



HPV, VIN and Vulvar Disease

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Disclosures

- Speaker/consultant for:
- Novonordisk
- Neogyn
- Sprout
- Sempra
- Shionogi



OBJECTIVES

- Identify the pathogenesis and symptoms associated with VIN
- List 4 colposcopic presentations of VIN
- Describe techniques used for vulvar biopsy
- Explain appropriate treatment options for women with preinvasive and invasive vulvar disease

INCIDENCE:VIN

- VIN= Vulvar Intraepithelial Neoplasia increased by 411% from 1973-2000
- Displays varying degrees of cytoplasmic and nuclear maturation, abnormal nuclei, disruption of normal architecture and mitotic figures

CLASSIFICATION: revised ISSVD 2004

- VIN previously paralleled that of CIN

- *VIN 1 = mild atypia

- *VIN 2 = moderate atypia

- *VIN 3 = severe atypia

However this classification system did not reflect biologic observation



Current classification system

- Current system: 3 types of VIN

FIRST: VIN “Usual” type

- 3 histologic sub types
- (warty, basiloid and mixed)
- Most common: Young women
- HPV related

VIN usual type

- Uni or multiple foci ;
PreMW-40% nulliparous
- May have history
condyloma (HPV 6,11)
and /or LGSIL/HGSIL
(HPV16,18 etc)
- Have demonstrated
potential to progress to
invasive SCC
- Onset associated with
pregnancy



VIN usual type

- Likelihood of progression depends upon risk factors:
- -smoking
- -hx cervical, vaginal, perianal neoplasia /Ca
- -age
- -immune status







Classification system

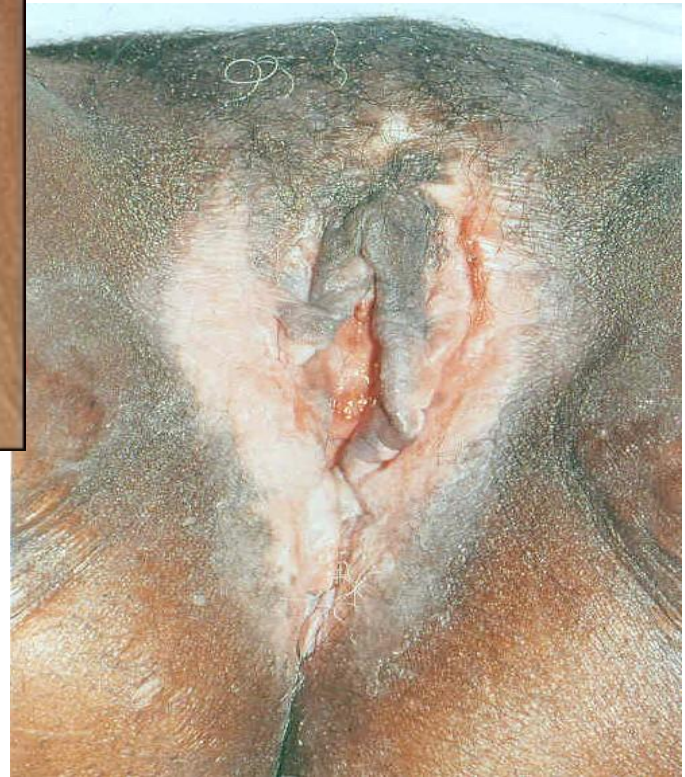
- **Second**= VIN differentiated type
- Older women
- Not HPV related
- Seen in women with hx Lichen Sclerosus or Squamous Cell Hyperplasia (LSC)

VIN: Differentiated (simplex) type

- Often unifocal
- Ulcer, warty papule or hyperkeratotic plaque
- Common in postMPW (but does occur in preMPW)
- Hx chronic irritation & vulvar dermatoses
- Negative for HPV DNA

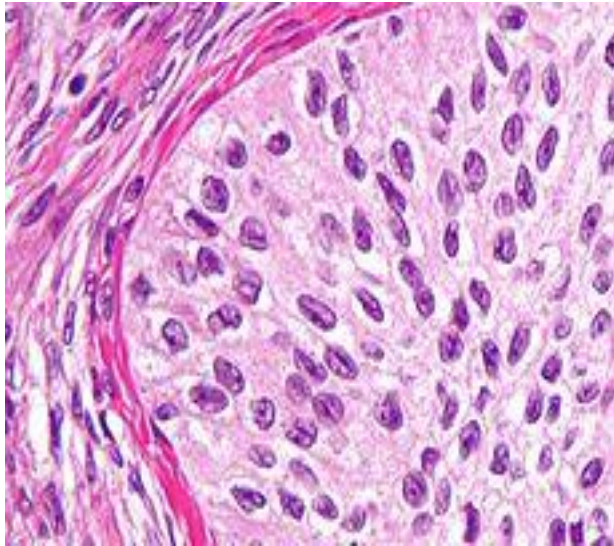
“Hyperplastic skin eruptions characterized by hardening /thickening of skin with accentuation of normal skin markings”





VIN= third type

- Unclassified (rare)
- Unknown origin



Epithelial stromal tumor

Vulvoscopy: challenging for the examiner

- 3 distinct tissue types
- complex architecture
- many artifacts

○ Unlike CIN, VIN can appear different, Depending on where it is located.

Female external genitalia



VIN SYMPTOMS

○ Lesions can appear on:

labia majora

labia minora

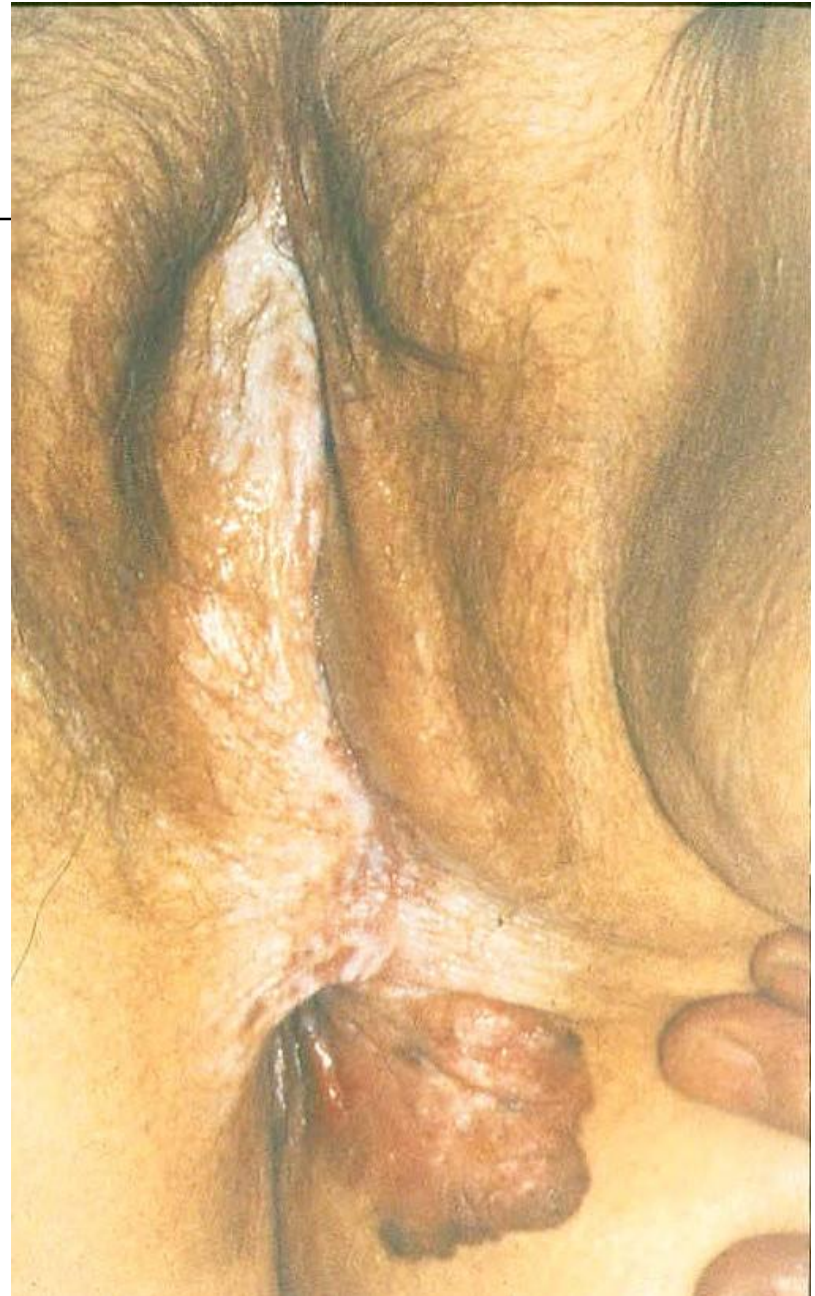
posterior fourchette

perineum

anus

medial thighs

buttocks



VULVOSCOPY



- “Any lesion that cannot be positively identified as benign deserves a biopsy”



VIN SYMPTOMS

- Progresses slowly, often asymptomatic
- First s/s: pruritus
- Physical signs include:
 - ***RED..WHITE..BROWN
 - ***PLAQUES, PAPULES, ULCERS

SYMPTOMS

- Red ulcerated areas in keratinized or nonkeratinized tissue OR hypervascular pink papules or plaques on mucosa



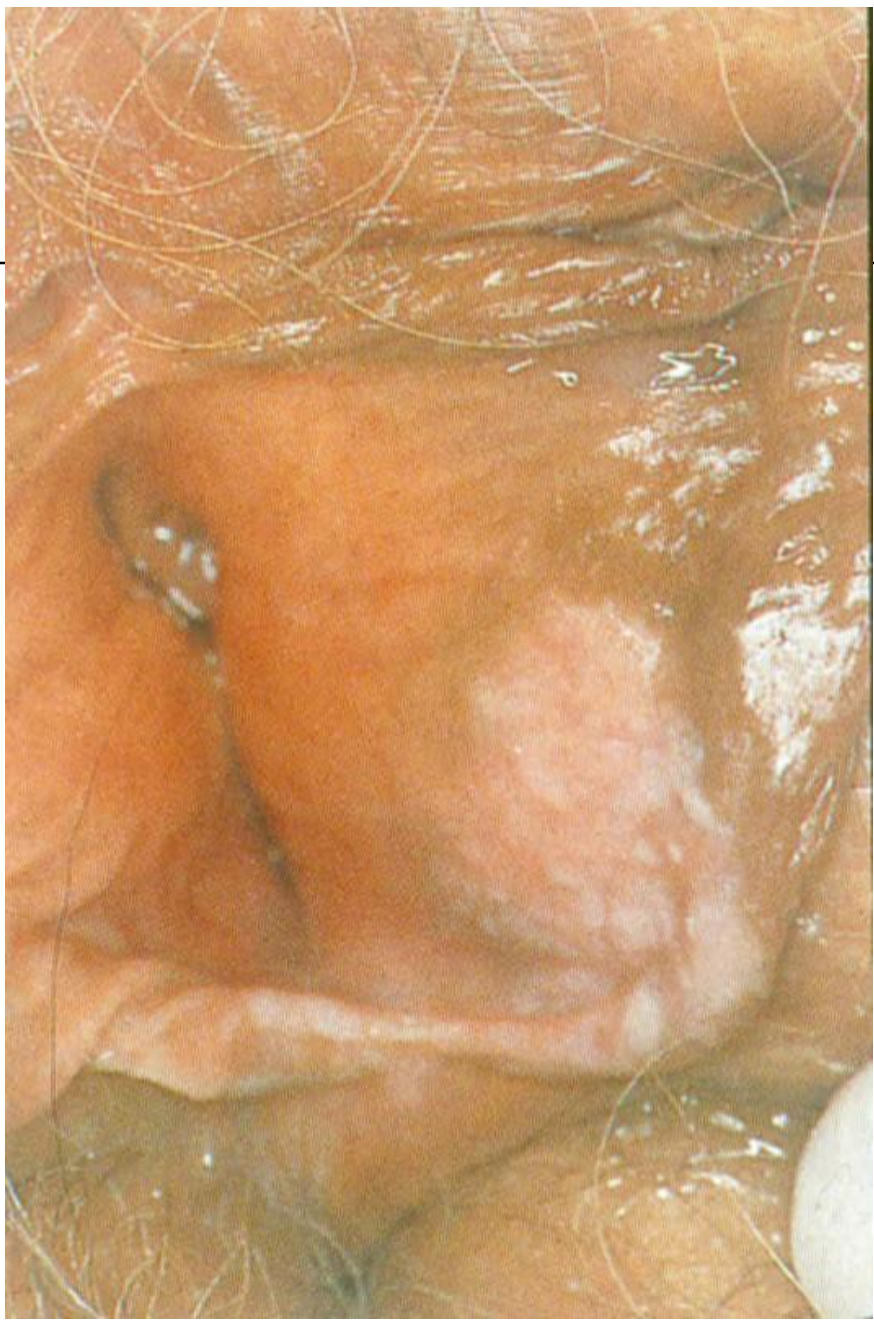




SYMPTOMS

- **White** hypopigmented keratotic nodules or plaques on non-hairbearing epithelium





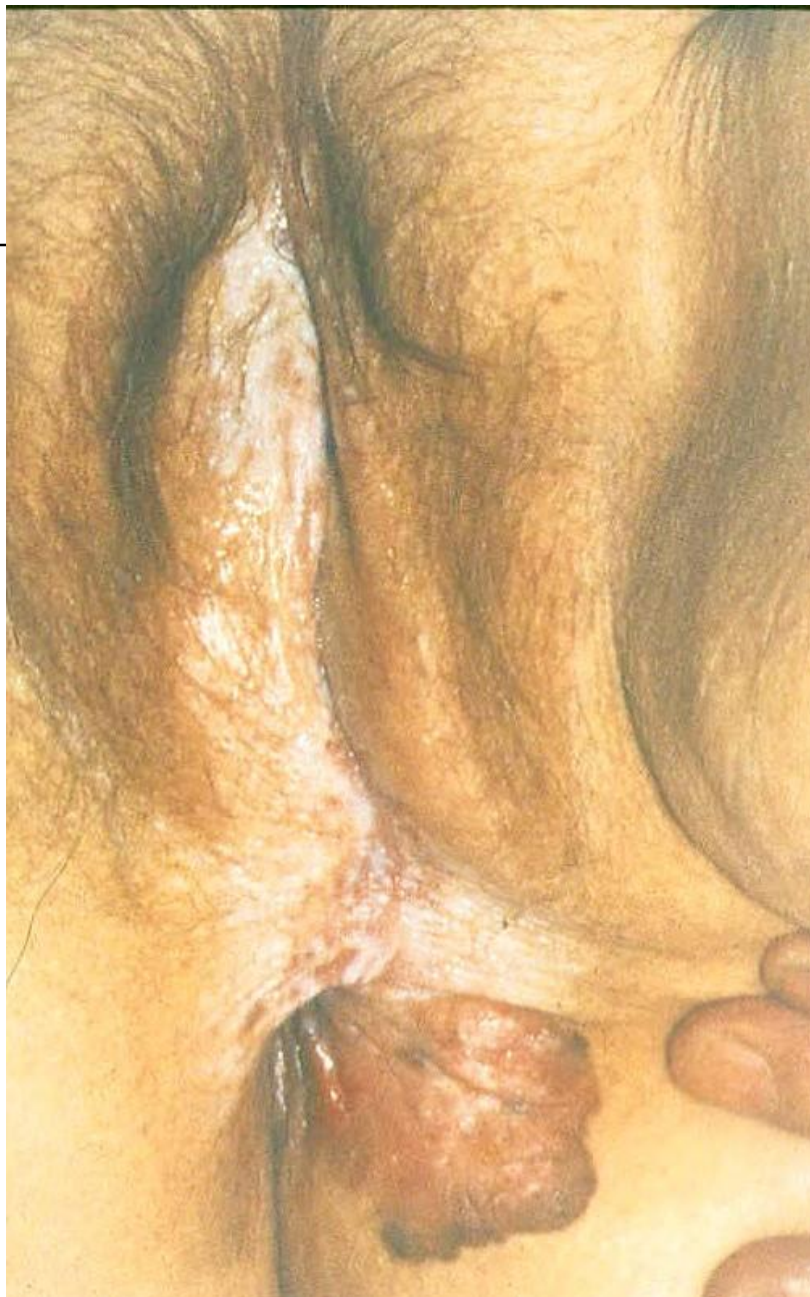




SYMPTOMS

- **Brown** (or grey) pigmented lesions on hair bearing epithelium (1/3 this type)





VIN: Progression to SCC

Differentiated type- progress to invasion-

9% if untreated / 3.3% if treated

Usual type- rate of progression related to:

HPV DNA (E6,7 oncoproteins)

Risk factors (smoking, immunocompetence)

Worldwide human papillomavirus genotype attribution in over 2000 cases of intraepithelial and invasive lesions of the vulva.

Eur J Cancer. 2013 Nov;49(16):3450-61. doi: 10.1016/j.ejca.2013.06.033. Epub 2013 Jul 22.
de Sanjosé S1, Alemany L, Ordi J,etal

BACKGROUND:

- Human papillomavirus (HPV) contribution in vulvar intraepithelial lesions (VIN) and invasive vulvar cancer (IVC) is not clearly established.

METHODS:

- Histologically confirmed VIN and IVC from 39 countries were assembled at the Catalan Institute of Oncology (ICO).

RESULTS:

- Of 2296 cases, 587 were VIN and 1709 IVC. HPV-DNA was detected in 86.7% and 28.6% of the cases respectively. Amongst IVC cases, 25.1% were HPV-DNA and p16(INK4a) positive.
- IVC cases were largely keratinising squamous cell carcinoma (KSCC) (N=1234).
- HPV 16 was the commonest type (72.5%) followed by HPV 33 (6.5%) and HPV 18 (4.6%). Enrichment from VIN to IVC was significantly high for HPV 45 (8.5-fold).

CONCLUSION:

- Our results indicate that HPV contribution in invasive vulvar cancer has probably been overestimated.

Vulvar Carcinoma can arise from other origins

- Melanoma
- (melanocytes;nevi)
- blue-black hyperpigmented flat or slightly raised lesion: 5% of all invasive Vulvar Ca



Vulvar Carcinoma can arise from other origins

- Paget's Disease (apocrine origin):
- Very dark red granular filed with white nodules +/- ulcers in the labial or perianal
- Aggressive lesions, even in the absence of malignancy





Vulvar Ca Diagnosis:

****OFTEN MISSED!!**

- Comprises 4% GYN Cancers
- 35% Dx delayed by 1 year or more..
- Pt: up to 9 mos of s/s before seeking care
- Provider: up to 7 mos of observing s/s before Bx
- **Immunocompetence is KEY in terms of progression / invasion (5yr survival:75%)

BEYOND the VULVA : **REMEMBER HPV r/t OTHER Cancers**

OROPHARYGEAL

HPV 16 with E6-7 oncogene viral integration

- **OPC: 6th most common**
- **worldwide**
- **>11,000 US cases/yr**
- **White men >35yo with >6 oral recep partners**

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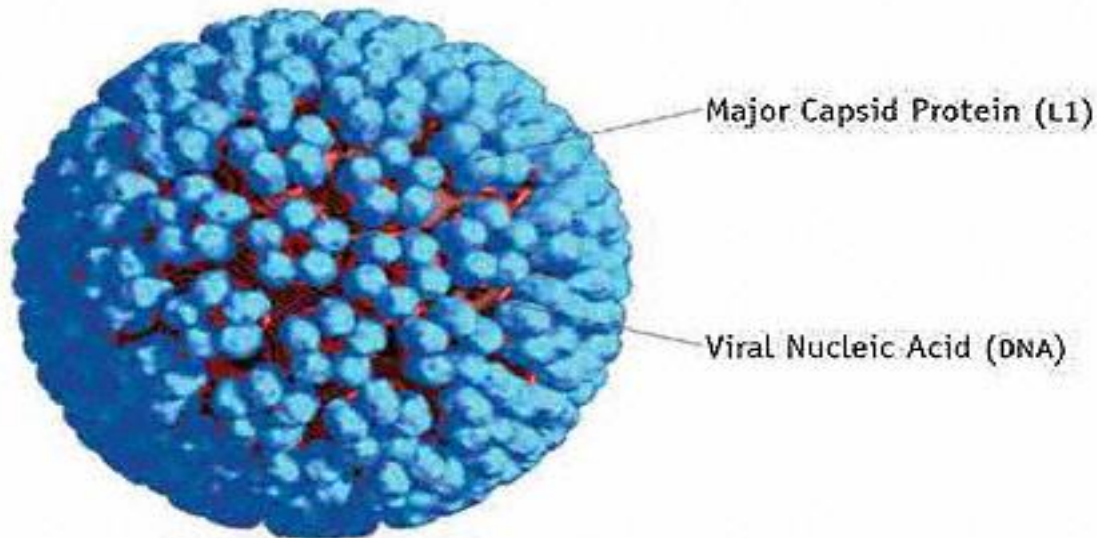
○ **ANAL**

- **HPV 16/18**
- **6000 new cases /yr**
- **400 deaths**
- **1-2% all GI cancers**



Thank you for your kind attention!

THREE-DIMENSIONAL MODEL OF HUMAN PAPILLOMAVIRUS



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Published in The PRN Notebook, Volume 6, Number 3, September 2001 and
The PRN Notebook Online at www.prn.org
Three-dimensional model of HPV Created by Louis E. Henderson, PhD,
Frederick Cancer Research Center.