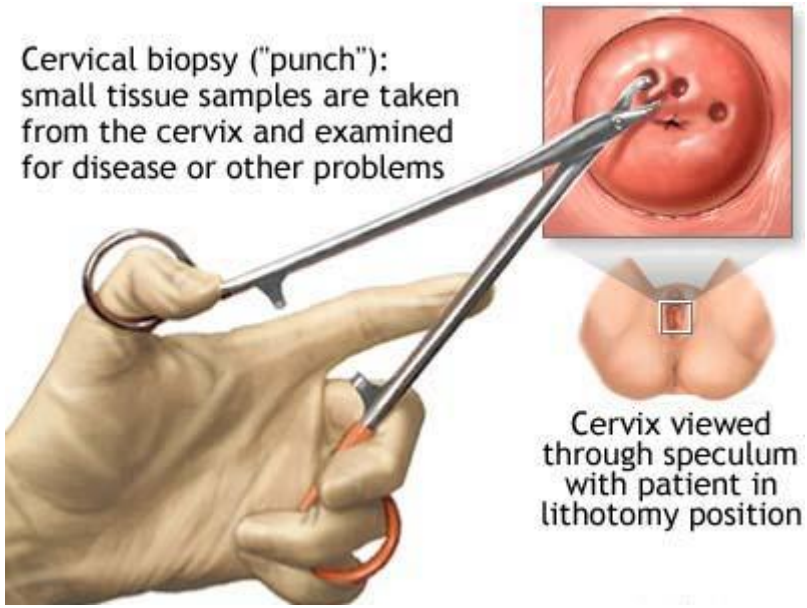
429 Pathology Team



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*** Pathology of the Uterine Cervix***

Benign

- Erosion
- Polyp
- Cervicitis

Malignant

- Cervix Carcinoma

Highlighted; Very important note
or Highlighted; An MCQ

	Erosion (Ectropion)	Polyp	Cervicitis: inflammation of the cervix, can be:	
			NON INFECTOUS	INFECTIOUS
About	Is a **benign** condition which has no malignant potential.	They are inflammatory proliferations of cervical mucosa and ***are not true neoplasms***. ***Most originate from***: **The Endocervix** (endocervical polyps) ***Some From***: the Ectocervix (ectocervical polyps).	An Inflammation of cervix which is ***often acute*** but may be chronic	**Most often involves** : the Endocervix.
Clinical Manifestation	**Erythematous** area.	Small Pedunculated mass Or Sessile(often) mass.	- Noninfectious cervicitis which is often asymptomatic. - The cervix appears red and swollen	➢ Often asymptomatic ➢ may manifest as ***vaginal discharge***
Morphology	***Histologically*** **Columnar Epithelium** replacing ***Squamous Epithelium*** ↓ ***Grossly*** resulting in the ***Erythematous Area***	***The Lesion is Characterized By***: - Overgrowth of benign stroma - Covered by epithelium. **Endocervical polyps :** **Are Covered By:** Endocervical, squamo-columnar or metaplastic squamous epithelium **Ectocervical Polyps:** **Are Covered By**: stratified squamous epithelium. **The Stroma:** **Contains:** - Thick-walled blood vessels - Fibrous Tissue - Some inflammatory cells.	***Histologically:*** nonspecific. **The inflammatory infiltrate may comprise:** - Neutrophils - Plasma cells - Lymphocytes *((or a combination of these cells))* **Nabothian Cysts:** When often some of the mucous glands are obstructed and dilate to form mucus-filled cysts **Common in Chronic Cervicitis:** ***Squamous metaplasia*** of the ***endocervical glandular epithelium***. (unlike ***The Erosion*** which is vice versa)	
ETIOLOGY	**Respond to variety of stimuli including:** - Hormones - Chronic irritation - Inflammation (chronic cervicitis).		**Caused by:** - ***Chemical*** irritation (e.g. douche, deodorant) - ***Mechanical*** irritation (e.g. tampon, diaphragm)	**Caused by *Various* Organisims:** ❖ Staphylococci ❖ Enterococci ❖ Gardnerella Vaginalis ❖ Trichomonas Vaginalis ❖ Candida Albicans ❖ Chlamydia Trachomatis.

5 Types of Infectious Cervicitis:

	CANDIDIASIS "MONILIASIS"	TRICHOMONIASIS	CHLAMYDIA TRACHOMATIS CERVISITIS	HERPES SIMPLEX VIRUS	HUMAN PAPILLOMA VIRUS
Etiology	Common form of *Vaginitis* or *Cervicitis* caused by **Candida albicans** (normal component of the vaginal flora) **Associated with**: ❖ Diabetes Mellitus. ❖ Pregnancy. ❖ Broad Spectrum Antibiotic Therapy. ❖ Oral Contraceptive Use ❖ Immunosupression.	A sexually transmitted disease **Caused by:** a *Unicellular Flagellated Protozoan* called : **Trichomonas vaginalis.** **Involves:** the vagina and cervix.	- An obligate, **gram-negative** intracellular pathogen. - A frequent cause of pelvic inflammatory disease - May also cause a condition known as: **lymphogranuloma venereum** ***The most common sexually transmitted disease in the developed countries.*** ***May coexist with*** Neisseria gonorrhoeae infection.	**HSV Type 2 infection** accounts for majority of genital herpes cases and is spread by sexual contact.	• HPV infection of the cervix is common. • Over 20 serotypes infect the female genital areas • Cause a variety of different lesions with the different serotypes. • Some are malignant and others are benign
Clinical Manifestations	**Characterized by** - White, Patchy, Mucosal *Lesions.* - Thick White *Discharge*. - Vulvovaginal Pruritis.	***Mostly***: asymptomatic ***Occasionally***: - Copious, thin, frothy, yellow green-gray offensive **discharge is produced.** - There may be vulvas itching/burning or dyspareunia	May be symptomatic or asymptomatic. ***In symptomatic cases:*** ❖ There is ***A Mucopurulent Cervical Discharge*** ❖ ***Reddened, Congested*** and ***Edematous Cervix.*** ❖ - May be associated with ***Urethritis.***	**Produces :** ***vesicles*** and ***ulcers*** **in:** ❖The Cervix, ❖Vagina ❖Vulva ❖Urethra ❖Perianal Skin	**Associated with:** increased risk of subsequent cervical cancer → long-term follow-up with attention to the cervix, vagina and vulva is necessary.
			NO MORPHOLOGY	**NO** MORPHOLOGY	MORPHOLOGY ↓

Morphology

- **Colonies of the fungus** ((*Present on the surface and extend into → the epithelium - but not into the underlying tissues)*)
- **Mild edema** & **Chronic ` Inflammatory Cells** are present.
- **Ulcers** may develop.

Cytological smears show:
Yeast Forms and **Branching Pseudohyphae**

Inflammatory Infiltrate:
lymphocytes and plasma cells.

The organisms *not seen in biopsies*
because they do not invade the vaginal wall.

Diagnosis
made by examination of
1) ***saline wet preparation***
((in which the motile trophozoites are seen))
2) ***Pap-stained vaginal smears.***

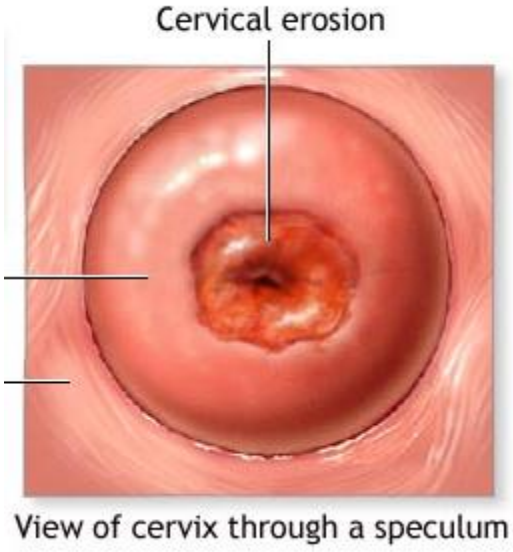
Human Papilloma Virus **infection may cause any of the following:**
((depending on the serotype))

1- **Condyloma:**
Develops in
- The squamous epithelium of ***The Ectocervix***
- In foci of squamous metaplasia in ***The Endocervix.***

The lesions may be flat or exophytic condylomma acuminatum.
Can be *caused by any HPV serotype* but more commonly by types 6 and 11.

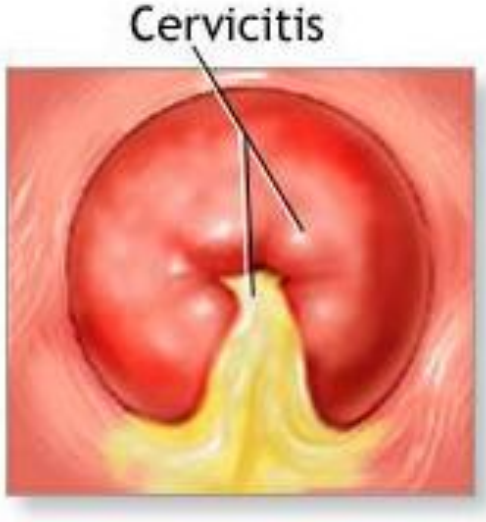
2- **Mild dysplasia:** usually caused by "low risk" HPV serotypes, 6 and 11

3- **High- grade dysplasia**
caused by
- "High risk" HPV (types16 and 18)
- Moderate risk HPV(types 31,33,35).



View of cervix through a speculum


Cervical polyps
As viewed through a speculum



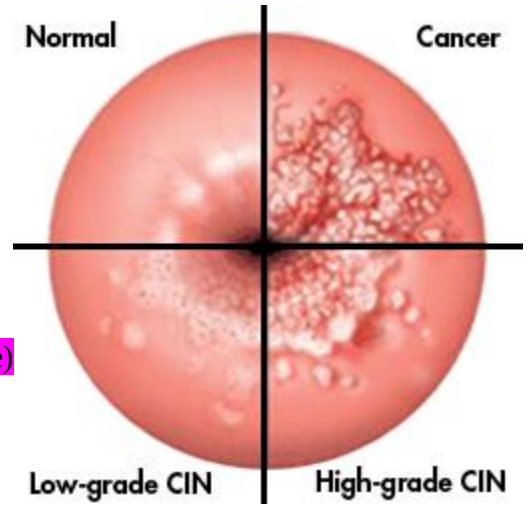
Cervix Carcinoma:

The most common cancer in female genital tract: Endometrium Cancer - **In women:** breast cancer

One of the **major causes** of **cancer-related death** in women (especially in developing world), but nowadays its prognosis dramatically improved (WHY?!)
Due to the wide use of ***PAP screening*** which lowered the incidence of invasive cancer and helped in **Early Diagnosis** and **Treatment.**

Types:

- Squamous cell carcinoma (most common)
- Adenocarcinoma
- Neuroendocrine Carcinoma



1) If Early Diagnosis; Precancerous Lesion: pre-cancer epithelial change referred as:
Cervical Intra-epithelial Neoplasia (**CIN**) or Squamous Intra-epthelial Lesion (**SIL**)
It is a pre-cancerous, non-invasive lesion → its detection makes curative treatment possible
Changes may develop to a cancer and may take years beginning as low grade or high grade.
(high grade become invasive in 6-75% of cases)
(but not all cases of CIN progress to cancer as some may spontaneously regress- if they are not a **high grade**)

Human Papilloma Virus and CIN:
high-risk HPV types are found in increasing frequency in the ***higher grade precursors*** of CIN (they are associated together)

CIN DIAGNOSIS

PAP Cytology Screening

1st: examin cervix & cell lining at ***Transformation zone***

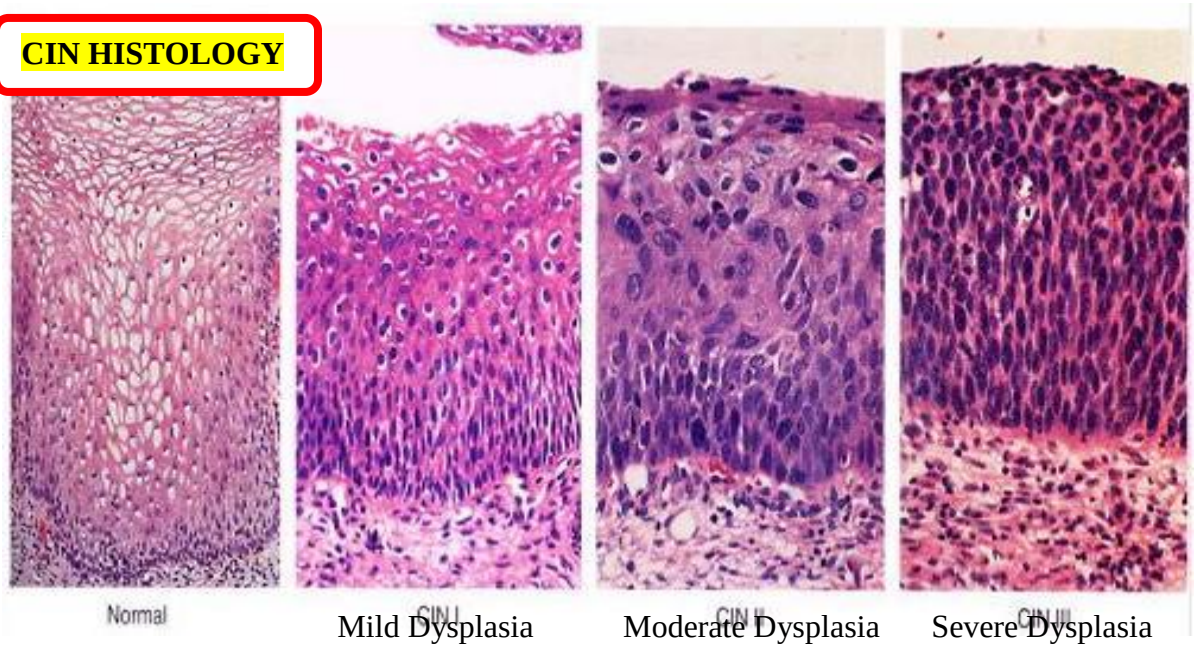
2nd: scrap and sample with a ***Spatula***

3rd: spread on a slide and stain with ***PAPanicolaou stain***

4th: examine under a ***Light microscope***

Then we grade it as low grade and high grade (see histology)

CIN HISTOLOGY



Mild Dysplasia | Moderate Dysplasia | Severe Dysplasia & Carcinoma in situ

CIN Risk Factors

-Early age at first intercourse
-Low socioeconomic group (rare among virgins)
-Multiple sexual partners
-Multiple pregnancies
-Persistent high risk HPV infection (detected in 85-90%)

High risk types HPV: 16, 18, 31, 33, 35, 39, 45, 52, 56, 58 & 59.
Low risk types HPV: 6, 11, 42, 44 which result in ***Condyloma ((infection of the genitals)***

2) Cervix Carcinoma:

About

75-90% of invasive cancers are ***Squamous cell carcinomas*** (generally evolves from a pre-cancerous CIN) and the remaineder are ***Adenocarcinomas***.

Peak Incidence: 45-years old (now appearing in younger females)

Causes

HPV is the number one reason for abnormal cells of the cervix.

It is a ***Skin Virus*** which results in: Warts – common warts – flat warts – genital warts – condylomas – plantar warts – ***Precancerous Lesions***.

Detected by:

- PAP-exam (annual exam is the common testing procedure).
- HPV DNA ISH test, Diegene Hyprid Capture test → determine the type of the strain of the virus whether high grade or low.

Diagnosis

It is usually ***Asymptomatic*** and the detection of the ***Dysplasia of the cervix*** is the only way to Diagnose it **by** Pap-exam

There should be a regular pap-exam made to detect any normal cells

Morphology

Encircling Os and at the transitional zone:

Microscopic foci early stromal invasion **Grossly** frank tumors (tumors may be invisible or exophytic).

Grading:

from 1 to 3 based on **cellular differentiation**

Staging:

From 1 to 4 depending on **clinical spread** as:

0 – Carcinoma in situ
1 – Confined to the cervix
2 – Extension cervix (without extension to lower part of the vagina or pelvic wall)
3 – Extension to pelvic wall and/or lower third of the vagina
4 – Extension to adjacent organs

Prognosis

Many → diagnosed in early stages
Vast majority → diagnosed in pre-invasive phase

If the woman never had a pap-smear or have waited many years since the prior one, she may present with ***more advanced stages***

Management:

Laser or **cone biopsy** is the most effective way **with** ***High grade SIL in cancer prevention***