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Dr.Ro,aa S.Mahdi

**THE CERVIX**

**Cervicitis**

is a very common condition that is associated with a mucopurulent discharge ,cytologic examination of the discharge reveals inflammatory cells admixed with cervical epithelial cells, and possible microorganisms.

**\**Etiology:*** It isoften due to vaginal flora, streptococci, staphylococci, and *E. coli.* Much more important are *Chlamydia trachomatis, Ureaplasma, Trichomonas vaginalis, Candida spp., Neisseria gonorrhoeae, herpes simplex II (genitalis), and HPV.* Many of these microorganisms are transmitted sexually, and so the cervicitis may represent a sexually transmitted disease. Among these pathogens,***C. trachomatis is by far the most common***sexually transmitted cervicitis***. Herpetic infections*** of the cervix are important because the infection may be transmitted to the infant during its passage through the birth canal, sometimes resulting in a serious, sometimes fatal, systemic infection.

***\*Pathologic features***

Nonspecific cervicitis may be either *acute or chronic***.** *The chronic form* *is very common* and usually referred to as *nonspecific cervicitis****.*** Chronic cervicitis consists of inflammation and epithelial regeneration. These changes may occur in both squamous and columnar mucosa. Eventually, the columnar epithelium undergoes squamous metaplasia.

**Cervical Tumors**

Despite dramatic improvements in early diagnosis and treatment, cervical carcinoma continues to be one of the major causes of cancer-related deaths in women in the developing world.

**Cervical Intraepithelial Neoplasia (CIN)**

The Pap smear, introduced 50 years ago by Papanicolaou, remains the most successful cancer screening test ever developed. *In populations that are screened regularly, cervical cancer mortality is reduced by up to 99%*. Nearly all invasive cervical squamous cell carcinomas arise from precursor epithelial changes referred to as cervical intraepithelial neoplasia (CIN). Detection of CIN by the Pap smear at an early stage permits curative treatment. *Cytological examination can detect CIN long before any abnormality can be seen grossly*. CIN begins as low-grade lesion that may progress to higher grade CIN, or it is a high-grade lesions from the outset; this depends on the location of the HPV infection in the transformation zone, the type of HPV infection (high versus low risk), and other host factors.

*On the basis of histology, precancerous changes are graded as*

*CIN I: Mild dysplasia*

*CIN II: Moderate dysplasia*

*CIN III: Severe dysplasia/carcinoma in situ*

The new **Bethesda system** divides the precancerous lesions into only two groups:

*1. Low-grade SIL* (SIL for squamous intraepithelial lesions), equivalent to CIN I

*2. High-grade SIL*. Equivalent to CIN II & III

Progression from low- to high-grade SIL ***may or may not occur***. The higher the grade of CIN the greater the likelihood of progression to invasive carcinoma, this reaches to 70% with CIN III.

***Epidemiology and Pathogenesis***

* The peak age of CIN incidence is about 30 years, whereas that of invasive carcinoma is about 45 years i.e. precancerous changes usually take many years to evolve into overt carcinomas.
* *Important risk factors for the development of CIN and invasive carcinoma are:*

*1.**Early age at first intercourse*

*2. Multiple sexual partners*

*3. Persistent infection by "high-risk" papilloma viruses*

*4. Low socio-economic status*

* All of the above favor a sexually transmitted causative agent (HPV). Indeed, *HPV can be detected by molecular techniques in nearly all precancerous and cancerous lesions*. Specifically, *high-risk HPV types including* ***16 & 18****,* account for the majority of cervical carcinomas. By contrast, condylomas, which are benign lesions, are caused by *low-risk HPV* types (i.e., 6 & 11). In these benign lesions the viral DNA does not integrate into the host genome.
* By contrast, *HPV types 16 & 18 usually integrate into the host genome with subsequent inactivation of the tumor suppressor genes p53 and RB.* The result is a transformed cell, capable of autonomous growth and susceptible to the acquisition of further mutations (cancer progression). *The recently introduced HPV vaccine is very effective in preventing HPV infections and hence cervical cancers.*
* Although many women harbor these viruses, only a few develop cancer, suggesting other pathogenetic influences play a role e.g. cigarette smoking and immunodeficiency states such as AIDS.

***Microscopic features***

***CIN & Carcinoma in situ***

* CIN begins with *CIN I***.** This lesion is characterized by koilocytotic changes mostly in the superficial layers of the epithelium**.( *Koilocytosis*** is composed of nuclear hyperchromasia and angulation with perinuclear vacuolization produced by cytopathic effect of HPV). The dysplastic epithelium is limited to the lower third of the mucosa.
* In *CIN II* the dysplasia is more severe, involving the lower two-thirds of the mucosa. The superficial layer in some cases shows the koilocytotic changes.
* *CIN III*shows dysplastic changes that affect virtually all layers of the epithelium. Surface cells and their koilocytotic changes are usually absent.
* In time, dysplastic changes become more atypical and may extend into the endocervical glands, but the alterations are confined to the epithelial layer and its glands**.** These changes constitute *carcinoma in situ*.
* The next stage is *invasive canrcinoma*.

The above progression sequences do not occur in all the cases.

*Cervical cytology and cervical colposcopy remain the basis of cervical cancer prevention.*

***Invasive Carcinoma of the Cervix***

***Clinically:*** unexpected vaginal bleeding, leukorrhea, painful coitus (dyspareunia), dysuria, and may be asymptomatic.

*The most common cervical carcinomas are* (in descending order)

*1. Squamous cell carcinomas (75%)*

*2. Adenocarcinomas and adenosquamous carcinomas (20%)*

*3. Small-cell neuroendocrine carcinomas (<5%).*

The squamous cell carcinomas are increasingly appearing in younger women, (peak incidence at about 45 years); 10 to 15 years after detection of their precursors (CIN).

Invasive carcinomas of the cervix develop in the region of the transformation zone (the squamo-columnar junction) and range from invisible microscopic foci of early stromal invasion to grossly visible exophytic ulcerating masses or deeply infiltrative cancer that encircle the os ,then it may:

\_ penetrate into the underlying stroma

\_ Extend into the parametrial soft tissues and *fix the uterus* to the pelvic structures

**\_** Spread to pelvic lymph nodes

\_ have Distant metastases, including para-aortic nodal involvement, remote organ involvement, or invasion of adjacent structures such as bladder or rectum, occur late in the course of disease

Three microscopic variants of cervical SCC squamous cell carcinoma exist, although admixtures and intermediate forms occur:

*1. Large cell nonkeratinizing*

*2. Keratinizing*

*3. Small cell;* this should be distinguished from small cell neuroendocrine carcinoma

With the exception of neuroendocrine tumors, which are uniformly aggressive, cervical carcinomas are graded from 1 to 3 based on the degree of cellular differentiation and staged from 1 to 4 depending on the extent of clinical spread.

Ideally cervical carcinomas should be diagnosed in the preinvasive phase; these appear as white areas on colposcopic examination after application of dilute acetic acid (Schiller test). More advanced cases of cervical cancer are invariably seen in women who either have never had a Pap smear or have waited many years since the prior smear. Mortality is most strongly related to the tumor stage. The 5-year survival in stage 1 is 90% but this figure drops to 10% in stage 4.

**Endocervical Polyp**

Thismay protrude, sometimes, through the exocervix. The trend is to regard these polyps as inflammatory rather than neoplastic. They are generally small, soft, and have smooth, glistening surface and subjacent cystically dilated spaces filled with mucinous secretion.