**Uterine Cervix**

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**Erosion/Ectropion**

Is characterized by columnar epithelium replacing squamous epithelium, grossly resulting in an erythematous area.

It is a typical response to a variety of stimuli including hormones, chronic irritation and inflammation (chronic cervicitis).

It is benign and has no malignant potential.

**Cervical polyp**

This is a small, pedunculated, often sessile mass. Most originate from the endocervix (endocervical polyps) with a few from the ectocervix (ectocervical polyps).

They are inflammatory proliferations of cervical mucosa and are not true neoplasms.

The lesion is characterized by overgrowth of benign stroma covered by epithelium.

Endocervical polyps are covered by endocervical, squamocolumnar or metaplastic squamous epithelium while ectocervical ones are covered by stratified squamous epithelium. The stroma contains thick-walled blood vessels and fibrous and some inflammatory cells.

**CERVICITIS**

Inflammation of cervix.

Can be non-infectious or infectious.

**I)Noninfectious (Nonspecific) Cervicitis**

This is inflammation of the cervix caused by chemical (e.g. douche, deodorant) or mechanical (e.g. tampon, diaphragm) irritation. It is often acute but may be chronic.

Clinical appearances

Noninfectious cervicitis is often asymptomatic. The cervix appears red and swollen

Histology

The histologic features are nonspecific. The inflammatory infiltrate may comprise neutrophils or plasma cells and lymphocytes or a combination of these cells.

Squamous metaplasia of the endocervical glandular epithelium is common in chronic cervicitis. Often some of the mucous glands are obstructed and dilate to form mucus-filled cysts called nabothian cysts.

**II) Infectious cervicitis**

Can be caused by various organisims e.g.staphylococci, enterococci, Gardnerella vaginalis, Trichomonas vaginalis, Candida albicans and Chlamydia trachomatis.

Most often involves the endo cervix.

Is often asymptomatic, may manifest as vaginal discharge

**a)Candidiasis (moniliasis)**

Common form of vaginitis /cervicitis.

Caused by Candida albicans, a normal component of the vaginal flora.

Associated with diabetes mellitis, pregnancy, broad spectrum antibiotic therapy, oral contraceptive use and immunosupression.

Characterized by white patchy mucosal lesions with thick white discharge and vulvovaginal pruritis.

Histology.

Colonies of the fungus are present on the surface and extend into the epithelium but not into the underlying tissues. Mild edema and chronic inflammatory cells are present. Ulcers may develop. Cytological smears show yeast forms and branching pseudohyphae

**b)Trichomoniasis**

caused by a unicellular flagellated protozoan, Trichomonas vaginalis. It is sexually transmitted disease

Involves the vagina and cervis also.

Clinical presentation

Most infections are asymptomatic and pass unnoticed. Occasionally, a copious, thin, frothy, yellow green to gray offensive discharge is produced. There may be vulvar itching or burning or dyspareunia

Histology

an inflammatory infiltrate of lymphocytes and plasma cells. The organisms are not seen in biopsies because they do not invade the vaginal wall. Diagnosis is made by examination of a saline wet preparation in which the motile trophozoites are seen. The organism can also be found in Pap-stained vaginal smears.

**c)Clamydia trachomatis Cervicitis**

Clamydia trachomatis is an obligate, gram-negative intracellular pathogen.

Clamydial cervicitis is the most common sexually transmitted disease in the developed countries. It may coexist with Neisseria gonorrhoeae infection.

It is a frequent cause of pelvic inflammatory disease.

Is most often asymptomatic.

 Chlamdial infection may also cause a condition known as lymphogranuloma venereum

Clinical appearances

The disease may be symptomatic or asymptomatic. In symptomatic cases there is a mucopurulent cervical discharge with a reddened, congested and edematous cervix. It may be associated with urethritis.

Histology

endocervix shows a dense infiltrate of lymphocytes , plasma cells and macrophages. Occasionally, many lymphoid follicles with germinal centers (called follicular cervicitis) are present. Diagnosis is confirmed by demonstrating the organisms in glandular epithelial cells by immunohistochemical or immunofluorescent techniques or by culture

Complications**:** It is usuallydue to spread from cervix and includes the following

Endometritis ,salpinghitis.

Generalized infection of the pelvic adnexal organs (pelvic inflammatory disease) and tubal blockage with infertility or ectopic pregnancy.

Infants born to mothers with C. trachomatis cervicitis may develop inclusion conjunctivitis or neonatal pneumonia

**d)Herpes simplex virus (HSV) Cervicitis**

HSV Type 2 infection accounts for majority of genital herpes cases and is spread by sexual contact.

It produces vesicles and ulcers that can involve the cervix, vagina, vulva, urethra and perianal skin.

**e)Human papilloma virus (HPV) Infection**

HPV infection of the cervix is common.

Over 20 serotypes infect the female genital areas. They cause a variety of different lesions with the different serotypes.

Clinical behavior

HPV infection is associated with increased risk of subsequent cervical cancer and so long-term follow-up with attention to the cervix, vagina and vulva is necessary.

HPV infection may cause any of the following depending on the serotype

**1)Condyloma**. This develops in the squamous epithelium of the ectocervix and 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** is usually caused by "low risk" HPV serotypes, 6 and 11.

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

**CANCER CERVIX**

One of the major causes of cancer-related death in women, specially in developing world.

Most common cervical cancer is squamous cell carcinoma. Other types are adenocarcinoma, neuroendocrine carcinoma etc.

Nowadays there is dramatic improvement because of early diagnosis and treatment.

The wide use of PAP screening lowered the incidence of invasive cancer .

**Precancerous lesion**

The majority of cancers are preceded by a precancerous lesion. This lesion may exist in the noninvasive stage for as long as 20 years and shed abnormal cells that can be detected on cytologic examination

All invasive squamous cell carcinomas arise from pre-cancer epithelial changes referred as Cervical Intraepithelial Neoplasia (CIN ) or Squamous intraepithelial lesions.

Squamous Intraepithelial Lesion (SIL) is the pre-cancerous(non invasive) lesion and detection of these lesions made curative treatment possible.

Not all cases of CIN progress to invasive cancer.

These precancerous changes:

(1) they do not invariably progress to cancer and may spontaneously regress,

the risk of persistence or progression to cancer increases in the high grade precancerous lesions;

(2) they are associated with papillomaviruses, and high-risk HPV types are found in increasing frequency in the higher-grade precursors

**CERVICAL INTRA-EPITHELIAL NEOPLASIA /CIN**

Cytologic examination can detect CIN (SIL) long before any abnormality can be seen grossly .

Pre-cancer changes can precede the development of an overt cancer by many years.

CIN lesions may begin as Low Grade CIN and progress to High Grade CIN, or they might start as HG lesion.

**CIN histology.**

On the basis of histology ,pre-cancer lesions are graded as follows:

-CIN I : Mild Dysplasia

-CIN II : Moderate Dysplasia

-CIN III : Severe Dysplasia and Carcinoma in situ.

Cancer is invasive once the basement membrane is ruptured and tumor cells extend into the underlying tissue.

On gross examination in CIN the cervix looks relatively normal. There is no tumor mass.

**Cytology screening for precancerous lesions**

The cervix is examined and the cells lining the cervical wall at the transformation zone are scrapped/ sampled with a spatula and then spread on a slide. They are then fixed, stained (Papanicolaou stain) and examined under a light microscope. This is called as cytology Pap Screening

In cytology smears we separate pre-cancer lesions into two groups :

1) Low Grade SIL

2) High Grade SIL

1-5 % of Low Grade SIL become invasive carcinoma.

6-74% of High Grade SIL become invasive carcinoma

CIN I = Low grade SIL

CIN II = High grade SIL

CIN III = High grade SIL

**CIN , Risk Factors**

Early age at first intercourse

Multiple sexual partners

A male partner with multiple previous sexual partners

Persistent infection by high risk papillomaviruses

Some other risk factors; low socioeconomic groups

rare among virgins, multiple pregnancies.

**CIN ,causes**

HPV can be detected in 85 -90 % of pre-cancer lesions

High risk types HPV : 16, 18, 31, 33, 35, 39, 45, 52, 56, 58, and 59 .

Low risk types HPV : 6, 11, 42, 44 . These types result in condylomas.

**Cervix Carcinoma ,Cause**

The cause is determined to be HPV virus .The HPV is the number one reason for abnormal cells of the cervix.

HPV is a skin virus, which results in warts, common warts, flat warts, genital warts (condylomas), and planter warts and precancerous lesions.

**Cervical carcinoma , Sign**

There are no visible symptoms that you have dysplasia of the cervix ,without a Pap smear or Pap exam .

This is why we should have regular pap exams, as to detect any abnormal cells .

**Cervical Carcinoma , Screening**

The Pap smear detects early HPV infection.

The common testing procedure for HPV infection is an annual pap exam .

There is the HPV DNA ISH test ,the Diegene Hyprid Capture test . This test will determine whether you carry high or low risk strains of the virus.

**Invasive cancer**

75 -90% of invasive cancers are Squamous cell carcinomas ,which generally evolves from pre-cancer CIN.

The remainder are Adenocarcinoma.

Squamous cell cancers are appearing in increasingly younger women ,now with a peak incidence at about 45 years, about 10-15 years after detection of their precursors.

**Cervical Carcinoma ,Morphology**

Mainly in the region of the transformation zone ,and range from microscopic foci of early stromal invasion to grossly frank tumors encircling the Os .

The tumors may be invisible or exophytic .

Cervical carcinomas are graded from 1 to 3 based on cellular differentiation and staged from 1 to 4 depending on clinical spread.

**Cervical Carcinoma, Staging**

0 Carcinoma in Situ

1 Confined to the cervix

2 Extension beyond the cervix without extension to the lower third of Vagina or Pelvic Wall

3 Extension to the pelvic wall and / or lower third of the vagina

4 Extends to adjacent organs

**Cervical Carcinoma ,Clinical Course and survival**

Many of cervical cancers are diagnosed in early stages , and the vast majority are diagnosed in the pre-invasive phase.

More advanced cases are seen in women who either have never had a Pap smear or have waited many years since the prior smear.

Laser or cone biopsy is the most effective method of managing patients with High grade SIL in cancer prevention .