

# FEMALE GENITAL SYSTEM, LECTURE 1

## VULVA AND VAGINA

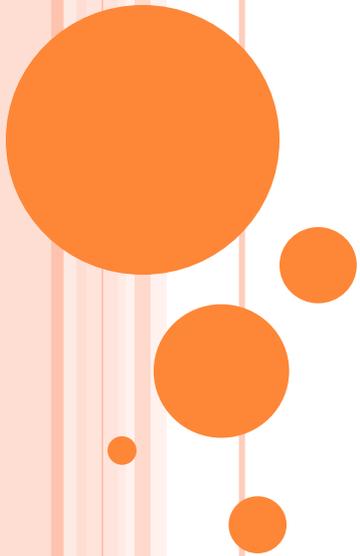


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# VULVA

**The vulva is the external female genitalia and includes the moist hair-bearing skin and mucosa in that region.**



# VULVITIS

- One of the most common causes of vulvitis is reactive inflammation in response:
  - To an exogenous stimulus, whether an irritant (contact irritant dermatitis) or an allergen (contact allergic dermatitis).
  - Vulvitis also may be caused by infections, which in this setting often are sexually transmitted and including:
    - **Human papillomavirus (HPV)**: the causative agent of condyloma acuminatum and vulvar intraepithelial neoplasia.
    - **Herpes simplex virus (HSV-1 or -2)**: Characteristic by vesicular eruption;
    - **N. gonorrhoeae**, a cause of suppurative infection of the vulvovaginal glands.
    - **Treponema pallidum**, the syphilis pathogen, in association with the primary chancre at a vulvar site of inoculation.
    - **Candida**.
- An important complication of vulvitis is obstruction of the excretory ducts of Bartholin glands. This blockage may result in painful dilation of the glands (a Bartholin cyst) and abscess formation.

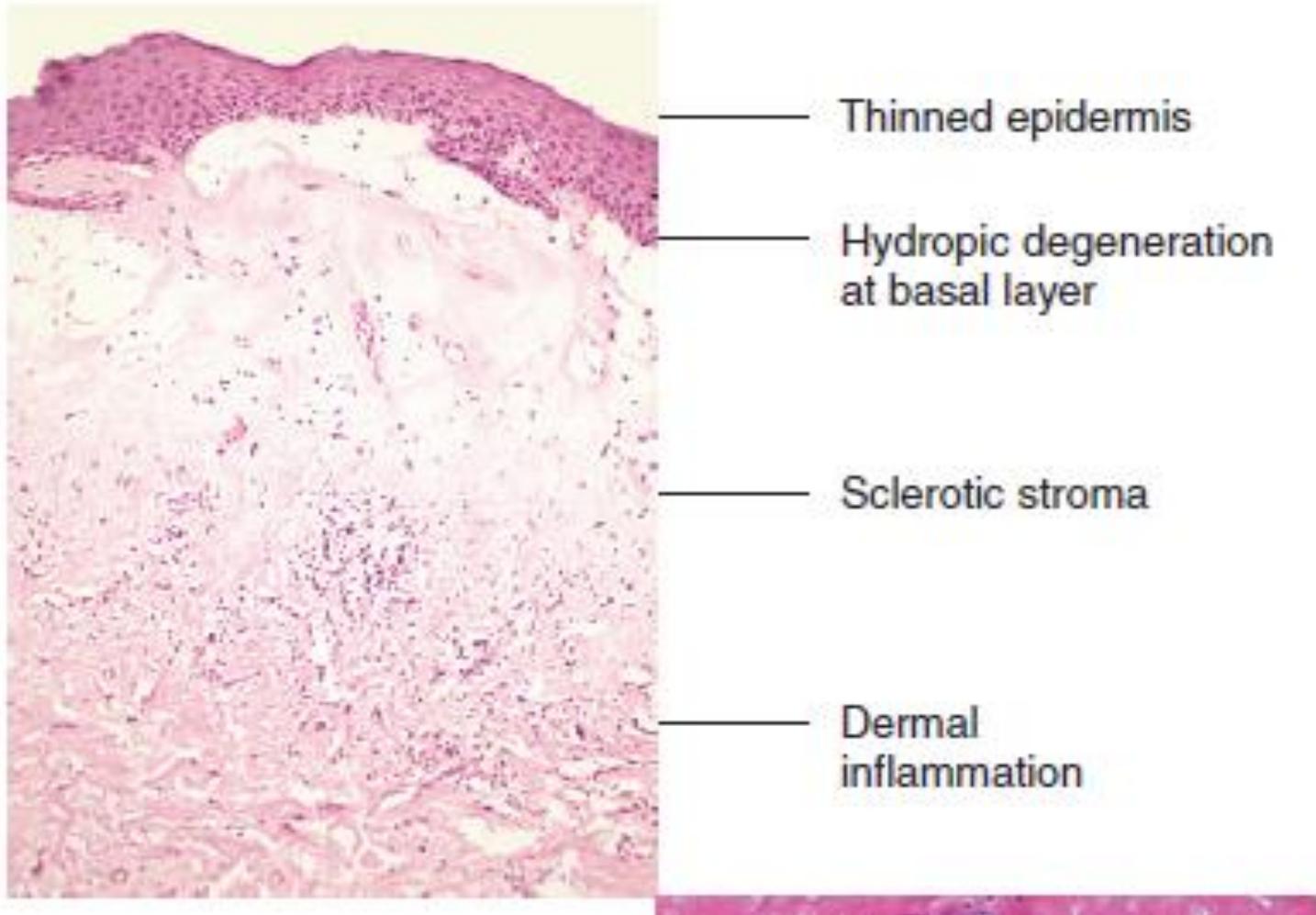


# NON-NEOPLASTIC EPITHELIAL DISORDERS

## 1-Lichen Sclerosus:

- It appears as smooth, white plaques (termed *leukoplakia*) or papules that in time may extend and coalesce.
  - Lichen sclerosus occurs in all age groups but most commonly affects postmenopausal women.
  - The pathogenesis is uncertain, autoimmune disorders??.
  - Lichen sclerosus is benign; however, a small percentage of women (1% ) with symptomatic lichen sclerosus develop squamous cell carcinoma of the vulva.
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Lichen sclerosus is characterized by thinning of the epidermis, disappearance of rete pegs, hydropic degeneration of the basal cells, dermal fibrosis, and a scant perivascular mononuclear inflammatory cell infiltrate.

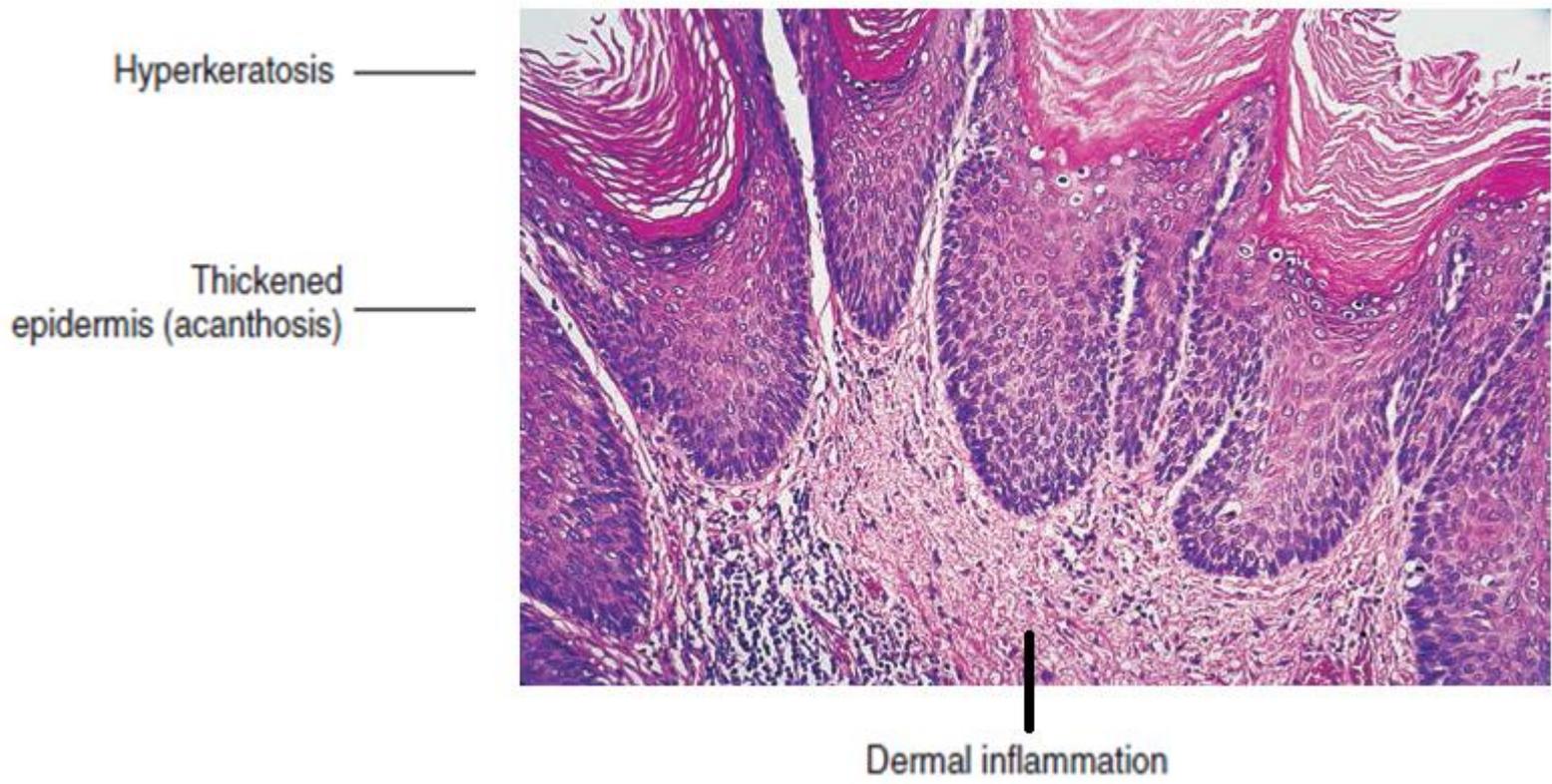


## 2-LICHEN SIMPLEX CHRONICUS

- Lichen simplex chronicus appears as white patches or plaques( an area of leukoplakia).
- These nonspecific changes are a consequence of chronic irritation, often caused by pruritus related to an underlying inflammatory dermatosis.
- With isolated lesions, no increased predisposition to cancer has been found, but lichen simplex chronicus often is present at the margins of established vulvar cancer, raising the possibility of an association with neoplastic disease.



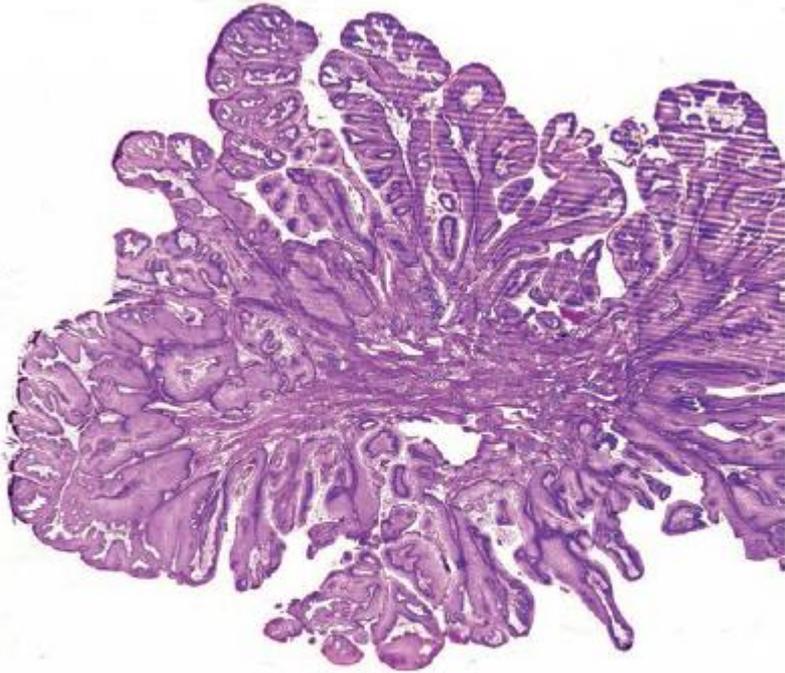
- Lichen simplex chronicus is marked by epithelial thickening (particularly of the stratum granulosum) and hyperkeratosis. Increased mitotic activity is seen in the basal and suprabasal layers; however, there is no epithelial atypia. Leukocytic infiltration of the dermis is sometimes pronounced.



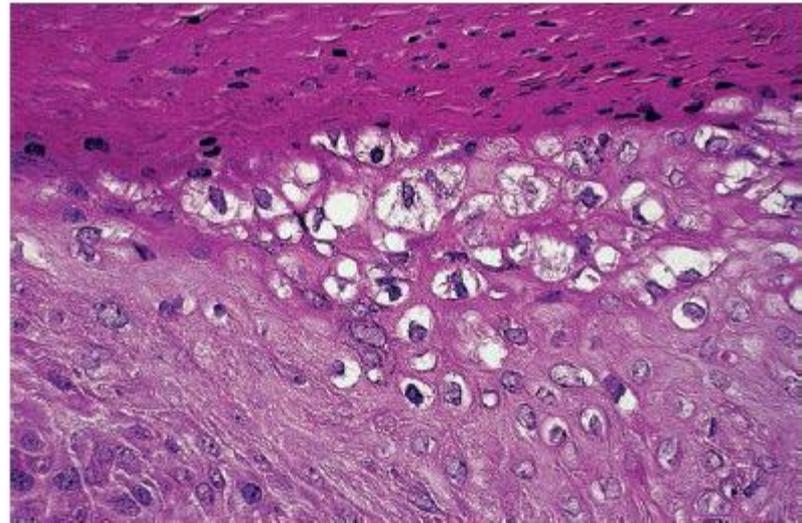
# CONDYLOMAS

- *Condyloma* is the name given to any warty lesion of the vulva.
- Most such lesions can be assigned to one of two distinctive forms.
  1. *Condylomata lata*, not commonly seen today, are flat, moist, minimally elevated lesions that occur in secondary syphilis.
  - 2- The more common *condylomata acuminata* may be papillary and distinctly elevated or somewhat flat and rugose.
- They can occur anywhere on the anogenital surface, sometimes as single but more often as multiple lesions.
- When located on the vulva, they range from a few millimeters to many centimeters in diameter and are red-pink to pink-brown.
- Indeed, condylomata acuminata are strongly associated with HPV subtypes **6 and 11**.
- HPV 6 and 11 infections carry a low risk of malignant transformation, and hence, vulvar condylomas do not commonly progress to cancer.

On histologic examination, the characteristic cellular feature is **koilocytosis**, a cytopathic change characterized by perinuclear cytoplasmic vacuolization and wrinkled nuclear contours that is a hallmark of HPV.



Whole mount of condyloma acuminatum of vulva.

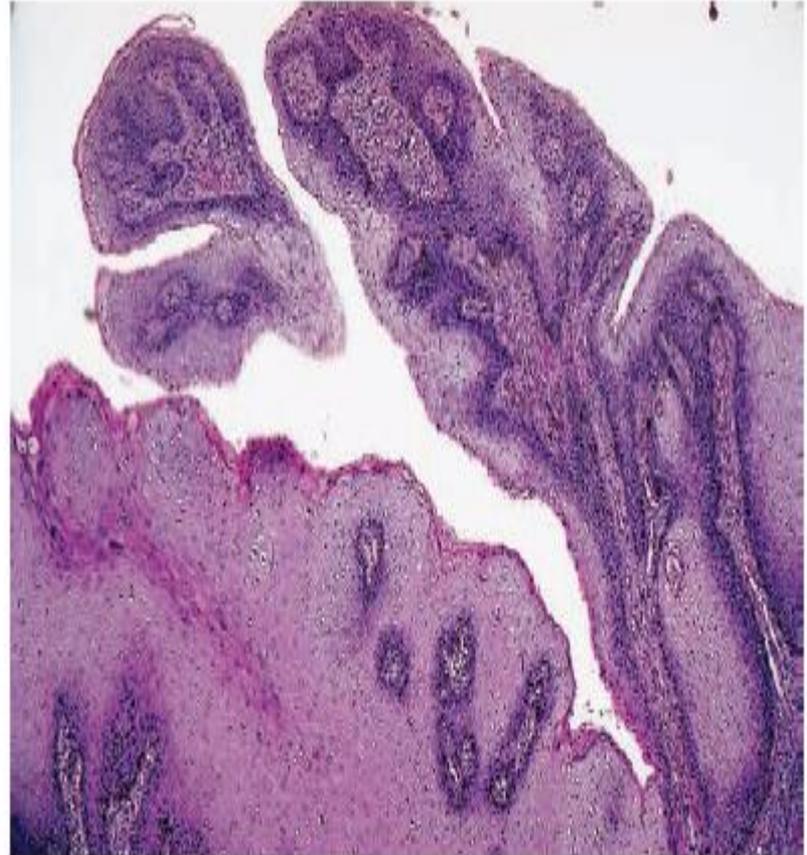


Prominent koilocytotic changes in vulvar epithelium.





Large condyloma of vulva.



Papillomatous shape of vulvar condyloma.



# CARCINOMA OF THE VULVA

- Carcinoma of the vulva represents about 3% of all female genital tract cancers, occurring mostly in women older than age 60.
  - Approximately 90% of carcinomas are squamous cell carcinomas; the other tumors are mainly adenocarcinomas or basal cell carcinomas.
  - There appear to be **two** distinct forms of vulvar squamous cell carcinoma:
    - 1- The less common form is related to high-risk HPV strains (especially HPV subtypes 16 and 18) and occurs in middle-aged women, particularly cigarette smokers. In this form, the onset of carcinoma often is preceded by precancerous changes in the epithelium termed *vulvar intraepithelial neoplasia* (VIN).
    - 2- A second form of vulvar carcinoma occurs in older women. It is not associated with HPV but often is preceded by years of reactive epithelial changes, principally lichen sclerosus. The overlying epithelium frequently lacks the typical cytologic changes of VIN, but it may display subtle atypia of the basal layer and basal keratinization. Invasive tumors of this form tend to **be well differentiated and highly keratinizing.**
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- VIN and early vulvar carcinomas manifest as areas of leukoplakia in the form of whitish patches of epithelial thickening.
- Over time, these areas are transformed into overt exophytic or ulcerative endophytic tumors
- VIN progresses in most patients to greater degrees of atypia and eventually undergoes transformation to carcinoma in situ; however, progression to invasive carcinoma is not inevitable and often occurs after many years.
- Environmental factors such as cigarette smoking and immunodeficiency appear to increase the risk of such progression.



- HPV-positive tumors often are multifocal and warty and tend to be **poorly differentiated squamous cell carcinomas**, whereas HPV-negative tumors usually are unifocal and typically manifest as **well-differentiated keratinizing squamous cell carcinomas**.
- Both forms of vulvar carcinoma tend to remain confined to their site of origin for a few years but ultimately invade and spread, usually first to regional nodes.
- The risk of metastasis correlates with the size of the tumor and the depth of invasion. Women with tumors less than 2 cm in diameter have about a 90% 5-year survival rate after radical excision, whereas only 20% of those with advanced-stage lesions survive for 10 years.

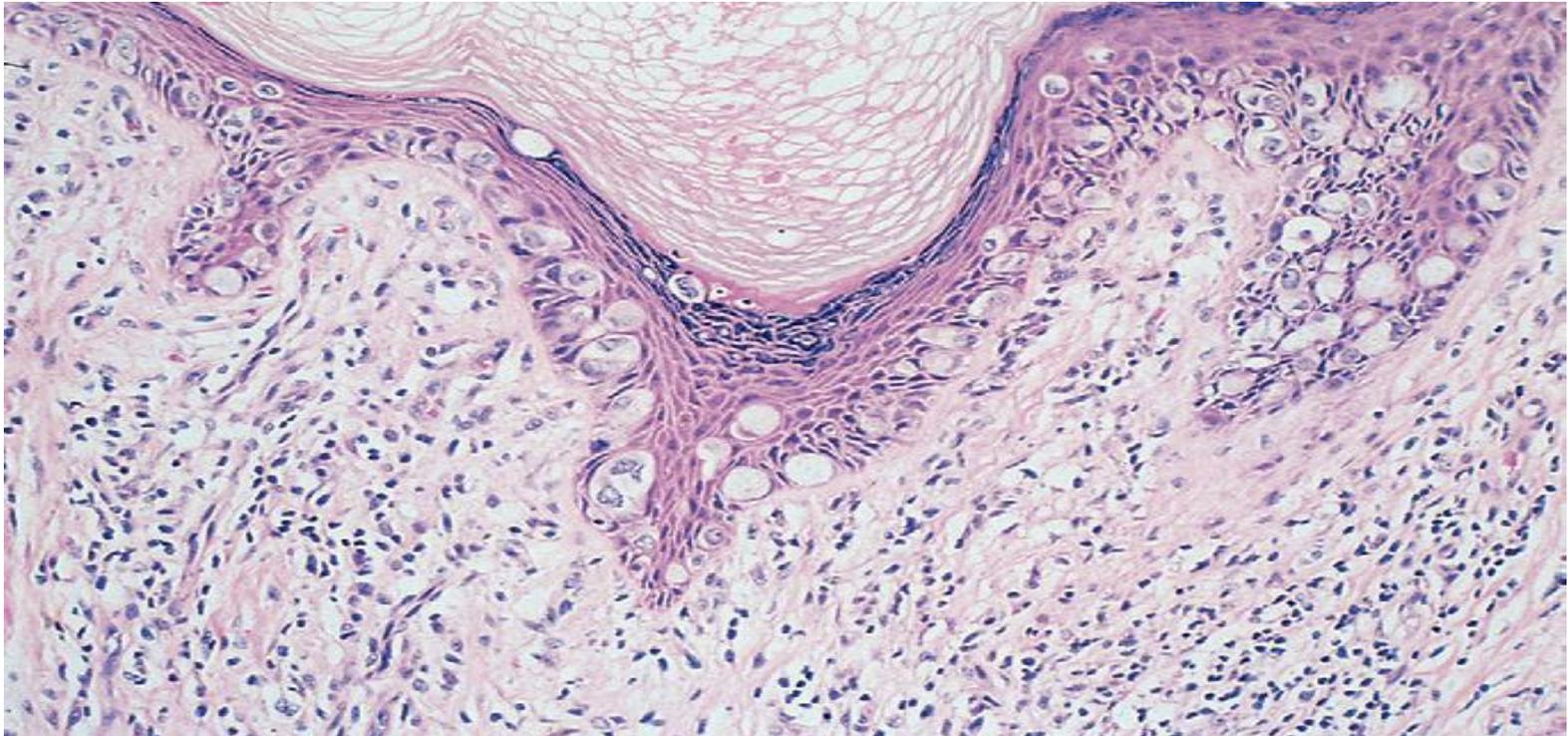


# EXTRAMAMMARY PAGET DISEASE

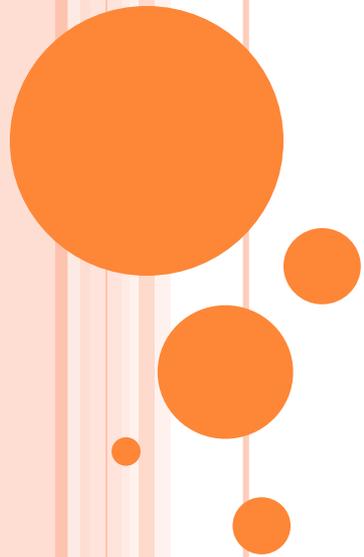
- Paget disease is an intraepidermal proliferation of malignant epithelial cells that can occur in the skin of the vulva or nipple of the breast.
- A majority of cases of vulvar (extramammary) Paget disease have no demonstrable underlying tumor.
- Only occasionally, Paget disease in this location is accompanied by a subepithelial or submucosal tumor arising in an adnexal structure, typically sweat glands.
- Paget disease manifests as a red, scaly, crusted plaque that may mimic the appearance of an inflammatory dermatitis.
- Intraepidermal Paget disease may persist for years or even decades without evidence of invasion. However, when there is an associated tumor involving skin appendages, the Paget cells may invade locally, and ultimately metastasize. Once metastasis occurs, the prognosis is poor.



On histologic examination, large epithelioid cells with abundant pale, finely granular cytoplasm and occasional cytoplasmic vacuoles infiltrate the epidermis, singly and in groups. The presence of mucin, as detected by periodic acid–Schiff (PAS) staining, is useful in distinguishing Paget disease from vulvar melanoma, which lacks mucin.



# VAGINA



- The vagina is seldom a site of primary disease.
- More often, it is involved secondarily by cancer or infections arising in adjacent organs (e.g., cervix, vulva, bladder, rectum).
- Congenital anomalies of the vagina fortunately are uncommon and include entities such as total absence of the vagina, a septate or double vagina (usually associated with a septate cervix and, sometimes, septate uterus), and lateral Gartner duct cysts arising from persistent wolffian duct rests.



# VAGINITIS

- Vaginitis is a relatively common condition that is usually transient and of no clinical consequence. It is associated with production of a vaginal discharge (leukorrhea).
- A large variety of organisms have been implicated, including bacteria, fungi, and parasites. Many are normal commensals that become pathogenic only in the setting of diabetes, systemic antibiotic therapy (which causes disruption of normal microbial flora), immunodeficiency, pregnancy, or recent abortion.

**Candidal vaginitis** is characterized by a curdy white discharge. This organism is part of the normal vaginal flora in about 5% of women, so the appearance of symptomatic infection almost always involves one of the predisposing influences.

***Trichomonas vaginalis*** produces a watery, copious gray-green discharge in which parasites can be identified by microscopy.



# MALIGNANT NEOPLASMS

- Squamous Cell Carcinoma
- Squamous cell carcinoma of the vagina is an extremely
- uncommon cancer that usually occurs in women older than 60 years of age.
- Vaginal intraepithelial neoplasia VIN is a precursor lesion that is nearly always associated with HPV infection.
- Invasive squamous cell carcinoma of the vagina is associated with the presence of HPV DNA in more than half of the cases, presumably derived from HPV-positive VIN.



# CLEAR CELL ADENOCARCINOMA

- Clear cell adenocarcinoma, a very rare tumor, was identified in a cluster of young women whose mothers took diethylstilbestrol DES during pregnancy to prevent threatened abortion. Now, Clear cell adenocarcinoma is very rare.
- In about one third of exposed women, small glandular or microcystic inclusions appear in the vaginal mucosa. These benign lesions are seen as red, granular-appearing foci that on histologic examination are lined by mucus-secreting or ciliated columnar cells. This clinical condition is called *vaginal adenosis*, and it is from such precursor lesions that clear cell adenocarcinoma arises.



# SARCOMA BOTRYOIDES

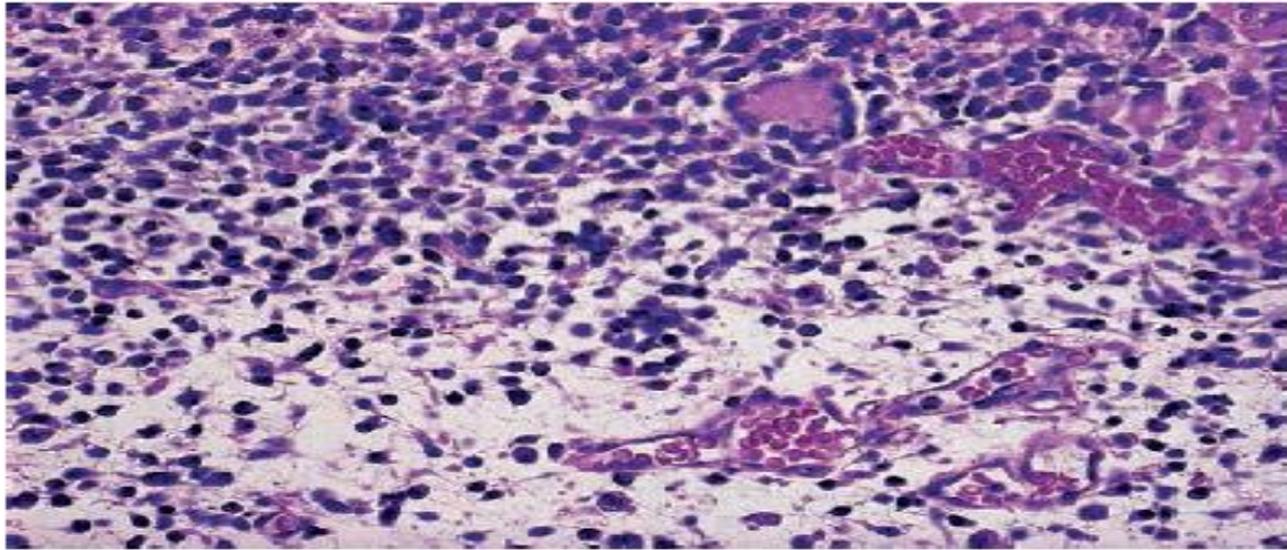
- Sarcoma botryoides (embryonal rhabdomyosarcoma) is a rare form of primary vaginal cancer.
- It usually is encountered in infants and children younger than 5 years of age. It also may occur in other sites, such as the urinary bladder and bile ducts.
- Grossly, it presents as a conglomerate of soft polypoid masses resembling a bunch of grapes—hence its designation as “botyroid.”



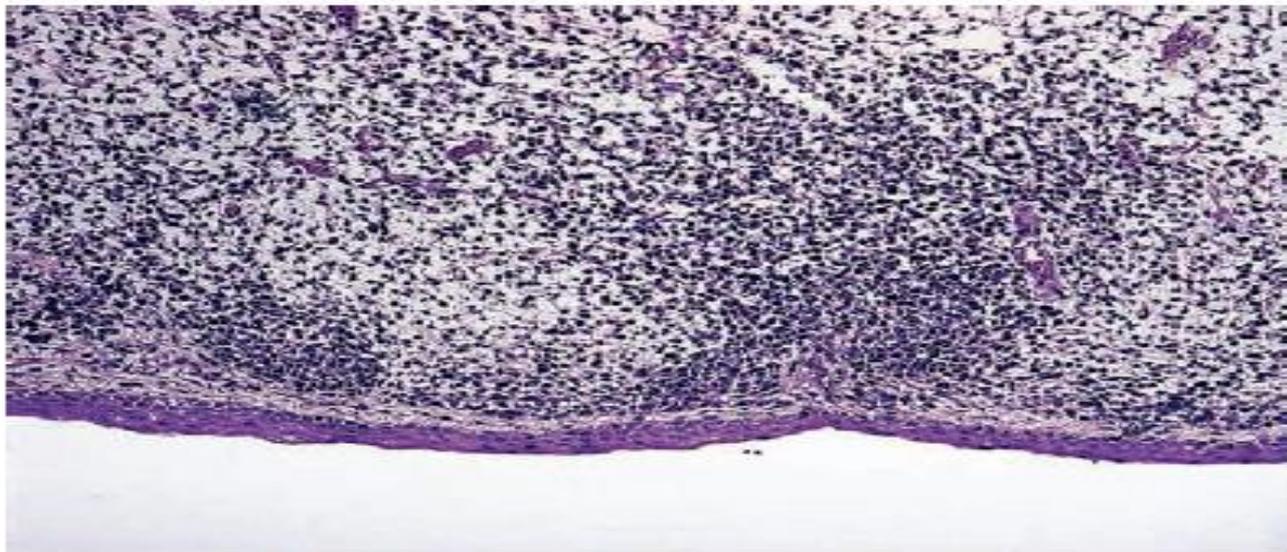
THE GRAPE-LIKE CONFIGURATION OF BOTRYOID EMBRYONAL RHABDOMYOSARCOMA OF VAGINA. IS CHARACTERISTIC.



- Microscopically, a myxoid stroma is seen containing a mixture of fusiform, round, or spindle cells. Some of these cells contain a bright eosinophilic granular cytoplasm suggestive of rhabdomyoblastic differentiation.
- Cross striations may or may not be present.
- An important diagnostic feature is the crowding of the tumor cells around blood vessels and, most important, beneath the squamous epithelium.
- The latter results in a distinctive subepithelial dense zone (the “cambium layer”).



... Microscopic Appearance of Embryonal Rhabdomyosarcoma. The differential diagnosis is that of small round cell tumors.



So-called cambium layer beneath non-neoplastic epithelium in embryonal rhabdomyosarcoma.

