# Treatment of Vulvar intraepithelial neoplasia

The goals of treatment of VIN are to
prevent development of vulvar squamous carcinoma ,
relieve symptoms,and
preserving normal vulvar anatomy and function.

Management options include:

- Surgical excision
- Ablative therapy
- Topical treatment

The choice of excision versus other treatments for VIN depends primarily upon the
risk of invasive disease
histology
risk factors
location
extent of disease and
symptoms.
Surgical excision is the mainstay of treatment,
but ablative therapy or pharmacologic treatment is an option for some patients.
The major surgical interventions appear to be similarly effective.
Excision provides both treatment and a diagnostic specimen.

The frequency of recurrence after :

vulvectomy : ١٩%

partialvulvectomy : ١٨%

local excision : ٢٢ %

and laser ablation : ٢٣%

For women with VIN, who have

possible invasive disease:

a lesion that is raised,
ulcerative, and/or has
irregular borders ,
previous VIN or vulvar carcinoma,
immunosuppression,
tobacco use,
age ≥۴۵ years,
lichen sclerosus,

surgical excision is required.

# Point:

*in ١٠ to ٢٢ % of women with VIN on initial biopsy Invasive SCC is present at the time of excision .

*It is also important to take the multifocal nature of VIN into consideration.

*Excision may be performed, but ablative therapy or topical pharmacologic treatment are the most likely to preserve vulvar anatomy.

for women in whom malignancy is not suspected or has been excluded, treat with excision for single lesions that allow complete removal with satisfactory cosmetic and functional results.

prefer laser ablation for those with the following characteristics:
young women;
multifocal disease;
lesions that involve the clitoris, urethra, or anus;
and lesions that involve the vaginal introitus (excision in this area may result in dyspareunia).

For women with recurrent lesions
use imiquimod to
avoid
multiple excisional procedures
that may distort anatomy or
result in impairment of function or
chronic pain.

risk factors for recurrent disease:
heavy smokers, immunocompromised patients.

# ۵-fluorouracil(efudex)

use only rarely and as a last treatment

when:

other therapies have failed because it is painful and in our experience it has not successful treatment outcomes.

For women with VIN, differentiated type is associated with a high risk of developing invasive carcinoma. recommend surgical excision rather than ablation or pharmacologic therapy.

# Excision

For excisional treatment, wide local excision is the preferred procedure.

# Wide local excision

defined as excision of lesion with a ١ cm margin followed by reapproximation of the defect generally provides satisfactory cosmetic results.

# Skinning vulvectomy

The procedure requires removing the vulvar skin along avascular plane beneath the epidermis,
while preserving the subcutaneous tissue.
Primary closure can be achieved by either reapproximation or by using a split thickness skin graft.

Skinning vulvectomy is rarely indicated and
is reserved for extensive VIN lesions that are either
multifocal or large and confluent.
It is used in the small proportion of patients in whom
prior treatments such as topical treatments,
laser ablation,
or smaller excisions have failed to control disease.

# vulvectomy

vulvectomy refers to removal of the entire vulva together with perineal tissues and usually includes some subcutaneous tissue.

It may be performed for benign and premalignant conditions of the vulva that are extensive or multifocal.

Vulvectomy is reserved for women in whom

vulvar carcinoma is suspected and

large or multifocal lesion, and

cannot be treated with a wide local excision or ablative therapy.

# Depth of excision:

removal of the epidermis provides sufficient depth for treatment of VIN as long as the margins are clear.

Removing a small amount of dermis helps to ensure the absence of early invasive disease.

Excision can be performed with a knife, electrosurgery, or carbon dioxide laser.

A negative margin will only reduce the recurrence risk at that site, not the life-long risk of reccurrence of VIN on the vulva

Positive epithelial margins are common and is a risk factor for recurrent disease.

If there is a grossly visible residual lesion, it should be treated.

If a margin is positive microscopically, but there is no visible residual disease, the patient may be followed by close clinical observation and colposcopy.

Re-treatment is provided if another visible lesion occurs.

# Ablative therapy

Laser vaporization is the most commonly used ablative therapy, but argon beam ablation and ultrasonic surgical aspiration have also been used as alternatives to excisional therapy, especially for women with multifocal and extensive lesions.
It is most advantageous when there are multiple small lesions.

Since tissue is ablated, prior to procedure the coexistence of invasive cancer must be carefully excluded by use of colposcopically directed biopsies.

Colposcopy is used to control the depth of tissue destruction to less than ١ mm, which will ablate the intraepithelial lesion and allow for rapid healing.

١ mm depth is sufficient ablation for hair-free epithelium,
٣ mm depth is required in hairy areas of the vulva
because the hair root sheet tends to extend as deep as ٢.٥ mm.

Superficial ablative therapy may cosmetic advantages,
deep laser vaporization results in destruction of the skin appendage, which leads to hypertrophic scar formation(negating the cosmetic advantages of laser ).
The limitations of laser ablation are that special training is required,
and another method may be preferred for lesions in hair-bearing areas because laser treatment destroys the hair follicle .

# Topical therapy

Conservative treatment with topical therapies aimed at preserving the vulvar anatomy particularly in younger patients.

Careful colposcopic examination with biopsies to exclude invasive disease is mandatory prior to beginning treatment with any of these drugs.

# Imiquimod

Imiquimod cream (Aldara) is a topical immune response modifier;
its antiviral and antitumor effects are mediated through the stimulation of local cytokine production and cell-mediated immunity.
Imiquimod appears to be effective therapy for high-grade VIN.
two randomized trials found that imiquimod was significantly more effective than placebo.

Imiquimod is applied topically to lesions, not to the entire vulva.
A typical course of therapy is ۱۶ weeks.

Side effects of imiquimod are common; up to two-thirds of patients reduce the number of applications due to local side effects.

Side effects of imiquimod consist mostly of inflammation at the application site, including mild to moderate erythema or erosions.

To reduce the incidence of local inflammation,
suggest an escalating dose regimen starting with an application once a week for two weeks, then twice a week for two weeks, then, if tolerated well, three times a week.

# Topical ٥fluorouracil

Application of ٥-fluorouracil (٥-FU) cream causes a chemical desquamation of the VIN lesion; response rates as high as ٧٥% have been reported. A disadvantage of this approach is poorly tolerated because of significant burning, pain, inflammation, edema, or painful ulcerations. For this reason, topical ٥-FU has a limited role in the primary therapy of VIN

## Investigational therapies

Photodynamic therapy and the use of chemopreventive agents, such as retinyl acetate gel and cidofovir, a potent antiviral agent are also being investigated.

# SPECIAL PATIENT POPULATIONS

# Management of VIN in pregnancy

Data regarding VIN and pregnancy are extremely limited.
Approximately ١٥% of vulvar carcinomas have been reported to occur in women under the age of ٤٠.

Thus, any vulvar lesion noted during pregnancy should be biopsied as the non-pregnant patient.

Management options for the pregnant patient with VIN fall principally into two main categories:

- Surgical therapy with local excision or ablative therapy

should follow the same general principles as for the non-pregnant patient.

This is the preferred treatment option for VIN in pregnancy especially for the patient remote from delivery.

- Expectant management until after delivery

Once invasive carcinoma has been ruled out histologically, clinicians may consider deferring treatment of VIN to the postpartum period,especially in patients who are diagnosed in the third trimester.

Small series suggest a possibility for spontaneous regression, particularly in asymptomatic women who are younger than ٣٠ years and who present with multifocal pigmented VIN .

- Medical therapy is generally not recommended:

Imiquimod is classified as a category C ,The safety of topical therapy with imiquimod during pregnancy has not been clearly established.

٥-fluorouacil (٥-FU) is a category D drug and should not be used for the treatment of VIN in pregnancy.

# Management of VIN in HIV-infected women

VIN occurs commonly among women infected with HIV.

Individuals infected with HIV are at greater risk of HPV-related cancers.

# PROGNOSIS

# Natural history

untreated VIN may …… persist,or progress, or resolve.

A systematic review of patients with VIN involving ٦١ untreated patients and٢٧ patients in whom macroscopic VIN was left behind after treatment.

٩% progressed to invasive vulvar carcinoma over ١ to ٨ years;
(٤of these women had had previous radiation therapy to the lower genital tract, and ١ was immunosuppressed.)
In addition reported complete spontaneous regression in a total of ٤١ patients.
All of these women were under age ٣٥ years (mean age ٢٠ years); regression was related to pregnancy in ١٧ cases.
It has been suggested that differentiated VIN has a higher risk of progression to squamous cell carcinoma than undifferentiated VIN (٥.٧ versus ٣٣ percent), with a shorter time to progression for differentiated VIN.

# Risk of malignancy

# Histologic type

The risk of synchronous or subsequent vulvar carcinoma differs by histologic type:

- VIN, usual type – ۴ to ۸%.
- VIN, differentiated type , is not well established, since this is an uncommon histologic type, and data are limited to a few small studies; however,the risk appears to be quite high .

In addition, it is likely to occur in postmenopausal patients, and age may also play a role in the risk of malignancy.

# Recurrence after treatment

With prolonged follow-up, approximately one-third of women develop recurrent VIN.

Risk factors for recurrent disease include:
immunosuppression,
the presence of multifocal or multicentric disease,
larger lesion size, or
positive margins on the excisional specimen.
Some series found higher rates of recurrence associated with laser than with excision (٤٢ versus ٢٦%).

In a large series of ٣٠٣ patients treated for VIN, ٨٧ patients (٢٨.٧%) developed recurrent disease at a median of ٢٥ months from primary diagnosis.

There appear to be two distinct patterns of invasive vulvar carcinoma in women treated for VIN:

One pattern is the development of invasive carcinoma at a prior site of incompletely treated VIN and reflects disease progression.

In these cases, carcinoma is observed after a median of ۲۵ month following VIN treatment.

In the other pattern, an invasive carcinoma develops several years later at a site distinct from the previously treated VIN and represents a new neoplasm in the area at risk.

# Follow_ up

suggest follow-up every six months for five years after the last treatment, and then annually.

Cigarette smoking is a significant risk factor for recurrence.
Patients should be encouraged to stop using tobacco to reduce their recurrence risk and for the general health benefits of not smoking.

# PREVENTION

Immunization with quadrivalent human papillomavirus (HPV) vaccine, which is active against HPV subtypes ٦, ١١, ١٦, and ١٨, has been found to decrease the risk of VIN.

The bivalent HPV vaccine (subtypes ١٦ and ١٨) has not been studied for VIN prevention.

Smoking cessation and treatment of vulvar dermatoses that may develop into vulvar neoplasia (ie, lichen sclerosus) may also help prevent VIN.

THANKS FOR YOUR ATTENTION