النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : Summary lec 12 (female 2)

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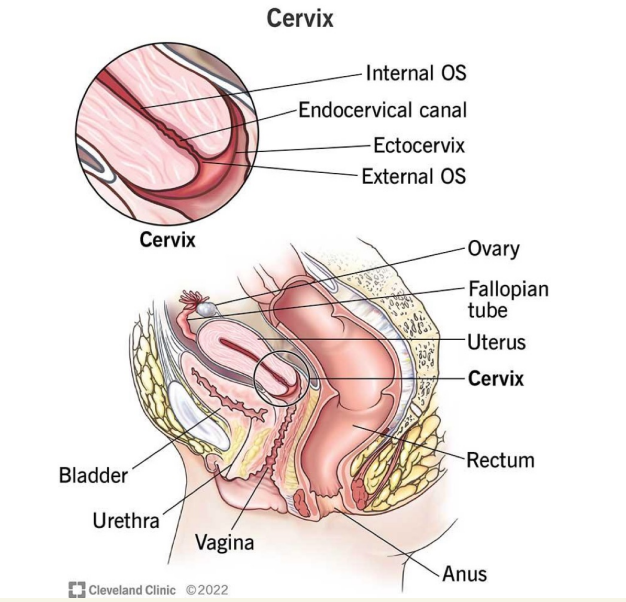
وَقُل رَّبِّ زِدْنِي عِلْمًا

Cervix

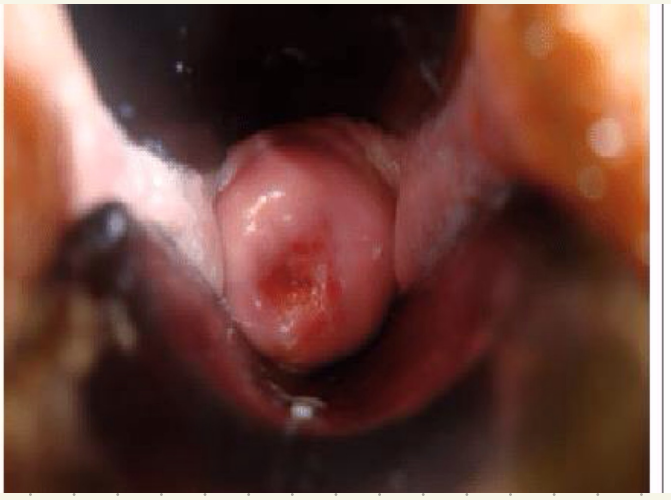
CERVICITIS

Cervicitis, inflammation of the cervix, can result from various factors:

1. **Trauma**, such as during childbirth or instrumentation during vaginal examination.
2. **Fluctuations in estrogen levels**, both high and low.
3. **Excessive cervical secretions**.
4. **The alkaline environment** of the cervical canal during ovulation.



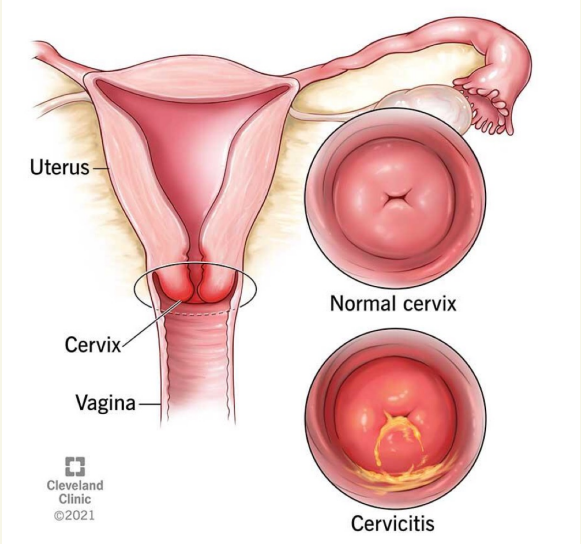
Cervicitis is highly prevalent and often presents with a **mucopurulent to purulent vaginal discharge**. Cytologic examination of the discharge typically reveals white blood cells and inflammatory changes in shed epithelial cells, along with possible microorganisms.



Acute cervicitis can be caused by childbirth or sexually transmitted diseases like gonorrhea, chlamydia, herpes, or trichomoniasis. It's frequently mistaken for vaginitis.

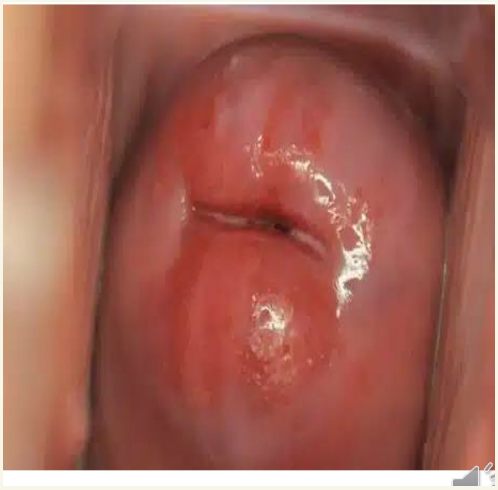
Chronic cervicitis, more common, refers to persistent discharge lasting three months despite resolution or exclusion of infection Chronic cervicitis is associated with symptoms such as **leukorrhea** (vaginal discharge), **destruction of the stratified squamous** epithelium of **the ectopic cervix,** growth of columnar epithelial cells of the endocervix leading to **cervical erosion** (reddening of the ectocervix), granularity of the ectocervix, development of nabothian cysts, and endocervical polyps.

If left untreated, cervicitis can be caused by organisms that may ascend into the uterus and fallopian tubes, leading to pelvic inflammatory disease (PID). PID can result in infertility and peritonitis, a life-threatening infection. These organisms can also be transmitted through sexual activity..



Grossly, **nonspecific cervicitis** may present as either the relatively uncommon acute nonspecific form, which is limited to postpartum women and typically caused by staphylococci or streptococci, or the common chronic nonspecific cervicitis, which is nearly ubiquitous and ever-present.

In chronic cervicitis, overgrowth of the regenerating squamous epithelium can block the orifices of endocervical glands in the transformation zone, leading to the formation of small Nabothian cysts lined by columnar mucus-secreting epithelium.

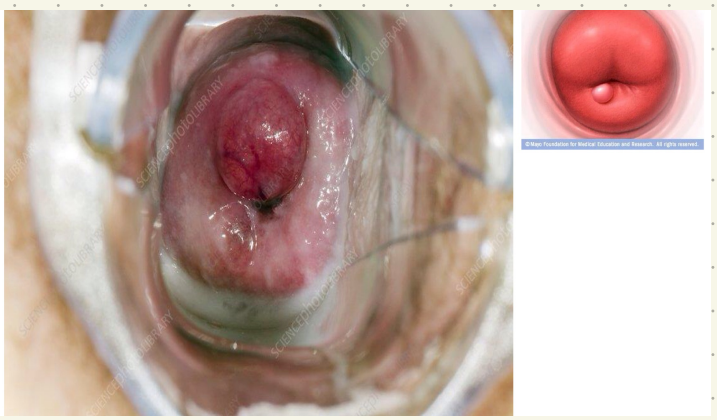


Cervical ectropion

Cervical ectropion, also known as cervical erosion, occurs when the endocervix everts, exposing the columnar epithelium to the vaginal environment. Despite its name, no actual erosion of cells occurs.

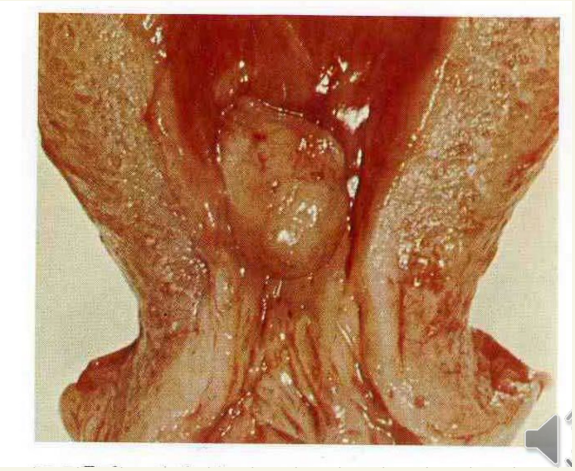
This condition is considered a normal physiological occurrence and is commonly observed during cervical examinations in adolescents, during pregnancy, and in women using estrogen-containing contraceptives.

This change is thought to be induced by high level of estrogen and does not represent metaplasia



Nabothian cysts

Nabothian cysts are mucus-filled cysts found on the cervix's surface. They typically develop when the stratified squamous epithelium of the ectocervix grows over the simple columnar epithelium of the endocervix, blocking the cervical crypts and trapping mucus inside them. These cysts often appear as firm bumps on the cervix's surface and usually resolve on their own without treatment. However, if nabothian cysts occur alongside chronic cervicitis, the underlying cause of the inflammation must be addressed.



endocervical polyp

An endocervical polyp is an inflammatory lesion that may protrude as a polypoid mass through the exocervix. Typically, it can be large, soft, and smooth with a glistening surface and underlying cystically dilated spaces filled with mucinous secretion. Importantly, these polyps have no malignant potential and often present as rounded, soft, sessile gelatinous growths filling the endocervical canal.

Neoplasia of the cervix

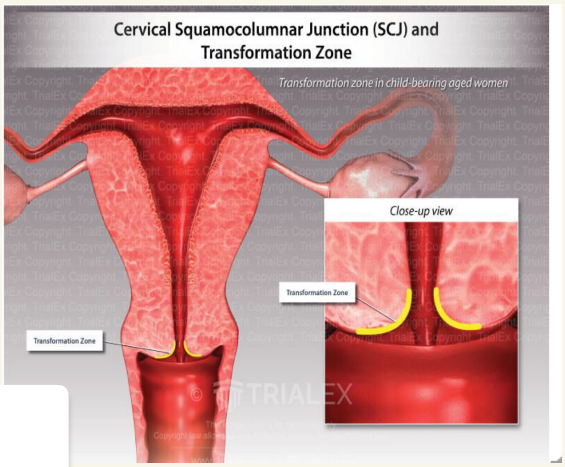
Pathogenesis

High-risk strains of HPV play a crucial role in cervical cancer development, with infections lasting longer on average than low-risk strains. Persistent infection increases the risk of precursor lesions and carcinoma. Risk factors include early sexual activity, multiple partners, and persistent infection by high-risk HPV strains.

Cervical tumors, mostly epithelial in origin, are linked to oncogenic strains of HPV. The junction of columnar and squamous epithelium at the cervix forms the transformation zone, where tumors typically develop due to HPV infection.

HPV's carcinogenic effect hinges on its E6 and E7 proteins, which disrupt the function of tumor suppressor proteins p53 and RB, respectively. This interference allows infected cells to evade growth arrest, crucial for viral replication and shedding. E6 induces p53 degradation and boosts telomerase expression, while E7 binds to RB, releasing E2F transcription factors and driving cell cycle progression.

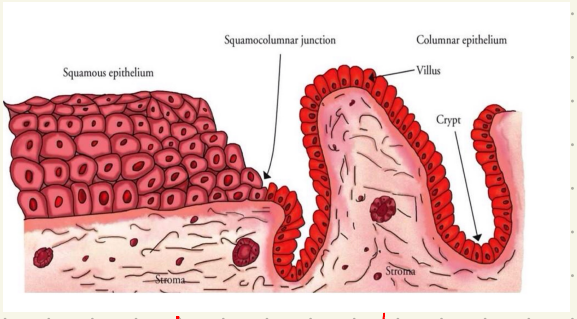
Approximately 70% of cervical intraepithelial neoplasia (CIN) and cervical carcinoma cases are attributed to two high-risk HPV types, 16 and 18. These types are prone to integrating into the host cell genome, a process linked to disease progression



Cervical Intraepithelial Neoplasia (CIN)

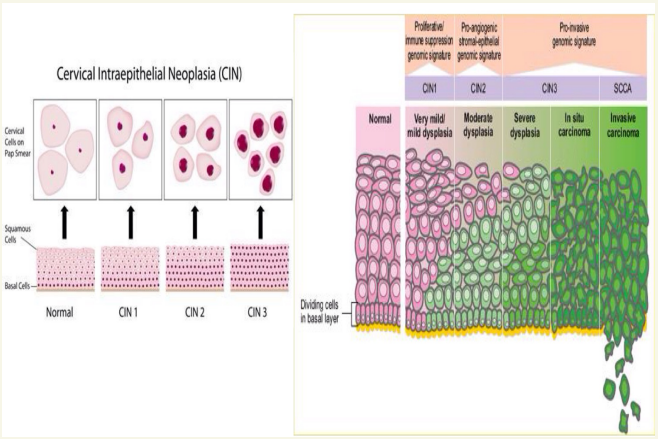
Dysplasia is graded based on epithelial involvement:
- CIN I: Mild dysplasia (< one-third of full epithelial thickness)
- CIN II: Moderate dysplasia (up to two-thirds of full epithelial thickness)
- CIN III: Severe dysplasia involving the full epithelial thickness (carcinoma in situ)

Cervical intraepithelial neoplasia (CIN) affects women primarily around the age of 30, with invasive cervical cancer typically emerging around age 45. Molecular methods allow for the detection of human papillomavirus (HPV) in nearly all precancerous lesions and invasive neoplasms. High-risk HPV types, notably 16, 18, 45, and 31, are responsible for the majority of cervical cancer cases. It's crucial to note that most invasive cervical squamous cell carcinomas originate from precursor CIN lesions. However, not all instances of CIN progress to invasive cancer; many remain stable or regress spontaneously over time.



Normal squamocolumnar junction

HPV types 16 and 18 integrate into the host genome, leading to increased expression of E6 and E7 proteins, which interfere with tumor suppressor genes p53 and RB, respectively. A recent HPV vaccine introduced in the USA and Europe effectively prevents HPV infections and subsequent cervical cancers. Cytological examination enables the detection of cervical intraepithelial neoplasia (CIN) long before any visible abnormalities arise. Follow-up studies have shown that precancerous CIN lesions may precede the development of cervical cancer by many years, or even decades, although only a fraction of CIN cases progress to invasive cancer.

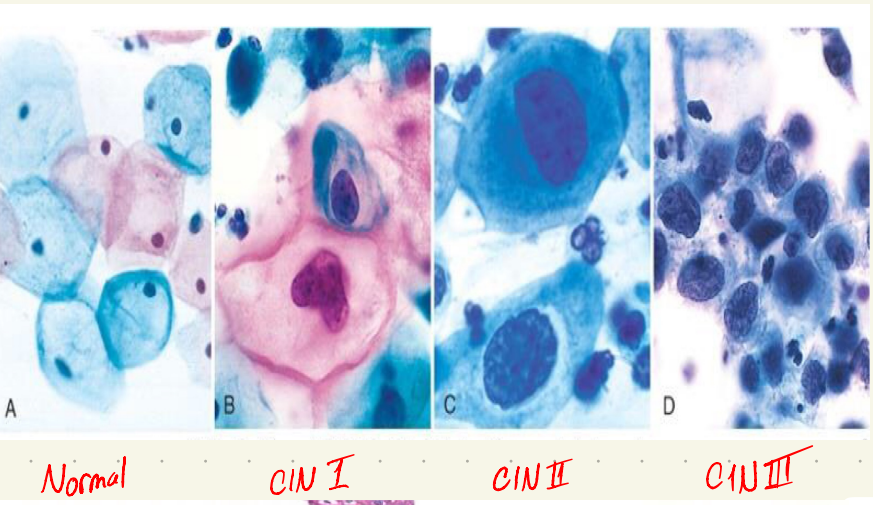


Precancerous cervical intraepithelial neoplasia (CIN) can originate in two ways: either as low-grade lesions that progress to higher CIN grades over time, or as high-grade lesions that develop de novo. The progression pattern depends on factors such as the location of the HPV infection in the transformation zone, the type of HPV involved (high or low risk), and other host-related factors.

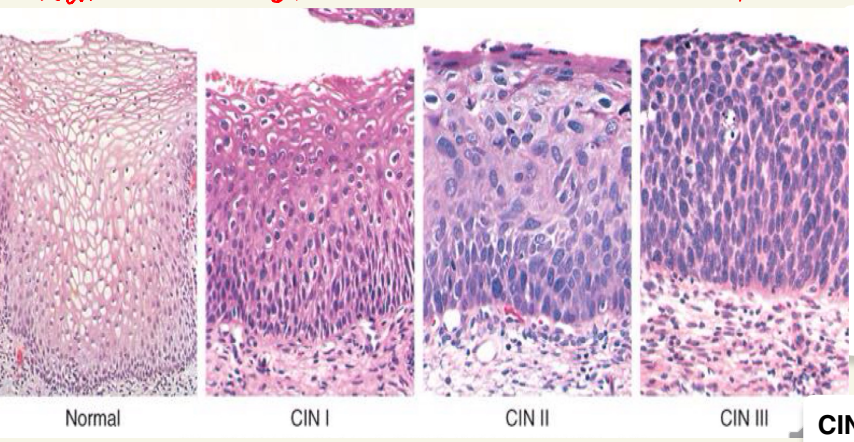
Important risk factors associated with the development of cervical intraepithelial neoplasia (CIN) and invasive cervical cancer include early age at first intercourse, having multiple sexual partners, having a male partner with multiple previous sexual partners, and persistent infection by high-risk HPV papillomaviruses. These factors are often linked to socioeconomic status, multiple pregnancies, and are rare among virgins, indicating the likelihood of sexual transmission of HPV, the causative agent in most cases.

Morphology

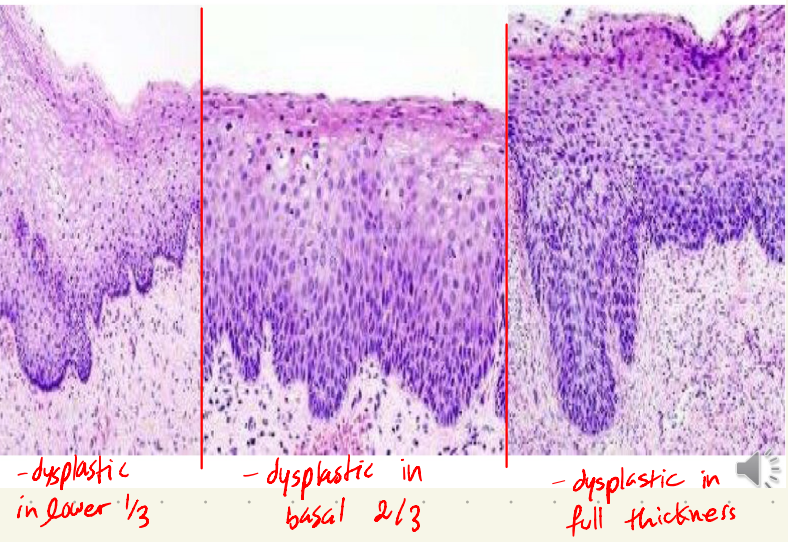
Cervical intraepithelial neoplasia (CIN) exhibits progressive morphological changes indicative of increasing severity.



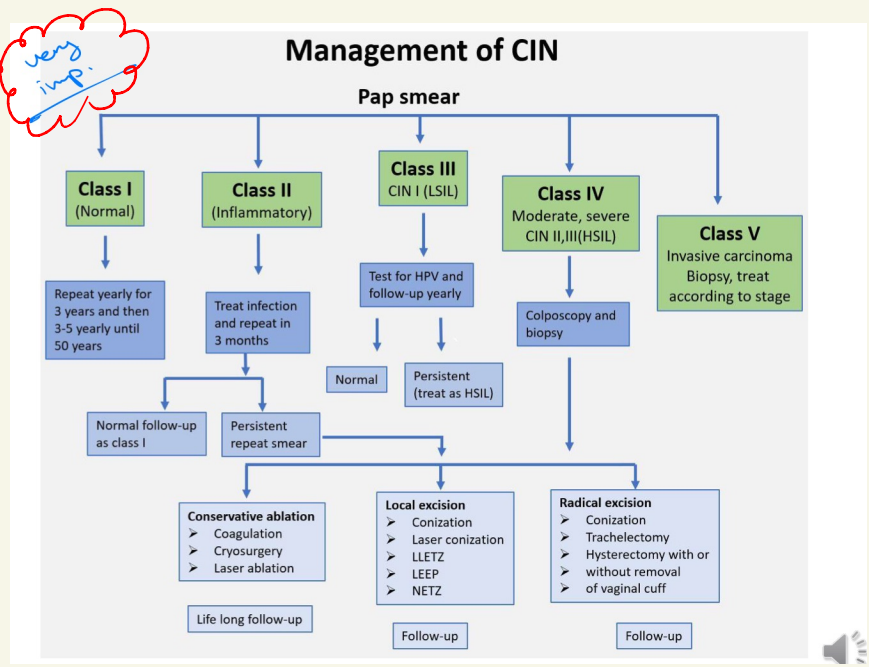
CIN I presents with mild dysplasia characterized by Koilocytosis, mainly affecting the superficial layers of the epithelium, with nuclear hyperchromasia and perinuclear vacuolization



CIN II displays more severe dysplasia, with delayed keratinocyte maturation extending into the middle third of the epithelium. This stage is marked by cellular and nuclear pleomorphism, heterogeneity of nuclear chromatin, and mitoses above the basal layer, reaching into the middle third of the epithelium. Additionally, some differentiation is observed in the superficial layer of cells. Overall, these changes signify the progressive nature of CIN, with implications for diagnosis and management.

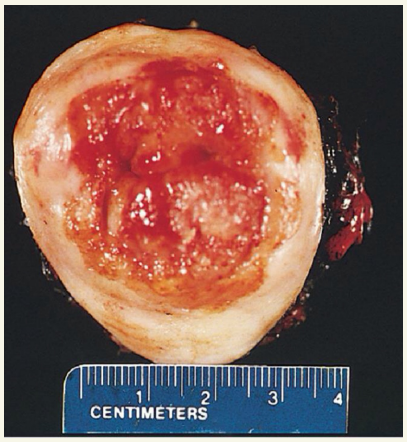


CIN III, the dysplastic changes become more pronounced, with greater pleomorphism in cell and nuclear size, marked hyperchromasia, and disorderly cell orientation. Mitoses, both normal and abnormal, are observed throughout the epithelium, indicating a loss of maturation. Koilocytotic changes typically disappear at this stage. As the dysplastic changes progress, they may extend into the endocervical glands, but remain confined to the epithelial layer and its glands, defining **carcinoma in situ**. While the next stage, invasive carcinoma, may occur, progression is not inevitable, underscoring the importance of early detection and intervention in managing cervical intraepithelial neoplasia.



Cervical Cancer

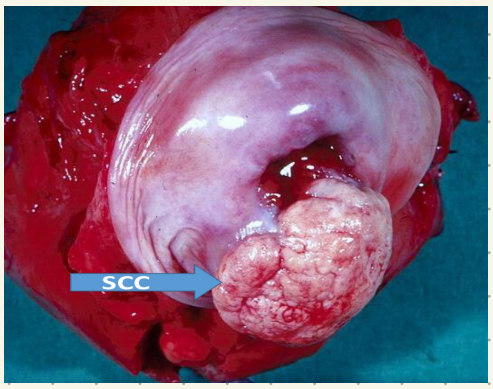
The most common type of cervical cancer is squamous cell carcinoma (SCC), accounting for about 75% of cases, followed by adenocarcinomas and adenosquamous carcinomas (20%), and neuroendocrine carcinomas (less than 5%). SCC typically peaks in incidence around the age of 45, approximately 10 to 15 years after the detection of precursors such as cervical intraepithelial neoplasia (CIN). Monitoring the course of the disease relies heavily on careful follow-up and repeat biopsies to track progression and inform treatment decisions.



- Advanced carcinoma of cervix

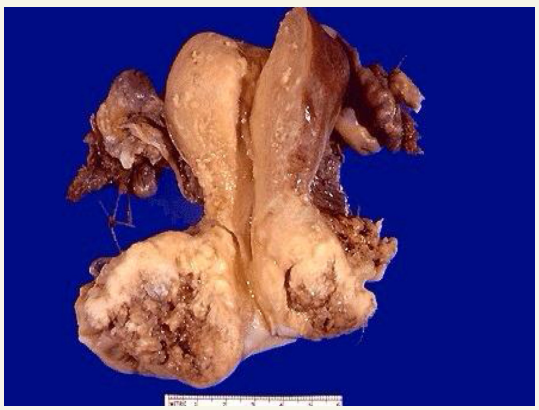
Morphology

Invasive cervical cancer develops in the transformation zone and can range from microscopic to grossly visible tumors encircling the cervix. It can lead to a "barrel cervix" and extend into nearby tissues, affecting the pelvic structures. The spread to pelvic lymph nodes is influenced by the depth(ranging from < 1% for T < 3 mm in depth to more than 10% once invasion is more than 5 mm) of invasion and lymphatic involvement.



- Squamous Carcinoma

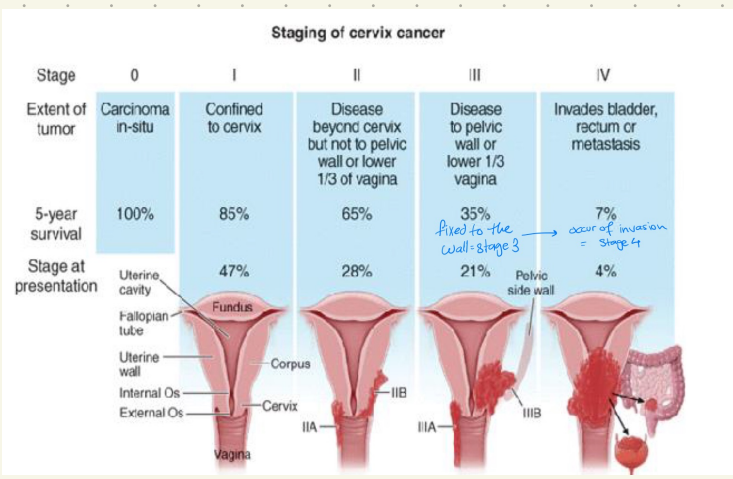
Invasive cervical cancer typically involves adjacent structures like the vagina, ureters, bladder, or rectum, and distant metastases occur later in the disease progression. Neuroendocrine tumors are consistently aggressive, while other types of cervical cancer are graded based on cellular differentiation and staged according to clinical spread, ranging from stages 1 to 4.



- Squamous Carcinoma spread to vagina

Clinical aspects

The introduction of the Pap smear has led to a higher proportion of cervical cancers being diagnosed early, often at stage 1. Most cervical tumors are identified in the preinvasive phase, appearing as white areas during colposcopy after acetic acid application. However, more advanced cervical cancers are typically found in women who have never had a Pap smear or have had long intervals between screenings. Clinically, these tumors may manifest with symptoms such as unexpected vaginal bleeding, leukorrhea, painful intercourse (dyspareunia), and dysuria, as well as post-coital bleeding.



Treatment for cervical intraepithelial neoplasia (CIN) typically involves procedures such as laser therapy or cone biopsy. In cases of invasive cancer, surgical excision is often necessary. Prognosis varies depending on the stage of the disease, with a 5-year survival rate of 100% for stage 0 (preinvasive), 85% for stage 1, 65% for stage 2, 35% for stage 3, and 7% for stage 4. **Prevention** strategies include vaccination against HPV, which can significantly reduce the risk of cervical cancer, as well as early detection of precursors through cytologic examination followed by interventions like laser vaporization or cone biopsy, which are highly effective in preventing cancer development.

بالتوفيق والنجاح