Clinical manifestation &diagnosis (HPV,warts)

Dr mojgan hajisafari
GYN oncologist
Assistant professor of shahidsadoughi university of medical sciences

Section 1

HPV diagnosis

Overview of diagnosis

- The clinical application of HPV detection is limited to testing of cervical specimens as part of cervical cancer screening and testing of oropharyngeal cancer biopsy specimens to inform appropriate staging and prognosis.

- Although HPV testing of other sites (vaginal, penile, and anal swabs, as well as oral rinses) has been used for surveillance and research purposes and is used clinically in special situations in some countries, such as the Netherlands and Australia, it is not approved for routine use in the United States.
- HPV testing in order to determine appropriateness of HPV vaccination is also not warranted.

- In the United States, there are no Food and Drug Administration (FDA)-approved tests clinically available to detect HPV infection of oropharyngeal, anal, or male genital specimens. There are also no FDA-approved serological or blood tests to detect HPV infection.

HOW TO OBTAIN A SAMPLE?

- Cell samples for cervical cytology and HPV testing are obtained during the speculum examination. With certain types of Pap tests (eg, ThinPrep), the same specimen can be used for analysis of both cytology and HPV.
- For conventional Pap smears, the ectocervical spatula is smeared and the endocervical brush is rolled uniformly onto a single slide promptly after obtaining the specimens.
- For liquid-based thin layer cytology, the collecting device is placed into a liquid "xative solution and vigorously swirled or rotated ten times in the solution

HPV testing

- HPV testing identifies oncogenic (ie, high-risk) HPV subtypes that are associated with cervical cancer . The subtypes that are tested have slight variation across the various testing systems, but all test for at least the 13 most common types.
- HPV genotyping refers to testing for individual HPV types, usually HPV 16 or 18, but some tests may also include HPV 45.
- HPV testing systems are approved for either primary HPV testing (without cervical cytology) or cotesting (with cervical cytology)

Cervical HPV testing

- Specimens for HPV testing can be collected from the endocervix using a cervical spatula or cervical brush, which is then placed in HPV test transport medium .
- With some liquid-based cytology sampling systems, the same specimen can be used for HPV testing and cytology.
- Self sampling: Patients can collect samples from the vagina using a tampon, Dacron or cotton swab, cytobrush, or cervicovaginal lavage.

Urine HPV testing

- Urine testing for HPV has been proposed, but is not clinically available.
- This testing method may have utility if HPV testing alone (without cervical cytology) is used for cervical cancer screening.
- The efficacy of urine testing was evaluated in a meta- analysis of 14 studies including 1443 patients . Most studies used commercial polymerase chain reaction methods, and cervical testing results were used as the reference standard.
- For detection of high-risk HPV, the sensitivity was 77 percent and specificity was 88 percent. For detection of HPV 16 and 18, sensitivity was 73 percent and specificity was 98 percent.
- Sensitivity was statistically signifcantly higher when urine samples were collected as first void compared with random or midstream.
- Such a test may have potential in large research studies or as an alternative test where routine cervicovaginal examinations are not economically feasible or less likely to be performed due to cultural barriers.

Biopsy of cervical visible lesions

- During Pap testing, any lesion that is raised, friable, or has the appearance of condyloma should be biopsied, regardless of previous cytology results or other risk factors for cervical cancer .
- The only visible lesions that do not require biopsy are Nabothian cysts and only when this diagnosis is confirmed by an experienced examiner.

SAMPLING CHALLENGES

- **Menses or other genital tract bleeding:**

We suggest performing rather than deferring the test, unless the blood cannot be cleaned from the cervix.

If there is obscuring blood, conventional Pap smears are more likely to be unsatisfactory for interpretation than liquid-based methods because liquid-based techniques filter out red blood cells.

- ✓ **HPV testing results are not affected by bleeding, although some data suggest that detection of high risk varies with the phase of the menstrual cycle**

SAMPLING CHALLENGES

- Interval between Pap tests:
- A Pap test may need to be repeated after a brief interval if the sample is unsatisfactory or at the time of colposcopy. A short interval between Pap tests (15 to 30 days) does not appear to affect sensitivity for detection of cervical neoplasia .
- Gel lubricants and other contaminants:
- In general, studies have not shown an adverse impact of lubricants on cervical cytology interpretation
- Vaginal intercourse, douching, and tampon use:
- may remove the most superficial layer of cervical cells. However, it appears that removal of cells by these activities or by swabbing (to remove blood or discharge) does not diminish the ability to diagnose cervical abnormalities or HPV infection.

Condyloma aquminatum

Section 2

Clinical manifestation

- External anogenital warts are typically found on the vulva, penis, groin, perineum, anal skin, perianal skin, and/or suprapubic skin .

- The CA can be single or multiple, flat, dome-shaped, caulifower-shaped, "liform, fungating, pedunculated, cerebriform, plaque-like, smooth (especially on the penile shaft), verrucous, or lobulated (picture 1A-H).
- The color varies; warts may be white, skincolored, erythematous (pink or red), violaceous, brown, or hyperpigmented.
- Anogenital warts are usually soft to palpation and can range from 1 mm to more than several centimeters in diameter.
- The warts are typically asymptomatic but can occasionally be pruritic

Clinical manifestion

- External anogenital warts can be accompanied by involvement of the cervix or urethra .
- CA may also develop in the anal canal, typically manifesting as small flat-topped to globoid-shaped papules, usually distal to the dentate line .
- Extensive CA can cause marked disfigurement of the anogenital area and may interfere with defecation.
- Urethral warts may result in urethral bleeding (including bleeding during coitus) and, in rare cases, urinary obstruction.

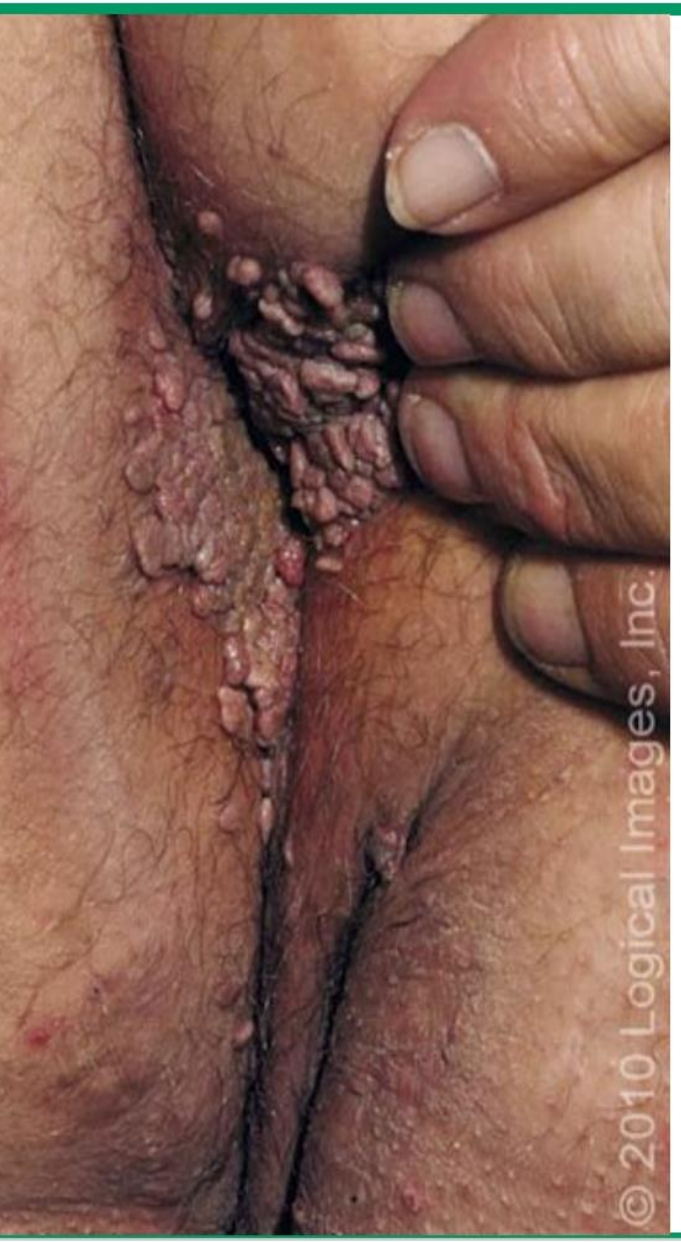
Clinical manifestion

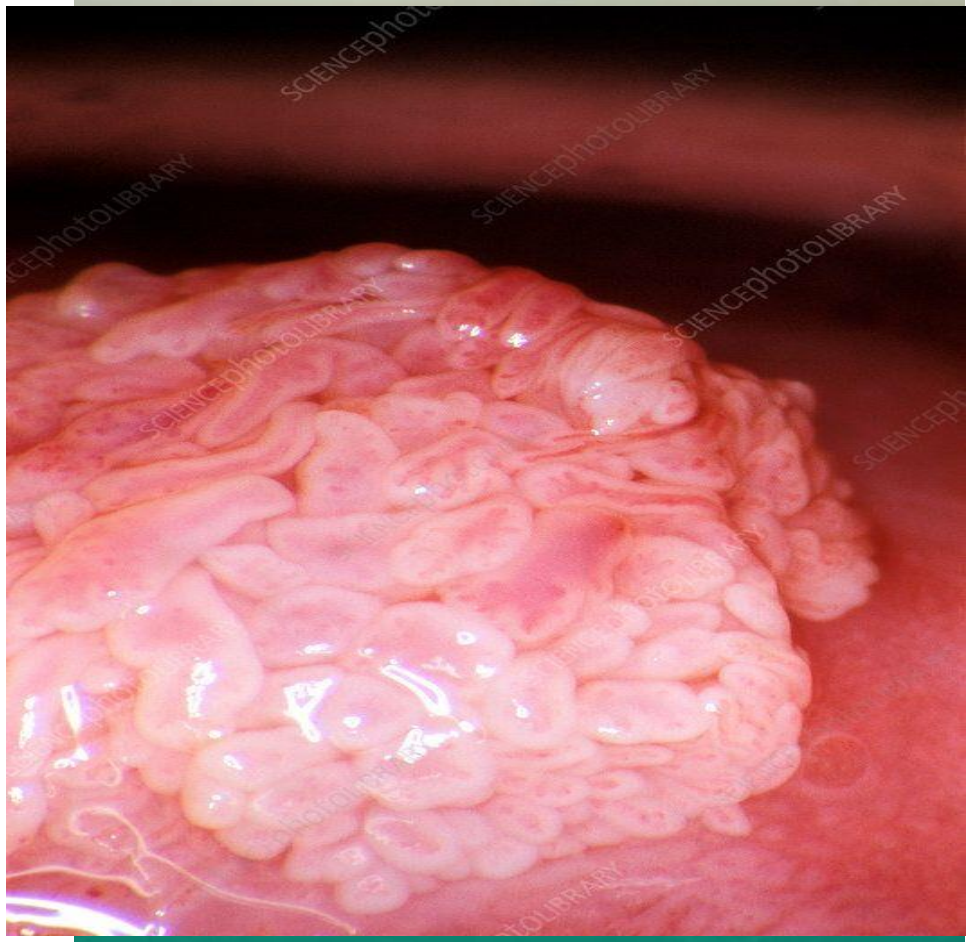
- The psychologic effects of CA should not be discounted.
- Patients with CA often experience stigmatization, social isolation, anxiety, depression, angst, and guilt, as well as concerns about future fertility and cancer risk .
- The emotional impact on sexual partners is also substantial and can lead to confict and relationship termination

Diagnosis

- **Dermoscopy :**
- **The dermoscopic features of CA have been described based upon morphologic patterns and vascular characteristics .**
- **The morphologic features may vary from a knob-like pattern to a finger-like pattern, and the vascular pattern can be dotted to glomerular. There is always papillomatosis**

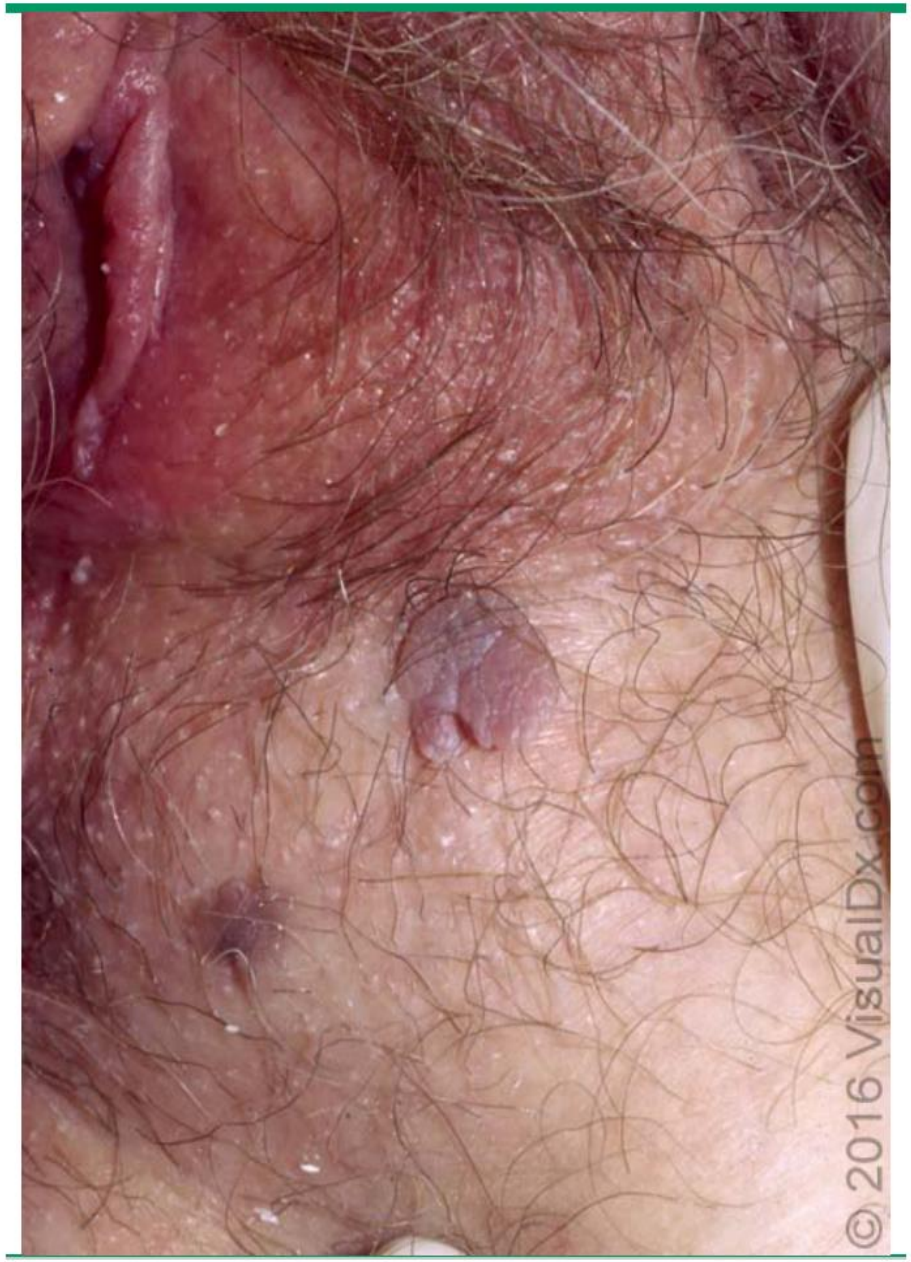
dyloma acuminatum





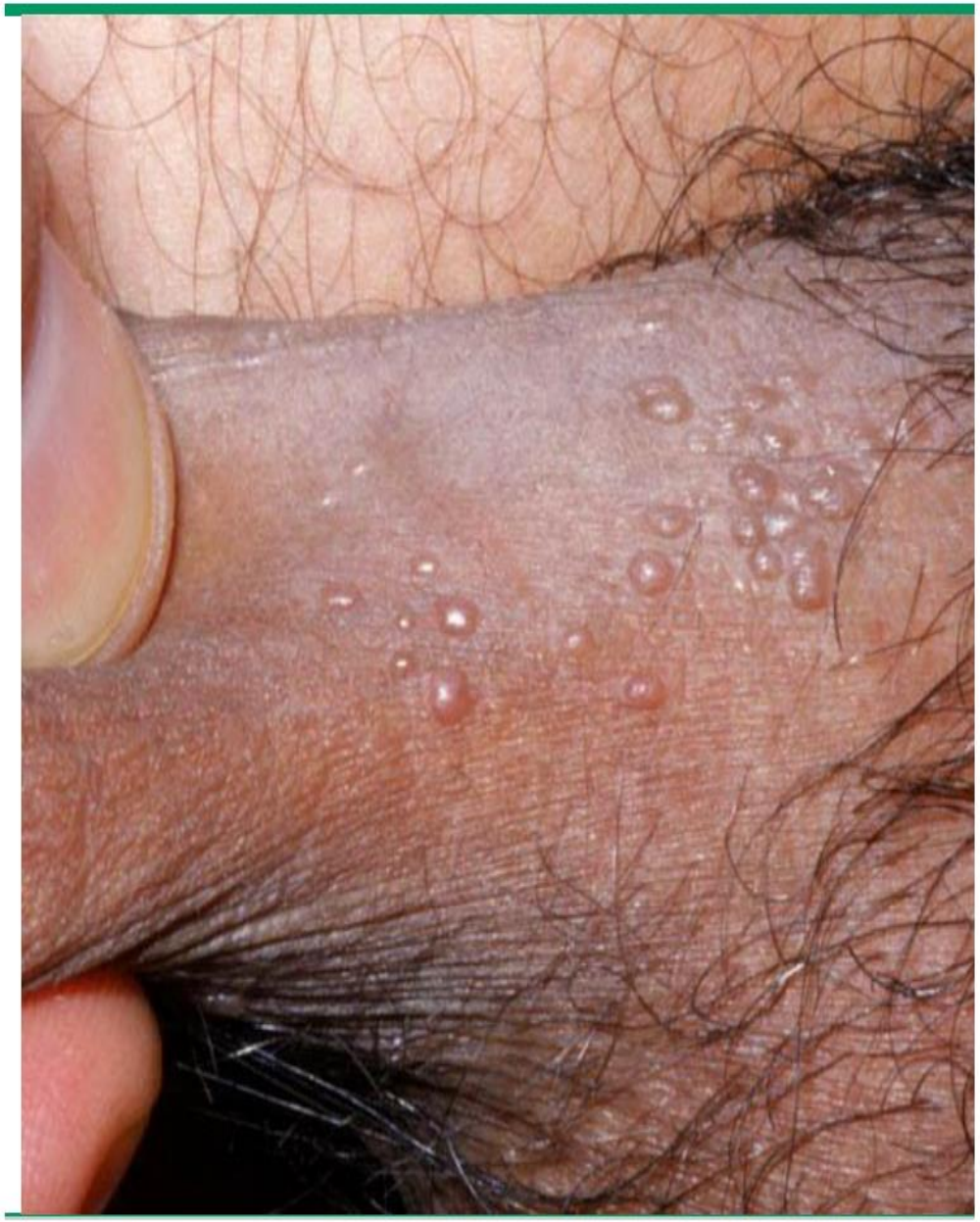
ssion from: www.visualdx.com. Copyright VisualDx. All rights

Condyloma acuminatum



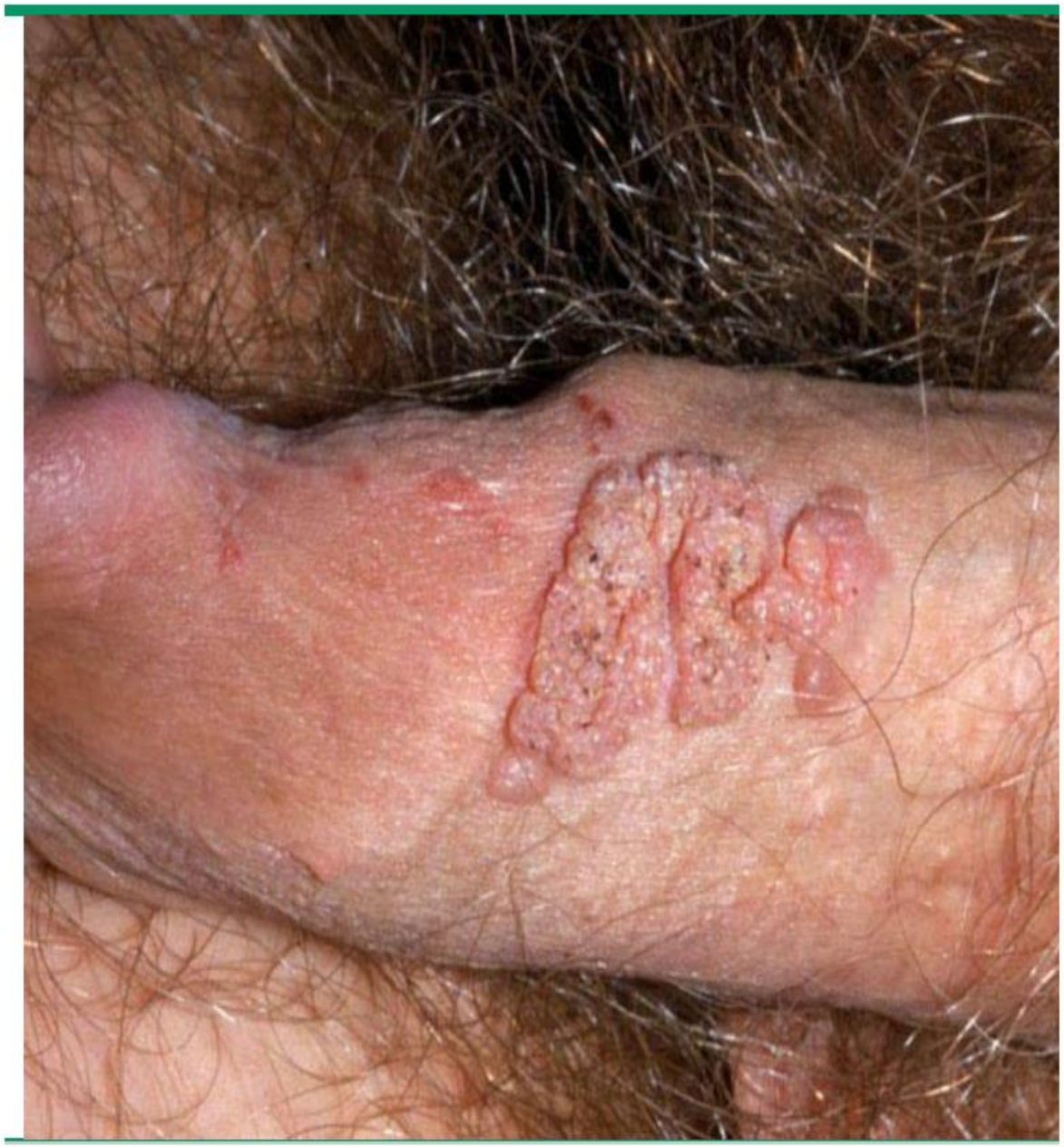
Condyloma acuminatum on the vulva

Condyloma acuminatum



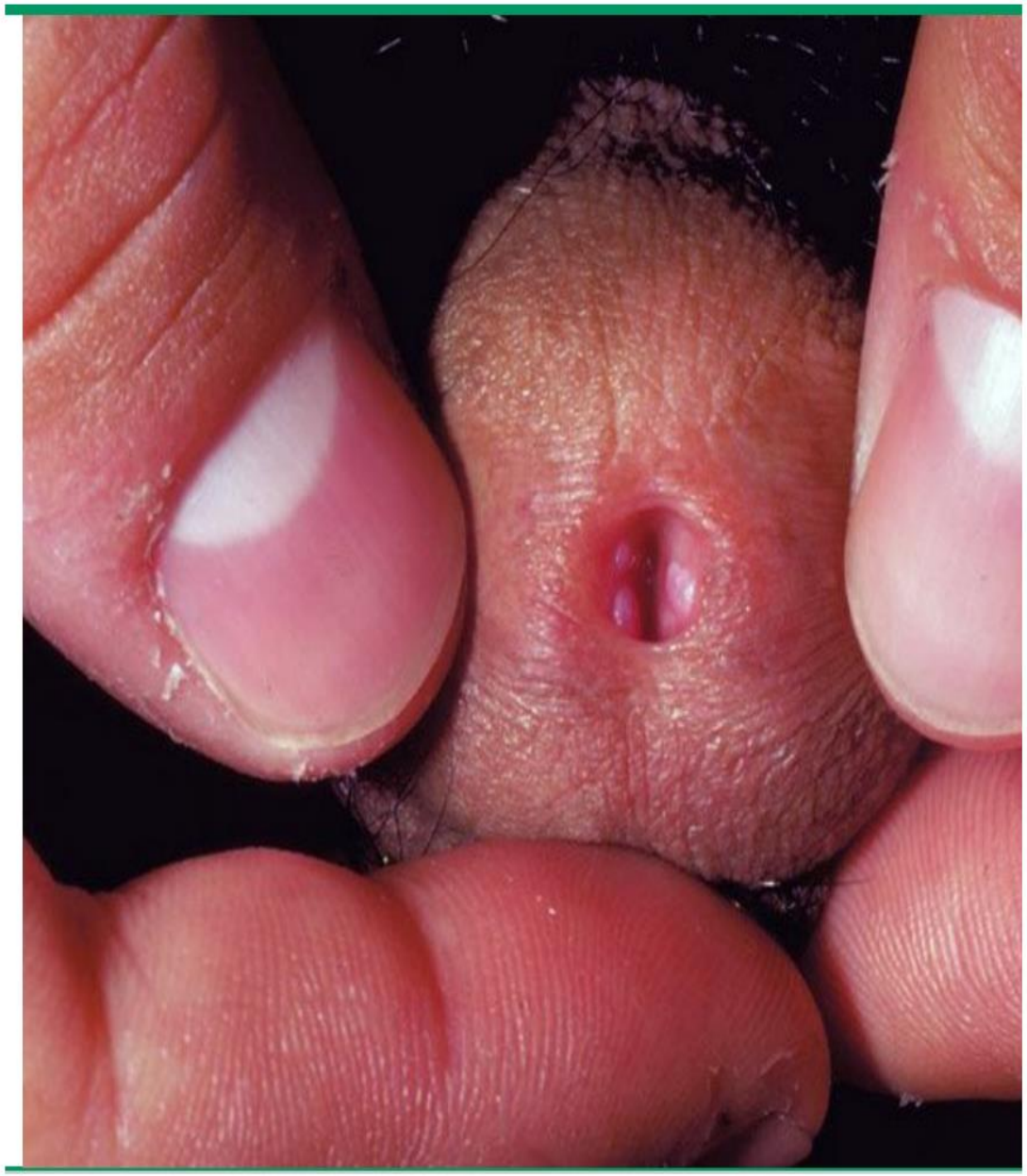
Multiple papules on the penis.

Condyloma acuminatum



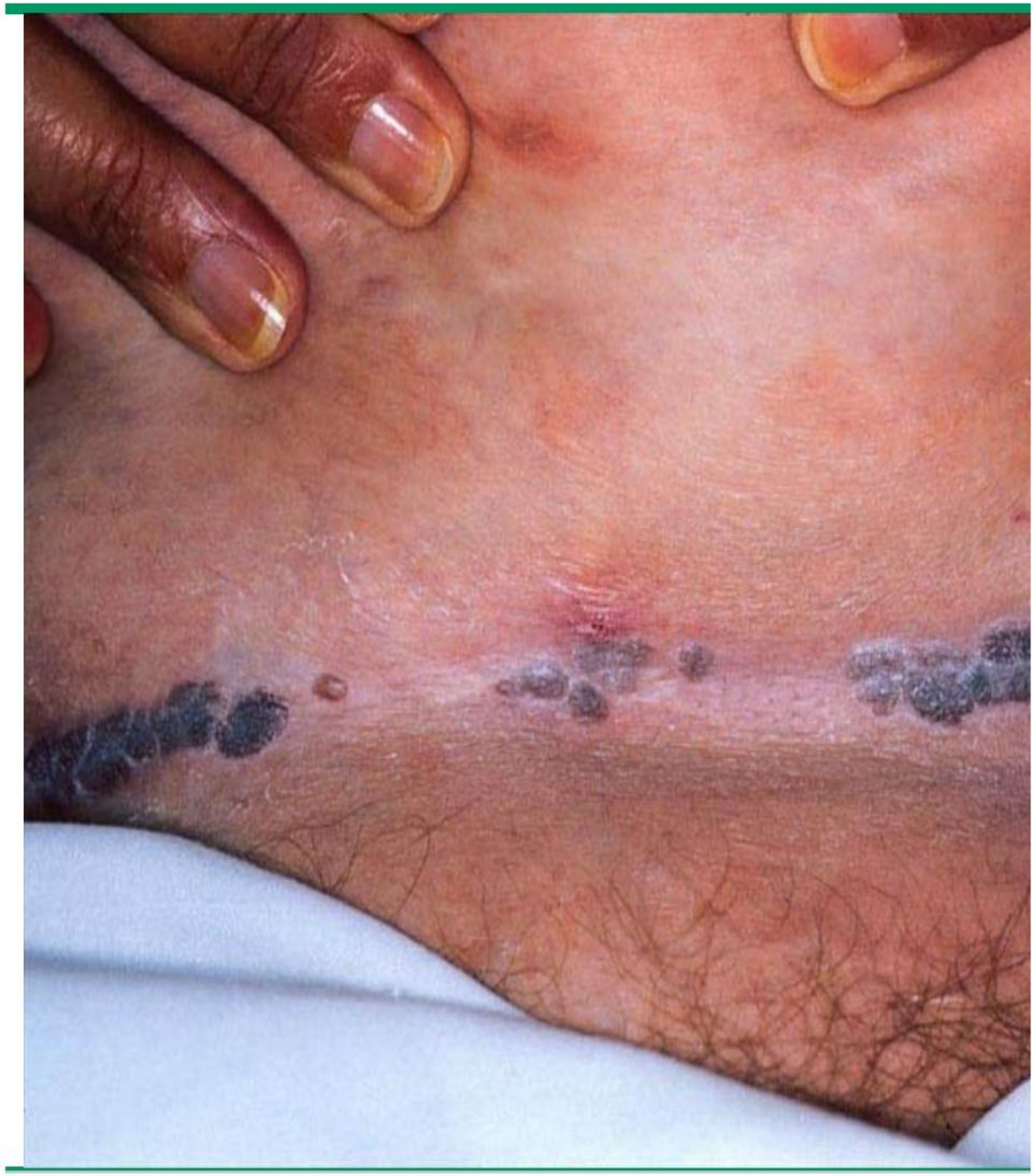
Verrucous plaque on the penis.

Condyloma acuminatum



Condylomata involving the urethral meatus.

Condyloma acuminatum



Suprapubic condyloma acuminatum.

Diagnosis

- **CLINICAL COURSE:**
- **After their initial appearance, anogenital warts may increase in number and size or regress spontaneously.**

- **It is estimated that approximately one-third of anogenital warts regress without treatment within four months .**
- **Human papillomavirus (HPV) infection may persist despite resolution of visible warts and may result in wart recurrence.**
- **Recurrence rates are not well defined.**

- ***Mechanical irritation, wounding*, immunosuppression, inflammation, and other extracellular influences affect viral copy number in the latently infected cells and *may predispose to reappearance***

ASSOCIATION WITH MALIGNANCY

- Although human papillomavirus (HPV) 6 and HPV 11, low-risk HPV types, are responsible for most cases of CA, coinfection with high-risk HPV genotypes linked to anogenital and head and neck cancers is common .
- A Danish study of 15,155 men and 32,933 women diagnosed with CA between 1978 and 2008 found increased risk for anogenital cancers and head and neck cancers, including anal (standardized incidence ratio [SIR] for men, 21.5; SIR for women, 7.8), vulvar (SIR 14.8), vaginal (SIR 5.9), cervical (SIR 1.5), penile (SIR 8.2), and head and neck cancers (SIR 2.8) .
- The SIR for subsites of head and neck cancer with confirmed HPV association was 3.5 for men and 4.8 for women

HISTOPATHOLOGY

- The primary histologic features of CA evident with hematoxylin-eosin (H&E) staining are papillomatosis, koilocytosis (multiple vacuolated cells with enlarged, irregular nuclei), and vascular distension . Coarse keratohyaline granules may also be present. Flat anogenital warts show acanthosis in the epidermal spinous layer.
- Additionally, the use of MIB1, an antibody targeting cell proliferation protein Ki-67, highlights cells infected with human papillomavirus (HPV)

DIAGNOSIS

- Physical examination
- Findings that suggest CA are single or multiple soft, smooth or papillated papules or plaques limited to the anogenital area.
- Select features that may suggest other disorders include umbilicated papules (molluscum contagiosum , keratotic plugs and hyperpigmentation (seborrheic keratosis , yellowish color (Fordyce spots , violaceous color (lichen planus), pinpoint papules (lichen nitidus), moist surface (condylomata lata of syphilis), and ulceration (other infection or malignancy)

Diagnosis (presentation)

- Patients may have simultaneous infection of the genital area and perianal skin.
- Therefore, all areas of predilection for CA (lower abdomen, vulva, penis, perineum, perianal skin, mons pubis, and crural folds) should be examined.
- Of note, uncircumcised foreskin or hair can obscure warts, warranting more careful examination

Biopsy

- If there is uncertainty about the diagnosis, a biopsy should be performed.
- A shave or scissor procedure to remove a suspected wart or sample a large suspected wart is usually suficient In addition, a biopsy to confirm the diagnosis and rule out malignancy is beneficial for CA that appear refractory to treatment, especially in immunosuppressed patients .
- Other indications for biopsy include atypical features (eg, induration, fixation to underlying structures, bleeding, atypical pigmentation, or ulceration)

HPV testing of warts?!

- **Human papillomavirus (HPV) testing of warts is not routinely indicated for diagnosis.**
- **Testing does not confirm the diagnosis and does not influence management of CA .**
- **Application of acetic acid has a low positive predictive value for diagnosing external anogenital warts .**
- **Therefore, use cannot be advocated for diagnosis . False-positive results commonly occur, resulting from parakeratosis in other pathologic processes (eg, psoriasis, candidiasis, squamous papilloma, healing epithelium, and lichen planus).**
- **The pain associated with acetic acid examination is another reason to avoid its use.**

Internal involvement

- Patients with external anogenital warts can have concomitant involvement of the anus, urethra, vagina, cervix, or rectum:

- Urethral involvement – Urethral CA occasionally occur and are most commonly found on the external meatus and distal urethra .
- but may also develop in more proximal sites within the urethra. Bladder obstruction is a rare complication .
- The physical examination should include a visual assessment of the urethral orifice.
- Patients with warts at this site should be referred to a urologist for further evaluation.

Internal involvement

- **Vaginal and cervical involvement – Women with genital warts should undergo speculum examination to evaluate for vaginal or cervical involvement.**
- **Cervical cancer screening should be performed according to standard guidelines.**

Internal involvement

- **Anal canal involvement –**
- **Clinicians should have a low threshold for performing anoscopy or referring patients to a gastroenterologist or colorectal surgeon for anoscopy to examine the anal canal.**
- **We suggest performing or referring patients for anoscopy whenever warts are present in the visible anal area.**


Have a nice
DAY!