IRIS AperTO

UNIVERSITÀ DEGLI STUDI DI TORINO

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

**2006 ISSVD classification of vulvar dermatoses: pathologic subsets and their clinical correlates**

**This is the author's manuscript**

*Original Citation:*

*Availability:*

This version is available http://hdl.handle.net/2318/39965 since

*Terms of use:*

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

12 October 2024

# 2006 ISSVD Classification of Vulvar Dermatoses

## *Pathologic Subsets and Their Clinical Correlates*

**Peter J. Lynch, M.D., Micheline Moyal-Barrocco, M.D., Fabrizio Bogliatto, Leonardo Micheletti and James Scurry, M.D.**

*The beginning of wisdom is calling things by their right name.*

—Anonymous

*The International Society for the Study of Vulvovaginal Disease (ISSVD) has, as one of its major societal goals, the development and promulgation of nomenclature and classification of vulvar disease. A committee of the ISSVD has developed new nomenclature and classification for the specific area of vulvar dermatoses. This classification was approved by the ISSVD members at the most recent international congress, held in New Zealand in February 2006.* (J Reprod Med 2007;52:3–9)

**Keywords:** vulvar diseases, skin dermatoses, International Society for the Study of Vulvar Disease.

**A primary goal of the society is to define and promulgate an international nomenclature for vulvar disease.**

The terminology and classification of disease are vitally important to the world of medicine. They are the common language used to communicate accurately and understandably with our patients and colleagues. Achieving consensus regarding the development of this "language" is difficult when it involves a set of diseases peculiar to a single medical specialty existing within a single country, but consensus is even more difficult when the area of medicine under consideration involves multiple specialties the members of which reside in numerous countries. Moreover, a consensus formulated on a one-time basis requires constant revision because of the subsequent evolution of knowledge.

Thirty years ago, the International Society for the Study of Vulvovaginal Disease (ISSVD) was founded by a multinational group of gynecologists, dermatologists and pathologists. A primary goal of the society is to define and promulgate an international nomenclature for vulvar disease. This has been partially accomplished, and the society currently has in place recently revised classifications for vulvar pain[1] and vulvar intraepithelial neoplasia.[2] The society's recommended classification of benign, noninfectious vulvar disease, which has been in place

From the Department of Dermatology, University of California, Davis, Sacramento; Private Practice in Dermatology, Paris, France; Department of Gynecology, University of Turin, Turin, Italy; and Private Practice in Pathology, Newcastle, NSW, Australia.

Address correspondence to: Peter J. Lynch, M.D., Department of Dermatology, University of California, Davis,3301 C Street, #1400, Sacramento, CA 95816.

*Financial Disclosure*: The authors have no connection to any companies or products mentioned in this article.

0024-7758/07/5201-0003/$15.00/0 © Journal of Reproductive Medicine®, Inc.

since 1987,[3] is considered to be controversial, outdated and unhelpful by both ISSVD members and others who care for women with vulvar disorders.

The early history of ISSVD involvement in the classification of benign, noninfectious vulvar disease was recently reviewed[4] but can be summarized as follows. Thirty years ago, the ISSVD recognized that a group of benign, noninfectious vulvar diseases ("white lesions") needed to be defined and classified in order to clearly separate these benign disorders from the premalignant and malignant epithelial conditions with which they had been historically confused. The ISSVD used the word *dystrophy*, as originally promulgated by Jeffcoate,[5] as the collective term for these benign conditions and then subdivided the dystrophies into 3 categories: lichen sclerosus, hyperplastic dystrophy and mixed dystrophy.[6] The term *dystrophy* was chosen as a "neutral" term that was to be substituted for the confusing and disparate nomenclature of leukoplakia, neurodermatitis, leukokeratosis, leukoplastic vulvitis, hyperplastic vulvitis and kraurosis vulvae, previously used by gynecologists and dermatologists.

This classification was widely accepted by gynecologists and led to a marked decrease in the performance of vulvectomies for benign conditions. However, dermatologists in general, and dermatopathologists in particular,[7] did not support this nomenclature. Specifically, Sanchez and Mihm recommended elimination of the term *dystrophy* "because of its imprecision and lack of usefulness."[7] Moreover, 2 members of the ISSVD, in a review of 1,000 patients cared for in a multispecialty vulvar disease clinic, found that the 3 categories contained in the ISSVD classification were too restrictive. These authors identified 14 specific diagnoses for white vulvar lesions alone.[8]

Increasing dissatisfaction with this nomenclature led the ISSVD, in 1987, to discontinue use of the term *dystrophy* and to reclassify the benign, noninfectious diseases of the vulva under the new rubric: nonneoplastic epithelial disorders. This new classification contained 2 specific categories ("lichen sclerosus" and "squamous cell hyperplasia") and 1 general category ("other dermatoses").[3]

While this classification system has remained in use to the present, it, too, has proven to be problematic and, once again, aroused the ire of dermatopathologists.[9] Due to increasing, widespread dissatisfaction, the ISSVD, in 2003, established a new Classification and Terminology Committee and asked it to review, and possibly revise, the 1987 nomenclature. The members of that committee are the authors of this paper. They represent 4 countries (Australia, France, Italy and the United States) and 3 specialties (gynecology, dermatology and pathology).

### *Principles Involving Terminology and Classification*

There are several important considerations involved in medical terminology and classification. The first is recognition of the difference between the terms *terminology* and *classification*: *terminology* (synonym: nomenclature) refers to the names of specific diseases, whereas *classification* refers to the placement of these diseases into categories, or "classes," based on features in common.

The second consideration is the principle on which the classification is to be based. In medicine, it might be ideal for classification to be formulated on *etiology* or *pathophysiology* (infectious diseases, metabolic diseases, malignant diseases, etc.) but unfortunately information regarding etiology and pathophysiology is not complete and too subject to change to make this approach feasible. An alternative approach would be to use disease *morphology*, involving either clinical patterns (papulosquamous diseases, eczematous diseases, etc.) or histologic patterns (lichenoid diseases, granulomatous diseases, etc.). These morphologic features are well established, and since they change very little with the passage of time and acquisition of new knowledge, this approach offers the advantage of relative stability.

The third consideration regards the completeness of the material (i.e., the number of diseases) contained within the classification. Greater completeness offers more precision but is offset by reduced usefulness at the practical, clinical level.

### *Committee Discussion Regarding Terminology*

The committee reviewed the terminology contained in the 1987 ISSVD classification. We concluded that the title of the classification, "nonneoplastic epithelial disorders," was misleading in that many of the conditions we might wish to include were not solely, or even primarily, "epithelial." We also agreed that the term *squamous cell hyperplasia* was inappropriate: (1) the term is not used by either dermatologists or pathologists for otherwise similar disorders occurring at sites other than the vulva, and (2) 20 years after its promulgation, it has not found favor with anyone, including our own ISSVD members. We concluded the discussion on terminology by agreeing that for the names of vulvar diseases, we

would employ the standard terminology used by dermatologists and dermatopathologists.

### *Committee Discussion Regarding Classification*

The committee then considered the basis on which we would formulate a classification. We discussed construction of a classification based on etiology and/or on pathophysiology but discarded this approach based on the objections mentioned above. Moreover, we recognized that such a classification would not be usable by clinicians for diagnostic purposes: one has to know what the diagnosis is before one can locate the disease within the classification.

We then deliberated over a classification system that would simply consist of a "laundry list" of standard dermatologic disorders but thought that this would be of little help to nondermatologic clinicians, who would likely be unfamiliar with this terminology. Moreover, such lists can be found in many textbooks, and we thought that there would be no justification for us to recapitulate this already-available information. Here, too, we thought that it would not be diagnostically helpful to the clinician. That is, a clinician faced with an unrecognized vulvar disorder would not find anything in such a classification that would assist in arriving at a diagnosis.

#### *Use of Clinical Morphology*

We next turned to the possibility of basing the classification on established categories of dermatologic clinical morphology ("papulosquamous diseases," "eczematous diseases," etc.), but we recognized that such terms, while helpful to dermatologists, would be useless for gynecologists and other nondermatologic clinicians. However, still wishing to stay with a classification based on clinical morphology, we considered using a problem-oriented algorithm such as was employed in an earlier textbook on genital disease.[10] This approach would involve grouping vulvar diseases into categories readily recognizable to all clinicians ("red lesions," "white lesions," etc.). Even though we agreed on the ultimate practicality of such an approach, we found that despite prolonged discussion, we could not reach a consensus on the morphologic terms, the names of individual disorders or the appropriate placement of those disorders within the various morphologic categories.

#### *Use of Histologic Morphology*

When it was apparent that we could not formulate a useful classification based on clinical morphology, we turned to the possibility of employing histologic morphology. We recognized that among various specialties and diverse languages, the nomenclature of histologic morphology is appreciably more standardized than that of clinical morphology. This already-existing standardization would represent a real advantage, but we were concerned that such an approach might not offer sufficient usefulness for a clinician faced with diagnostic uncertainty.

After much discussion, and in a collective moment of intuitive understanding, we came to the following conclusions: (1) A clinician who recognizes a specific disease at the time of examination has no need for any type of classification: with the diagnosis in hand, additional knowledge can easily be found by disease name in standard reference sources. (2) A clinician who does not recognize a specific disease on examination will likely carry out a biopsy. For many diseases, biopsy findings will lead the pathologist to identify a specific diagnosis. Here, too, no classification will be needed as once again additional knowledge can be found by disease name in standard reference sources. (3) The real need for a classification occurs when neither the clinician nor the pathologist can reliably arrive at a single, specific diagnosis. In this situation the pathologist will likely offer a description of the histologic pattern without committing to a specific diagnosis. (4) At that point, if the clinician had the name of the histologic pattern and a list of the diseases most commonly demonstrating that pattern, he or she could carry out a short reference review. Then, using clinicopathologic correlation, the clinician could almost always determine the most likely diagnosis.

With these thoughts in mind, we elected to construct a classification system based on the most common histologic patterns, within which, using standard dermatologic terminology, would be placed a list of the most likely diagnoses.

### *The Categories of Disease to Be Considered for Classification*

There are literally hundreds of disorders that involve the vulva. If all of these were to be included, our classification would be of textbook length and complexity. Fortunately, we could reduce the number of disease to be considered inasmuch as the ISSVD already had in place a classification of vulvar intraepithelial dysplasia,[2] and we think that the remaining neoplasms (both benign and malignant)

are sufficiently histologically distinctive to be readily recognized on biopsy. Likewise, infectious diseases have well-defined criteria for diagnosis in terms of culture and/or histologic identification, and thus they, too, are fairly easy to identify. On this basis we thought that we could exclude all neoplasms and infectious diseases from our classification.

The committee members then concluded that of the remaining disease possibilities, the most diagnostically troublesome for both clinicians and pathologists would be the benign inflammatory disorders. These conditions are clinically difficult to recognize (even for dermatologists) because the warm, moist, frictional environment of the vulva regularly obscures what otherwise would be their characteristic morphologic hallmarks. These disorders can also cause trouble for pathologists because of the "noise" contributed by these same adverse environmental factors. With these thoughts in mind we elected to confine our classification to noninfectious, nonneoplastic vulvar disease. In effect, what had been termed the "dystrophies" are now included within the "vulvar dermatoses."

### *Diseases to Be Considered Within the Vulvar Dermatoses*

In order to keep the classification simple and useful to a wide range of clinicians, we decided to include only the most common and most important histologic patterns and only the most common and important diseases exhibiting those patterns. Moreover, we excluded those dermatologic conditions involving the vulva that usually present with a widespread distribution pattern. We reasoned that patients with these diseases would almost certainly present first to dermatologists, who would then be able to establish the correct overall diagnosis.

### *Conclusions and the Classification*

We constructed a classification that includes the most commonly encountered noninfectious and nonneoplastic vulvar disorders as well as a few likely to cause diagnostic difficulty for both clinicians and pathologists. It has been kept simple and usable by virtue of excluding the histologically well-defined neoplasms and the readily recognized infections. It retains both the standardized histologic nomenclature for the most commonly encountered inflammatory patterns. For the diseases within those patterns, it retains the historically well-established dermatologic terminology. The committee members think that this is the best and most practical approach to meeting the needs of gynecologists, dermatologists and pathologists involved in the care of women with vulvar disease.

The classification we formulated is contained in Figure 1. It was presented to the members of the ISSVD in February 2006 at the society's XVIIIth World Congress. The members voted, by a slightly larger than two-thirds majority, to officially accept this new classification.

### *Definitions and Guidelines for Use of the Histologic Patterns*

The histologic patterns we have included in the classification are generally well accepted and widely used by pathologists. Nevertheless, we judged that for clinicians, better clarity and more usefulness could be achieved if simplified definitions and guidelines for use of the histologic patterns were to accompany the classification. The definitions we formulated for the histologic patterns are based largely on the widely used and highly respected dermatopathology textbooks by Weedon and

**Spongiotic pattern**
- Atopic dermatitis
- Allergic contact dermatitis
- Irritant contact dermatitis

**Acanthotic pattern** (formerly squamous cell hyperplasia)
- Psoriasis
- Lichen simplex chronicus
  - Primary (idiopathic)
  - Secondary (superimposed on lichen sclerosus, lichen planus or other vulvar disease)

**Lichenoid pattern**
- Lichen sclerosus
- Lichen planus

**Dermal homogenization/sclerosis pattern**
- Lichen sclerosus

**Vesiculobullous pattern**
- Pemphigoid, cicatricial type
- Linear IgA disease

**Acantholytic pattern**
- Hailey-Hailey disease
- Darier's disease
- Papular genitocrural acantholysis

**Granulomatous pattern**
- Crohn's disease
- Melkersson-Rosenthal syndrome

**Vasculopathic pattern**
- Aphthous ulcers
- Behçet's disease
- Plasma cell vulvitis

**Figure 1** 2006 ISSVD Classification of Vulvar Dermatoses: Pathologic Subsets and Their Clinical Correlates.

McKee.[11,12] We did also considered including definitions of the clinical entities contained within the histologic patterns but elected not to do so, reasoning that such definitions are readily available to clinicians in standard textbooks of dermatology and vulvology.

### *Spongiotic Pattern*

Spongiosis is the presence of intercellular edema within the epidermis leading to the widening of space between the epidermal cells. This pattern is characteristically seen in the eczematous (dermatitic) diseases.

Histology cannot distinguish between irritant contact dermatitis, allergic contact dermatitis and atopic dermatitis. The histologic diagnosis in each instance is "spongiotic dermatitis." These entities therefore have to be distinguished clinically. However, vulvar dermatitis is most often biopsied only when it is chronic. This occurs because the cause of acute dermatitis is more likely to be diagnosed clinically, and therefore such lesions uncommonly require biopsy. While clinical examples of acute and subacute dermatitis demonstrate spongiosis histologically, chronic dermatitis merges with lichen simplex chronicus (see below) and may exhibit minimal spongiosis. In itself, spongiosis is a nonspecific sign that may occur in many conditions other than the classical eczematous (dermatitic) diseases: e.g., infections (candidiasis) and trauma (excoriation). These other conditions generally demonstrate characteristic clinical, histologic or laboratory features that allow their correct recognition.

### *Acanthotic Pattern*

The acanthotic pattern represents an increase in the number of epithelial cells (keratinocytes), leading to a thickening of the epidermis. Some pathologists prefer the term *psoriasiform pattern* or *psoriasiform dermatitis*; the ISSVD formerly called this pattern *squamous cell hyperplasia*. Clinically, the acanthotic pattern is usually associated with thick, white plaques. The acanthotic pattern is normally a benign feature. However, in the setting of such diseases as lichen sclerosus and lichen planus, therapeutically resistant acanthosis can foreshadow the development of squamous cell carcinoma.

Psoriasis, acute and subacute dermatitis, chronic dermatitis (lichen simplex chronicus) and candidiasis form a common quartet of overlapping histology in vulvar biopsies. In some instances there may be distinctive histologic features (e.g., a positive periodic acid–Schiff stain for *Candida*) that permit a specific diagnosis, but often the pathologist can only place these diagnoses in order of likelihood and leave it to the clinician to make the final diagnosis. Lichen simplex chronicus is the clinical and histologic diagnosis when only the changes of chronic rubbing (irritation) are seen. However, in some cases, lichen simplex chronicus may be superimposed on some other underlying dermatologic disorder.

Acanthosis is a very common and nonspecific histologic finding that may be seen in situations other than the vulvar dermatoses. Thus, it can be present in infections (candidiasis, syphilis, human papillomavirus disease) and neoplasia (seborrheic keratosis, vulvar intraepithelial neoplasia of warty-basaloid and differentiated types, verrucous and conventional squamous cell carcinoma and extramammary Paget's disease). These other conditions usually have distinguishing features clinically and histologically.

### *Lichenoid Pattern*

Lichenoid inflammation is characterized by the presence of a bandlike lymphocytic infiltrate in the upper dermis and accompanying epidermal basal layer damage, as identified by cell death and/or vacuolar alteration. Some pathologists use the term *lichenoid pattern* even when a bandlike upper dermal inflammatory infiltrate occurs in the absence of epidermal alteration, but we think that this is insufficiently precise and therefore inappropriate.

Most biopsy specimens from lichen sclerosus show the characteristic feature of dermal homogenization. Occasionally, however, only a lichenoid reaction is seen, and in these instances, the histology overlaps with that of lichen planus. In chronic lichen sclerosus, the lichenoid reaction may be lost, and the dermis then exhibits fibrosis rather than homogenization. In this circumstance, the histology merges with that of lichen simplex chronicus.

Other erosive diseases of the vestibule and vagina, such as Stevens-Johnson syndrome, systemic lupus erythematosus and graft vs. host disease, may demonstrate a lichenoid pattern and thus may be histologically indistinguishable from the more commonly encountered lichen planus and lichen sclerosus. These conditions need to be separately identified on a clinical basis.

Plasma cell vulvitis, also termed Zoon's vulvitis, may show 1 aspect of the lichenoid pattern: an upper dermal, bandlike infiltrate of chronic inflam-

matory cells. However, this condition does not reveal "classical" lichenoid basal layer damage. We placed plasma cell vulvitis in the "vasculopathic pattern" based on the presence of extravasated red blood cells and hemosiderin-containing macrophages.

### *Dermal Homogenization/Sclerosis Pattern*

Dermal homogenization/sclerosis is a type of collagen change with partial or complete obliteration of the boundaries between bundles of collagen such that the dermis has a homogenized, "glassy" or "hyalinized" appearance. While dermal homogenization nearly always indicates lichen sclerosus, radiation dermatitis may show a nearly identical microscopic appearance.

### *Vesiculobullous Pattern*

Vesicles are small (< 5 mm), and bullae are large (≥ 5 mm) spaces containing loculated fluid (blisters). These blisters may occur within the epidermis or between the epidermis and the dermis. Blisters containing acantholytic epidermal cells are considered in the Acantholytic Pattern.

Due to local environmental trauma, most vulvovaginal vesicobullous diseases present both clinically and histologically with erosions rather than intact blisters. Direct immunofluorescence, from adjacent normal-appearing tissue, may help with the diagnosis of vesiculobullous disorders.

### *Acantholytic Pattern*

Acantholysis results from the breakage of desmosomal junctions between epidermal cells. This process results in separation ("clefting") between epithelial cells. Isolated, "rounded up," individual epithelial cells (acantholytic cells) are often present within these clefts.

Papular genitocrural acantholysis may have microscopic changes nearly identical to those found in Hailey-Hailey or Darier's disease. It is separated from these 2 conditions clinically by the lack of extragenital lesions and of a positive family history.

### *Granulomatous Pattern*

Granulomas consist of epithelioid macrophages, intermingled inflammatory cells and variable numbers of giant cells. Granulomatous inflammation occurs within the dermis and/or subcutaneous fat.

Vulvar instances of Crohn's disease and Melkersson-Rosenthal syndrome may be indistinguishable histologically. Melkersson-Rosenthal syndrome is distinguished by the absence of gastrointestinal disease. However, it is possible for vulvar Crohn's disease to precede the development of intestinal symptoms and signs. Other granulomatous disorders, such as infections (mycobacterium tuberculosis, deep fungal infection), keratin granulomas (folliculitis, hidradenitis suppurativa), foreign body granulomas, sarcoidosis and pyoderma gangrenosum, almost always demonstrate other clinical and histologic features permitting their diagnosis.

### *Vasculopathic Pattern*

The term *vasculopathy*, used in a general sense, represents any disruption of blood vessel function. Used narrowly, as in this classification, it is characterized histologically by blood vessel damage occurring in the setting of widespread dermal inflammation. The resultant deprivation of oxygen and nutrient flow generally leads to erosion or ulceration.

Aphthous-type ulcers, as seen in complex aphthosis and Behçet's disease, demonstrate blood vessel compromise due to an intense dermal inflammatory infiltrate consisting mostly of lymphocytes. Instances of pyoderma gangrenosum involving the vulva show similar ulceration due to an intense inflammatory infiltrate consisting mostly of neutrophils.

Plasma cell vulvitis is listed in the vasculopathic pattern based on the presence of extravasated red blood cells and hemosiderin-containing macrophages. (See additional discussion under "lichenoid pattern.")

## *References*

1. Moyal-Barracco M, Lynch PJ: 2003 ISSVD terminology and classification of vulvodynia: A historical perspective. J Reprod Med 2004;49:772–777
2. Sideri M, Jones RW, Wilkinson EJ, et al: Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med 2005;50:807–810
3. Ridley CM: International Society for the Study of Vulvar Disease: Progress report. Br J Dermatol 1988;118:732–733
4. Lynch PJ, Micheletti L: The demise of dystrophy: A history of the evolving terminology. CME J Gynaecol Oncol 2006;10:142–146
5. Jeffcoate TN: Chronic vulval dystrophies. Am J Obstet Gynecol 1966;95:61–74
6. New nomenclature for vulvar disease. Am J Obstet Gynecol 1976;124:325–326
7. Sanchez NP, Mihm MC Jr: Reactive and neoplastic epithelial alterations of the vulva. J Am Acad Dermatol 1982;6:378–388

8. Young AW Jr, Tovell HMM: Disease of the vulva presenting as white lesions. Clin Obstet Gynecol 1978;21:1023–1039
9. Kiryu H, Ackerman AB: A critique of current classifications of vulvar disease. Am J Dermatopathol. 1990;12:377–392
10. Lynch P, Edwards L: Genital Dermatology. New York, Churchill Livingstone, 1994
11. Weedon D: Skin Pathology. Second Edition. London, Churchill Livingstone, 2002
12. McKee PH, Calonje E, Granter SR: Pathology of the Skin. Third edition. London, Elsevier Mosby, 2003