Harvard-MIT Division of Health Sciences and Technology

HST.071: Human Reproductive Biology Course Director: Professor Henry Klapholz

Estimated New Cancers Cases 2003

Age Adjusted Death Rates - Males

Age Adjusted Death Rates - Females

Leading Sites of New Cancer Cases & Deaths

Probability of Developing Cancer

Five Year Survival Rates

Who is at risk for cervical cancer?

- Vastly more common in developing nations
- In the U.S., 13,000 women will developed cervical cancer in 2002
- 4100 women will died of cervical cancer in 2002
- 12th most common cancer that women develop
- 14th most common cause of cancer death for women in the U.S.
- 2nd most common cause of cancer death in developing nations
- 370,000 new cases annually having a 50% mortality rate
- 75% decrease in incidence and mortality from cervical cancer in developed nations over the past 50 years.
- Cervical cancer screening programs in the wealthier nations.

Who is at risk for cervical cancer?

- Infection with a sexually transmitted disease is a risk factor
- Any risk factors for developing sexually transmitted diseases are also risk factors
- Women who have had multiple male sexual partners
- Began having sexual intercourse at an early age
- Had male sexual partners who are considered high risk
 - many sexual partners
 - began having sexual intercourse at an early age
- Contracting any other sexually transmitted diseases
 - Herpes
 - gonorrhea,
 - syphilis,
 - chlamydia
- Any condition that weakens the immune system also increases risk
 - HIV
 - Having had an organ transplantation,
 - Hodgkin's disease.
- Male sexual partners who are uncircumcised.

WARTS

Human Papilloma Virus

- More than 70 different types of HPV have been classified.
- Type 6, 11, and 42, are associated with raised, rough, easily visible genital warts
- Types 16, 18, 31, 33, 35, 39, 45, 51, and 52. Associated with cervical cancer
- Presence of both HPV and herpes virus together good predictor of cervical cancer
- Infection with HPV is very common majority of people have no symptoms
- In several studies done on college women, nearly half were positive for HPV
 - Only 1 to 2% had visible warts and less than 10% had ever had any visible genital warts.
- Incidence of genital warts appears to be increasing rapidly
 - May be a result of increased diagnostic ability and awareness.
- Risk factors for genital warts
 - multiple sexual partners,
 - unknown partners,
 - early onset of sexual activity,
 - tobacco use,
 - nutritional status,
 - hormonal conditions,
 - age,
 - stress
 - concurrent viral infections (such as flu, HIV, Epstein-Barr and herpes).

Other risks for cervical cancer

- Smoking
 - At least twice as likely as non-smokers
 - Increase the importance of the other risk factors for cancer
- Low socioeconomic group
 - Increase your likelihood for developing and dying from cervical cancer
 - Increased smoking rates
 - More barriers to getting annual screening exams
- One of the few cancers that affects young women
 - In their twenties and even their teens
- No one who is sexually active is really too young to begin screening
- No one is too old to continue screening if at risk
- Even someone without any risk factors can still get cervical cancer
- Proper screening and early detection are our best weapons

The Ideal Cervix

Images removed due to copyright reasons.

The transformation zone of the cervix in the ideal cervix and in one with an ectropion (eversion)

The original squamous epithelium

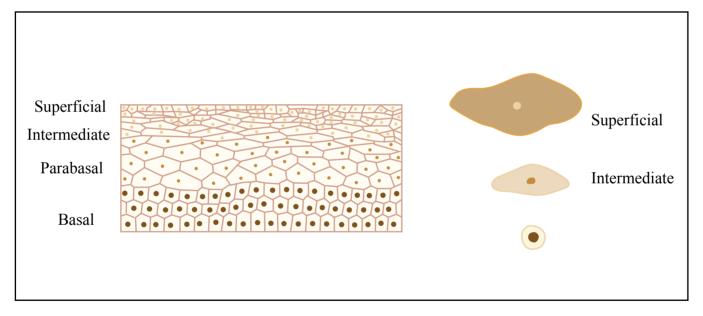


Figure by MIT OCW.

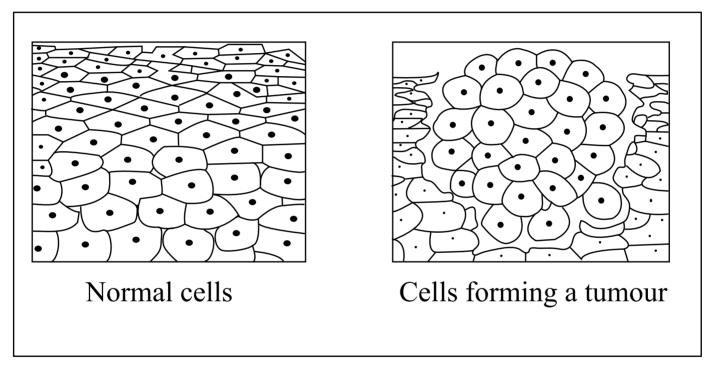


Figure by MIT OCW.

Using a spatula to obtain a PAP smear

Images removed due to copyright reasons. Commercially available cytologic sampling instruments

The endocervical brush (Cytobrush)

Ayre's cervical spatula and modifications

Pap Smear Abnormalities

- **Inflammation.** Common vaginal or cervical infections may appear on a Pap test. Your doctor will treat any infection and then repeat the Pap test a few months later.
- Atypical squamous cells of undetermined significance (ASCUS). This term is applied when a Pap test shows slightly abnormal cells, but the cells don't clearly indicate a cervical problem. Many times this finding represents a viral infection, which can be treated.
- Squamous intraepithelial lesion (SIL). This term is used to indicate that the cells seen on the Pap test are consistent with abnormalities in the cervix that may be precancerous (cervical intraepithelial neoplasia, or dysplasia). If the threat is low grade, the size, shape and other characteristics of the cells suggest that if a precancerous lesion is present, it's likely to be years away from becoming a cancer. If the threat is high grade, the certainty of something being wrong on the cervix is greatly enhanced, and the lesion is likely to be farther down the road to cancer.
- Atypical glandular cells of undetermined significance. This term is used when glandular cells appear to be slightly abnormal. Compared with ASCUS, this finding is far more likely to be serious. And it always demands further testing.
- Squamous cancer or adenocarcinoma cells. In either circumstance, the cells seen on the Pap test are so abnormal that the pathologist is almost certain a cancer will be found growing in the vagina, cervix or occasionally the uterus. Squamous refers to flat, skin-like cells. Adenocarcinoma refers to cancers arising in gland cells.

What screening tests are available?

- Pap test is highly effective
- Isn't a perfect test
- May miss cells
- Shouldn't be performed when you are menstruating
- Even the best laboratories can miss abnormal cells
- Need to have the tests performed on a regular basis
- It may miss abnormal cells one year
- Unlikely to miss anything two years in a row.
- Begin having yearly Pap tests done at the onset of sexual activity
- Age 18
- Continue to have Pap tests done on a yearly bas
- Three normal Pap tests
 - option of getting the tests done every two or three years
 - Women in low risk groups
 - monogamous with monogamous partners
- New sexual partner
- Back to yearly Pap testing
- Women who have had a hysterectomy
- "Subtotal or supracervical" hysterectomy
- Post-menopausal

What screening tests are available?

- HPV testing can theoretically find the vast majority of women who are at risk for developing cervical cancer
- Modern DNA analysis
- Subtype, or strain, of HPV a person is infected with
- Subtype of HPV predicts how likely it is to lead to a cervical cancer
- Can be done at home
 - Private
 - By a woman collecting a sample herself
 - Sending it to a laboratory via the mail
 - Less technical expertise required to correctly run an HPV test
 - Cuts down on errors and cost
 - Test isn't perfect
- Majority of women with HPV will not go on to have cervical cancer
- Positive test result creates the need for expensive and often unnecessary follow-up

Atypical cells

High Grade Dysplasia

What are the signs of cervical cancer?

- Early stages of cervical cancer usually do not have any symptoms.
- Abnormal bleeding
 - Bleeding after sexual intercourse
 - In between periods
 - Heavier/longer lasting menstrual bleeding
 - Bleeding after menopause
- Abnormal vaginal discharge (may be foul smelling)
- Pelvic or back pain
- Pain on urination
- Blood in the stool or urine
- Non-specific, and could represent a variety of different conditions

Staging of Cervical Cancer

- Stage IA microscopic cancer confined to the uterus
- Stage IB cancer visible by the naked eye confined to the uterus
- Stage II cervical cancer invading beyond the uterus but not to the pelvic wall or lower 1/3 of the vagina
- Stage III cervical cancer invading to the pelvic wall and/or lower 1/3 of the vagina and/or causing a nonfunctioning kidney
- Stage IVA cervical cancer that invades the bladder or rectum, or extends beyond the pelvis
- Stage IVB distant metastases

Type of Cancers

Cervical intraepithelial neoplasia (CIN). This is a term used to describe abnormal changes on the surface of the cervix after biopsy. CIN — along with a number (1, 2 or 3) — describes how much of the lining of the cervix contains an abnormal growth of cells. Another term for this condition is dysplasia.

Carcinoma in situ (CIS). This cancer involves cells on the surface of the cervix that haven't spread into deeper tissues. Treatment to remove the cancer is necessary and highly successful.

Cervical cancer. Abnormal cells will eventually invade deeper tissues and may spread into blood vessels and the lymphatic system, where they can be carried to distant sites. Both squamous and glandular cancers can arise in the cervix. Most of the time, abnormal Pap tests pick up precancerous tissue that can be treated before these more dangerous diseases arise.

Treatments

Conization. This is a procedure in which your doctor removes a coneshaped piece of cervical tissue containing the abnormal area.

Laser surgery. In this procedure, your doctor uses a laser to kill precancerous cells.

Loop electrosurgical excision procedure (LEEP). This is a technique in which a wire loop with an electrical current running through it is used like a surgeon's knife to remove abnormalities.

Cryosurgery. Your doctor may use this technique to freeze and kill precancerous cells.

Hysterectomy. This is the surgical removal of precancerous areas, including the cervix and uterus

Cervical Cancer Therapy

- SURGERY
 - Radical hysterectomy
 - Pelvic lymph nodes
- RADIOTHERAPY
 - External Beam
 - Brachytherapy HDR, LDR
- CHEMOTHERAPY
 - Cisplatin
 - 5-FU
 - Hydroxyurea
 - Ifosfamide
 - Paclitaxel

WHO NEEDS A PAP SMEAR?

- Begin 3 years after starting vaginal intercourse
- At age 21
- Yearly till age 30
- Every 2-3 years after 3 negative annual smears at age 30 unless risk factors
- May stop screening at age 70 if 3 or more negative smears in past 10 years she
- May stop screening after total hysterectomy if it was not done for cervical disease or vaginal disease