



The International Society
for the Study of Vulvovaginal Disease

Sister Society
Meeting



“Vulvar intraepithelial neoplasia. New classification. Diagnosis and treatment”

Veronica Suzuki, MD

Hospital de Clinicas “Jose de San Martin”
University of Buenos Aires - Argentina



“Programa de Prevención, Diagnóstico, Terapéutica y Vacunación en Patologías del Tracto Genital Inferior”

Director: Prof. Dr. Silvio Tatti

Hospital de Clínicas “José de San Martín” - U.B.A.

colpoclinicas@hotmail.com



- I have no financial relationships or conflicts of interest to disclose

Objectives

- Familiarize yourself with the new classification of Vulvar Squamous Intraepithelial Lesions
- Identify and treat VHSIL and VINd

TERMINOLOGY OF VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS

ISSVD 1986			
VIN 1			
VIN 2			
VIN 3			
VIN differentiated type			

Squamous Vulvar Intraepithelial Neoplasia

2004 Modified Terminology, ISSVD Vulvar Oncology Subcommittee

Mario Sideri, M.D., Ronald W. Jones, M.D., Edward J. Wilkinson, M.D., Mario Preti, M.D., Debra S. Heller, M.D., James Scurry, M.D., Hope Haefner, M.D., and Sallie Neill, M.D.

- The term VIN I will no longer be used. It is not reproducible and is not a cancer precursor
- Instead: Flat condyloma acuminatum or HPV effect
- The term VIN should apply only to histologically high grade squamous lesions (VIN 2 and 3)
- 2 categories:

VIN, usual type

- a. VIN, warty type
- b. VIN, basaloid type
- c. VIN, mixed (warty/basaloid) type

VIN, differentiated type

Figure 1 Squamous VIN terminology (ISSVD, 2004). The occasional example of VIN that cannot be classified into either of the above VIN categories (usual or differentiated type) may be classified as *VIN, unclassified type*. The rare VIN of pagetoid type may be classified as such or placed in this category.

TERMINOLOGY OF VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS

ISSVD 1986	ISSVD 2004		
VIN 1	Flat condyloma or HPV effect		
VIN 2	VIN usual (Warty, Basaloid o mixed)		
VIN 3			
VIN differentiated type	VIN differentiated type		



cap



Lower Anogenital Squamous Terminology Standardization of HPV-associated Neoplasia

Teresa M. Darragh, MD
*University of California, San Francisco
Steering Committee, ASCCP Co-Chair*

David C. Wilbur, MD
*Harvard Medical School, Massachusetts General Hospital
Steering Committee, CAP Co-Chair*

Terminology for human papillomavirus (HPV)-associated squamous lesions of the lower anogenital tract

The Lower Anogenital Squamous Terminology (LAST) Project was co-sponsored by the **College of American Pathologists** and the **American Society for Colposcopy and Cervical Pathology**

The final, approved recommendations standardize biologically relevant histopathologic terminology for HPV-associated squamous intraepithelial lesions and superficially invasive squamous carcinomas across all lower anogenital tract sites and detail the appropriate use of specific biomarkers to clarify histologic interpretations and enhance diagnostic accuracy.

Diagnostic terminology for a 2-tiered system

Low Grade Squamous Intraepithelial Lesion (LSIL)

High Grade Squamous Intraepithelial Lesion (HSIL)

(These may be further classified by the applicable –IN subcategorization)

TERMINOLOGY OF VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS

ISSVD 1986	ISSVD 2004	LAST 2012	
VIN 1	Flat condyloma or HPV effect	LSIL	
VIN 2	VIN usual (Warty, Basaloid o mixed)	HSIL	
VIN 3			
VIN differentiated type	VIN differentiated type		



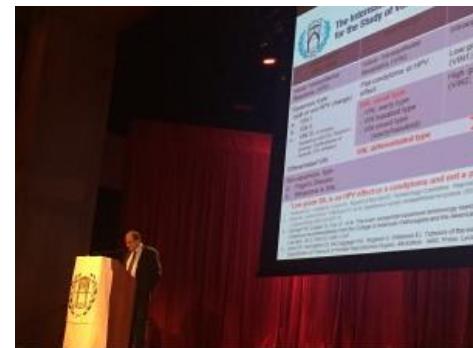
The 2015 International Society for the Study of Vulvovaginal Disease Terminology of Vulvar Squamous Intraepithelial Lesions

Jacob Bornstein MD, MPA,
Chairman of the 2013-2015 ISSVD Terminology Committee,
Past President ISSVD.

Table 1: 2015 ISSVD Terminology of Vulvar Squamous Intraepithelial Lesions

Low grade squamous intraepithelial lesion (Flat condyloma or HPV effect)
High grade squamous intraepithelial lesion (VIN usual type)
Intraepithelial neoplasia, differentiated-type

<http://issvd.org/resources/terminology/>



ISSVD APPROVES NEW TERMINOLOGY AT XXIII
WORLD CONGRESS

TERMINOLOGY OF VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS

ISSVD 1986	ISSVD 2004	LAST 2012	ISSVD 2015
VIN 1	Flat condyloma or HPV effect	LSIL	LSIL of the vulva (vulvar LSIL; flat condyloma, or HPV effect)
VIN 2	VIN usual (Warty, Basaloid o mixed)	HSIL	HSIL of the vulva (vulvar HSIL; VIN usual type)
VIN 3			DVIN - differentiated-type VIN.
VIN differentiated type	VIN differentiated type		

VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS

HSIL (VIN, usual type)

1. VIN, Warty type
2. VIN, Basaloid type
3. VIN, mixed (Warty-basaloid) type

- Younger women
- Related to HPV infection
- Lower progression to cancer.

VIN, differentiated type

- Older women. Menopause.
- No related to HPV infection
- Higher probability of progression to cancer



HSIL (VIN USUAL TYPE)

Epidemiology(1):VHSIL

- It is an increasingly common problem, particularly among women in their 40s.
- 75% premenopause
- HPV HR - 16

RISK FACTORS

- HPV infection in the lower genital tract
- Smoking
- Immunosuppression (HIV, solid organ transplant, oral steroids, other causes)

VHSIL in HIV+

Risk factors for incident lesions

- HPV infection ($p=0.0013$),
- Low CD4 ($p = 0.0395$)
- Endovenous drugs ($p=0.0199$).

VHSIL in HIV+

- Incidence 1.31 vs **4.67** per 100 person/year in HIV negative women versus HIV positive
- HSIL in 359 (23%) positive HIV women versus 35 (7%) HIV-negative
- HSIL was related to:
 - HAART
 - CD4
 - Abnormal PAP
 - HR-HPV

Diagnosis

- Inspection
- Dischromic.
Grey, white, red.
- Diagnosis: Biopsy.



When to suspect VIN?

- Always biopsy: Postmenop women with “genital warts”
- Always biopsy: No response to treatment (any age)

- Hyperpigmented, ulcerated, necrotic
- Immunosupressed





















- Although spontaneous regression has been reported, VIN should be considered a premalignant condition.
- Treatment is recommended for all women with vulvar HSIL (VIN usual type).
- Because of the potential for occult invasion, wide local excision should be performed if cancer is suspected, even if biopsies show vulvar HSIL.

- When occult invasion is not a concern, vulvar HSIL (VIN usual type) can be treated with
 - ❖ Excision,
 - ❖ Laser ablation,
 - ❖ Topical imiquimod (off-label use).

- Cigarette smoking is strongly associated with vulvar HSIL (VIN usual type), and cessation should be encouraged.
- 3% occult invasive carcinoma
- Recurrence post-treatment : 9 - 50%
- + when positive margins
- + when multiple lesions
- - when surgical treatment

VHSIL :

Recurrence after initial treatment

In 28.7% patients

- Smoking ($p < 0.001$)
- Size of lesion ($p = 0.016$)
- Positive margins ($p = 0.005$)

VHSIL: Risk factors – surgical margins

- 50% recurrence if surgical margins were positive versus 15% when negative margins

Original Article



Risk factors for unrecognized invasive carcinoma in patients with vulvar high-grade squamous intraepithelial lesion at vulvoscopy-directed biopsy

Mario Preti,¹ Lauro Bucchi,² Bruno Ghiringhello,³ Silvana Privitera,³
Valentina Frau,¹ Elisabetta Corvetto,¹ Chiara Benedetto,¹ Leonardo Micheletti¹

¹Department of Obstetrics and Gynaecology, University of Torino, Torino, Italy

²Romagna Cancer Registry, Romagna Cancer Institute (IRST) IRCCS, Meldola, Forlì, Italy

³Department of Pathology and Cytology of Female Cancer, Childhood Cancer, and Rare Cancers, AOU Città della Salute e della Scienza, Torino, Italy

OPEN ACCESS

216 patients median age 50 y.o
>35% multifocal lesion
11% % invasive carcinoma

Higher risk:

- ❖ Age ($p=0.008$)
- ❖ Size of lesion $\geq 20\text{mm}$ ($p=0.013$)
- ❖ Clitoral involvement ($p<0.001$)
- ❖ Nodular lesion ($p=0.078$)

Treatment modalities

- Young patients:
Esthetic/Psycological/Functional/Issues
- Recurrences



Medical Tx

5FU

IFN- α

cidofovir)

Photodynamic tx

Imiquimod

Surgical Tx

Vulvectomy

Local resection

Laser

Treatment modalities

- Surgery
- Laser therapy
- Imiquimod

Treatment modalities

Surgery

- Thickness of involved tissue does not generally exceed 2 mm
- Deeper lesions are in hair-bearing areas where VIN extends to the deepest hair follicles. Generally not more than 4 mm.

Skinning vulvectomy

- Removes all vulvar skin
- Is rarely needed
- It may be useful for cases of confluent multifocal lesions (immuno-compromised)

Treatment modalities

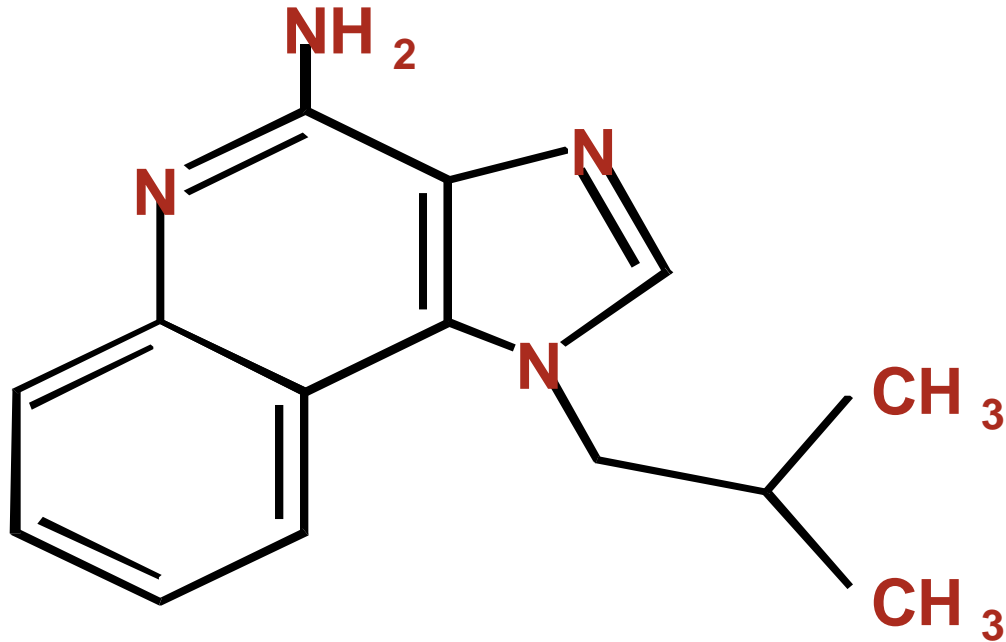
Laser CO₂

Laser ablation is acceptable for the treatment of vulvar HSIL (VIN usual type) when cancer is not suspected.

- It is performed under colposcopic control
- It is useful for mucosal regions
- Deep vaporization < 3 mm
- No scarring
- No histologic material

Treatment modalities.

Imiquimod



Treatment modalities.

Imiquimod

- Binds to toll-like receptor 7, a cell-surface receptor on the immature plasmacytoid dendritic cell.
- Binding initiates an intracellular signaling cascade that results in innate and cell-mediated immune responses.
- Promotes maturation of antigen-presenting cells and secretion of proinflammatory cytokines.
- Initiates a shift to type I T-cell-mediated immunity.
- Direct proapoptotic activity against tumor cells.

VIN differentiated type



Epidemiology (2): VIN differentiated type

- Median age 67 y.o
- Not related to HPV infection
- More probability of progression to invasive carcinoma
- Frequently associated to chronic dermatoses (vulvar lichen sclerosus, lichen planus, squamous cell hyperplasia)

RISK FACTORS: VIN differentiated type

- Past history of a chronic dermatoses (vulvar lichen sclerosis, lichen planus, squamous cell hyperplasia)

Lichen Sclerosus

2-5% risk squamous cell carcinoma



Squamous cell carcinoma

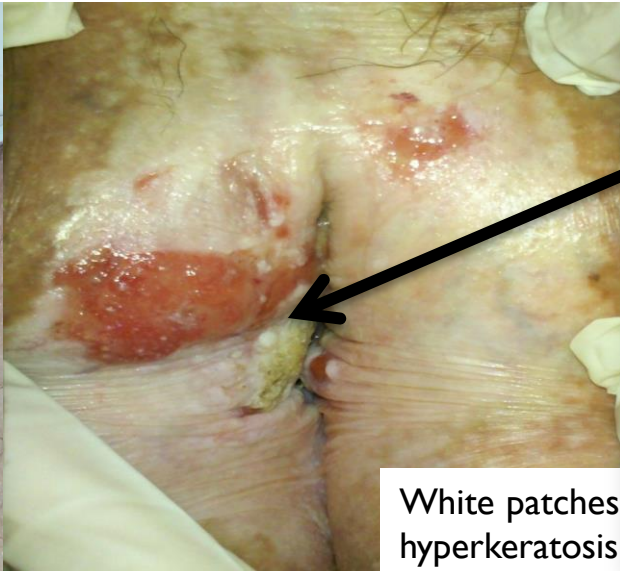


LS and dVIN

Lichen Sclerosus

DURING FOLLOW UP, ALWAYS CONSIDER BIOPSY IF

- Symptoms unresponsive to treatment
- Suspicious changes (persistent area of hyperkeratosis, erosions, new papular lesion)



❖ Patients with lichen sclerosus with dyskeratosis and parakeratosis, hyperplasia and/or basal cellular atypia should be kept under close surveillance as these lesions also tend to progress to squamous cell carcinoma.

- Parakeratosis (P=0.004)
- Dyskeratosis (P<0.001)
- Hyperplasia (P=0.048)
- Basal cellular atypia(P=0.009)

VIN differentiated type

TREATMENT

- SURGERY

IMPORTANT

- Vulvar HSIL in young women – more frequent.
- Detection is limited to visual assessment with confirmation by histopathology.
- Risk factors
- Differentiated VIN: importance of treatment of chronic vulvar dermatoses.



**THANK YOU FOR YOU
ATTENTION**

avsuzuki@gmail.com

colpoclinicas@hotmail.com