

Obstetrics & Gynecology TEAM



Cervical Intraepithelial Lesion

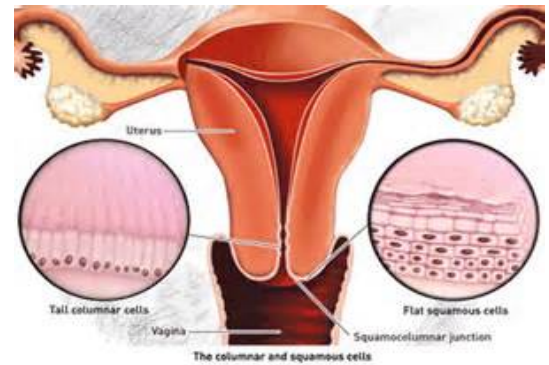
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ALL ABOUT CERVIX

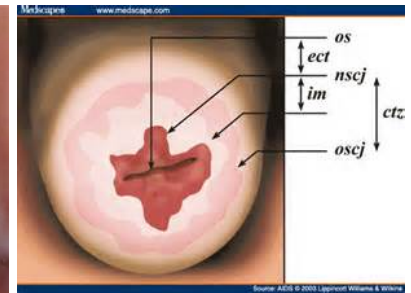
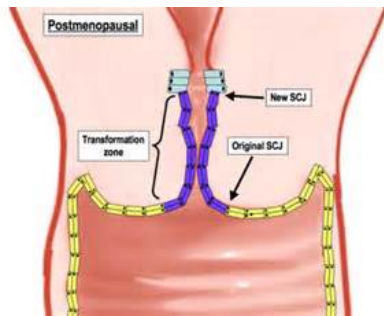
Anatomy :

- The ectocervix ..surface of the cervix that is visualized on vaginal speculum examination is covered in squamous epithelium, and the endocervix, including the cervical canal, is covered with glandular epithelium.



Transformation zone :

zone on the cervix at which squamous epithelium and columnar epithelium meet; changes location in response to a woman's hormonal status.



- SCJ is a dynamic point that change in response to
 - Puberty
 - Pregnancy
 - Menopause
 - Hormonal stimulation
- In neonate it located on the exocervix, at menarche, the production of estrogen causes the vaginal epithelium filled with glycogen.
- Lactobacilli “ vaginal normal flora “ act on glycogen to lower the PH, stimulate the subcolumnar reserve cells to undergo metaplasia.

HPV :

Human Papilloma virus – sexually transmitted virus .

- (HPV) is divided into two classes:
 - 1) oncogenic
 - 2) nononcogenic.
- Infection with oncogenic (or high-risk) HPV** usually is a necessary but not sufficient factor for the development of squamous cervical neoplasia. Therefore, only a small fraction of women infected with HPV will develop significant cervical abnormalities and cancer.
- HPV 16 has the highest carcinogenic potential** and accounts for approximately 55–60% of all cases of cervical cancer worldwide.
- HPV 18 is the next most carcinogenic genotype** and is responsible for 10–15% of cases of cervical cancer.
- Approximately 10 other genotypes are associated with the remainder of cases of cervical cancer.
- The current model of cervical carcinogenesis posits that HPV infection results in either transient or persistent infection.
- Most HPV infection is transient and poses little risk of progression.
- Only a small fraction of infections are persistent, but persistent infection at 1 year and 2 years strongly predicts subsequent risk of cervical intraepithelial neoplasia (CIN) 3 or cancer regardless of age.**
- Two low-risk types (6 and 11) cause benign disease of the HPV infection “anogenital warts and condyloma” .**

Risk factors :

- Cofactors that increase the likelihood of persistence infection include
 - Cigarette smoking and HPV infection have synergistic effects on the development of CIN and cervical cancer.
 - compromised immune system.
 - human immunodeficiency virus (HIV) infection
 - Oral contraceptives “ why ? because of estrogen “ — Long-term use of oral contraceptives has been implicated as a cofactor that increases the risk of cervical carcinoma in women who are.
 - The excess risk of cervical cancer declines after discontinuation of oral contraceptives, and by 10 years, returns to the baseline risk in nonusers
- Herpes simplex virus and chlamydia “sexually transmitted virus”
 - Infection with chlamydia, herpes simplex virus, or other sexually transmitted infections may be a surrogate marker of exposure to HPV rather than a causal factor itself .
 - Alternatively, these infections may modulate host immunity, thereby facilitating persistence of oncogenic HPV
- The risk of transmission of HPV correlates with the lifetime number of sex partners, but the prevalence of HPV infection is substantial (4 to 20 percent) even in those with one partner.
- In the United States (US), up to 50 percent of sexually active young women will have positive HPV tests within 36 months of first sexual activity, and up to 57 percent of sexually active female adolescents are infected with HPV at any one point in time
- Human papillomavirus infection is most common in teenagers and women in their early 20s, with a decrease in prevalence as women age.
- Most young women, especially those younger than 21 years, have an effective immune response that clears the infection in an average of 8 months or reduces the viral load in 85–90% of women to undetectable levels in an average of 8–24 months

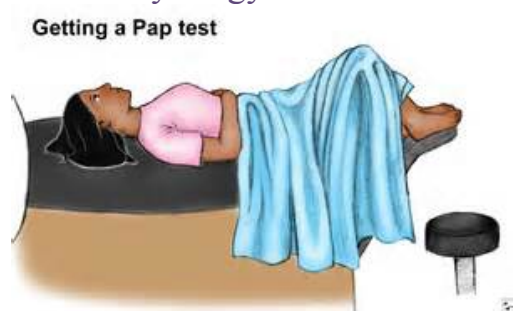
Screening :

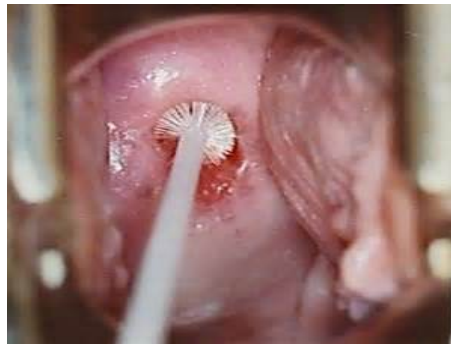
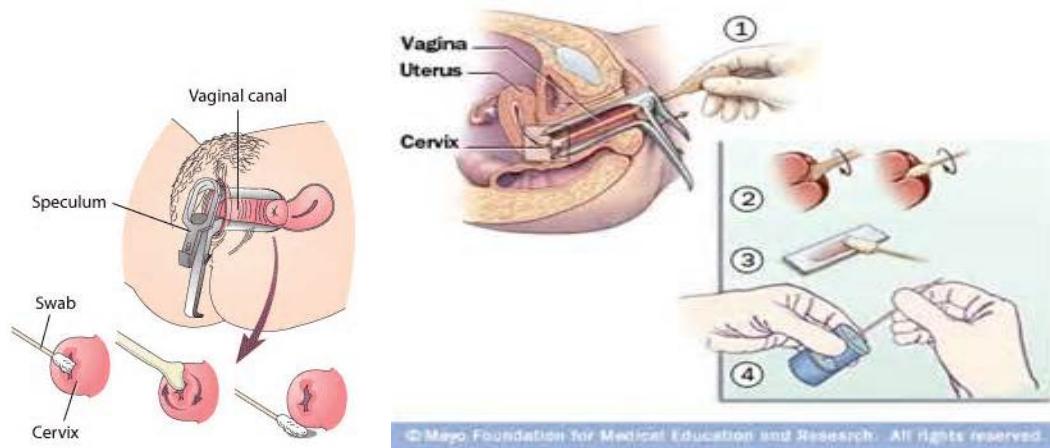
- Most cervical cancer occurs in women who were either never screened or were inadequately screened.
- Estimates suggest that 50% of the women in whom cervical cancer is diagnosed never had cervical cytology testing, and another 10% have not been screened within the 5 years before diagnosis.
- Thus, approximately 60% of diagnoses of cervical cancer are a result of inadequate screening

When to screen : “ imp as MCQ “

- Cervical cancer screening should begin at age 21 years
- 21-29yrs.... PAP every 3years.
- 30-65yrs.... PAP +HPV every 5years “preferable “
PAP every 3years.”acceptable “
- Above 65... no screening “if the patient does not have any abnormal PAP smear “ “ if she has previous event , we have to screen her till 20 years after the diagnosis “
- Vaccinated women should continue age specific screening protocol.

PAP... Cytology :



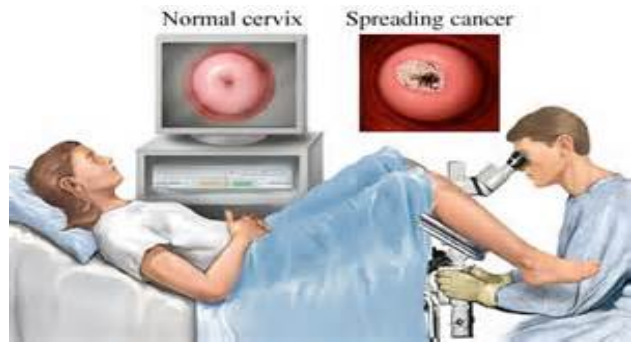


PAP... interpretation :

- Bethesda system classification
 - Squamous cell abnormalities
 - ASC “ Abnormal squamous cells”
 - ASC-US “atypical squamous cells of undetermined significance “
 - ASC-H “atypical squamous cells favoring high grade “
 - LSIL” low-grade squamous intraepithelial lesion” consistent with CIN 1
 - HSIL” high-grade squamous intraepithelial lesion” consistent with CIN2, CIN3, CIS
 - SCC “Squamous cell carcinoma”
 - Glandular cell abnormalities
 - Atypical glandular cell “ it gives you a hint that check above , if there is any abnormalities in the endometrium “
 - Atypical endocervical cell
 - Atypical endometrial call
 - No otherwise specific
 - Atypical glandular cell favor neoplastic
 - Endocervical
 - No otherwise specific.
 - AIS
 - Adenocarcinoma

Colposcopy :

- Steroscopic binocular microscope of low magnification.
- 3% acetic acid to remove adherent mucus & cellular debris.
- Green filter to accentuate the vascular changes.
- Original squamous epithelium appears gray & homogenous.
- The columnar epithelium appears red and grape like.
- TZ glands opening that are not covered by the squamous metaplasia and by the paler color of the metaplastic epithelium. “Normal colposcopic finding “



Who need colposcopy :

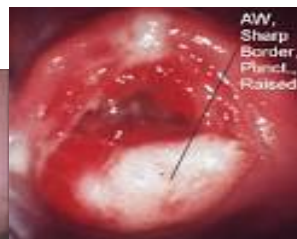
- Persistent atypical cells of undetermined significance (ASC-US) or ASC-US with positive high-risk human papillomavirus (HPV) subtypes
- ASC suggestive of high-grade lesion (ASC-H)
- Atypical glandular cells (AGC)
- Low-grade squamous intraepithelial lesions (LSIL)
- High-grade squamous intraepithelial lesion (HSIL)
- Suspicious for invasive cancer
- Malignant cells present

Abnormal finding on colposcopy :

Leucoplakia



Aceto-white area



Mosaicism



Punctation



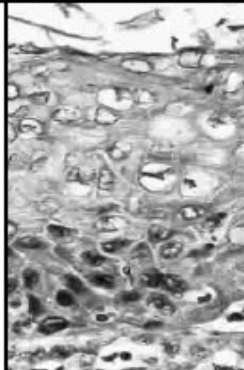
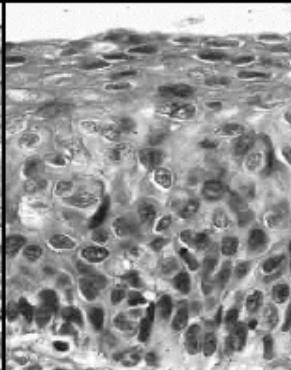
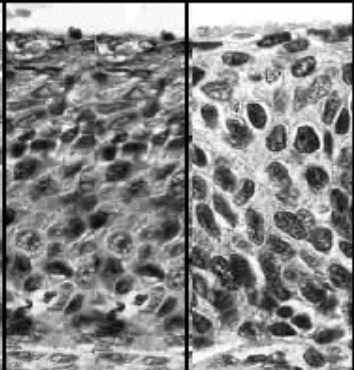
Biopsy and ECC :

- The most abnormally appearing areas are biopsied. Biopsies are relatively contraindicated in patients on anticoagulation medication, who have a known bleeding disorder, or who are pregnant.
- Endocervical curettage or sampling is performed in patients with ASC-H, HSIL, AGC, adenocarcinoma in situ (AIS), LSIL but no visible lesion, if ablative treatment is contemplated, and those with an unsatisfactory colposcopic examination

Histological definitions :

- CIN 1 is a low-grade lesion. It refers to mildly atypical cellular changes in the lower third of the epithelium. Human papillomavirus (HPV) cytopathic effect (koilocytotic atypia) is often present.
- CIN 2 is considered a high-grade lesion. It refers to moderately atypical cellular changes confined to the basal two-thirds of the epithelium (formerly called moderate dysplasia) with preservation of epithelial maturation.
- CIN 3 is a high-grade lesion. It refers to severely atypical cellular changes encompassing greater than two-thirds of the epithelial thickness and includes full-thickness lesions (previous terms were severe dysplasia or carcinoma in situ).

Biopsy... Histopathology :

LAST System ^[1]	Cytology	LSIL	HSIL	
	Histology	LSIL	p16 staining should be performed*	HSIL
Bethesda Classification System ^[2]	Cytology	LSIL	HSIL	
	Histology	CIN 1	CIN 2	CIN 3
Previous terminology		Mild dysplasia	Moderate dysplasia	Severe dysplasia Carcinoma in-situ
Histologic images				

CIN 1 , 2 , 3 = They are not crossing the basement membrane .

CIN to cancer :

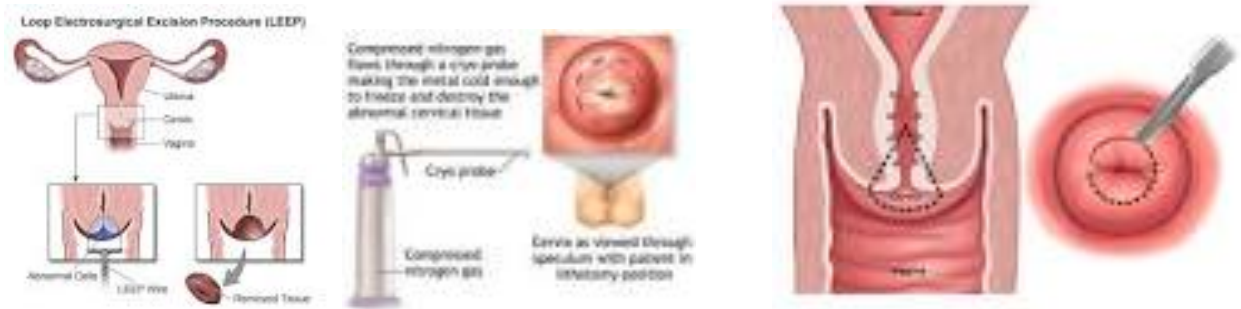
- The outcome of CIN 1 lesion depends upon the preceding cytology:
 - CIN 1 preceded by ASC-US or LSIL cytology –will be diagnosed with CIN 2,3 within 6 to 24 months of follow-up . No studies have reported invasive cervical cancer in this patient population within this follow-up period.
 - CIN 1 preceded by ASC-H or HSIL cytology, five-year risk of CIN 3+ of 15 percent
 - For CIN 2 lesions, 40 to 58 percent of lesions will regress if left untreated, while 22 percent progress to CIN 3, and 5 percent progress to invasive cancer
 - For CIN 3, the estimated spontaneous regression rate is 32 to 47 percent, with 12 to 40 percent progressing to invasive cancer if untreated

Management of CIN :

LEEP "office procedure"

cryosurgery

Cone biopsy



- Cone biopsy
 - Diagnostic and therapeutic
 - Under GA
 - **Complications**
 - **Bleeding**
 - **Infection**
 - **Cervical stenosis**
 - **Cervical incompetence**

Cone for whom :

- Diagnostic cone
 - Colposcopy is unsatisfactory
 - ECC shows High grade lesion
 - Discrepancy between PAP and biopsy
 - CIS or AIS on PAP
 - Biopsy confirm invasion

Cone as therapeutic :

- CIN 3
- Stage IAI

No PAP....NO colposcopy :

- Any patient **with grossly abnormal** cervix should have a punch **biopsy** regardless of any previous result.



Cervical cancer :

- 2008
 - 530,000 new cases ...275,000 deaths worldwide..
 - 8-6% in developing countries.
 - The tenth most common cause of death in developed countries 9 per 100,000 women
 - In the developing countries second most common type of cancer (17.8 per 100,000 women) and cause death 9.8 per 100,000 women.
- In USA
 - Over 12,000 new cases annually and 4000 cancer death
 - Third cause of death among gynecological cancer
 - With effective screening program and vaccination 75% decrease in incidence and mortality had noticed in the past 50 years in the developed countries.
- **There are two main types of cervical cancer:** squamous cell carcinoma and adenocarcinoma.
 - **Squamous cell carcinoma of the cervix is more prevalent than adenocarcinoma.**
 - Both types are found in sexually active women.
 - Infection with specific high-risk strains of human papillomavirus (HPV) is central to the pathogenesis of cervical cancer
 - Of the approximately 30 to 40 HPV genotypes that infect the mucosa of the genital tract, eight (types 16, 18, 45, 31, 33, 52, 58, and 35) are responsible for 95 percent of cervical cancers, and two (types 16 and 18) are responsible for about 70 percent of cervical cancer [5]. Two low-risk types (6 and 11) cause about 90 percent of benign anogenital warts.

How to evaluate :

- Symptoms
 - Abnormal vaginal bleeding
 - Postcoital
 - Intermenstrual
 - Postmenopausal.
 - Persistent vaginal discharge
 - Pelvic pain “ or pelvic pressure “
 - Leg swelling
 - Urinary frequency
 - Constipation and PR bleeding.
- Physical finding
 - Normal because it is a microscopic disease when it is stage 1a1
 - Weight loss?
 - Enlarged inguinal or supraclavicular LN.
 - Lower limb edema.
 - Local exam....
 - Normal cervix
 - Lesion in endocervix
 - Ulcerative, exophytic, granular or necrotic.
 - **Friable cervix ... bleeding to touch “very characteristic sign “**
- Clinical exam “ why ? because cervical cancer is clinical staging disease not surgical staging – This is MCQ trick “
 - Rectovaginal exam is essential to determine the extent of the tissues involvement
 - Evaluate the vaginal fornices
 - Evaluate the pelvic side wall

Pattern of spread : very imp

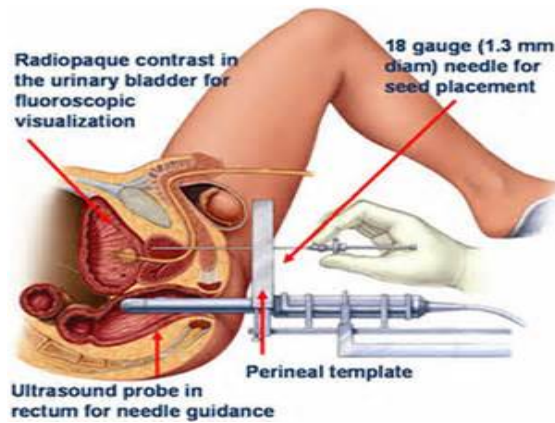
- Direct invasion of
 - Cervical stroma
 - Corpus
 - Vagina
 - Parametrium
- Lymphatic spread
 - Pelvic , inguinal & going up to supraclavicular
 - Paraaortic
- Haematogenous
 - Lung
 - Liver
 - Bone

Work up :

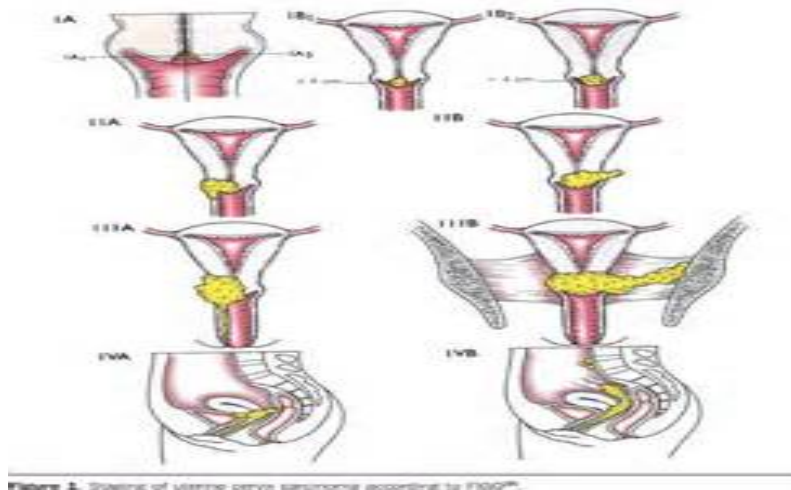
- History ... Examination
 - Ask about last PAP
 - When
 - Result
 - Any specific management
- Physical exam...
 - Biopsy for any gross lesion
 - PAP if no lesion seen
 - Sever bleeding... packing
 - LN assessment
- Blood work
 - CBC
 - Low HB in case of bleeding
 - KFT
 - High creatinin in case of ureteric obstruction
 - 30% in stage III disease.
 - 40% in stage IV disease.
 - Hypercalcemia indicate bone metastasis
 - LFT
 - Abnormal results indicate metastasis.
- Images
 - CXR
 - IVP
 - Abdominal CT
 - MRI pelvis

Cervical cancer stages :

- Clinical exam...underanesthesia?
 - Evaluation of the cervix
 - Upper and lower vagina
 - Rectovaginal exam to evaluate the parametria and pelvic side wall
- Cystoscopy
 - Bladder invasion
- Proctoscopy
 - Rectal invasion



Figo staging :



- Stage I
 - The carcinoma strictly confined to the cervix “ we know the depth of the invasion by doing cone biopsy “
 - IA microscopic disease... no gross lesion “manage by cone biopsy or hysterectomy “
 - IA1... invasion ≤ 3 mm extension ≤ 7 mm
 - IA2 ...invasion > 3 mm but not more than 5mm, extension not more than 7mm.
 - IB macroscopic disease more than stage IA or visible lesion , “manage by radical hysterectomy “ – radical means removal of parametrium .
 - IB1 visible lesion ≤ 4 cm in greatest dimension
 - IB2 visible lesion > 4 cm in greatest dimension
- Stage II
 - Extension beyond the cervix but not to the pelvic side wall or lower vagina
 - IIA...without parametrial invasion
 - IIA1 ... clinically visible lesion ≤ 4 cm in greatest dimension.
 - IIA2... clinically visible lesion > 4 cm in greatest dimension.
 - IIB... with parametrial invasion.” Only we know it by rectovaginal exam “
- Stage III
 - Tumor invade pelvic side wall & or lower third of the vagina & or causing hydronephrosis or non – functioning kidney.
 - IIIA only lower third of the vagina
 - IIIB invading pelvic side wall & or causing hydronephrosis or non – functioning kidney.
- Stage IV
 - Tumor extended beyond the true pelvis or has invade the mucosa of the rectum or the bladder.
 - IVA.. Tumor invading adjacent organ
 - IV B.. Tumor invading distant organ.

Summary : (from Kaplan)

1-The most common etiology of cervical cancer is HPV .

2- Risk Factors. These include early age of intercourse, multiple sexual partners, cigarette smoking and immunosuppression .

3- Pap smear classification :

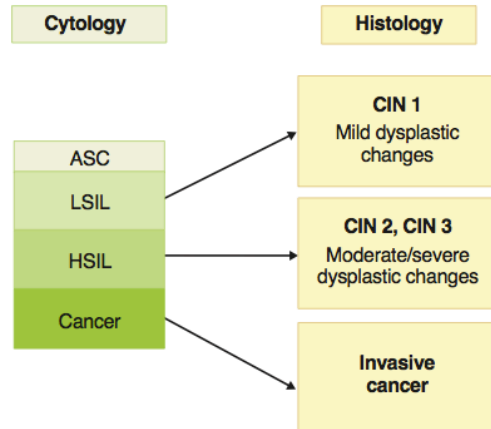


Figure II-4-4. Classification of Cervical Dysplasias

4-Invasive Cervical Cancer : is cervical neoplasia that has penetrated through the basement membrane .

5- Staging : is clinical based on **pelvic examination** .

6- Management :

- **Specific by stage:**

Stage Ia1: Total simple hysterectomy, either vaginal or abdominal

Stage Ia2: Modified radical hysterectomy

Stage IB or IIA: Either radical hysterectomy with pelvic and paraaortic lymphadenectomy (if premenopausal) and peritoneal washings or pelvic radiation (if postmenopausal). In patients who can tolerate surgery, a radical hysterectomy is preferred; however, studies have demonstrated equal cure rates with radiation or surgical treatment.

Stage IIB, III, or IV: Radiation therapy and chemotherapy for all ages.