Not surprisingly, it is not uncommon for the optimal therapy or combination of therapies to be arrived at after a year of trial and error.

In line with the above-mentioned principle, nonsteroid immunomodulators are first-line therapies, with topical steroids and oral medications reserved for intractable cases. Similarly, topical steroid therapy should start with less potent formulation first (eg. hydrocortisone), with a more potent formulation (eg. clobetasol) reserved for intractable cases.

In this case, the patient was started on tacrolimus and instructed on a regimen of topical skin care (Table 1.2). For pain management, she was started on topical lidocaine ointment (5%). Lastly, she was asked to contact us if she experienced burning with any of the topical treatments (eg, allergic dermatitis). After 4 weeks of therapy, her symptoms were markedly improved. Subsequently, over the ensuing 6 to 8 months, her treatment was titrated down to biweekly application of topical tacrolimus (0.03%). Vaginal estrogen tablets (Vagifem) and vitamin E cream were concurrently used throughout this period in order to correct atrophy and minimize superimposed dermatitis.

**Pathology notes**

Vulvar dystrophy

Vulvar punch biopsies may be interpreted by pathologists with various backgrounds, including dermatopathologists, general pathologists, and gynecologic pathologists. For inflammatory dermatoses involving the vulva, the first task of the pathologist is to integrate clinical history, physical exam findings, and histopathology to make as specific a diagnosis as possible to guide therapy. It is therefore important for the clinician to communicate physical exam findings, including description of affected nongenital sites, and clinical history to the pathologist. The second task for pathologists interpreting vulvar dystrophy biopsies is to exclude vulvar neoplasia and infectious conditions, sometimes with the help of special stains. The terminology used in articles and textbooks to describe vulvar inflammatory dermatoses is inconsistently applied. Classification of vulvar dermatoses using the same specific terminology applied to conditions affecting nongenital skin is advised. Descriptive diagnoses are not encouraged and are likely to be of little utility in determining the clinical management of the patient. Use of consistent terminology helps ensure that the clinician is more likely to understand the terminology and will be able to
Pathology notes (continued)

use the pathology report information to optimize patient therapy. A brief discussion of important pathologic aspects for the most common vulvar inflammatory dermatoses follows.

The most common inflammatory disorder involving the vulva is eczematous dermatitis, which is characterized histologically by the presence of intercellular edema, “spongiosis” within the epidermis, and a variably intense dermal chronic inflammatory infiltrate. There are several clinical variants of eczematous dermatitis based on clinical features of the condition; these variants usually cannot be subtyped on histology alone. Once the pathologist has made the diagnosis of eczematous dermatitis and excluded other dermatoses, it is then up to the clinician to then search for the specific etiology. Eczematous dermatitis is the histopathologic counterpart to contact dermatitis in most patients, with the differential diagnosis including both irritant contact dermatitis and allergic contact dermatitis. Common causes of irritant contact dermatitis include soaps, perfumes, cleansers, topical over-the-counter medications, urine, sweat, and friction. Irritant contact dermatitis results from direct damage to the skin by exogenous agents. Allergic contact dermatitis is rarer and may be more difficult to confirm without skin patch testing. Histopathologic features in skin biopsies favoring allergic contact dermatitis include the presence of increased eosinophils around superficial venules and occasionally within the spongiotic epidermal layer, and intraepidermal microgranulomas consisting of Langerhans cells. Allergic contact dermatitis represents a type IV hypersensitivity reaction to a specific allergen. Fungal infections may occasionally show histopathologic features similar to eczematous dermatitis and should be excluded by the pathologist, especially given the different treatment implications. The absence of fungal organisms in the biopsy can be confirmed with special stains such as the periodic acid–Schiff (PAS) stain.

Lichen simplex chronicus (LSC) is a reactive condition often seen in association with eczematous dermatitis. LSC is characterized histologically as showing epidermal acanthosis, hyperkeratosis, and hypergranulosis. LSC represents a cutaneous reaction to repeated physical trauma such as chronic scratching. LSC is not a distinct entity that explains the patient’s condition. The pathologist is expected to make an attempt to identify the underlying cause of LSC if possible. If there are no histopathologic features that identify an underlying etiology, the pathology report can so state. Eczematous dermatitis is the most common specific inflammatory condition to be seen in association with LSC. The differential diagnosis for LSC includes VIN simplex-type.

The diagnosis of well-established lichen sclerosus (LS) is typically straightforward due in large part to the characteristic homogenized dermal sclerosis seen on light microscopy. It should be noted that early lesions of LS may be difficult to diagnose and can show overlapping histologic features with lichen planus (LP). The presence of even subtle dermal sclerosis favors the diagnosis of LS over LP. Some cases of LS may be associated with superimposed LSC and have an unusual appearance on physical exam. The presence or absence of atypia should be noted in biopsies from elderly women showing LS. LS does appear to be associated with some risk for developing vulvar squamous cell carcinoma and VIN simplex-type in elderly women.

A whole host of other inflammatory disorders may involve the vulva, including infections, psoriasis, lichen planus, Behçet disease, Crohn disease, plasma cell vulvitis, and various acantholytic disorders. Biopsy evaluation by a pathologist with experience in evaluating inflammatory skin conditions is optimal to help ensure all diagnostic possibilities have been considered in a biopsy, especially for unusual or problematic cases.
References