


*“There are only two ways to live your life. One is as though nothing is a miracle. The other is as though everything is a miracle.”*



*“Today you are You, that is truer than true. There is  
no one alive who is Your than You.”*

# Cervical Cancer

- *Cervical cancer is the third most common gynecologic cancer diagnosis and cause of death among gynecologic cancers, as more than 500,000 new cases are diagnosed each year. The most common female cancer in many developing countries.*
- *In countries that do not have access to screening and prevention programs, cervical cancer remains the second most common type of cancer and cause of cancer deaths among all types of cancer in women.*
- *The incidence of invasive cervical cancer has declined steadily in the developed countries; however, it continues to rise in the under developed and developing countries.*
- *Cervical cancer has lower incidence and mortality rates than uterine corpus and ovarian cancer, as well as many other cancer sites. These rankings are similar to global estimates for other developed countries*

# *Facts*

- *Mean age: 50 years; two groups:*
  - \* *30-39 years,*
  - \* *60-69 years.*
  
- *Early diagnosis can be extremely challenging:*
  - \* *frequently asymptomatic nature of early stage disease.*
  - \* *the significant false negative rate for Pap smear.*
  - \* *the origin of some tumors from within the endocervical canal.*
  - \* *the origin of some tumors beneath the epithelium of the ectocervix.*

# Cervical Cancer

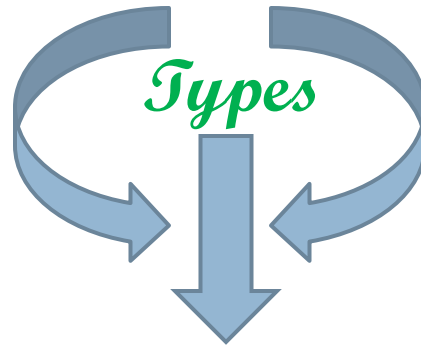
- *The key to preventing invasive cervical cancer is to detect **any cell changes early**, before they become cancerous.*
- *The most common finding is **an abnormal Papanicolaou** test result. **Regular pelvic examinations and Pap smears are the best way to do this.***
- **Vaccination**; of boys and girls before they are sexually active should significantly decrease the incidence of cervical cancer in the future.

# Cervical Cancer

- *A major mistake is to rely on a Pap test to rule out a cancer in a woman who has symptoms or findings that could be due to a cancer. No test in symptomatic women.*
- *A normal Pap test never excludes a cancer.*
- *Biopsy is the only scientific way to confirm or to rule out cancer.*

# Cervical Cancer

\* *Strong evidence now implicates human papillomaviruses (HPVs) as prime suspects.*



- *Squamous cell carcinoma as the major group (85%).*
- *Less common adenocarcinoma, small cell carcinoma, melanoma, and lymphoma.*

# Human Papilloma Virus (HPV) infection

- HPV is group of nonenveloped, double-stranded DNA viruses in Papovaviridae family
- Types of HPV that cause genital warts are different from types that cause anogenital cancers
- > 120 subtypes of HPV
  - HPV-6/11 are low malignant risk subtypes and cause 90% of genital warts
  - HPV-16/18 are high malignant risk subtypes associated with cervical cancer and anogenital cancers, usually with co-infection with HPV-6/11
- Up to 20% of patients with HPV may be infected with multiple strains
- HPV 16 can survive on dry inanimate surfaces for > 7 days



# History

- *Clinically, the first symptom is abnormal vaginal bleeding, usually postcoital.*
- *The most common laboratory finding is an abnormal Pap smear test result.*
- *± Vaginal discomfort, malodorous discharge, and dysuria.*
- *Advanced disease may present with pelvic or lower back pain,*
- *Bowel or urinary symptoms*

# Bleeding Symptom

- \* Cancers *must make new* blood vessels as they grow. These new blood vessels are *often abnormal* and *break easily*.
- \* The cancer also *outgrows* some of its blood supply, so portions of it are *deficient in oxygen*.
- \* The *atypical vessels* usually prone to bleed.

# Sexual Activity

- *Age of starting sexual activity,*
- *Multiple sexual partners,*
- *Promiscuous male partners, his occupation.*
- *Sexual partner with multiple sexual partners,*
- *High parity.*
- *History of sexually transmitted diseases.*
- *Smoking.*

- *Oral contraceptive pills.*
- *Young age at first pregnancy,*
- *History of vulvar or vaginal squamous intraepithelial neoplasia or cancer.*
- *Immunosuppression.*
- *Low socioeconomic status is associated with an increased risk of cervical cancer*

## *The four major steps in the development of cervical cancer*

- *1. Infection of the metaplastic epithelium of the transformation zone with one or more carcinogenic HPV types; Oncogenic HPV infection*
- *2. Viral persistence rather than clearance reflecting the host immune response,*
- *3. Clonal progression of persistently infected epithelium to cervical precancerous state (CIN),*
- *4. Development of carcinoma: **Invasion**; through the basement membrane*

# *Investigations / Clinical Staging*

- \* Physical examination*
- \* Examination for distant metastases*
- \* Colposcopy; biopsy*
- \* Conization*
- \* Hysteroscopy*
- \* Proctoscopy*
- \* Blood tests; CBC, CA 125, HE4, KFF*
- \* Pelvic examination*
- \* Cervical biopsy*
- \* Endocervical curettage*
- \* Endoscopy*
- \* Cystoscopy*
- \* Imaging studies*

# Physical Findings

- *Can be relatively normal.*
- *As the disease progresses, the cervix may become abnormal in appearance, .....*
- *Rectal examination may reveal an external mass or gross blood from tumor erosion.*
- *Bimanual examination findings often reveal pelvic metastasis.*
- *Leg edema suggests lymphatic/vascular obstruction from tumor.*

# *Imaging Studies*

- *Ultrasound; to assess tumor size and local extent of disease.*

- *Intravenous pyelogram (IVP)*


□ *A routine chest radiograph should be obtained to help rule out pulmonary metastasis.*

□ *CT scan of the abdomen and pelvis; assess involvement of pelvic and paraaortic lymph node involvement.*

□ *MRI - To assess tumor size and local extent of disease.*

□ *The use of positron emission tomography (PET).*

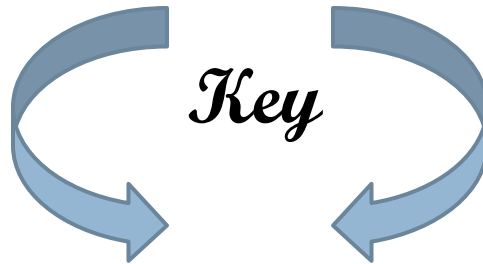


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- *Pretreatment surgical staging is the most accurate method to determine the extent of disease. ????*
  - *Pretreatment surgical staging should be individualized after a thorough nonsurgical workup.*

# *Role of Surgery for Early Cervical Cancer*

- *\* Age            \* Stage            \* Fertility            \* Co-morbidity*
- *\* Access to other modalities of treatment.*
  
- *Modified radical hysterectomy; type II hysterectomy.*
- *Fertility-sparing surgery;*
- *Primary radiation therapy (RT) with or without chemotherapy.*

## *Advantages of Surgery over Radiotherapy*



- 1. Preservation of ovarian function.*
- 2. Better preservation of sexual function.*
- 3. Accurate assessment of lymph node status.*
- 4. Avoidance of long term sequelae of Radiotherapy.*
- 5. Fertility preservation if needed.*

# *What is new in this issue?*

- *Cancer of the uterine cervix has traditionally been staged clinically, but surgical and radiologic evaluations are now part of assigning stage.*
- *In 2018, (FIGO) expanded the list of tests and procedures that may be used in assigning stage to include imaging and pathologic findings where available.*

# Stage/ I

*The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded)*

- *IA Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion  $<5$  mm*
  - *IA1 Measured stromal invasion  $<3$  mm in depth*
  - *IA2 Measured stromal invasion  $\geq 3$  mm and  $<5$  mm in depth*
- *IB Invasive carcinoma with measured deepest invasion  $\geq 5$  mm (greater than stage IA), lesion limited to the cervix uteri*
  - *IB1 Invasive carcinoma  $\geq 5$  mm depth of stromal invasion and  $<2$  cm in greatest dimension*
  - *IB2 Invasive carcinoma  $\geq 2$  cm and  $<4$  cm in greatest dimension*
  - *IB3 Invasive carcinoma  $\geq 4$  cm in greatest dimension*

# Stage/II

*The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall*

- *IIA Involvement limited to the upper two-thirds of the vagina without parametrial involvement*
  - ▣ *IIA1 Invasive carcinoma <4 cm in greatest dimension*
  - ▣ *IIA2 Invasive carcinoma ≥4 cm in greatest dimension*
- *IIB With parametrial involvement but not up to the pelvic wall*

# Stage/III

*The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes*

- *IIIA Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall*
- *IIIB Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)*
- *IIIC Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)*
  - ▣ *IIIC1 Pelvic lymph node metastasis only*
  - ▣ *IIIC2 Paraaortic lymph node metastasis*

# Stage/IV

*The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV*


- *IVA Spread of the growth to adjacent organs*
- *IVB Spread to distant organs*



# *Treatment/ Principles*

- *The treatment of cervical cancer varies with the stage of the disease.*
- *For early invasive cancer, surgery is the treatment of choice.*
- *In more advanced cases, radiation combined with chemotherapy is the current standard of care.*
- *In patients with disseminated disease, chemotherapy or radiation provides symptom palliation.*
- *Treatment of these premalignant changes is usually simple and almost 100% effective.*

# Treatment/IA

- *Stage IA: surgery; 1a1: total hysterectomy, 1a2: modified radical hysterectomy, pelvic lymphadenectomy.*
- *Bilateral Ovarian Translocation.*
- *Pelvic radiation therapy is now a category 1.....*   
*recommendation for women with stage IA disease and negative lymph nodes after surgery who have high-risk factors, including large primary tumor, deep stromal invasion and/or lymphovascular space invasion.*
- *Conization versus trachelectomy.*

# *Primary therapy/ Radical hysterectomy*

- *The standard treatment for stage IA2 and most IB1 cervical cancers is a modified radical hysterectomy.*
- *Pelvic lymphadenectomy is performed at the time of radical hysterectomy; paraaortic lymphadenectomy is performed if the pelvic nodes are suspicious for metastatic disease.*

# Stage IB111 or 11A

- \* *Radical hysterectomy with bilateral pelvic lymphadenectomy. Bilateral Ovarian Translocation.*
- \* *Combined external beam radiation with brachytherapy*
- \* *Radical trachelectomy (cervicectomy) with pelvic lymph node dissection is appropriate for fertility preservation in women with stage 1A2 disease, and those with stage 1B1 disease whose lesions are less than 2 cm.*

# Stage IB or IIA

*A randomized trial showed that patients with parametrial involvement, positive pelvic nodes, or positive surgical margins benefit from a postoperative combination of cisplatin-containing chemotherapy and pelvic radiation.*

# Stage IIB-IVA

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*For locally advanced cervical carcinoma (stages IIB, III, and IVA), dramatic improvement in survival with the combined use of **chemotherapy** and **radiation**.*

# *Stage IVB and recurrent cancer*

- \* These patients are treated with combined chemotherapy.*
- \* Palliative radiation is often used on an individualized basis to control bleeding, pelvic pain, or urinary or partial large bowel obstructions from pelvic disease.*

# Complications of Surgery

- \* *The most common complication of radical hysterectomy is urinary dysfunction as a result of partial denervation of the detrusor muscle.*
- \* *The most serious complication of radical hysterectomy is ureterovaginal fistula or stricture.*
- \* *Other complications include foreshortened vagina,, hemorrhage, infection, bowel obstruction, fibrosis of the intestine or rectosigmoid colon, bladder and rectovaginal fistulas.*



# Prognosis

- *Most early cancers are cured; most advanced cancers are not.*
- *If a cancer was removed surgically then it cannot come back.*
- *If it recurs that means that a cancer cell had already spread by the time the cancer was removed, and it took a couple of years to grow large enough to be detected.*
- *If a cervical cancer is destined to recur, about 85% will recur within the first two years after treatment.*
- *If there has been no recurrence by five years, then the cancer is unlikely to recur and is considered cured.*

# *Five Year Survival*

<i>Stage I</i>	<i>90%</i>
<i>Stage II</i>	<i>75%</i>
<i>Stage III</i>	<i>50%</i>
<i>Stage IV</i>	<i>25%</i>

# *Take home messages*

- *Cigarette smoking is a risk for the development of cervical cancer.*
- *Vaginal bleeding after menopause is never normal.*
- *Any abnormality found on a Pap smear mandates further evaluation. Not necessary to be cancer.*
- *As an abnormal Pap test is not a diagnosis. It is only an abnormal screening test that must be evaluated*
- *A normal Pap test never excludes a cancer. Cancer can only be excluded by the proper biopsies.*

# Key Points

- *Radical hysterectomy with lymph node dissection is the classical option for treatment of early cervical cancer, up to stage IA1.*
- *Radiation may be used for every treatable stage of cervical cancer.*
- *Radical trachelectomy is increasing popular fertility preserving surgery for stage IA2 or IB1.*

*Imaging and pathology can be used, where available, to supplement clinical findings with respect to tumor size and extent, in all stages.*

*The involvement of vascular/ lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.*


*Δ Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to Stage TTN.*

*The type of imaging modality or pathology technique used should always be documented.*

*When in doubt, the lower staging should be assigned.*



*“Yesterday is history, tomorrow is a mystery, today is a gift of God, which is why we call it the present.”*



*“A person needs just three things to be truly happy in this world: someone to love, something to do, and something to hope for.”*