E le isterectomizzate?

Dott. Claudio Zanardi
BOLOGNA

Vaginal Cancer

- Rare tumor representing only 1-2% of all gynecologic malignancies:
  - **primary vaginal cancer**
  - **metastatic cancer to the vagina**
- 80-90% are metastatic
- Mean age of patients with primary vaginal cancer is 60-65 years
- Most primary tumors are squamous cell in origin

VAGINAL CANCER

- **Relatively uncommon tumor**

Incidence of vaginal cancers is about 1-2/100.000/yr

100.000 women would require screening to detect one vaginal cancer

Vaginal Cancer

- **84% of cancers in vaginal area are secondary**
  - **Cervical**
  - **Uterine**
  - **Colorectal**
  - **Ovary**

Fu YS, Pathology of the Uterine Cervix, Vagina and Vulva, 2nd ed. 2002

Vaginal Carcinoma

- Squamous Cell 80-85%
- Clear Cell 10-14%
- Sarcoma 3-4%
- Melanoma 2-3%

NEOPLASIA INTRAEPITELIALE VAGINALE (VAIN)

LA NEOPLASIA INTRAEPITELIALE VAGINALE (VAIN) RAPPRESENTA UNA PATOLOGIA DELLA VAGINA CON SIGNIFICATO PRENEOPLASTICO, MA LA RELATIVA RARITÀ RAPPRESENTA UN IMPEDIMENTO AD UNA COMPRENSIONE COMPLETA DEL PROCESSO DELLA MALATTIA E DELLA SUA STORIA NATURALE.

Di conseguenza, molte delle informazioni rappresentano un'estrapolazione della nostra conoscenza sulla fisiopatologia della neoplasia intraepiteliale cervicale e vulvare.

Cancer 1984 Sep 1;54(5):869-75

VAIN
CLASSIFICATION

- The disease is classified according to the depth of epithelial involvement: VAIN 1 and 2 involve the lower one-third and two-thirds of the epithelium, respectively, and VAIN 3 involves more than two-thirds of the epithelium.Carcinoma in situ, which encompasses the full thickness of the epithelium, is included under VAIN 3.
- Intraepithelial dysplasia of glandular origin, or atypical vaginal adenosis, is a separate entity. This lesion has a well-established association with in utero diethylstilbestrol (DES) exposure. In addition, it may be a precursor to DES-associated clear-cell adenocarcinoma.

VAIN
EPIDEMIOLOGY

- The true incidence of VAIN is unknown, but is estimated at 0.2 to 0.3 cases per 100,000 women in the United States

Am J Obstet Gynecol 1977 Nov 1;129(5):525-32

- The average patient is between 43 and 60 years of age, slightly younger than the age for vaginal carcinoma

Int J Cancer 1997 Jul 29;72(3):412-5.

Vaginal Cancer precursors

- VAIN – avg age of VAIN 3 is 53
- Ratio of VAIN to CIN is 1:100
- 5-9 % progress to Vaginal Ca
- Hallmark of VAIN
  - cytologic atypia-Pleomorphisim, irreg nuclear contours and chromatin clumping
  - Abnormal maturation
  - nuclear enlargement

Vaginal Intraepithelial Neoplasia Grade 2-3 (VAIN 2-3)

- Natural history of HPV-related vaginal cancer closely mimics that of cervical cancer
- Cancer arises from VAIN 2-3 lesions
  - In a series of untreated VAIN 2-3, 2% progressed to invasive cancer at a median follow-up of 2 years

Obstetrics & Gynecology Clinics of North America. 23(2):325-45, 1996 Jun.

Vaginal Cancer Etiology

- Infection with certain high-risk types of the human papillomavirus (HPV 16 and 18)

  may be associated with up to 80% of cases of VAIN

Cancer Research UK (2002)

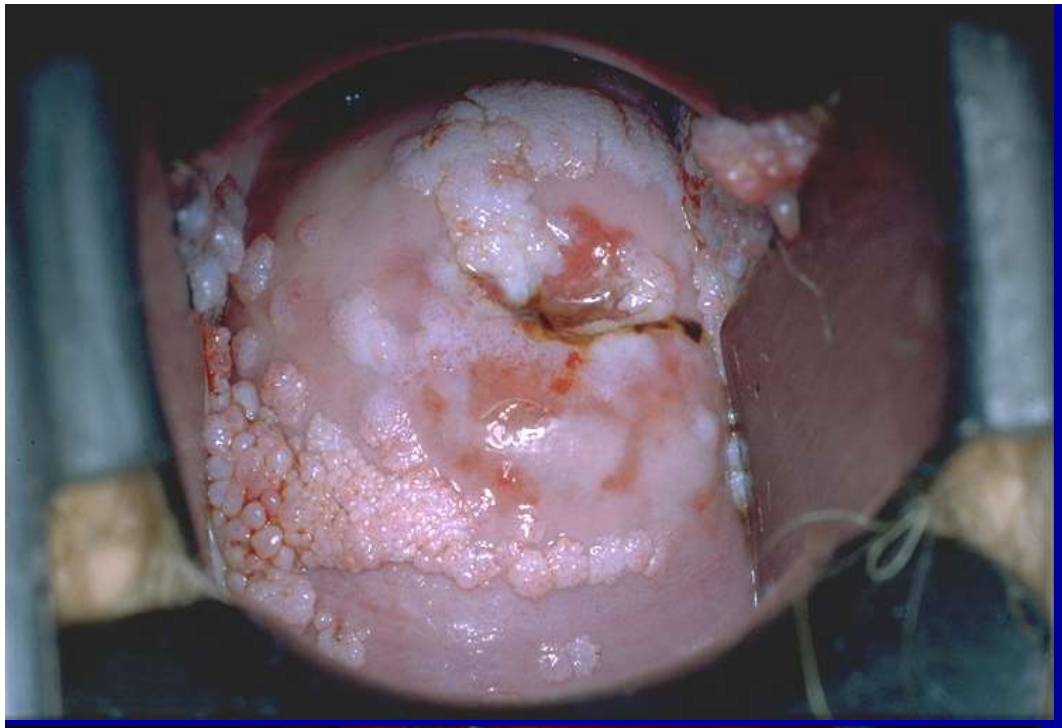
PATOLOGIA VAGINALE

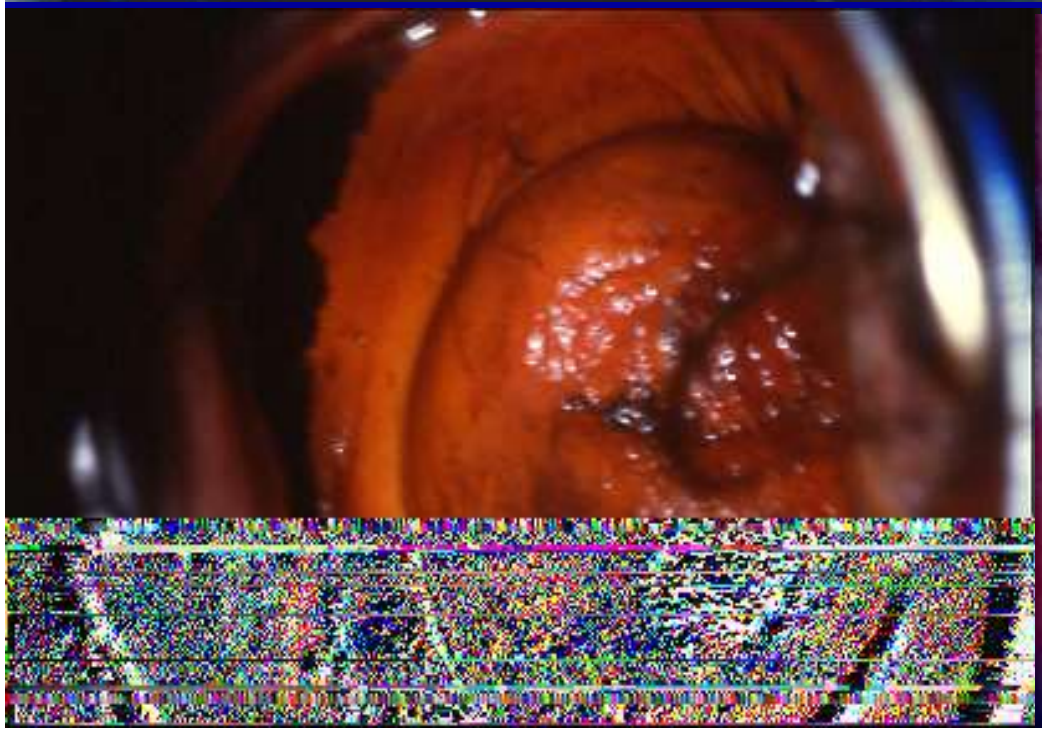
•Alcuni tipi di Papillomavirus Umano (HPV) possono indurre a livello vaginale la formazione di lesioni uniche o associate ad altre del basso tratto genitale (BTG).

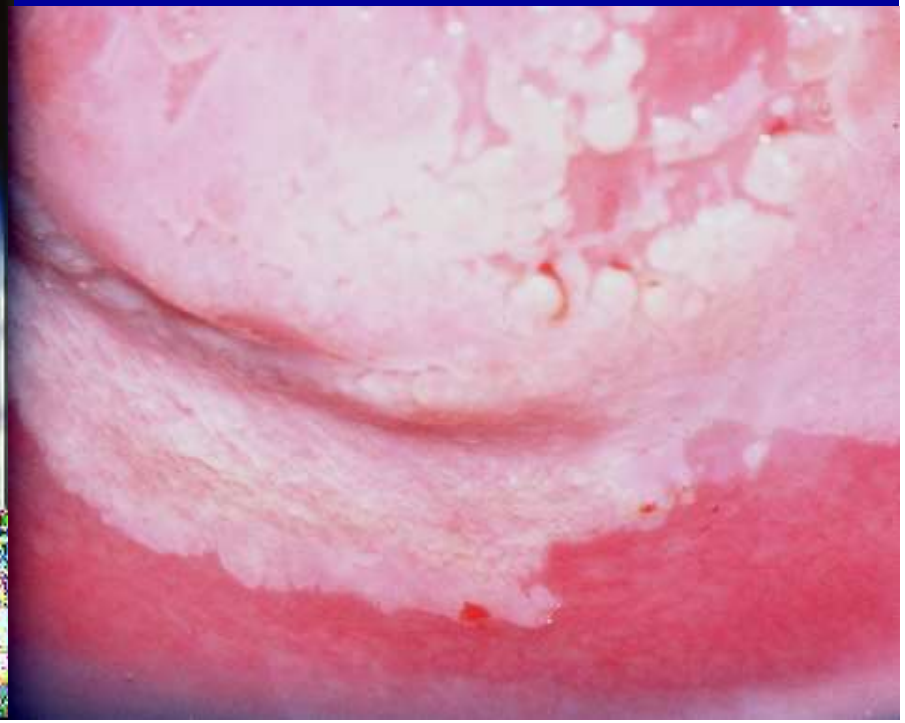
• Nella maggior parte dei casi, lesioni HPV-associate coesistono a livello della cervice uterina.

•Le lesioni vaginali mostrano aspetti colposcopici simili a quelli presenti sulla portio, allorché la zona di trasformazione (ZT) si estenda gradualmente, in modo variabile, sulle pareti della vagina.

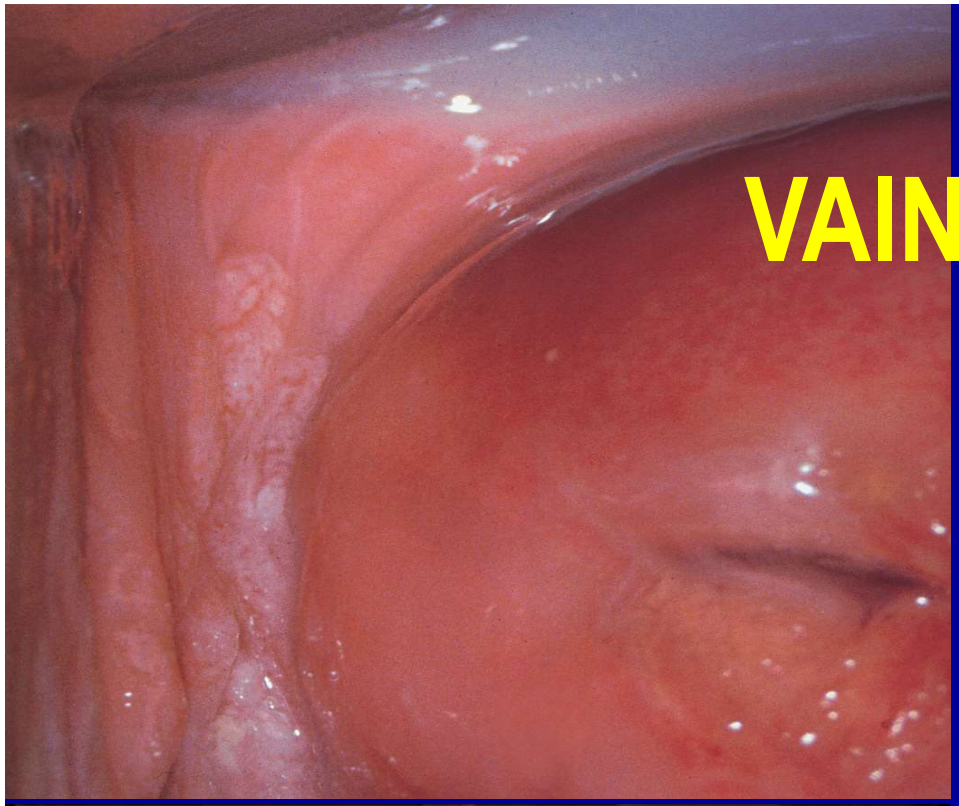
LESIONI HPV-ASSOCIATE CERVICALI E VAGINALI

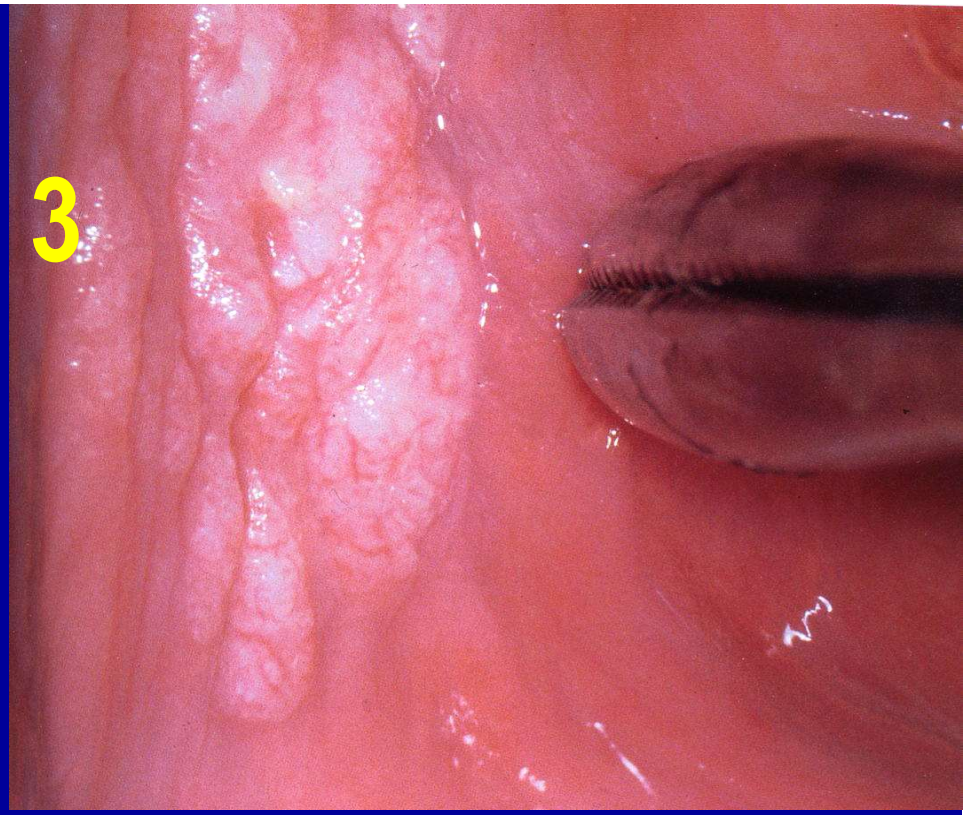


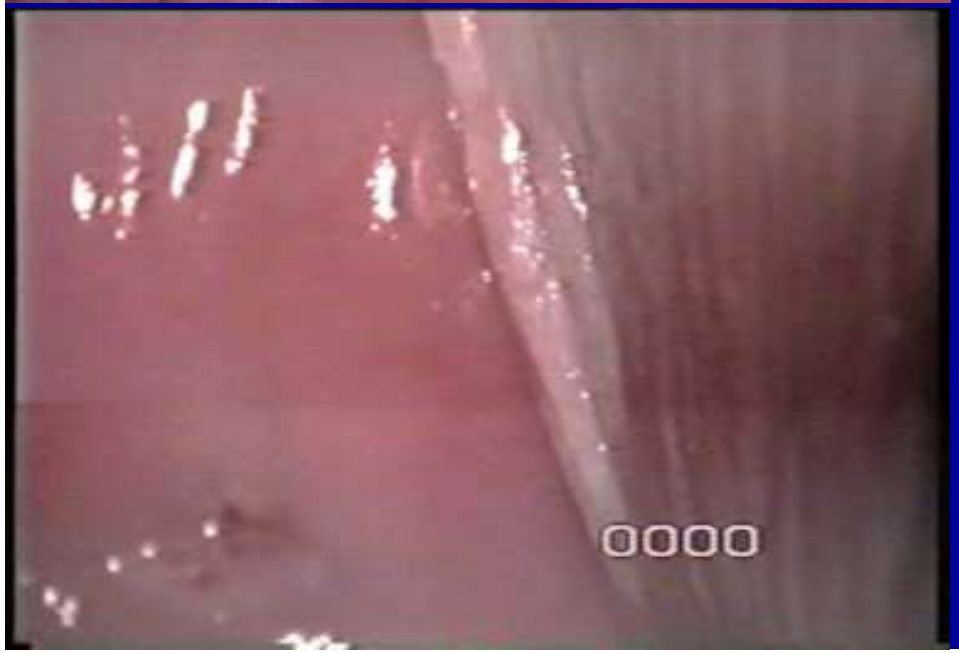




VAIN 3



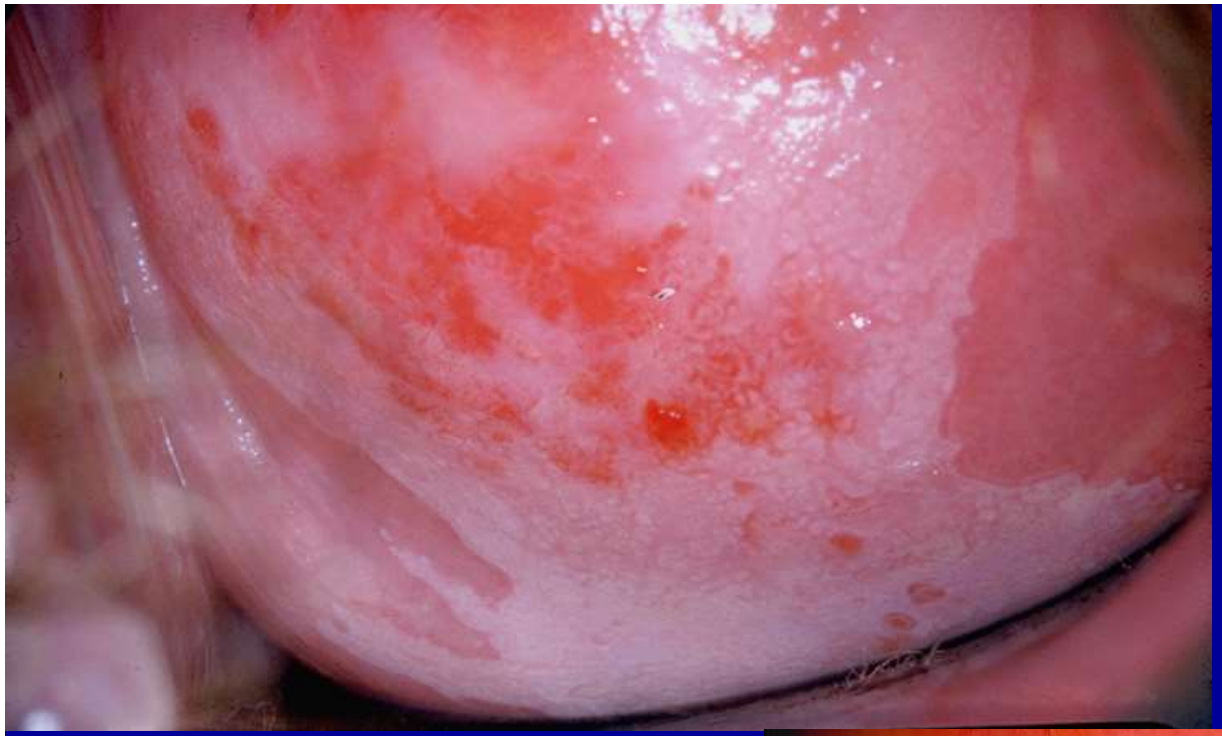




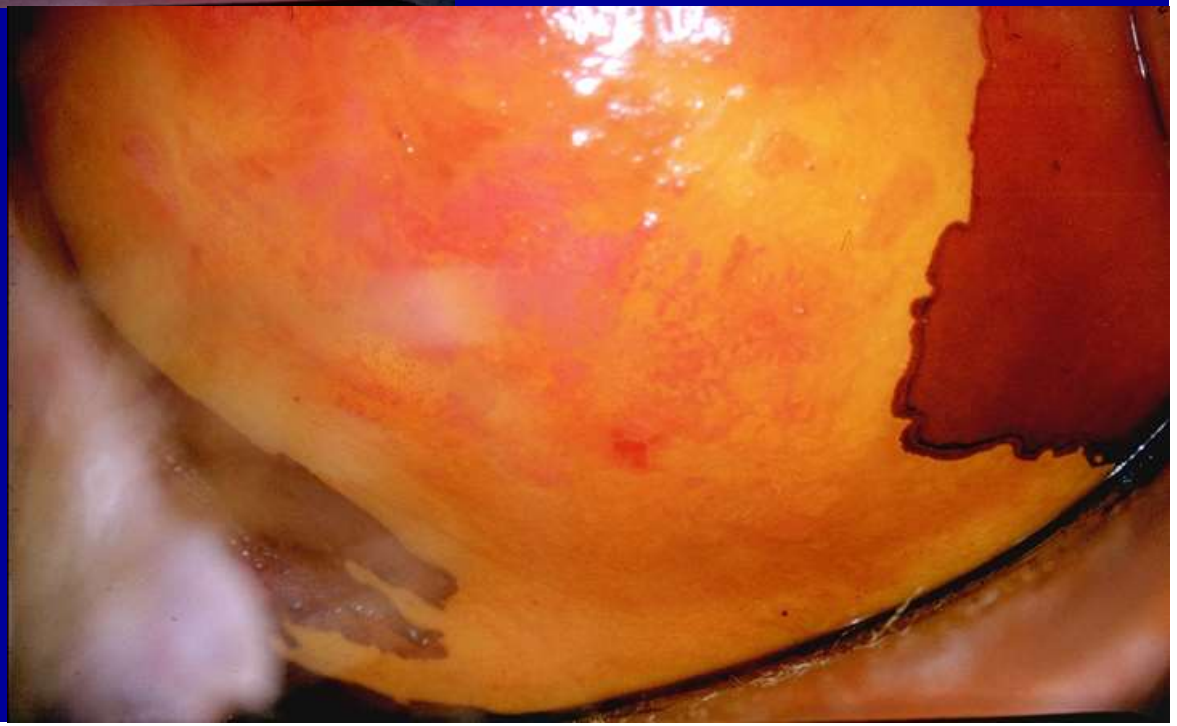
Se la colposcopia risultasse normale dopo un pap-test anormale,prima di praticare un cono cervicale diagnostico, sarebbe bene effettuare un attento controllo di tutto l'epitelio vaginale al fine di escludere una VAIN.

LA VAIN È SPESSO CONCOMITANTE A NEOPLASIE INTRAEPITELIALI CERVICALI E VULVARI HPV CORRELATE

- l'associazione con la CIN è stata riscontrata nel 65-70% dei casi
- l'associazione con la VIN nel 10% dei casi
- oltre i 2/3 delle donne con VAIN sono state precedentemente sottoposte ad isterectomia



VAIN E CIN CONCOMITANTI



Tra le donne isterectomizzate per carcinoma in situ cervicale il rischio è maggiore, e la VAIN compare in circa il 5-10% dei casi: nel 50% dei casi il suo grado sarebbe simile a quello della CIN pregressa.

Il 70% delle VAIN si riscontra in donne isterectomizzate per CIN o per cancro, con un tempo medio di comparsa dopo l'intervento di circa 41 mesi.

•Kalogirou D., Antoniou G., Karakitsos P Botsis D., Papadimitriou A., Giannikos L.: Eur J Gynaecol Oncol 1997;18:188-91

•Coronel-Brizio P., Olivares Nowak J., Palafox Sanchez F.: Recurrence of high grade squamous intraepithelial lesions following hysterectomy. Ginecol Obstet Mex 1999;67:415-8

•Schockaert S., Poppe W., Arbyn M., Vreguts T., Verguts J.: Incidence of vaginal intraepithelial neoplasia after hysterectomy for cervical intraepithelial neoplasia: a restrospective study. Am J Obstet Gynecol 2008;199:113.e1-113.e5

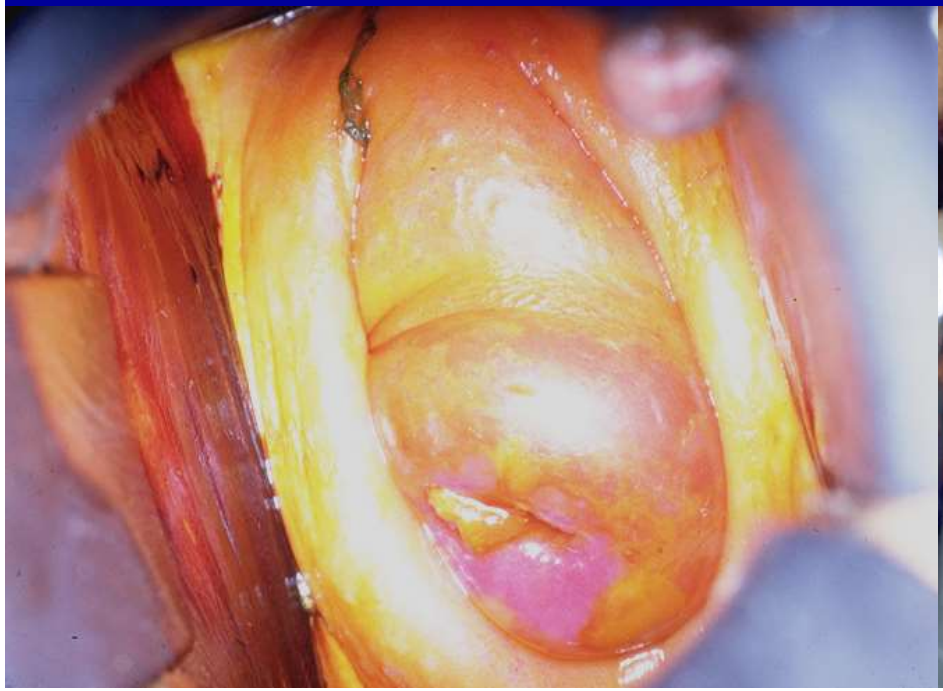
Incidence of vaginal intraepithelial neoplasia after hysterectomy for cervical intraepithelial neoplasia:

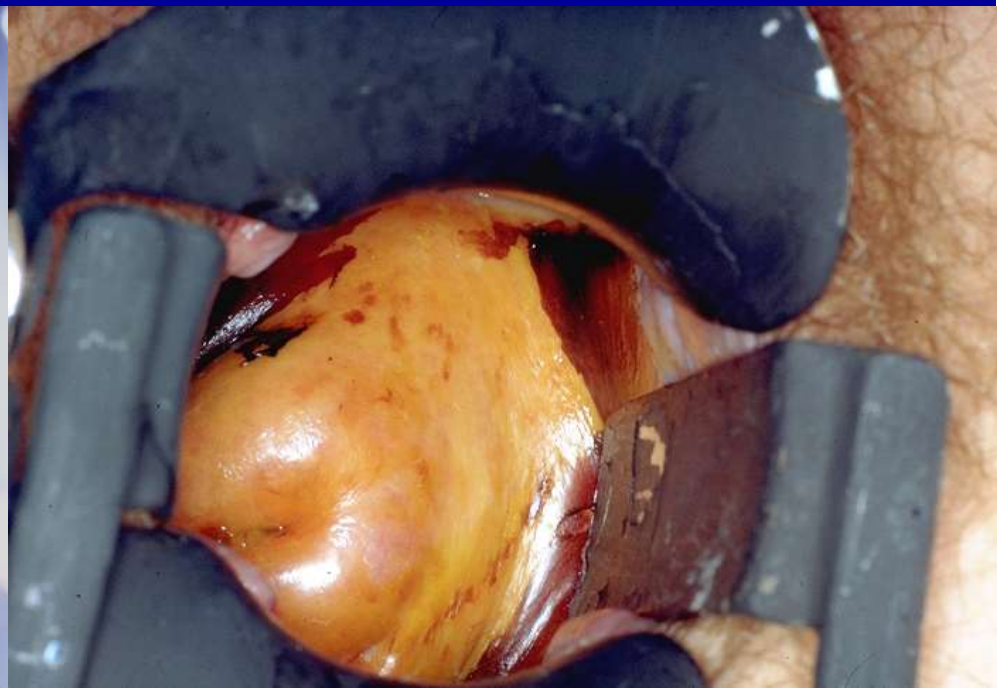
Hysterectomy may not be considered as a definitive therapy for CIN2+ because the incidence rate of subsequent VAIN2+ is as high as 7.4%.

Schockaert S et al.
Am J Obstet Gynecol. 2008

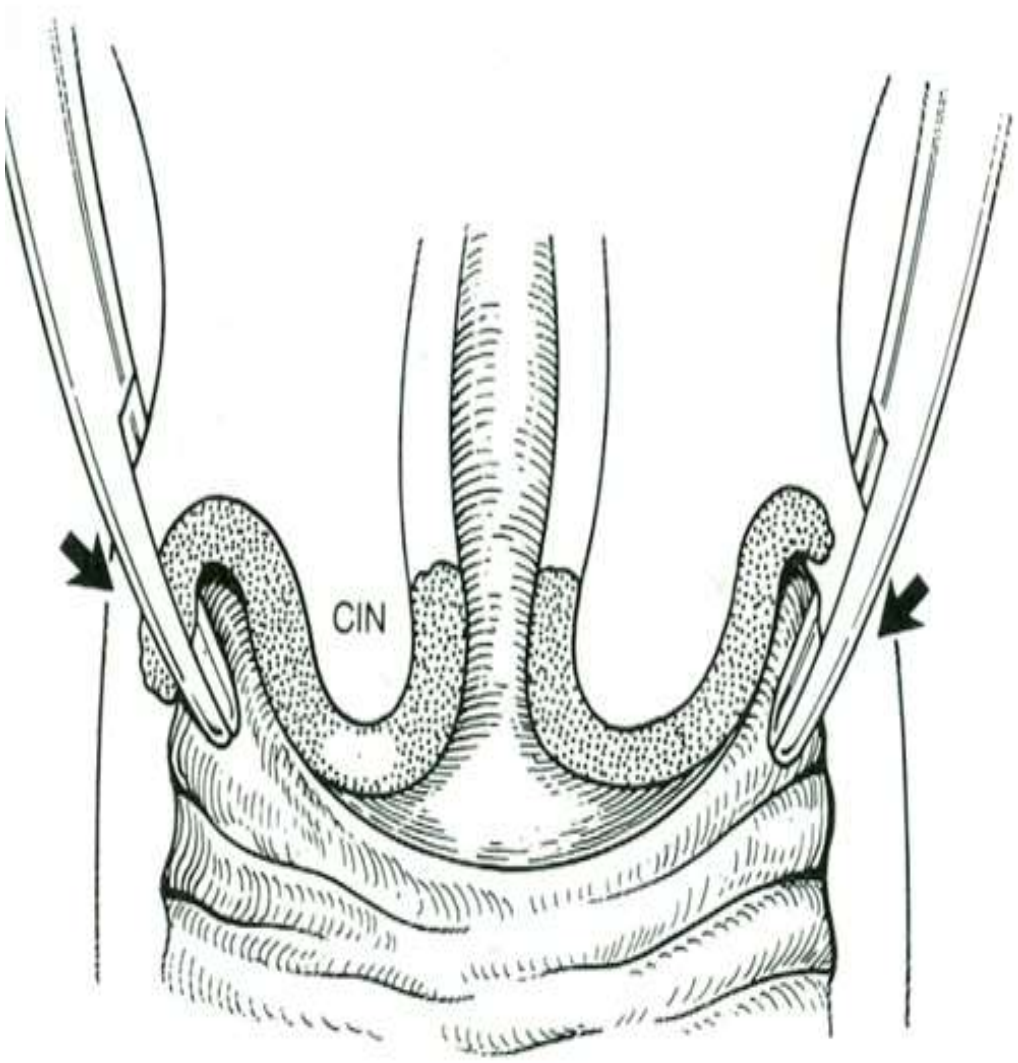
PATOLOGIA VAGINALE

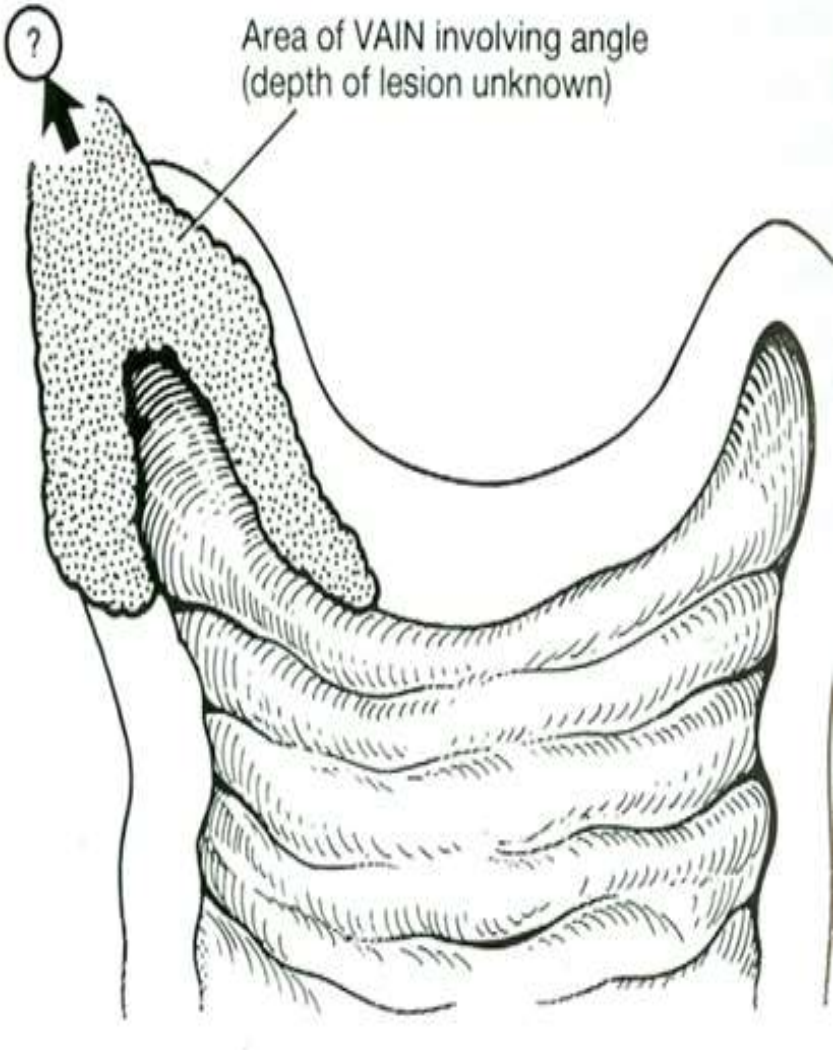
- **Colposcopicamente, la zona di trasformazione anormale (ANTZ) può interessare la maggior parte della cervice e allargarsi fino al terzo superiore della vagina.**





VAIN

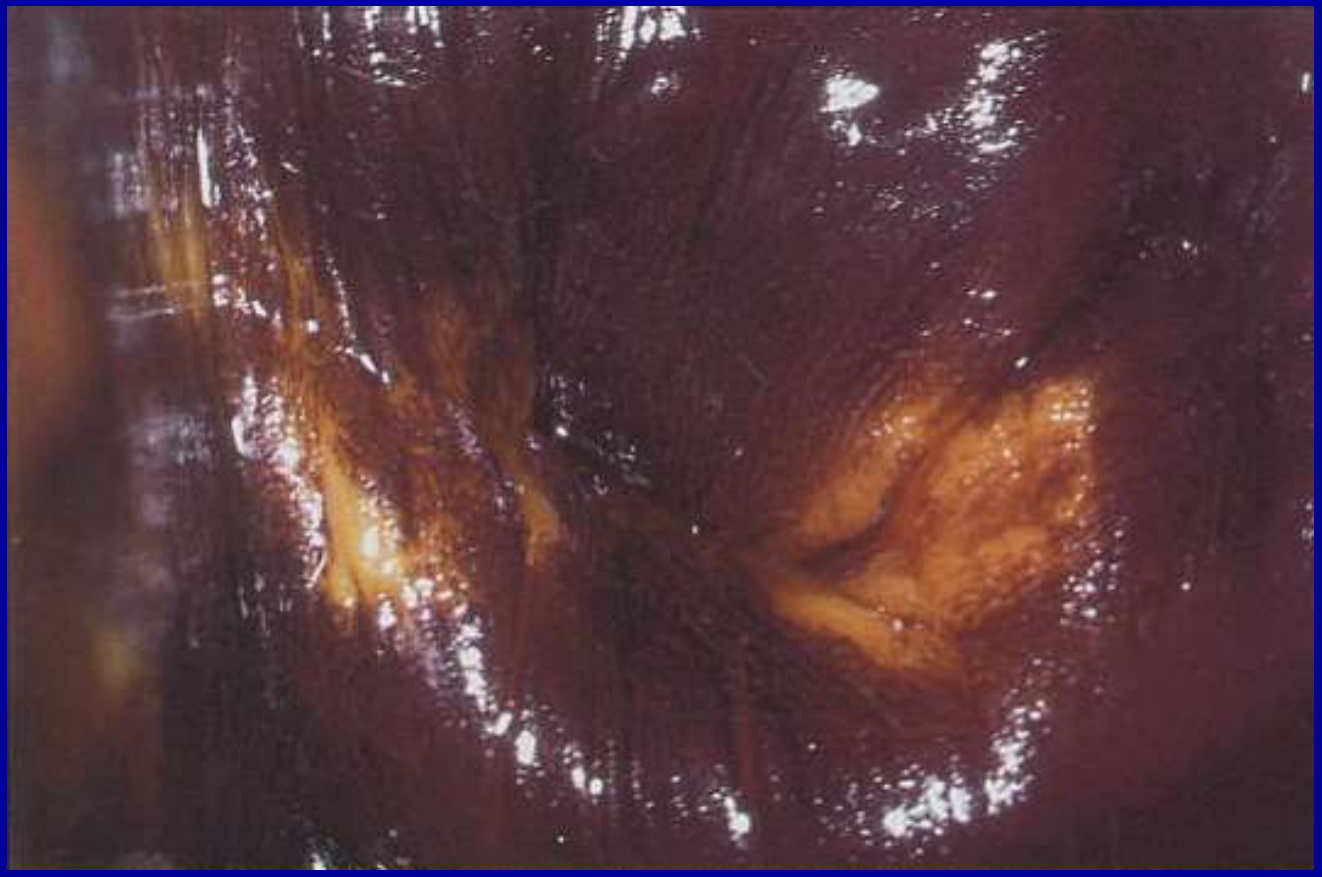




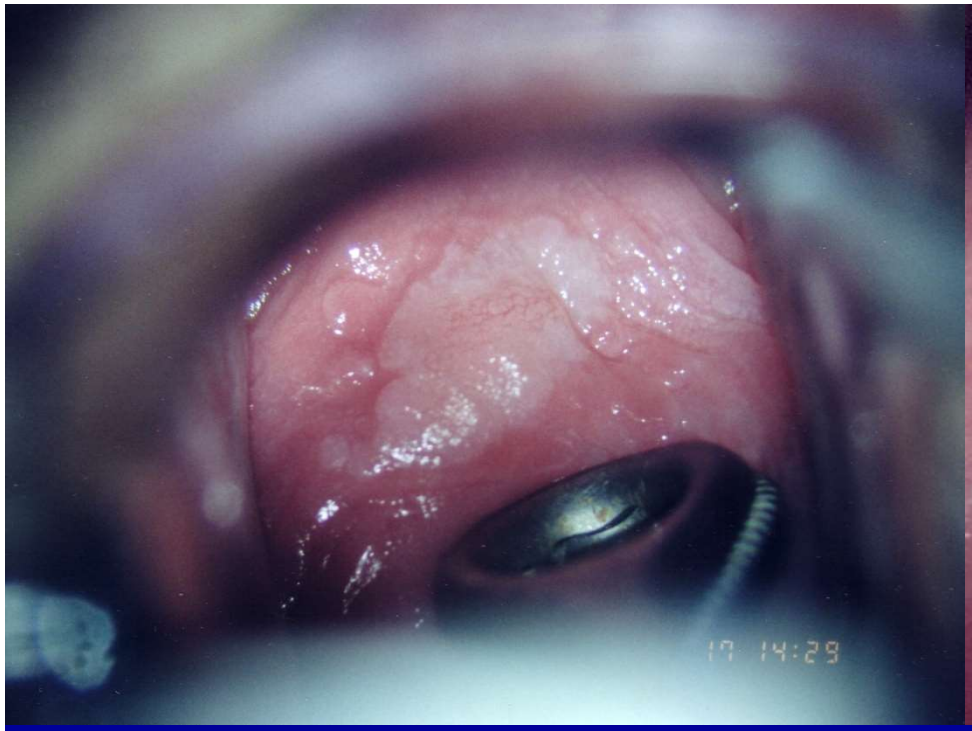
Vaginal Cancer precursors

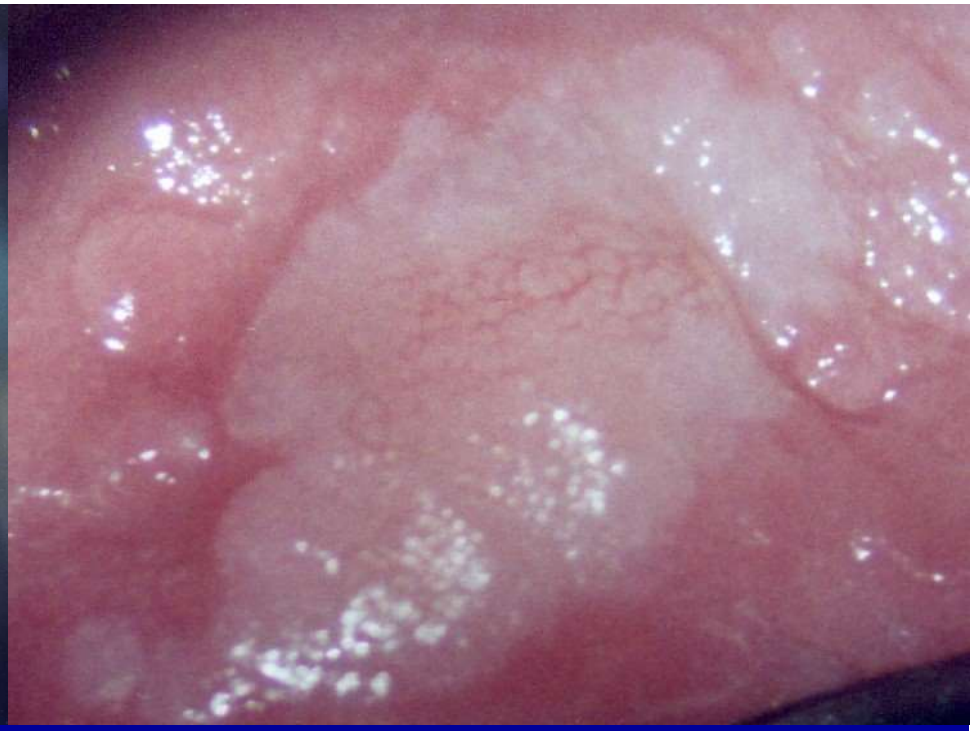
- VAIN 3
  - usually occurs in upper third of vagina and is multifocal and diffuse in half the cases.
  - Colposcopic findings are similar to those of CIN (aceto white epithelium with punctations and mosaic patterns)

PATOLOGIA VAGINALE



Lesioni intraepiteliali isolate, e quindi al di fuori della ZT, possono essere evidenziate soprattutto a livello del terzo superiore della vagina oppure della cupola vaginale dopo isterectomia.



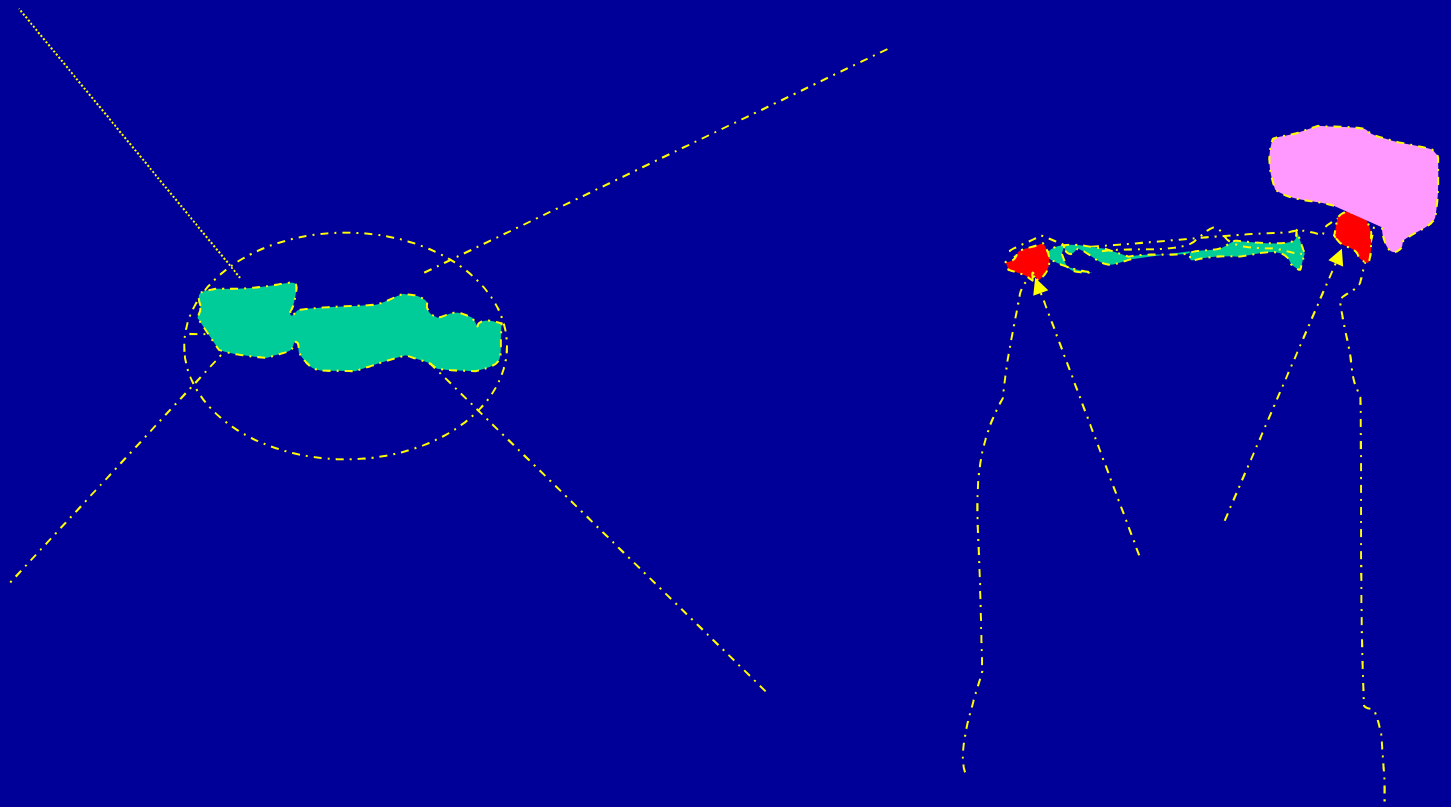


VAIN

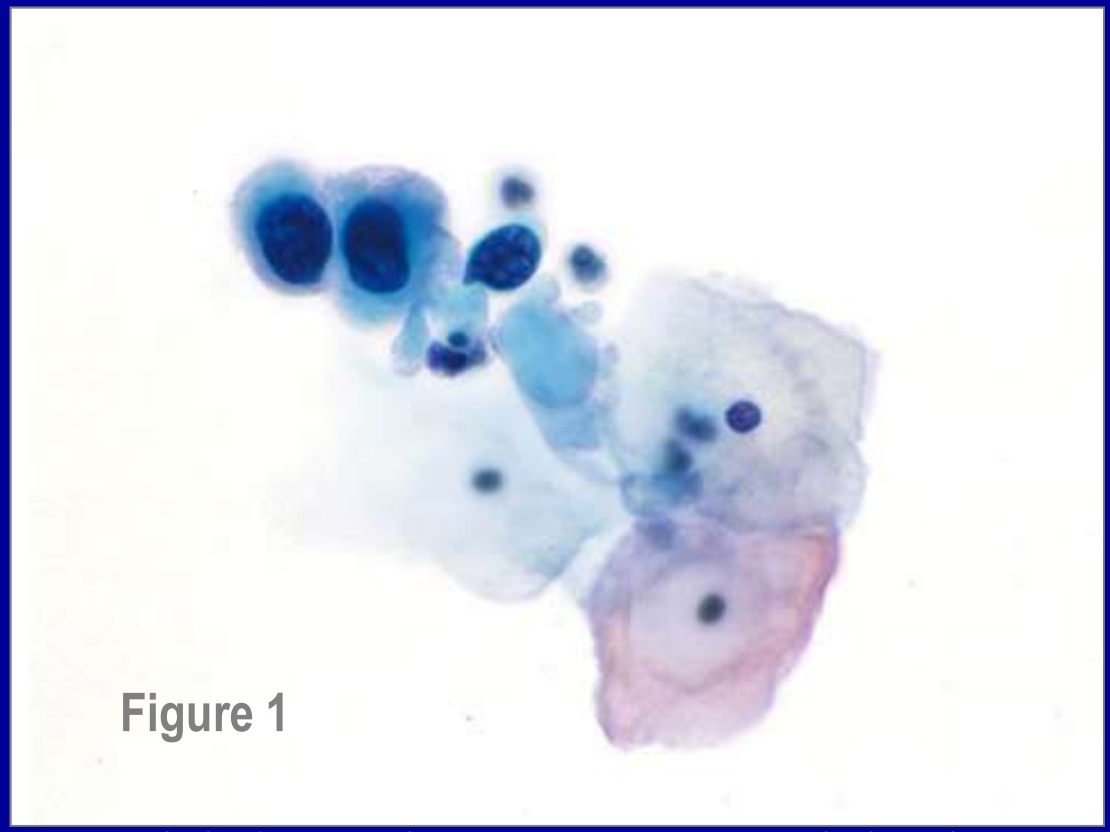
PATOLOGIA VAGINALE

- In caso di VAIN 3 in corrispondenza della colporrafia della cupola vaginale dopo isterectomia, è bene accertarsi, prima di ogni trattamento, dell'assenza di patologie neoplastiche a livello pelvico, mediante indagini strumentali adeguate (ecografia 3D, TAC, RM, Laparoscopia).

PATOLOGIA VAGINALE



Initial Presentation



A 43-year-old female presents with the vaginal smear shown in Figure 1. The patient previously had a vaginal hysterectomy for a CIN 2 lesion.

Given a Cytologic Diagnosis of HSIL, the Preferred Management Option at This Time Is:

Question 2

A. Reflex HPV-DNA testing

B. Repeat cytology in 3-6 months

C. Colposcopy

Given a Cytologic Diagnosis of HSIL, the Preferred Management Option at This Time Is:

Answer 2

C. Colposcopy: Correct

The diagnosis of HSIL requires colposcopy to detect high-grade lesions. Reflex HPV-DNA testing, although appropriate for triage of ASC-US cytology, does not have a role in the management of HSIL. Observation and repeat cytologic surveillance is also not appropriate for HSIL. Treatment with 5-FU cream should not be initiated until a definitive diagnosis is made.

Diagnostic Study

Colposcopy of This Patient Can Be Seen in Figures 2 and 3.
Figure 2 Shows a Lesion at the Apex of the Vagina Within the Left Fornix After Acetic Acid.
Figure 3 Shows the Same Lesion Under a Green Filter.

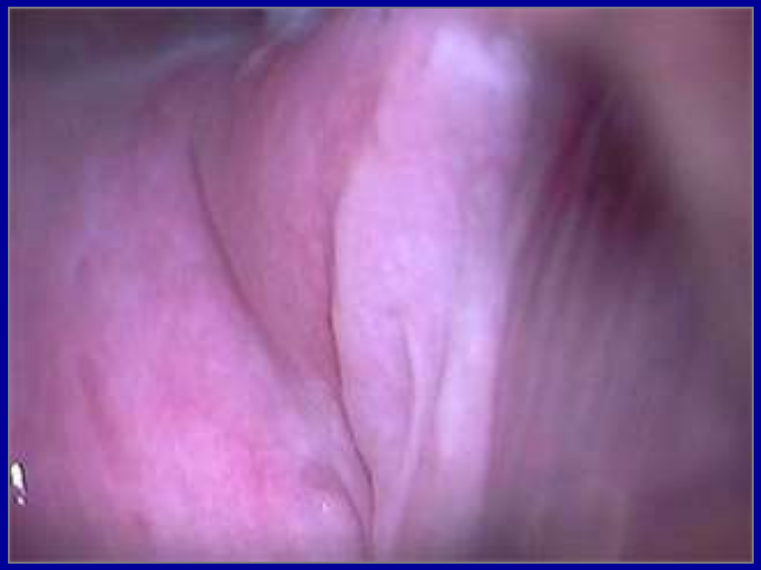


Figure 2: Image without filter

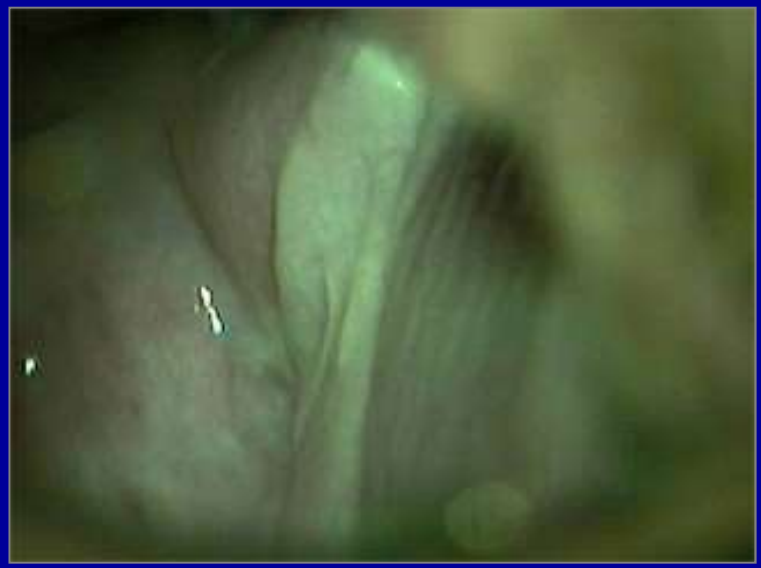


Figure 3: Image with filter

Diagnostic Study

The Next Appropriate Step Is:

Answer 4

A. Lugol's staining of the vagina: Correct

In order to determine if there are other lesions in the vagina, Lugol's iodine should be applied. This will help to highlight the lesion and eventually direct therapy. Biopsy will eventually be necessary for diagnosis, but Lugol's staining prior to this may be helpful. Lugol's staining is very important in vaginal colposcopy as the multiple folds and rugae of the vagina make a colposcopic exam more difficult. The use of Lugol's can also highlight areas where lesions can be missed.

Treatment such as laser ablation or cryotherapy should not be initiated until a diagnosis is made.

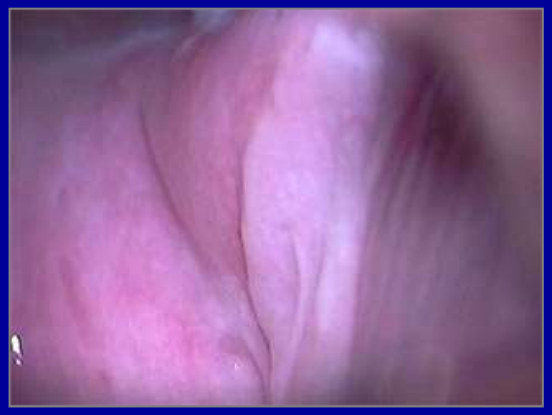


Figure 2: Image without filter

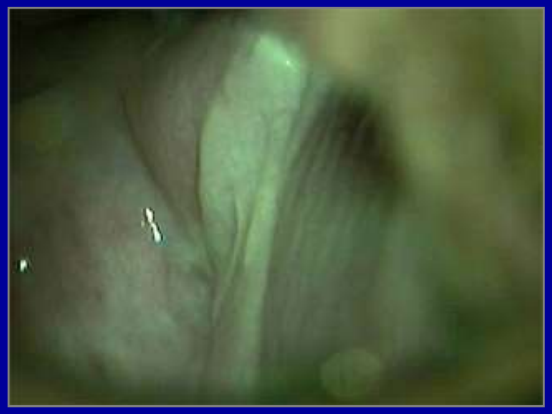


Figure 3: Image with filter

Final Diagnosis

The Result of Lugol's Staining Is Seen in Figure 4, Highlighting the Lesion Seen in the Left Vaginal Fornix. The Pathology From a Biopsy of This Lesion Is Seen in Figure 5.

Figure 4: Lugol's staining

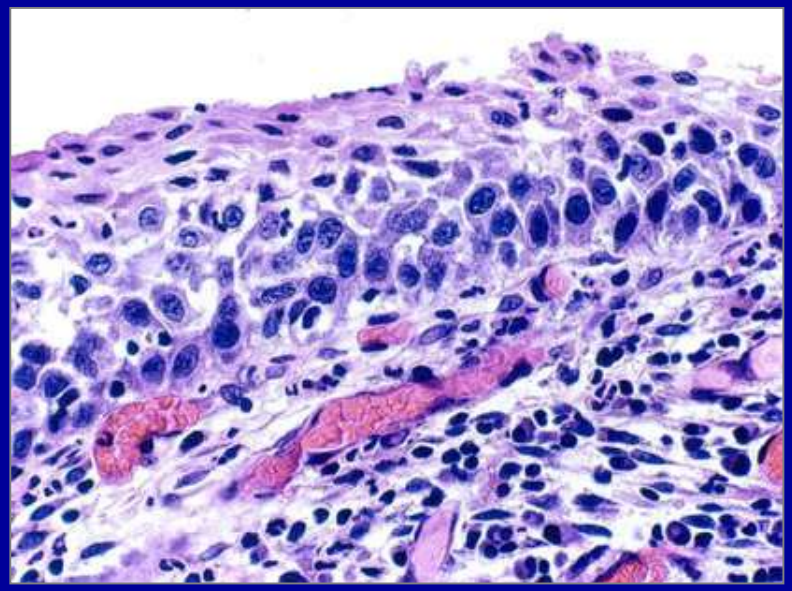


Figure 5: Pathology

VAIN

- **LA MULTIFOCALITÀ DELLE LESIONI È STATA DESCRITTA FINO AL 61% DEI CASI (4).**
- **DOPO ISTERECTOMIA LE LESIONI SAREBBERO SINGOLE FINO ALL'80% DEI CASI (11).**

4. Dodge J.A. et Al. Gynecol Oncol 2001;83:363-9
11. Murta EF. et Al. Arch Gynecol Obstet 2005;272(4):261-4

VAIN

TERAPIA

- Vaporizzazione laser
- Escissione locale laser,Leep
- Vaginectomia parziale o totale

For This Patient, the Correct Management Option at This Time Is:

Question 6

A. Cryotherapy

B. Laser vaporization or excision

C. Loop excision

D. 5-Fluorouracil cream

Treatment

The Correct Management Options Are:

Answer 6

B. Laser vaporization: Correct

Most clinicians would treat this lesion with laser vaporization, which is the preferred technique and allows for adequate treatment to a depth of 1-2 mm and destruction of the entire lesion. If there is any concern that an invasive component is present, excision of the lesion should be performed.

Laser CO_2

- **Il trattamento con laser CO_2 sarebbe curativo nel 42- 90% dei casi, la facile ripetitività e gli scarsi effetti collaterali, unito alla precisione del trattamento, che può combinare escissione e vaporizzazione, viene considerato da molti Autori il trattamento di scelta. L'uso del laser non è gravato dalle complicanze riportate con altri metodi, ma si tratta di una tecnica che richiede importanti investimenti economici e una lunga curva di apprendimento, soprattutto per quanto riguarda le tecniche escissionali sulla vagina; è una tecnica molto versatile che in mani esperte è in grado di trattare aree vaginali altrimenti difficilmente raggiungibili, quali i recessi angolari alla cupola dopo isterectomia.**

- *Rome R.M., England P.G. Int J Gynecol Cancer 2000;10:382-90*

Treatment

The Correct Management Options Are:

Answer 6

continued

C. Loop excision: Correct

Loop excision has been reported for vaginal lesions and, in the hands of experienced operators, it may be possible to use loop excision, but laser vaporization may be more precise in controlling the depth of treatment.

D. 5-Fluorouracil cream: Correct

5-FU cream has been used for resistant cases, but there is an increased incidence of ulcerations with this technique.

Treatment

The Correct Management Options Are:

Answer 6

continued

A. Cryotherapy: Incorrect

Cryotherapy is not the preferred method as it is difficult to control the depth of treatment.

HPV-DNA TEST NELLE DONNE ISTERECTOMIZZATE

E' STATO SUGGERITO DI AGGIUNGERE L'HPV-DNA TEST PER LA RICERCA DEI CEPPI ONCOGENI NEL FOLLOW-UP, IN QUANTO SAREBBE MAGGIORE LA CAPACITÀ DI PREDIRE LA PERSISTENZA O PROGRESSIONE DELLA VAIN DOPO TRATTAMENTO PRIMA DEL RISCONTRO DI UNA COLPOCITOLOGIA ANORMALE.

Frega A. et Al. Cancer Lett 2007;249:(2)235-41

Summary

- Women treated for CIN with hysterectomy remain at risk for VAIN.
- Cytologic surveillance should continue for these patients.
- The colposcopic criteria for a diagnosis of VAIN are the same as for CIN.
- Vaginal lesions may be more difficult to diagnosis due to the larger area to be evaluated colposcopically.
- Lugol's iodine is helpful in detection of these lesions.
- While most VAIN lesions are located in the upper third of the vagina, clinicians should inspect the entire vagina for abnormalities.
- After excluding an invasive lesion, treatment consists of excision or destruction of the noninvasive lesions.

A.G.E.O.

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