بسم الله الرحمن الرحيم
Carcinoma of the Cervix

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Anatomy of the cervix

- It is the lower third of the uterus
- 2.5 cm in length
- Divided into supra- and infravaginal portions by the attachments of the vagina
- The portion projecting into the vagina is referred to as the *portio vaginalis* or ectocervix.
- The ectocervix's opening is called the external os.
- The passageway between the external os and the uterine cavity is referred to as the endocervical canal.
- The endocervical canal terminates at the internal os which is the opening of the cervix inside the uterine cavity.
The ectocervix is composed of nonkeratinized stratified squamous epithelium. The endocervix is composed of simple columnar epithelium. The border of the endocervix and ectocervix is known as the transformation zone or squamocolumnar junction. The Transformation zone undergoes metaplasia physiologically.
Carcinoma of the cervix
Introduction

- It is the second commonest female cancer affecting over 500,000 women each year, and killing more than 270,000 women per year. Cervical cancer occurs mainly in developing countries, accounting for about 85% of cases worldwide.
- The incidence of cervical cancer has declined dramatically since the 1950s.
- Screening in developed countries has reduced cervical CA death by 70%
Pathogenesis

- Site where squamous epithelium of vagina meets columnar epithelium of endocervix known as squamocolumnar junction (SCJ)
- Before puberty: SCJ located just inside the cervical os
- At puberty, increasing levels of estrogen lead to squamous metaplasia of columnar epithelium to squamous epithelium
- Results in repositioning of the SCJ further towards the uterus
Transformation zone is the site of 95% of the cervical cancer development.

Exposure of transformation zone to carcinogens begins process of intraepithelial neoplasia (dysplasia).

While exact role of carcinogens in this process remains poorly understood, it is clear that HPV and cigarette smoking can cause dysplasia at the transformation zone.
Risk factors

1. Human papillomavirus (HPV) infection is the major risk factor for development of cervical cancer.
Small double stranded DNA virus with protein capsid.

About 120 types of HPV described

HPV infection is very common and does not lead to cancer in the majority of cases. Genital infections with HPVs typically cause no symptoms and go away on their own. Sometimes, however, the infection persists. Precancerous changes or ultimately cervical cancer only arises when there is a persistent infection by one of the HPV types associated with cervical and other cancers.
• Low risk types — HPV types 6 and 11 can cause genital warts and are low-risk types because they rarely cause cervical cancer.

• High risk types — HPV types 16 and 18 are considered high-risk types because they may cause cervical cancer in some women.
The major difference between the 2 types is that after infection, the low-risk HPVs are maintained as extrachromosomal DNA episomes, while the high-risk HPV genome is found integrated into the host cellular DNA.
The recombination event often leaves E6 and E7 directly coupled to the viral promoter and enhancer sequences, allowing their continued expression after integration
Because E7 binds and inactivates the Rb protein while E6 binds p53 and directs its degradation, the functional loss of both \( P53 \) and the \( RB \) genes leads to resistance to apoptosis, causing uncensored cell growth after DNA damage. This ultimately results in progression to malignancy.
• HPV is spread by direct skin-to-skin contact, including sexual intercourse, oral sex, anal sex, or any other contact involving the genital area (eg, hand to genital contact). It is not possible to become infected with HPV by touching an object, such as a toilet seat. In 2006, a vaccine became available in the United States to help prevent infection with certain types of HPV.
Most people who are infected with HPV have no signs or symptoms. Most HPV infections are temporary and resolve within two years. When the virus persists (in 10 to 20 percent of cases), there is a chance of developing cervical precancer or cancer. However, it usually takes many years for HPV infection to cause cervical cancer.
Condylomata accuminata
Cont...Risk factors

- 2-Giving birth to many children.
- 3-Having many sexual partners.
- 4-Having first sexual intercourse at a young age.
- 5-Smoking cigarettes.
6- Using oral contraceptives ("the Pill").
7- Having a weakened immune system
8- Diethylstilbestrol (DES): Some studies have suggested that DES-exposed daughters may be at increased risk of developing precancerous cervical cancer and squamous cell carcinoma of the cervix.
• 9-Age: Most cases of cervical cancer tend to occur in women younger than 50 years of age.

• 10-Socioeconomic status
Histological Types

- SSC 80-95%
- ADENO 5-20%
- OTHERS: clear cell; sarcoma
Adenocacinoma
STAGING

**STAGE 0** *(precancerous)*

**CIN** refers to the histopathological description in which a part or the full thickness of the stratified squamous epithelium replaced by cells showing varying degrees of *dysplasia*, but basement membrane intact

**Mild dysplasia – CIN I**

- Undifferentiated cells are confined to lower 1/3 of epithelium
Moderate dysplasia – CIN II

• Undifferentiated cells occupy lower 50 to 75% of epithelial thickness.

Severe dysplasia & CA insitu – CIN III

• Entire thickness replaced by abnormal cells, but basement membrane intact

• CIN – II, III: HSIL/high grade squamous intra epithelial lesions
NORMAL CERVIX
CIN I
CIN II
CIN III
Stage I

- In stage I, cancer is found in the cervix only. Stage I is divided into stages IA and IB, based on the amount of cancer that is found.

- Stage IA: A very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. Stage IA is divided into stages IA₁ and IA₂, based on the size of the tumor.
In stage IA₁, the cancer is not more than 3 millimeters deep and not more than 7 millimeters wide.
In stage IA₂, the cancer is more than 3 but not more than 5 millimeters deep, and not more than 7 millimeters wide.
Stage IB is divided into stages IB₁ and IB₂. In stage IB₁:
the cancer can only be seen with a microscope and is more than 5 millimeters deep and more than 7 millimeters wide; or
the cancer can be seen without a microscope and is 4 centimeters or smaller.

In stage IB₂, the cancer can be seen without a microscope and is larger than 4 centimeters.
In stage II, cancer has spread beyond the cervix but not to the pelvic wall or to the lower third of the vagina. Stage II is divided into stages IIA and IIB, based on how far the cancer has spread.

• Stage IIA: Cancer has spread beyond the cervix to the upper two thirds of the vagina but not to tissues around the uterus. Stage IIA is divided into stages IIA1 and IIA2, based on the size of the tumor.
• In stage IIA1, the tumor can be seen without a microscope and is 4 centimeters or smaller.
• In stage IIA2, the tumor can be seen without a microscope and is larger than 4 centimeters.

Stage IIB: Cancer has spread beyond the cervix to the tissues around the uterus.
Stage III

In **stage III**, cancer has spread to the lower third of the vagina, and/or to the pelvic wall, and/or has caused kidney problems. Stage III is divided into stages IIIA and IIIB, based on how far the cancer has spread.

• **Stage IIIA**: Cancer has spread to the lower third of the vagina but not to the pelvic wall.
• **Stage IIIIB:**
  - Cancer has spread to the pelvic wall; and/or
  - the tumor has become large enough to block the ureters (the tubes that connect the kidneys to the bladder). This blockage can cause the kidneys to enlarge or stop working.
In **stage IV**, cancer has spread to the bladder, rectum, or other parts of the body. Stage IV is divided into stages IVA and IVB, based on where the cancer is found.

- **Stage IVA**: Cancer has spread to nearby organs, such as the bladder or rectum.
- **Stage IVB**: Cancer has spread to other parts of the body, such as the liver, lungs, bones, or distant lymph nodes.
INVASIVE CA
In the early stages of cervical cancer, the woman may or may not experience symptoms. It is important to note that some symptoms of cervical cancer can also be caused by other health conditions.

- Abnormal vaginal bleeding or spotting between periods
- Pain during sexual intercourse or bleeding after intercourse
- Clear, watery, or foul-smelling discharge from the vagina
- Increased amount of vaginal discharge
Late symptoms can occur as the tumours grow large or invade other organs of the body:
• pelvic or back pain
• urine leakage (incontinence) or blood in the urine (hematuria)
• weight loss
• appetite loss or anorexia
• shortness of breath
• anemia (causing lack of energy and shortness of breath)
• blood in the stool
• constipation
Diagnosis

1- Hx. And Ex.
2- Screening tests
   a- PAP SMEAR.
   b- HPV test
3- Other test mentioned later on.
Pap smear

A procedure to collect cells from the surface of the cervix and vagina. A piece of cotton, a brush, or a small wooden stick is used to gently scrape cells from the cervix and vagina. The cells are viewed under a microscope to find out if they are abnormal.
The test can find early cell changes that are not yet cancer. If cell changes are found, they can be treated. This can prevent them from becoming cervical cancer. This test also can find cervical cancer at a stage that is easy to treat.
 HPV test

- **Human papillomavirus (HPV) test:** A laboratory test used to check DNA (genetic material) for certain types of HPV infection. Cells are collected from the cervix and checked to find out if an infection is caused by a type of human papillomavirus that is linked to cervical cancer.
• This test may be done if the results of a Pap smear show certain abnormal cervical cells. This test is also called the HPV DNA test.
These tests are good, but they are not perfect. They can sometimes report that there are precancers present when there really are not. These “false-positive” results can lead to treatments that are not needed. Pap tests have been done yearly in the past, but now we know that yearly Pap tests are not needed. In fact, yearly Pap tests can lead to harm from treatment of cell changes that would never go on to cause cancer.
The new screening recommendations (shown below) keep the benefit of testing but lower the risks of unneeded treatment (called ‘overtreatment’).

Regular cervical cancer screening is not helpful before age 21 years. Women should start screening at age 21 years and be tested every 3 years with a Pap test. At age 30 years, HPV tests are a useful addition to Pap test.
If a woman tests positive for HPV, she will need further testing to find out if she is likely to have a precancer.
If she tests negative on both the Pap and HPV tests, her risk of precancer and cancer is so low that she does not need to be tested again for another 5 years.
1) Cervical cancer screening should begin at age 21 years. Women younger than age 21 years should not be tested with either the Pap test or the HPV test.

2) Women between the ages of 21 and 29 years should have a Pap test every 3 years. HPV testing should not be used in this age group unless it is needed after an abnormal Pap test.
Colposcopy: A procedure in which a colposcope is used to check the vagina and cervix for abnormal areas. Tissue samples may be taken using a curette and checked under a microscope for signs of disease.
• **Biopsy**: If abnormal cells are found in a Pap smear, the doctor may do a biopsy. A sample of tissue is cut from the cervix and viewed under a microscope by a pathologist to check for signs of cancer. A biopsy that removes only a small amount of tissue is usually done in the doctor’s office. A woman may need to go to a hospital for a cervical cone biopsy (removal of a larger, cone-shaped sample of cervical tissue).
In a cone biopsy, the patient lies on her back, and a speculum is inserted into the vagina (A). The cervix is visualized, and a cone-shaped piece of the cervix is removed (B and C). A cauterizing tool is used to stop any bleeding (D).
Pelvic exam: An exam of the vagina, cervix, uterus, fallopian tubes, ovaries, and rectum.
After Dx.

- Chest x-ray
- CT scan
- Lymphangiogram
- Pretreatment surgical staging
- Ultrasound
- MRI
- Fine-needle aspiration (FNA) biopsy
MODE OF SPREAD

- 1-CONTINUITY
- 2-CONTIGUITY
- 3-LYMPHATIC SPREAD
- 4-VASCULAR
Three types of standard treatment are used:

1. SURGERY
   - Conization
   - Hysterectomy
   - Bilateral salpingo-oophorectomy
   - Pelvic exenteration
   - Cryosurgery
   - Laser surgery
   - Loop electrosurgical excision procedure (LEEP)
There are two types of radiation therapy. **External radiation** therapy uses a machine outside the body to send radiation toward the cancer. **Internal radiation** therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.
Treatment according to the stage

- **Carcinoma in Situ (Stage 0)**
  - Treatment of carcinoma in situ (stage 0) may include the following:
    - Loop electrosurgical excision procedure (LEEP).
    - Laser surgery.
    - Conization.
    - Cryosurgery.
    - Total hysterectomy for women who cannot or no longer want to have children.
    - Internal radiation therapy for women who cannot have surgery.
Stage IA Cervical Cancer
Treatment of stage IA cervical cancer may include the following:
• Total hysterectomy with or without bilateral salpingo-oophorectomy.
• Conization.
• Modified radical hysterectomy and removal of lymph nodes.
Internal radiation therapy
Stage IB Cervical Cancer
Treatment of stage IB cervical cancer may include the following:
• A combination of internal radiation therapy and external radiation therapy.
• Radical hysterectomy and removal of lymph nodes.
• Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy.
Stage IIA Cervical Cancer

Treatment of stage IIA cervical cancer may include the following:

• A combination of internal radiation therapy and external radiation therapy plus chemotherapy.
• Radical hysterectomy and removal of lymph nodes.
• Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy.
Stage IIB, III, IV

Treatment of stage IIB cervical cancer may include **internal** and **external radiation therapy** combined with **chemotherapy**.
CA CERVIX AND PREGNANCY

- EARLY PREGNANCY
  - External irradiation

- LATE PREGNANCY
  The uterus must be emptied by hysterostomy or CS. b/f radiotherapy

Most surgeons prefer to treat these cases by Wertheim hysterectomy at the time of CS.
Women can minimize their risk of developing cervical cancer by reducing their risk of HPV infection. The virus is most commonly transmitted via sexual contact and intercourse.

If a woman smokes, quitting also reduces her chance of developing cervical cancer.
Another effective way to prevent cervical cancer is through vaccination.
The world's first vaccination against HPV was approved in Canada and the United States in 2006. The vaccination provides protection from 4 different types of HPV. Two of these HPV types cause 70% of cervical cancer.
Recombinant Human Papillomavirus (HPV) Bivalent Vaccine

US Brand Name(s):
- Cervarix

FDA Approved

Used in:
- Cervical cancer
- Lesions that sometimes lead to cervical cancer
2-Recombinant Human Papillomavirus (HPV) Quadrivalent Vaccine

Name: Gardasil

FDA approved
Used in:

- **Anal cancer**.
- **Cervical cancer**.
- **Vaginal cancer**.
- **Vulvar cancer**.
- **Lesions** that sometimes lead to anal, cervical, vaginal, or vulvar cancer.

**Genital warts**
5 YEAR SURVIVAL IS
- Stage I: 80%
- Stage II: 74%
- Stage III: 47%
- Stage IV: 25%
REFERENCES

- New recommendations from the American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology modified at 14-3-2012
- National Cancer Institute modified at 4-4-2012
- Gynecology By Ten Teachers
Thank You!

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