



HEALTHY CARIBBEAN COALITION

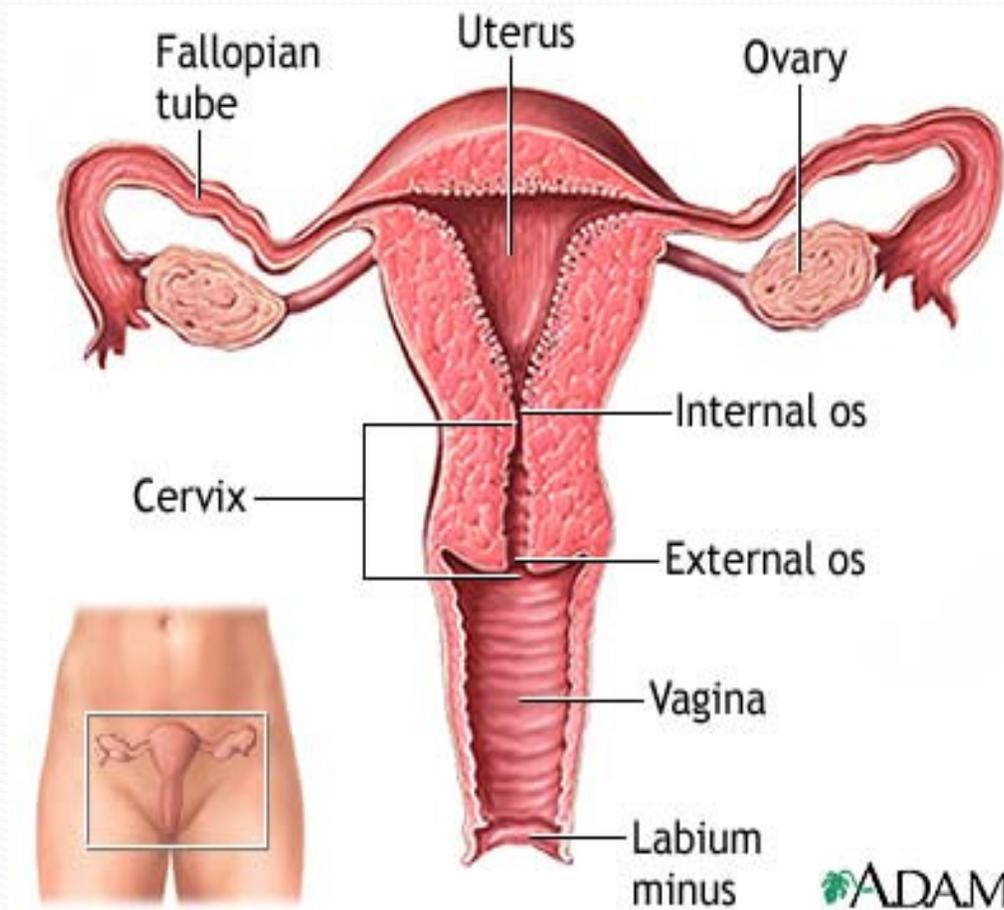
"a civil society alliance for combating chronic diseases"

HCC CERVICAL CANCER ADVOCACY CAPACITY BUILDING WORKSHOP

CANCER OF THE CERVIX TREATMENT

Dr. Homer Bloomfield
Cancer Society of the Bahamas

Pelvic Anatomy (Female)



Cancer of the Cervix

“ IS A SEXUALLY TRANSMITTED DISEASE ”

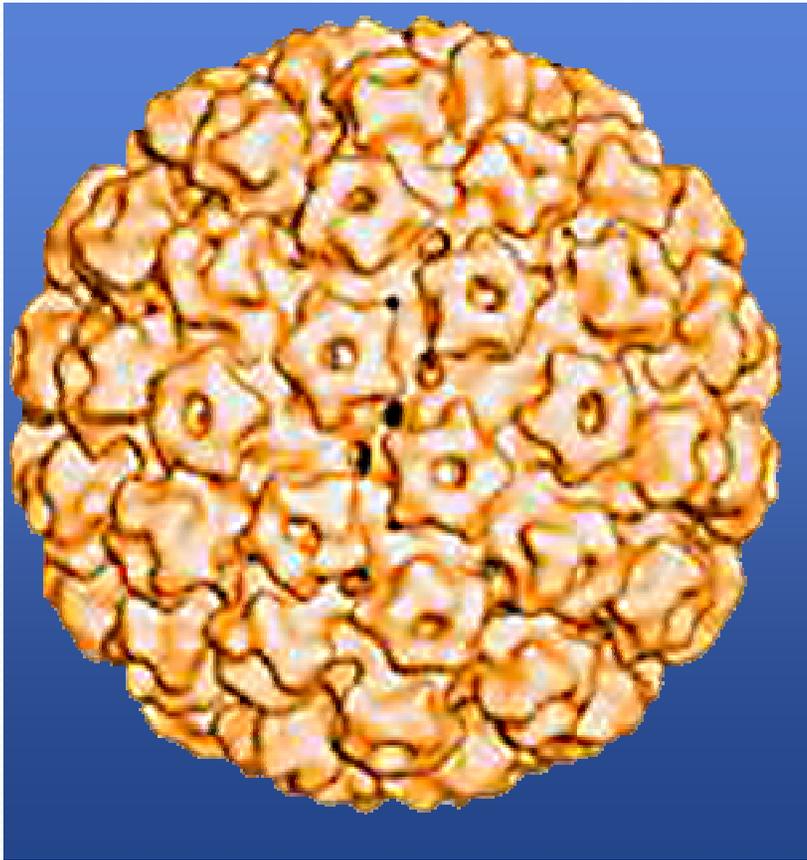
caused by the HPV virus – 16, 18, 31, 33, 35, 45, etc.

“ IS A PREVENTABLE DISEASE ”.

The American Cancer Society estimates that in 2008, about 11,070 women in the United States will be diagnosed with invasive cervical cancer, and about 3,870 US women will die from this disease.^{[19](#)}

Human Papilloma Virus

Nonenveloped double-stranded DNA virus¹



- **>100 types identified²**
- **~30–40 anogenital^{2,3}**
 - **~15–20 Oncogenic/High risk,^{2,3}**
 - **HPV16 and HPV18 types account for the majority of worldwide cervical cancers.⁴**
 - **Nononcogenic/Low risk types**
 - **HPV6 and 11 are most often associated with external anogenital warts.³**

1. Howley PM, Lowy DR. In: Knipe DM, Howley PM, eds. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229.

2. Schiffman M, Castle PE. *Arch Pathol Lab Med.* 2003;127:930–934. 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis.* 2002;35(suppl 2):S210–S224. 4. Muñoz N, Bosch FX, Castellsagué X, et al. *Int J Cancer.* 2004;111:278–285.

Reprinted from *J Virol.* 1994;68:4503–4505 with permission from the American Society for Microbiology Journals

Department.

HPV Infections

- *The commonest sexually transmitted viral infection.*
- *Infection occurs most commonly at age 15 -29 years.*
- *About 130 strains of the HPV virus have been identified.*

Certain strains are implicated in cancers ;

- *HPV can lead to cancers of the cervix, vulva, vagina, and anus in women.*
- *In men, it can lead to cancers of the anus and penis.*

Human Papillomavirus (HPV)

- *Strong association of CIN and Cervical cancer with HPV infection of the cervix.*
- *HPV Types - **16** (50%) & **18** (24%)*
 - *others **31, 33, 35, 39, 42, 45, 51, 52, 56, 58.***



Cancer of the Cervix - Facts

- *Most women presenting with cancer of the cervix have never had a PAP Smear.*
- *Many women presenting with cancer of the cervix have not had a PAP Smear in > 5yrs.*

Cancer of the Cervix

- *Worldwide, it continues to be the number two cancer affecting women, with approximately 500,000 cases occurring annually.*
- *Accounts for ~ 250,000 deaths per year/worldwide.*
 - *Most deaths occur in 'third world countries'.*
- *Bimodal age distribution with peaks in the late 30s and in the early 60s.*

Cancer of the Cervix

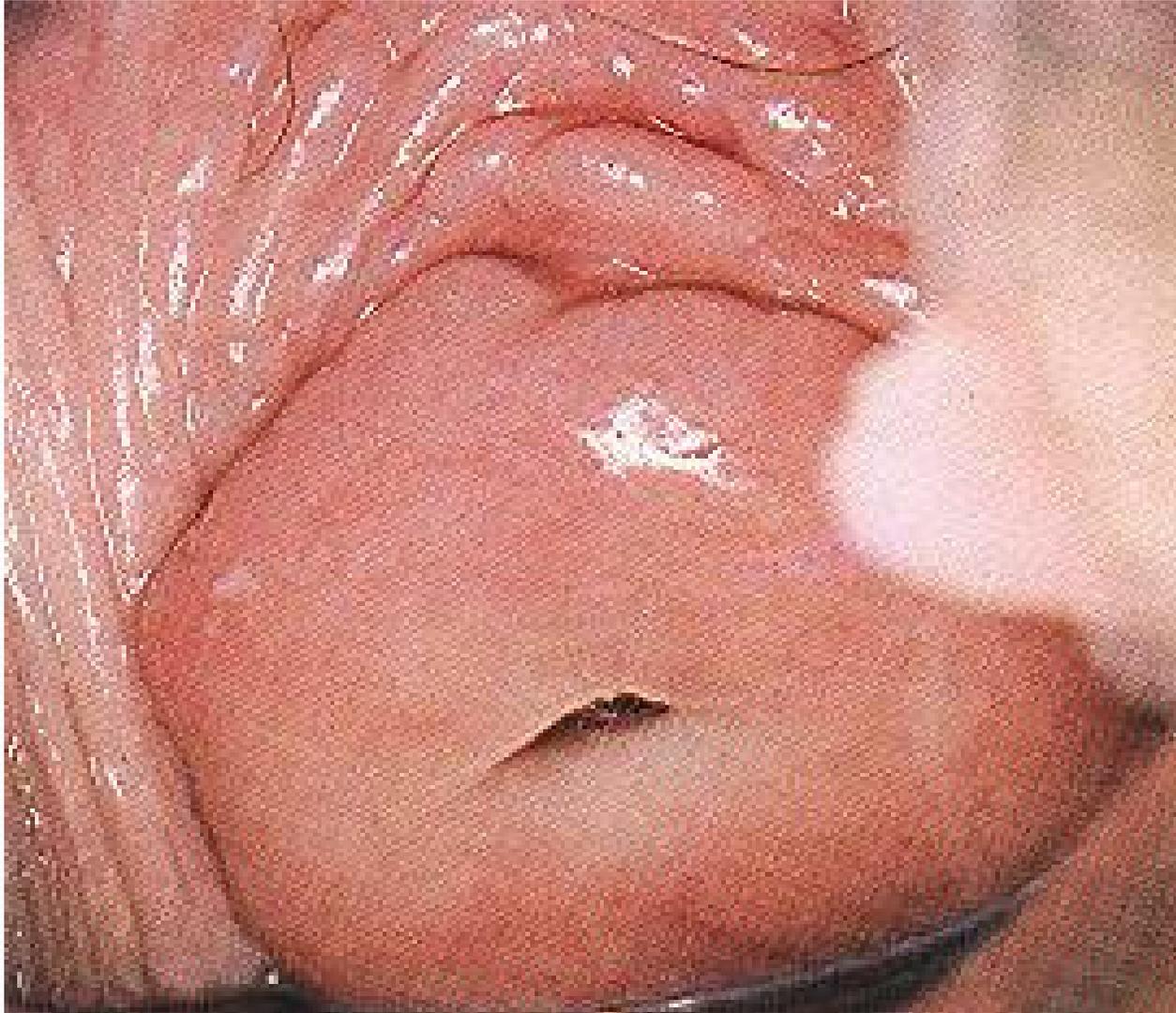
- *Death rates are higher for women older than 55 years, than among those less than 55 years.*
- *Invasive cancer develops about 10 years after failure to detect and treat early, non-invasive lesions.*
- *Early disease is often*

Asymptomatic.

Cervical cancer - Types

- **Squamous cell carcinomas**
 - Cancer of the flat epithelial cell
 - 80 – 90%
- **Adenocarcinomas**
 - Cancer arising from glandular epithelium
 - 10 – 20%
- **Mixed carcinomas**
 - Features both types
- **Rare types - small cell, neuroendocrine, glassy cell, villoglandular adenocarcinoma.**

Healthy cervix



Abnormal cervix - inflamed





Diagnosis

Screening

- Cervical Cytology (PAP Smear)
 - Cells are removed from the cervix and examined under the microscope.
 - Thin Prep – liquid base test.
 - HPV DNA analysis.

Diagnosis

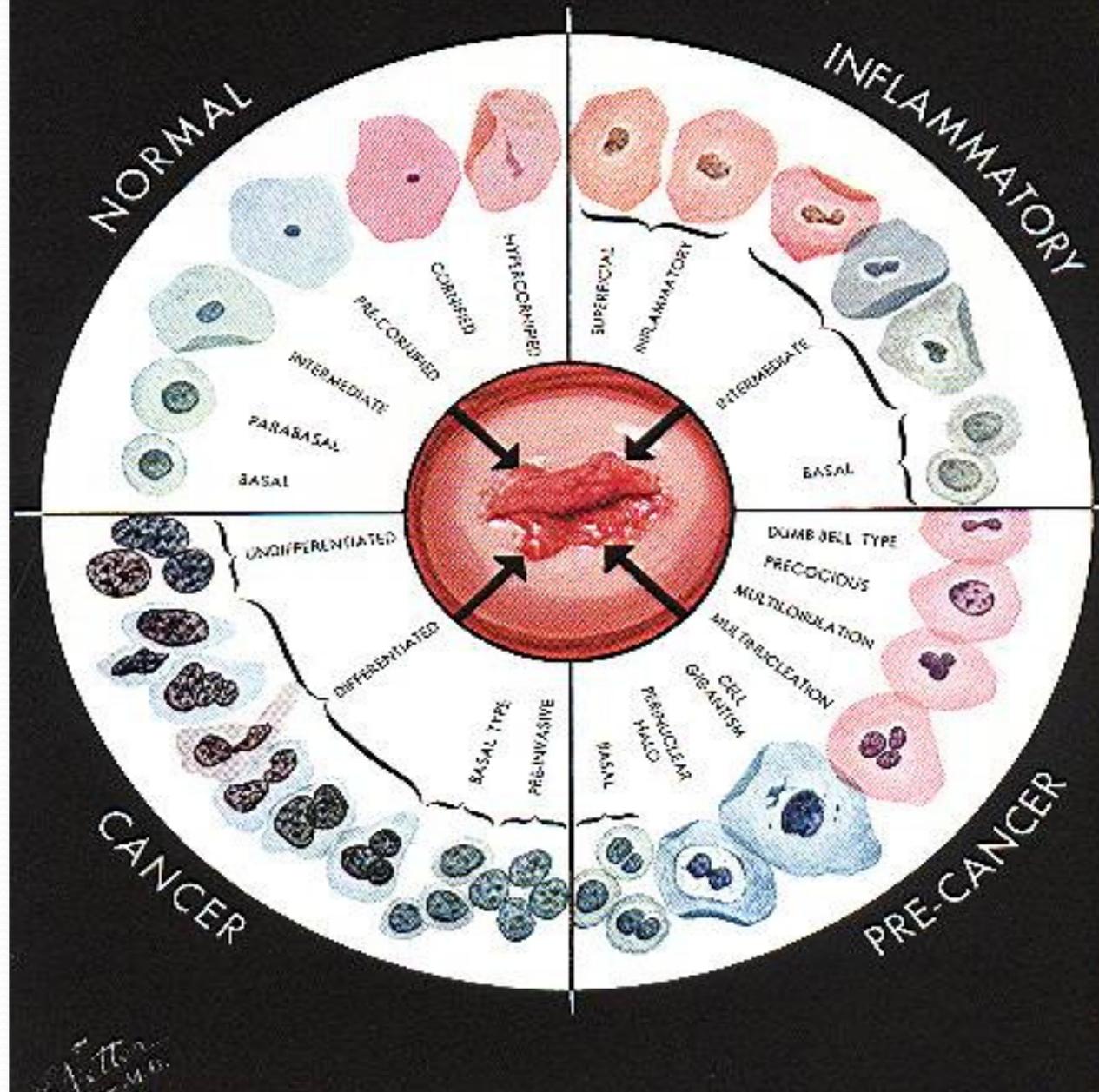
Symptoms/Signs

- Vaginal Bleeding (intermenstrual or postcoital)
- Vaginal discharge (foul-smelling/ blood-stained)
- Pelvic pain, backache
- Pain during intercourse (postcoital) etc.

CERVICAL CELL PATHOLOGY IN SQUAMOUS TISSUE

GRADES AND CELL TYPES

- *PAP Smear*
- *Cells from the cervix.*
- *Squamo-columnar junction.*



Speculum Examination

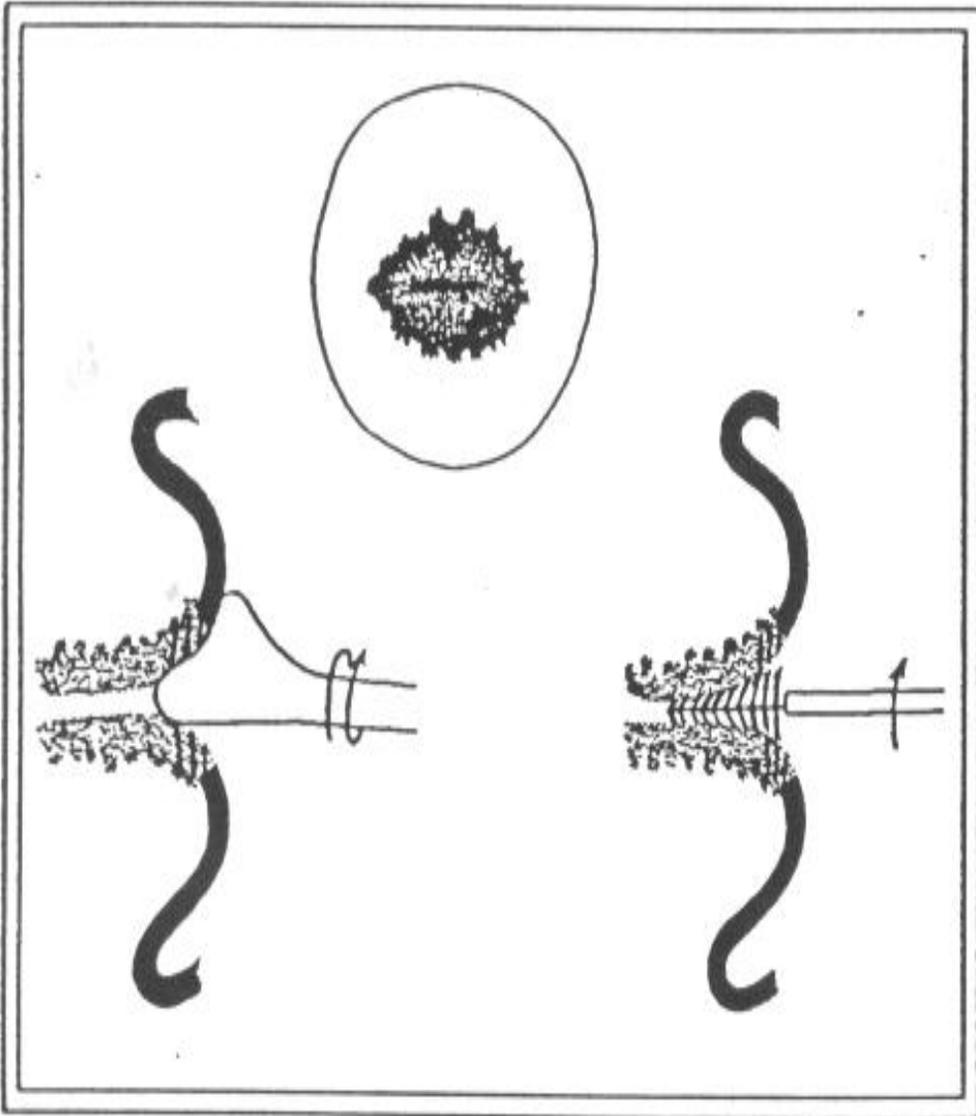


Fig. 9.2 Examination with the **duckbill speculum**, which is easily manipulated by one hand

Visualize the Cervix



PAP Smear Preparation



VISUALIZE CERVIX

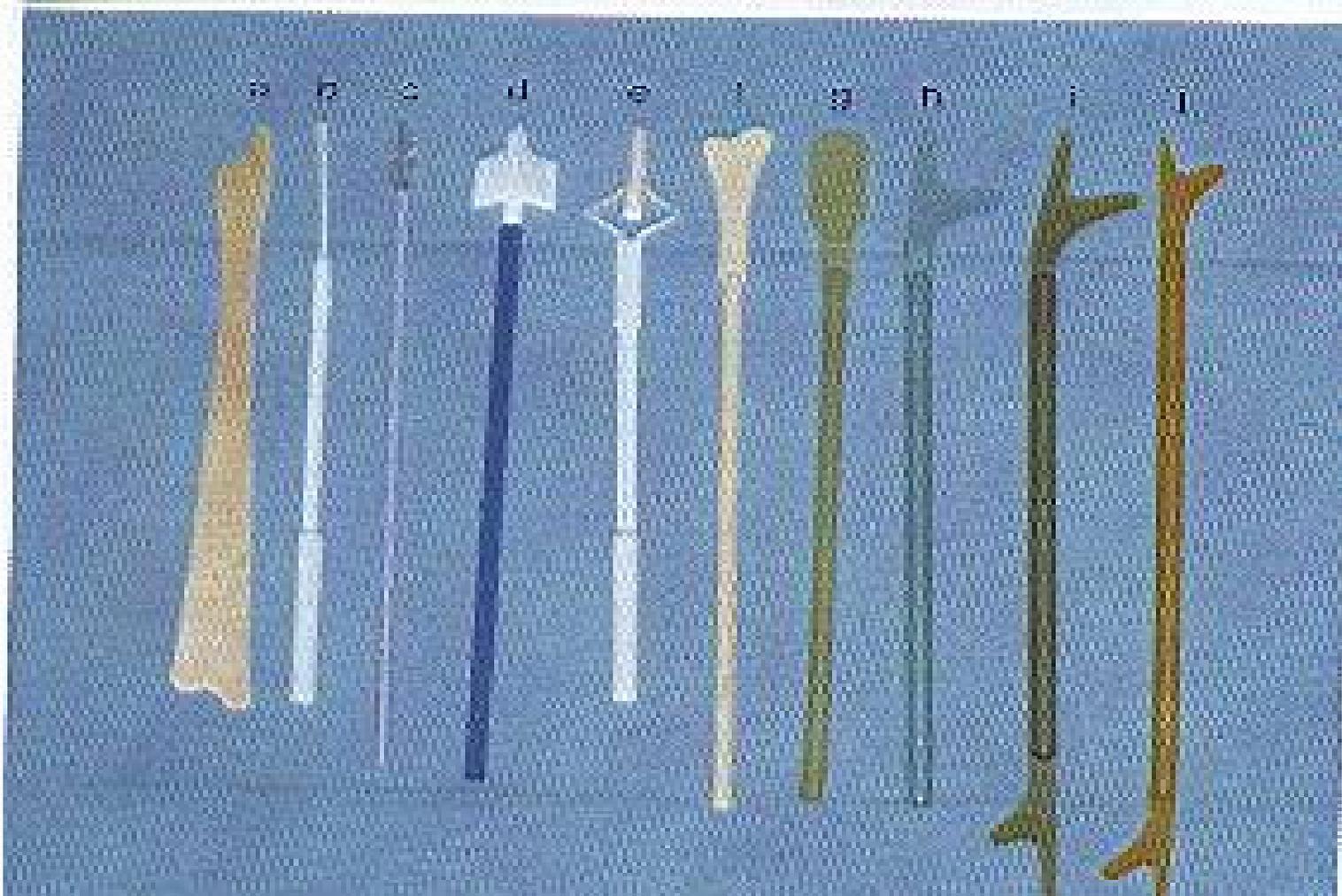
Refer to *Adequate "Pap" Smears*, FIGURE 1

- lubricate speculum with warm water
- rinse talcum from outer surface of gloves
- do not use lubricant gel

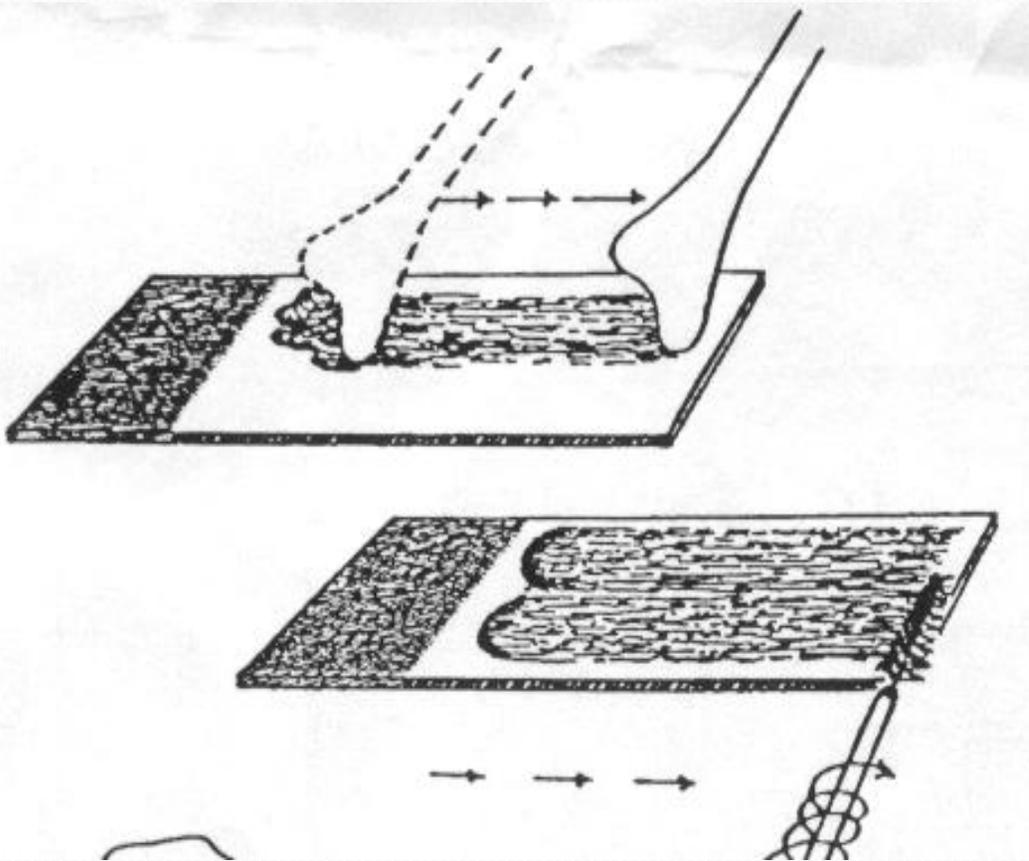
Assess position of transformation zone.

Ensure zone will be sampled with appropriate device.

Spatulae and brushes



PAP Smear Preparation



Apply Sample

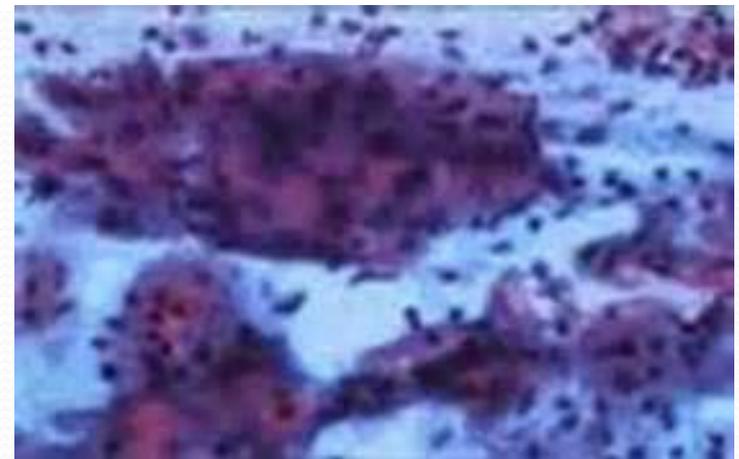
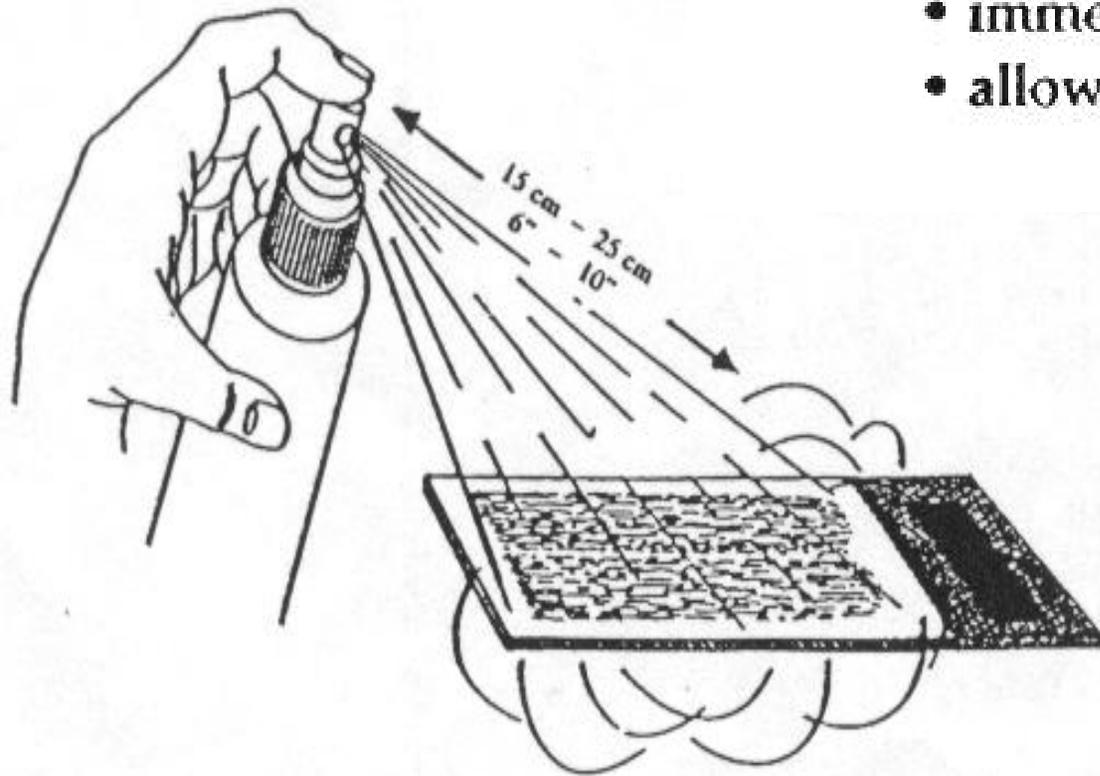
Use ONE SLIDE. Apply each sample on one half of slide as shown-keep separate

- 1. Spatula-spread in a single uniform motion**
- 2. Brush-sample will dry quickly**
 - roll on in one motion

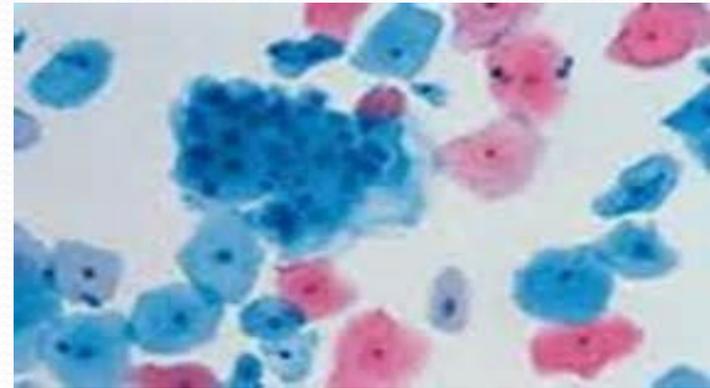
PAP Smear Preparation

FIX SAMPLE

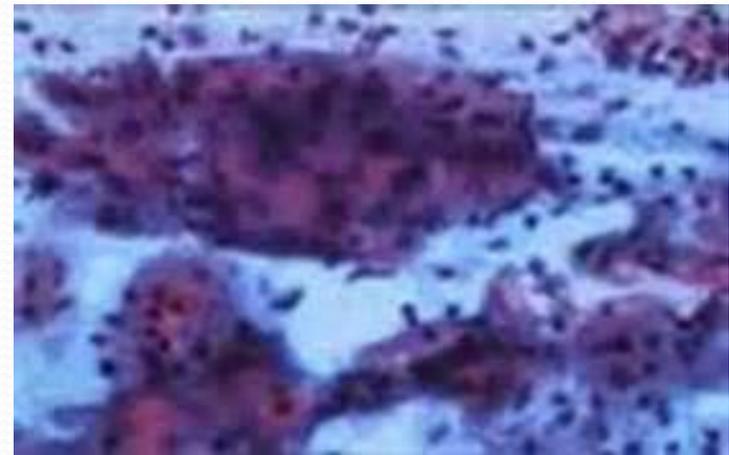
- immediately
- allow sample to dry before closing mailer



Thin Prep – Liquid Base



Thin Prep



Conventional PAP

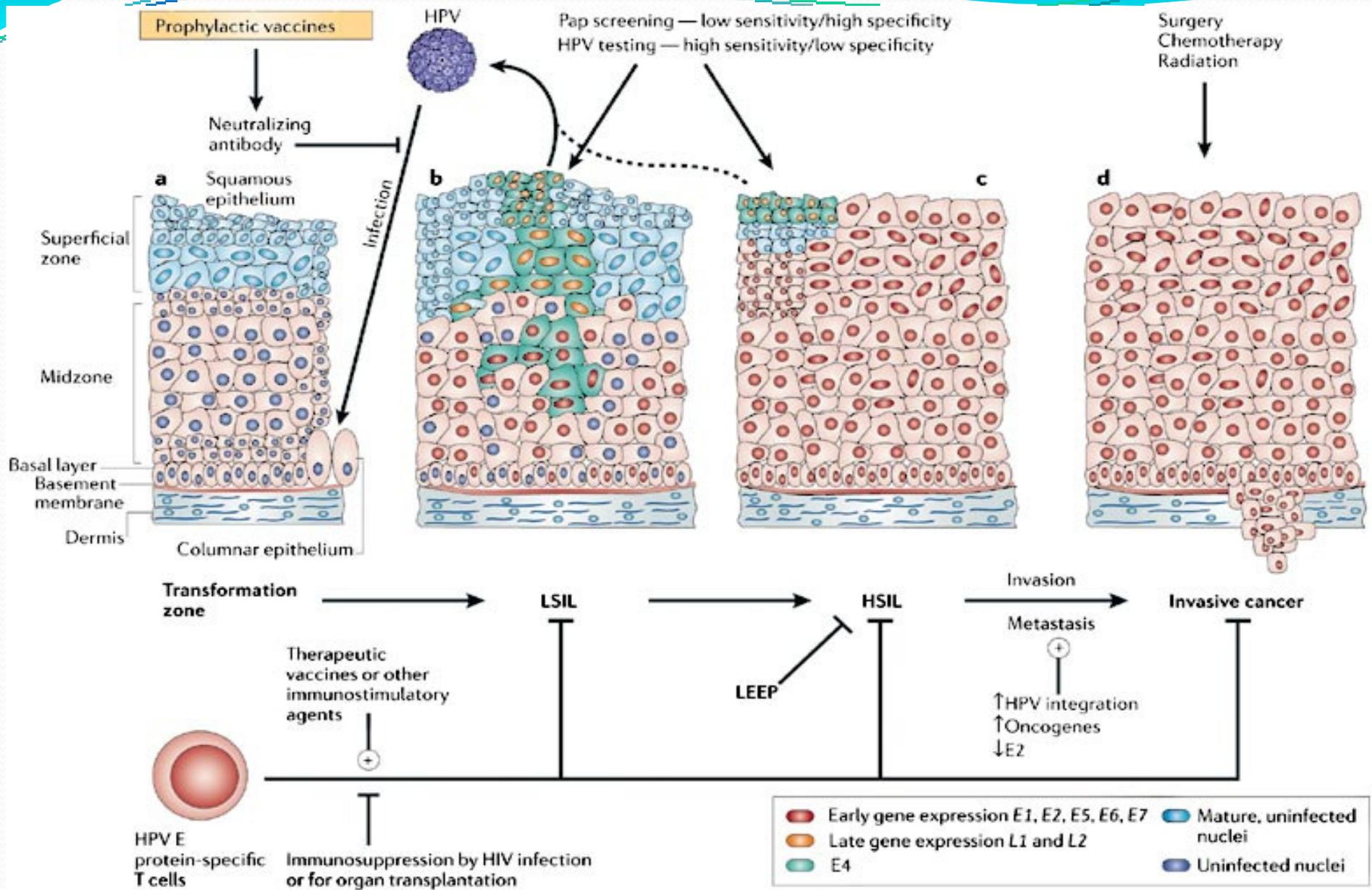
PAP Reports

- *Normal.*
- *Abnormal – inflammatory changes.*
- *Abnormal – Dysplasia*
 - *CIN 1*
 - *CIN 11*
 - *CIN 111*
- *Suspicious for Cancer – In situ*
 - *Invasive*

**** CIN - Cervical intraepithelial neoplasia**

PAP Reports

- ***Normal.***
- ***Abnormal – inflammatory changes.***
- ***ASCUS - Atypical Sq Cells of undetermined significance***
- ***LSIL – Low grade Sq intraepithelial lesion***
- ***HSIL – High grade Sq intraepithelial lesion.***
- ***ASCH – Atypical Sq Cells that cannot exclude HSIL***



Treatment of CIN

- *Most effective treatment is excision of precursor lesions*
- *Ways to Remove Lesions*
 - *Cryocautery- freezing, thawing, & refreezing lesion*
 - *Colposcopic Laser Therapy- more accurate, capable of removing low and high grade lesions*
 - *LEEP Biopsy- performed on low and high grade lesion*
- *Always schedule follow-up Pap Smears to assure lesions have not returned*

Diagnosis / CONFIRMATION

- **Cervical biopsy (punch)** – lesion visible.
- **Colposcopic – directed biopsy** – microscopically diagnosed.
- **Endocervical Curettage** – lesions in the endocervical canal.
- **Diagnostic Cone Biopsy** – microinvasive disease.

Diagnosis / CONFIRMATION

- **Comprehensive physical examination**
 - Cervical and vaginal inspection
 - Rectovaginal examination
 - Palpation of the liver and lymph nodes
(inguinal and supraclavicular)

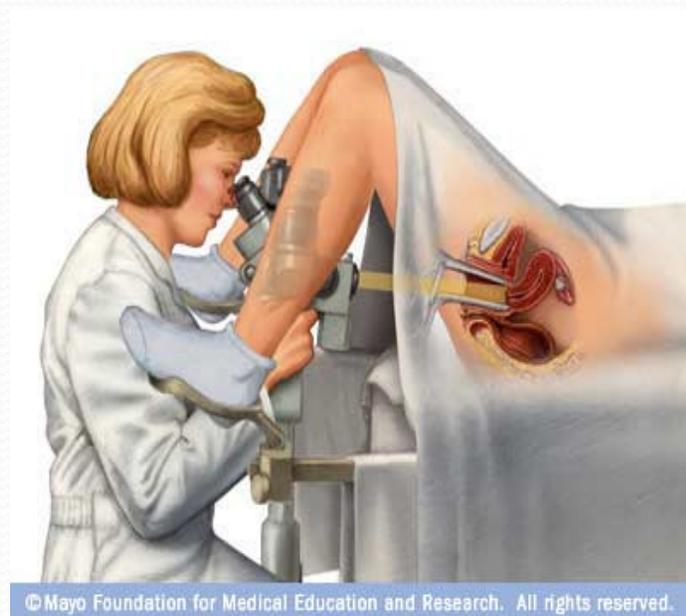
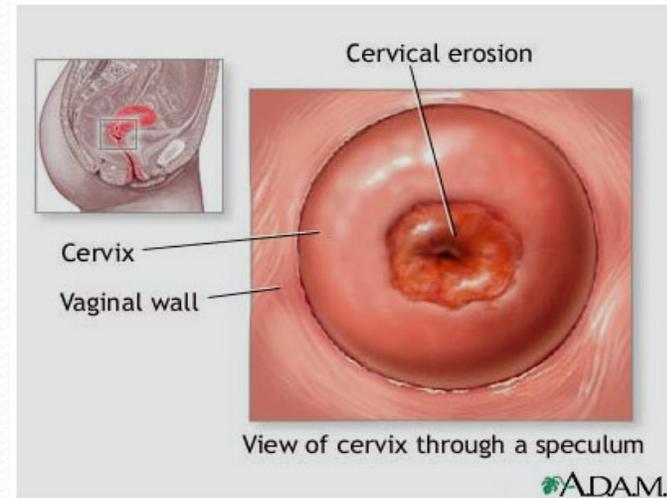
Diagnosis / CONFIRMATION

- **Laboratory and Imaging Tests**
 - CT, MRI, and ? Lymphangiography.
 - Intravenous pyelogram/ cystoscopy/USS.
 - Renal / Liver function tests.
 - Barium enema.

Colposcopy

Colposcope:

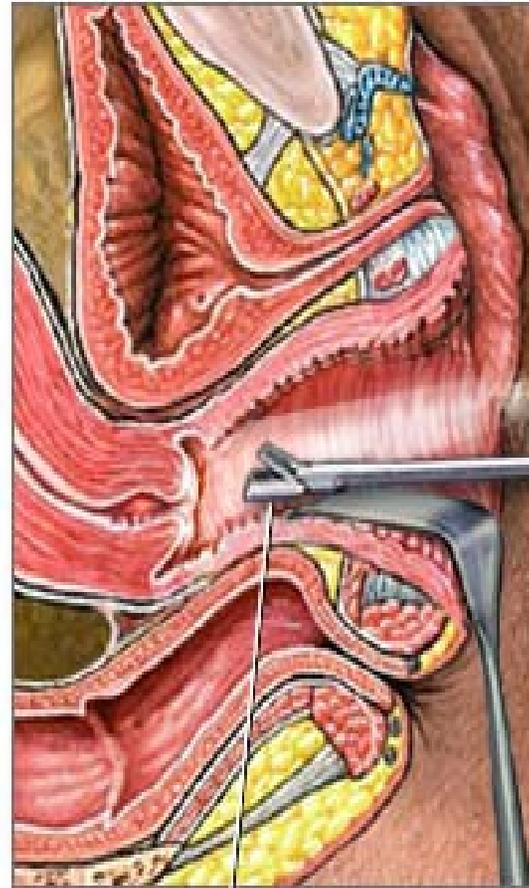
- *A stereomicroscope that enables investigators to examine areas of dysplasia and select best sites to biopsy*
- *device has green filter that helps identify presence of blood vessels (an ominous sign)*
- *Before colposcopy, cervix coated with acetic acid which enhances presence of dysplasia*
- *Key to colposcopy is complete visualization of transformation zone*



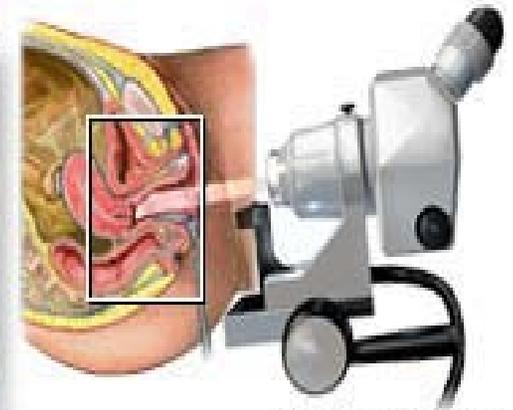
Colposcopic Biopsy



Figure 7. Cervigram photograph after the application of vinegar. Immature transformation zone. SCJ completely visible. Low-grade lesions visible as acetowhite epithelium attached to the squamo-columnar junction on the anterior ectocervix.



Biopsy forceps are used to sample the cervix



Colposcope illuminates the cervix for biopsy

CIN as Seen in Colposcopy

Colposcopy findings confirmed by histology¹

- CIN 1: Mild dysplasia; includes condyloma (anogenital warts)²
- CIN 2: Moderate dysplasia²
- CIN 3: Severe dysplasia; cancer in situ (CIS); FIGO Stage 0^{2,3}

CIN 1



Photo courtesy of Dr. J. Monsonego

CIN 2



Photo courtesy of Dr. J. Monsonego

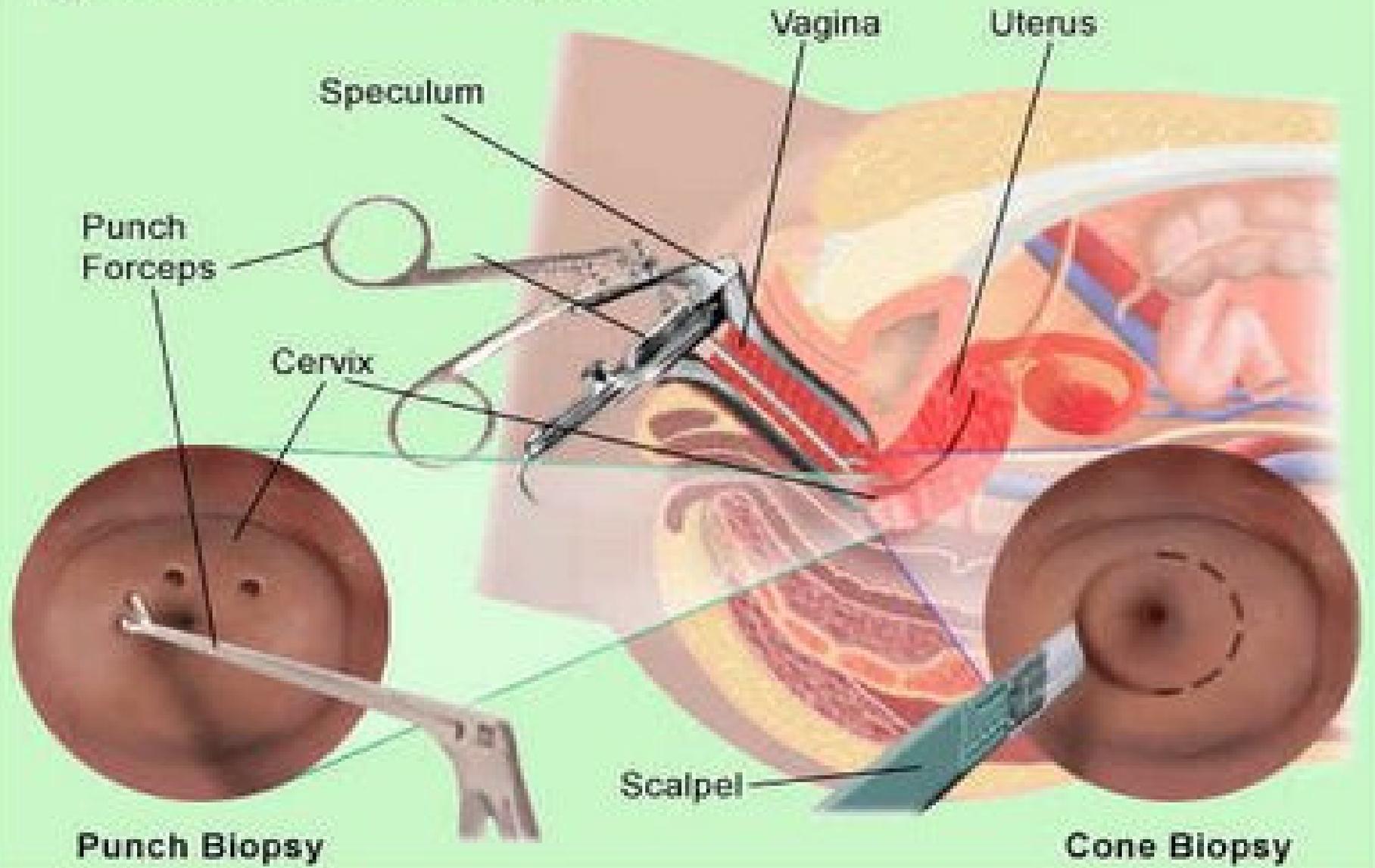
CIN 3



From IARC, 2003.⁴

1. Wright TC Jr, Cox JT, Massad LS, et al, for the ASCCP-Sponsored Consensus Congress. *JAMA*. 2002;287:2120-2129. 2. Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. Washington, DC: American Society for Microbiology Press; 2002:557-596. 3. Canadian Cancer Society. Cervical Cancer: What you need to know. Available at: http://www.cancer.ca/vgn/images/portal/cit_86751114/63/40/151140772cw_library_wyntk_cervical_en.pdf. Accessed March 13, 2006. 4. Reprinted with permission from Sellors JW, Sankaranarayanan R, eds. *Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual*. Lyon, France: International Agency for Research on Cancer; 2003.

Types of Cervical Biopsies



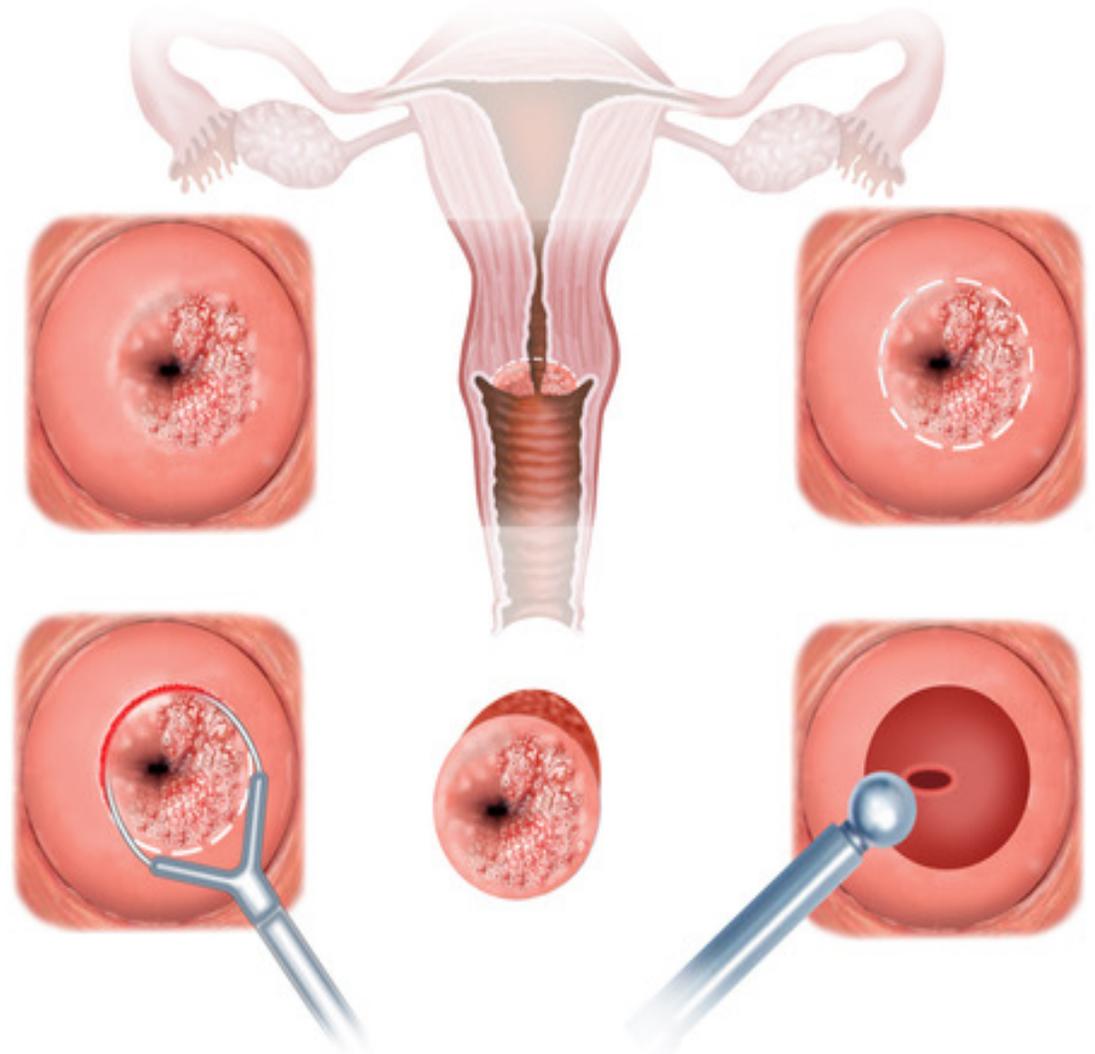
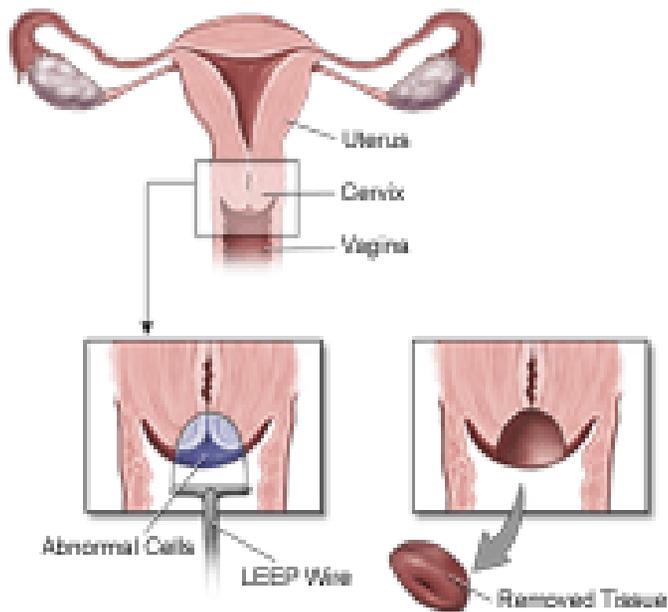
Cone Biopsy

- *Cone biopsy is a minor surgical procedure to further investigate the transformation zone*
- *Performed using a scalpel, laser, or LEEP*
- *Reasons for Performing Cone Biopsy*
 - *Investigator is unable to visualize the entire transformation zone*
 - *Endocervical curettage shows dysplastic changes*
 - *Results of Pap Smear are remarkably different than results from colposcopy*



“LEEP” Excision

Loop Electrosurgical Excision Procedure (LEEP)



Prognostic Indicators for Squamous cell carcinoma

1. Stage of disease (most important)
2. Lymph node involvement
3. Tumor size
4. Depth of stromal invasion
5. Invasion of lymphovascular space.

Staging

- **FIGO System** (International Federation of Gynaecology and Obstetrics)
- **Stage O** Carcinoma in situ.
- **Stage I** Invaded the cervix, but has not spread.
- **Stage II** Has spread to nearby areas, but not leaving the pelvic area.
- **Stage III** Has spread to the lower part of the vagina.
- **Stage IV** Cancer has spread to nearby organs; metastasis.

Survival Rates/Staging

- ***FIGO System*** (International Federation of Gynaecology and Obstetrics)
- Stage I > 90%.
- Stage II 75%.
- Stage III 40%.
- Stage IV < 15%.

FIGO staging of cervical carcinomas

- Stage I

Stage I is carcinoma strictly confined to the cervix; extension to the uterine corpus should be disregarded.

Stage IA: Invasive cancer identified only microscopically. All gross lesions even with superficial invasion are stage Ib cancers. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm* and no wider than 7 mm.

Stage IA₁: Measured invasion of the stroma no greater than 3 mm in depth and no wider than 7 mm diameter.

Stage IA₂: Measured invasion of stroma greater than 3 mm but no greater than 5 mm in depth and no wider than 7 mm in diameter.

Stage IB: Clinical lesions confined to the cervix or preclinical lesions greater than stage IA.

Stage IB₁: Clinical lesions no greater than 4 cm in size. Stage IB₂: Clinical lesions greater than 4 cm in size.

Stage II

Stage II is carcinoma that extends beyond the cervix but has not extended onto the pelvic wall. The carcinoma involves the vagina, but not as far as the lower third.

Stage IIA: No obvious parametrial involvement. Involvement of up to the upper two-thirds of the vagina.

Stage IIB: Obvious parametrial involvement, but not onto the pelvic sidewall.

Stage III

Stage III is carcinoma that has extended onto the pelvic sidewall. On rectal examination, there is no cancer free space between the tumor and the pelvic sidewall. The tumor involves the lower third of the vagina. All cases with a hydronephrosis or nonfunctioning kidney should be included, unless they are known to be due to other causes.

Stage IIIA: No extension onto the pelvic sidewall but involvement of the lower third of the vagina.

Stage IIIB: Extension onto the pelvic sidewall or hydronephrosis or nonfunctioning kidney.

Stage IV

Stage IV is carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.

Stage IVA: Spread of the tumor onto adjacent pelvic organs.

Stage IVB: Spread to distant organs.

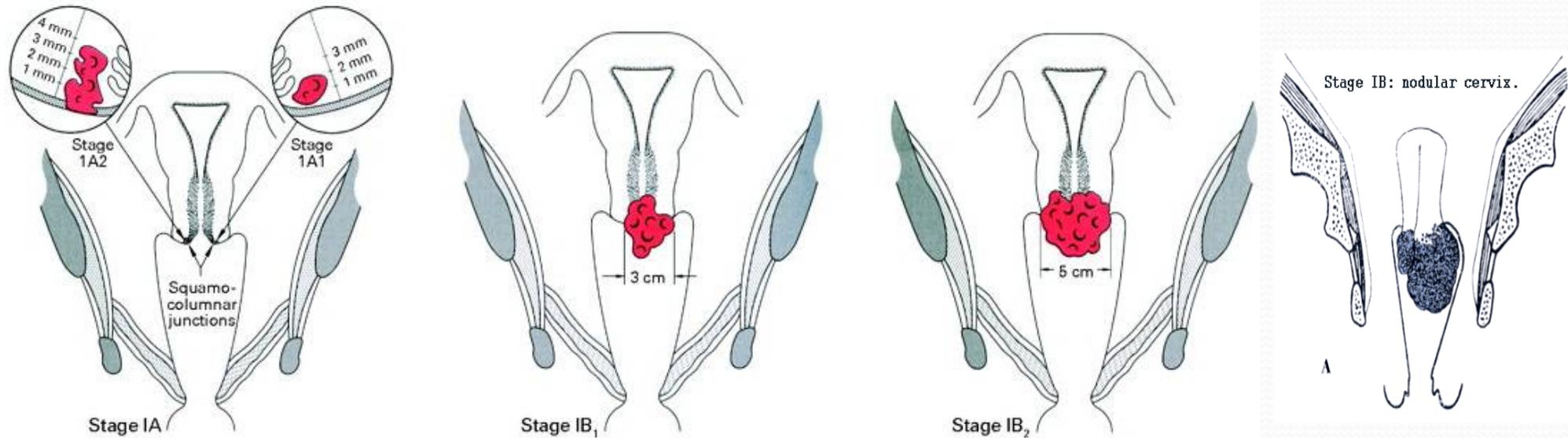
FIGO staging of cervical carcinomas

- TNM Staging TX: Primary tumor cannot be assessed
- To: No evidence of primary tumor
- Tis: Carcinoma in situ
- T1/I: Cervical carcinoma confined to uterus (extension to corpus should be disregarded)
 - T1a/IA: Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions--even with superficial invasion--are T1b/IB. Stromal invasion with a maximal depth of 5 mm measured from the base of the epithelium and a horizontal spread of 7 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification
 - T1a1/IA1: Measured stromal invasion 3 mm or less in depth and 7 mm or less in horizontal spread
 - T1a2/IA2: Measured stromal invasion more than 3 mm and not more than 5 mm with a horizontal spread 7 mm or less
 - T1b/IB: Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a2/IA2
 - T1b1/IB1: Clinically visible lesion 4 cm or less in greatest dimension
 - T1b2/IB2: Clinically visible lesion more than 4 cm in greatest dimension
- T2/II: Cervical carcinoma invades beyond uterus but not to pelvic wall or to the lower third of the vagina
 - T2a/IIa: Tumor without parametrial involvement
 - T2b/IIb: Tumor with parametrial involvement
- T3/III: Tumor extends to the pelvic wall and/or involves the lower third of the vagina, and/or causes hydronephrosis or nonfunctioning kidney
 - T3a/IIIA: Tumor involves lower third of the vagina, no extension to pelvic wall
 - T3b/IIIB: Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney
- T4/IVA: Tumor invades mucosa of the bladder or rectum, and/or extends beyond true pelvis (bullous edema is not sufficient to classify a tumor as T4)
 - M1/IVB: Distant metastasis
- Regional lymph nodes (N)
- NX: Regional lymph nodes cannot be assessed
- No: No regional lymph node metastasis
- N1: Regional lymph node metastasis

Stage 0

- Stage 0 is carcinoma in situ, intraepithelial carcinoma. There is no stromal invasion.
- Lesion often not visible with the naked eye.

Stage 1



- Stage IA: Invasive cancer identified only microscopically.
- All gross lesions even with superficial invasion are stage Ib cancers. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm* and no wider than 7 mm.

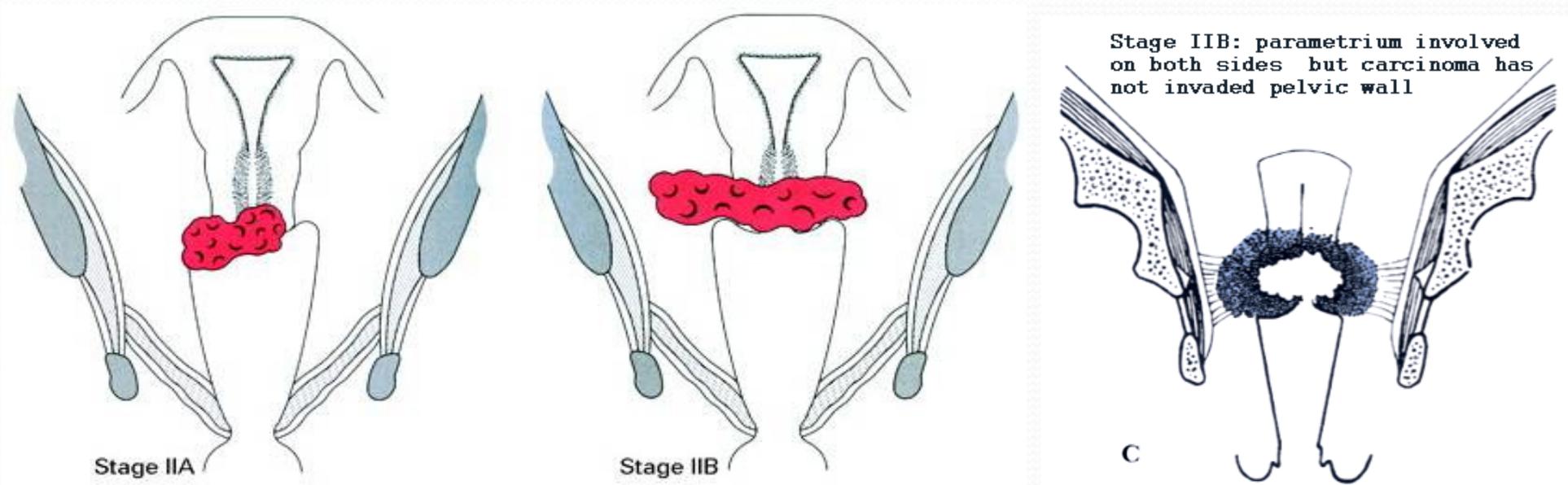
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Stage 11

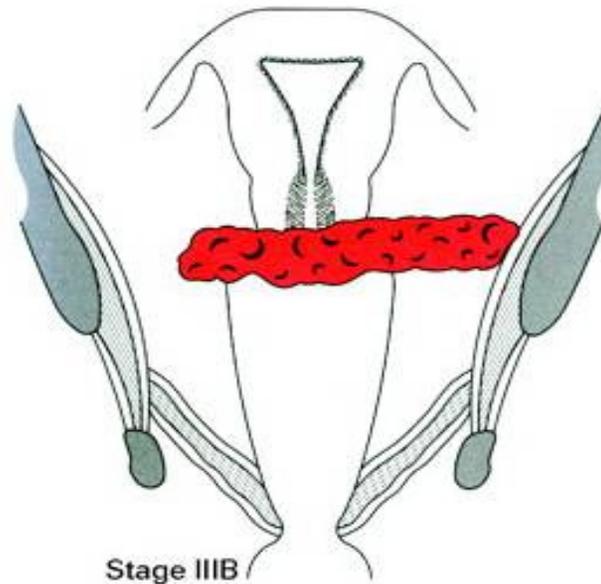
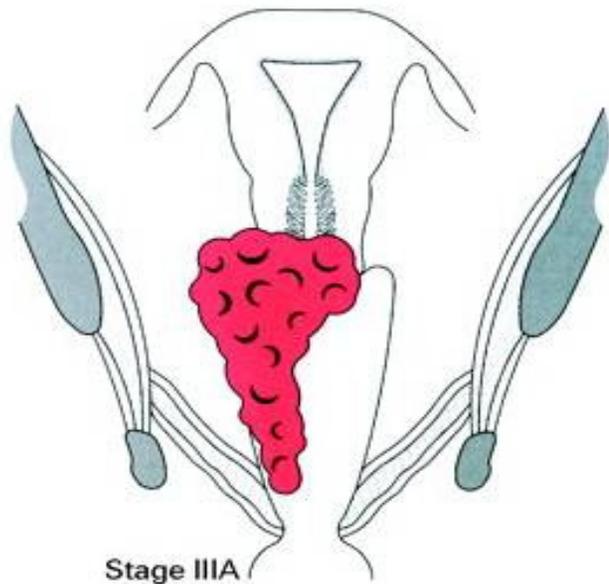


- Stage II
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Stage IIA: No obvious parametrial involvement. Involvement of up to the upper two-thirds of the vagina.

Stage IIB: Obvious parametrial involvement, but not onto the pelvic sidewall.

Stage 111



Stage IIIB: parametrium involved on both sides; at left, carcinoma has invaded pelvic wall

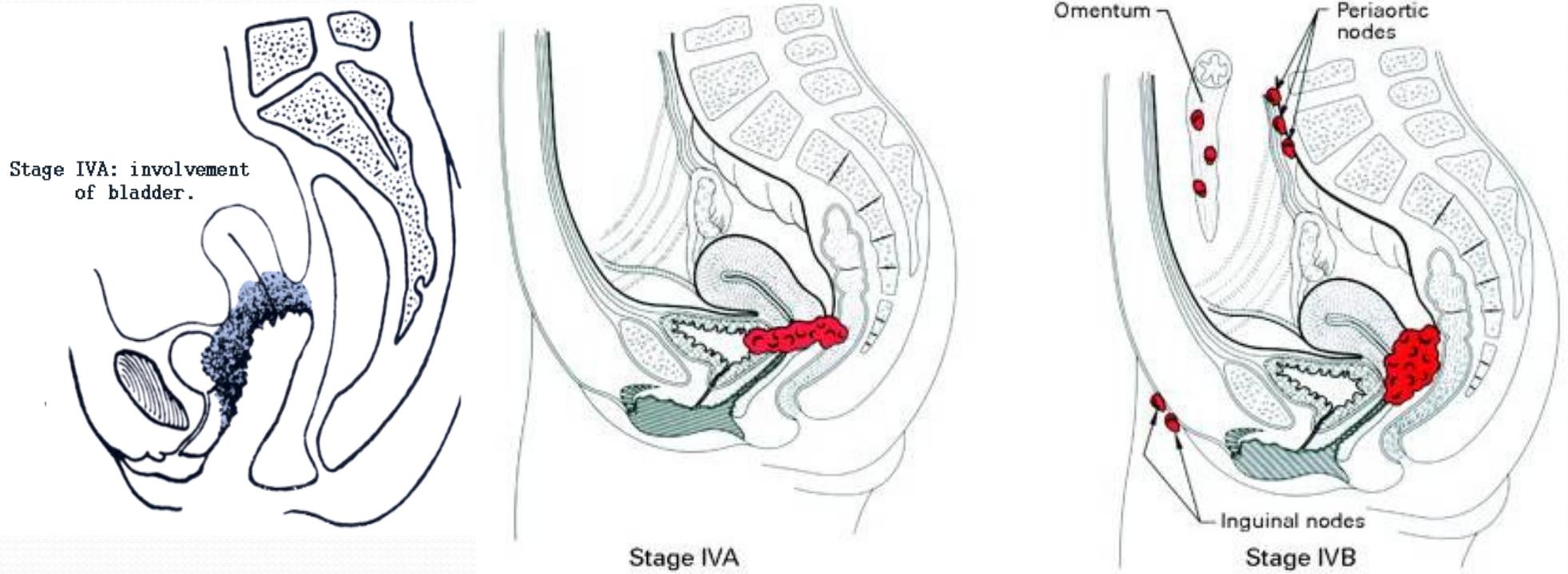


- Stage III
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- Stage IV
Stage IV is carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.
Stage IVA: Spread of the tumor onto adjacent pelvic organs.
Stage IVB: Spread to distant organs.

***Recommended Rx
for each of the following stages of squamous cell ca.***

Preinvasive cervical lesion

- **Cryosurgery**
- **Laser surgery**
- **Conization**

Recommended Rx

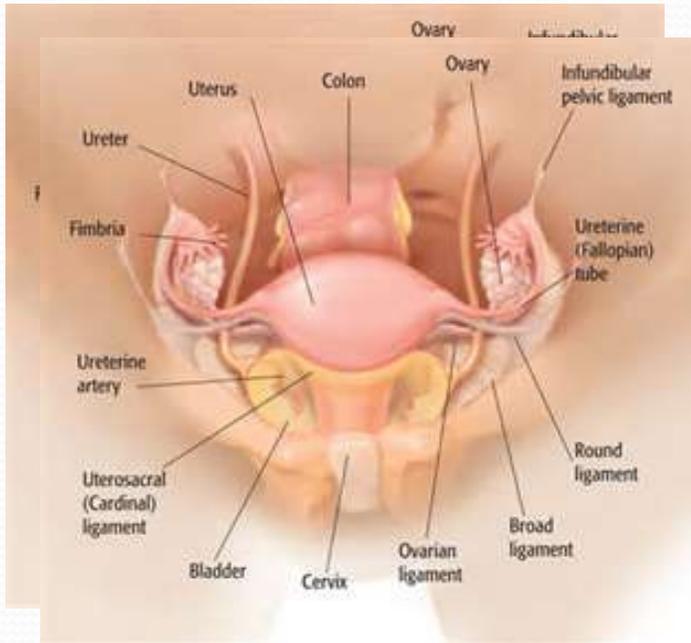
for each of the following stages of squamous cell ca.

Invasive cervical lesion

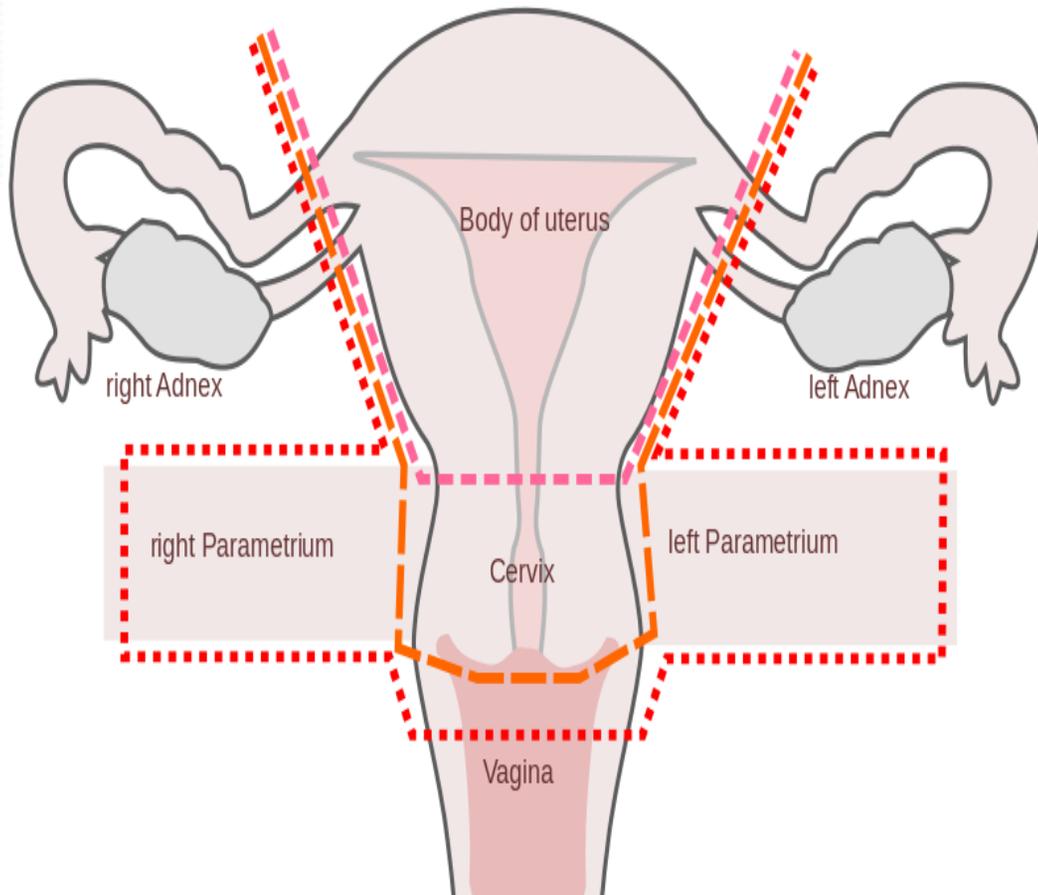
- Simple hysterectomy
- Radical hysterectomy with pelvic lymphadenectomy with or without chemoradiation.
- Chemoradiation
- Combined chemotherapy.

Treatment of Cervical Cancer

- *Option 1: Surgery*
 - *Useful in patients with Stage I and II cancer*
 - *Radical hysterectomy with pelvic lymphadenectomy is procedure of choice for early invasive cancer*
 - *When performing surgery, spare ovaries so they can continue to manufacture estrogen*

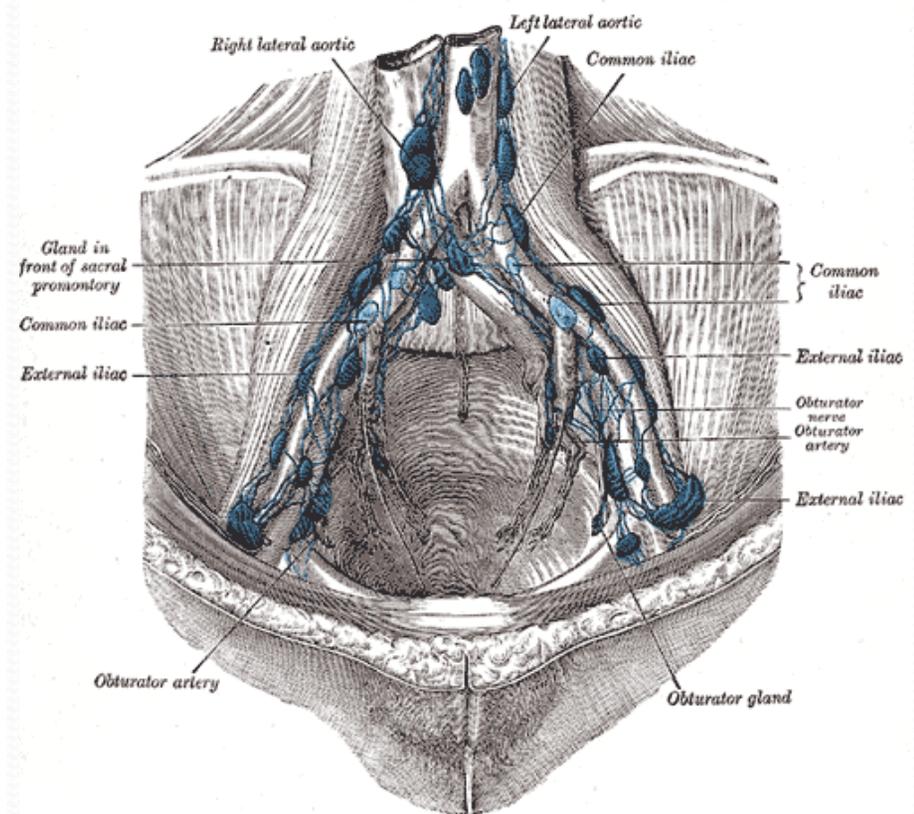


Radical Hysterectomy



- - - subtotal
 - - - total
 - - - radical

Hysterectomy



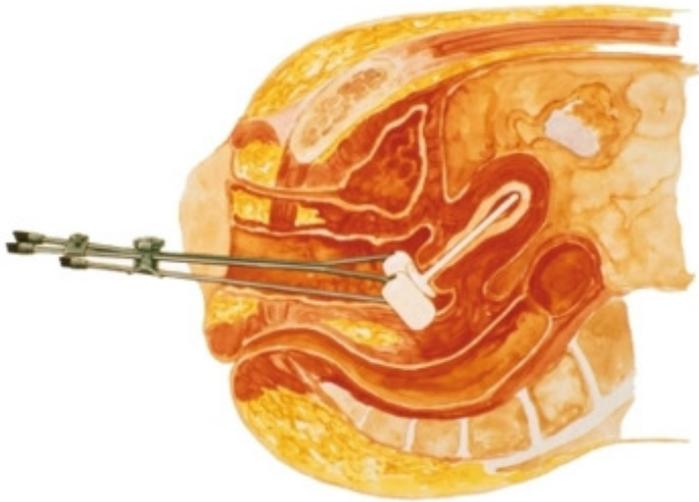
Treatment of Cervical Cancer

- *Option 2: Radiation*
 - *Reserved for poor surgical candidates or patients with advanced disease*
 - *Problems with radiation- infertility, radiation cystitis, fibrosis*
 - *Usually ineffective in patients with recurrent cervical cancer*
- *Options 3: Radiation + Chemotherapy*

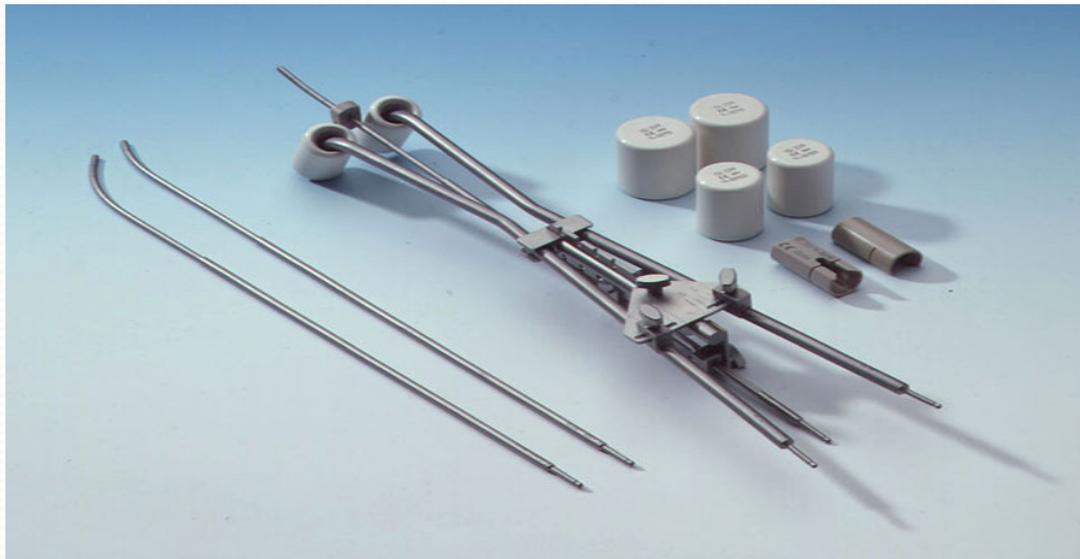
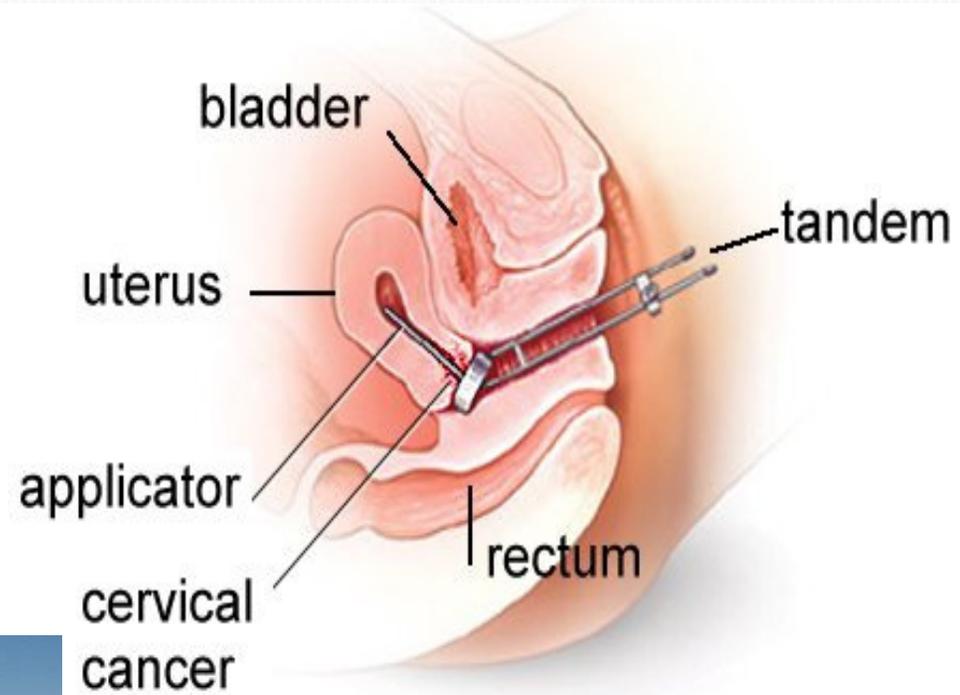
Treatment of Cervical Cancer

- *Radiation Therapy*
- **Intracavitary Brachytherapy**
 - adequate treatment for Stage IaI disease
- **External radiation therapy:**
 - *added to brachytherapy to improve pelvic control with more advanced disease.*

Radiation Therapy



Delivery of brachytherapy using applicators placed in the cervix



There are three types of brachytherapy which can be used to treat cervical cancer:

- ***Low dose rate (LDR) brachytherapy***
 - ***High dose rate (HDR) brachytherapy***
 - ***Pulsed dose rate (PDR) brachytherapy***
-
- **All three types provide effective radiotherapy for cervical cancer, by placing a source of radiation directly next to the cancer.**
 - **The difference between them is how often the radiation is delivered and how ‘intense’ the radiation is.**

Chemo-Radiation



Chemotherapy

- **Cisplatin** with or without **5-FU**.
 - Positive resection margins
 - Positive lymph nodes
 - Parametrial involvement.
 - Recurrence after surgery or previous radiation therapy.
-
- FDA (2006) approved the drug combination of **HYCAMPIN** and **CISPLATIN** for Stage IVB

Advanced Cervical Cancer Treatments and Possible Complications¹

Although effective, treatment options for advanced-stage disease are associated with complications.¹

Surgery ^{*,1,2}	Radiation ^{1,2}	Chemotherapy ¹
<ul style="list-style-type: none"> ▪ Infertility ▪ Excessive bleeding ▪ Wound infection ▪ Damage to urinary or intestinal systems ▪ Sexual life impairment <ul style="list-style-type: none"> – Fear of pain – Change in body image 	<ul style="list-style-type: none"> ▪ Fatigue ▪ Upset stomach ▪ Diarrhea ▪ Vaginal stenosis (and consequent sexual discomfort) ▪ Premature menopause ▪ Problems with urination ▪ Sexual life impairment <ul style="list-style-type: none"> – Fear of pain – Change in body image 	<ul style="list-style-type: none"> ▪ Multiple side effects that vary by agent and regimen ▪ Common side effects: <ul style="list-style-type: none"> – Fatigue – Nausea and vomiting – Hair loss – Mouth sores – Loss of appetite – Increased risk of infection – Bleeding or bruising

*

1. American Cancer Society. Available at: <http://documents.cancer.org/115.00/115.00>. Accessed January 4, 2005.
 Bukovic D, Strinic T, Habek M, et al. *Coll Antropol*. 2003;27:173–180.

Maintaining Fertility

- Radical Trachelectomy and lymphadenectomy makes it possible for young women to maintain their fertility
- Cervix is removed vaginally, the lymph nodes are removed laparoscopically and a suture is inserted at the utero-cervical junction.
- Post-op issues : recurrence, need for C/section delivery, miscarriages etc.

Management in Pregnancy

- Rare.
- Gestational status
- Stage of the disease
- Frank discussion with patient and supporting family member(s).

HPV Vaccine

- **The Food and Drug Administration (2006)**
licensed these vaccines for use in girls/women, ages 9-26 years.
- *The vaccine is given through a series of three shots over a six-month period.*
- *The retail price of the vaccine is ~ \$100 per dose (\$300 for full series).*

HPV Vaccines

- The vaccine, **Gardasil®** protects against four HPV types, which together cause 70% of cervical cancers and 90% of genital warts.
 - HPV 16 and 18 – cervical cancer,
 - and HPV 6 and 8 – genital warts.
- **CERVARIX** vaccine protects against HPV types 16 and 18.

Prevention

- *Improving Access to Pap Smears*
 - *50% of patients who die of cervical cancer have never had a Pap Smear*
- *Patients with CIS and cancer limited to the cervix - cure rate 90-100%*
- *Patients with advanced cervical cancer*
 - *cure rate is 25-50%*

Individual Burden of Cervical Cancer

- *Cancer tends to occur among women in their childbearing years and beyond (half between 35–55 years of age).^{1,2}*
- *Treatments for advanced cervical cancer have associated potential complications, including infertility.¹*
- *Quality of life of patients with cervical cancer is generally poor, especially during the course of the disease.^{3,4}*

1. American Cancer Society. Available at: <http://documents.cancer.org/115.00/115.00.pdf>. Accessed January 4, 2005.

2. American Cancer Society. Available at: www.cancer.org/downloads/PRO/CervicalCancer.pdf. Accessed August 15, 2005.

3. Nair MG. *Int Clin Psychopharmacol*. 2000;15 (Suppl 3):S47–S49.

4. Greimel E, Thiel I, Peintinger F, Cegnar I, Pongratz E. *Gynecol Oncol*. 2002;85:140–147.

QOL in Cervical Cancer Survivors

- *QOL persistently impaired*
 - *Sexual discomfort¹*
 - *Hot flashes¹*
 - *Vaginal dryness¹*
 - *Reproductive concerns (ie, inability to bear children)¹*
 - *Fearful of future diagnostic tests and cancer recurrence¹*
 - *Cancer-specific distress¹*
 - *Sexual-life impairment²*

Personnel and Equipment

- Medical personnel – Doctors, Nurses, Cytologist, Pathologist, Gynaecological Oncologist, Medical Oncologist, Radiation Oncologist/Therapist, Physicist, and Social workers/educators.
- Equipment/ Facilities - Clinics, Cyto-pathology labs., Tumor Registry, Imaging – Xray, CT Scan, MRI, PET Scan, Operating Room with general and laparoscopic facilities, Blood Banking, Chemo-Radiation Centers, Hospice care etc.

Treatment /Cost

- *PAP smear: Free - \$25*
- *Thin Prep/HPVDNA : \$100-\$200*
- *Vaccine (3 shots): \$100 x 3 = \$300*
- *Colposcopy / biopsy : \$ 150 - \$600*
- *LEEP/Cryo/Cone Biopsy : \$600 -\$1500*
- *Hysterectomy : \$4000*
- *Radical Hysterectomy : \$8000 – \$10,000*
- *Radiation : \$30,000 - \$50,000*
- *Chemotherapy : \$30,000 (\$5000 per cycle)*
- *Hospital cost*

Summary

- *Early detection = Effective treatment/ Better Outcome*
- *Annual PHYSICAL and PAP smear.*
- *Awareness/ Knowledge/ Information.*
- *Access to Treatment and Effective management with follow-up.*



Thank You