CERVICAL CANCER

Dr Hamza Al-Amoosh

JBOG, FRCOG, MSc laparoscopy, ATSM Urogynaecology

Assistant Professor Hashmite University

Statistics

- 10,520 new cases in the U.S. this year
- 3,900 will die
- 50% are diagnosed between ages 35 and 55.
- 20% at the age of 65 or over.
- Rarely occurs in women younger than 20
- Noninvasive is four times more common
- 74% decrease in deaths between 1955 and 1992 in the U.S.
- Death rate continuous to decline by 2% a year

Lifetime Probability of Developing Cancer, by Site, Women, US, 1998-2000

Site	Risk
All sites	1 in 3
Breast	1 in 7
Lung & bronchus	1 in 17
Colon & rectum	1 in 18
Uterine corpus	1 in 38
Non-Hodgkin lymphoma	1 in 57
Ovary	1 in 59
Pancreas	1 in 83
Melanoma	1 in 82
Urinary bladder	1 in 91
Uterine cervix	1 in 128

Source:DevCan: Probability of Developing or Dying of Cancer Software, Version 5.1 Statistical Research and Applications Branch, NCI, 2003. http://srab.cancer.gov/devcan

Cervical Cancer

- Begins in the lining of the cervix
- Cells change from normal to pre-cancer (dysplasia) and then to cancer

Three Types

- Squamous cell Carcinomas
  - Cancer of flat epithelial cell
  - 80% to 90%
- Adenocarcinomas
  - Cancer arising from glandular epithelium
  - 10% - 20%
- Mixed carcinoma
  - Features both types

Signs and Symptoms

- Vaginal bleeding
- Menstrual bleeding is longer and heavier than usual
- Bleeding after menopause or increased vaginal discharge
- Bleeding following intercourse or pelvic exam
- Pain during intercourse

Type of patient:

- Multiparous.
- Low socioeconomic class.
- Poor hygiene.
- Prostitutes.
- Low incidence in Muslims and Jews.

Symptoms:

Early symptoms	Late symptoms
- None. - Thin, watery, blood tinged vaginal discharge frequently goes unrecognized by the patient. - Abnormal vaginal bleeding Intermenstrual Postcoital Perimenopausal Postmenopausal - Blood stained foul vaginal discharge.	- Pain, leg oedema. - Urinary and rectal symptoms dysuria haematuria rectal bleeding constipation haemorrhoids - Uraemia

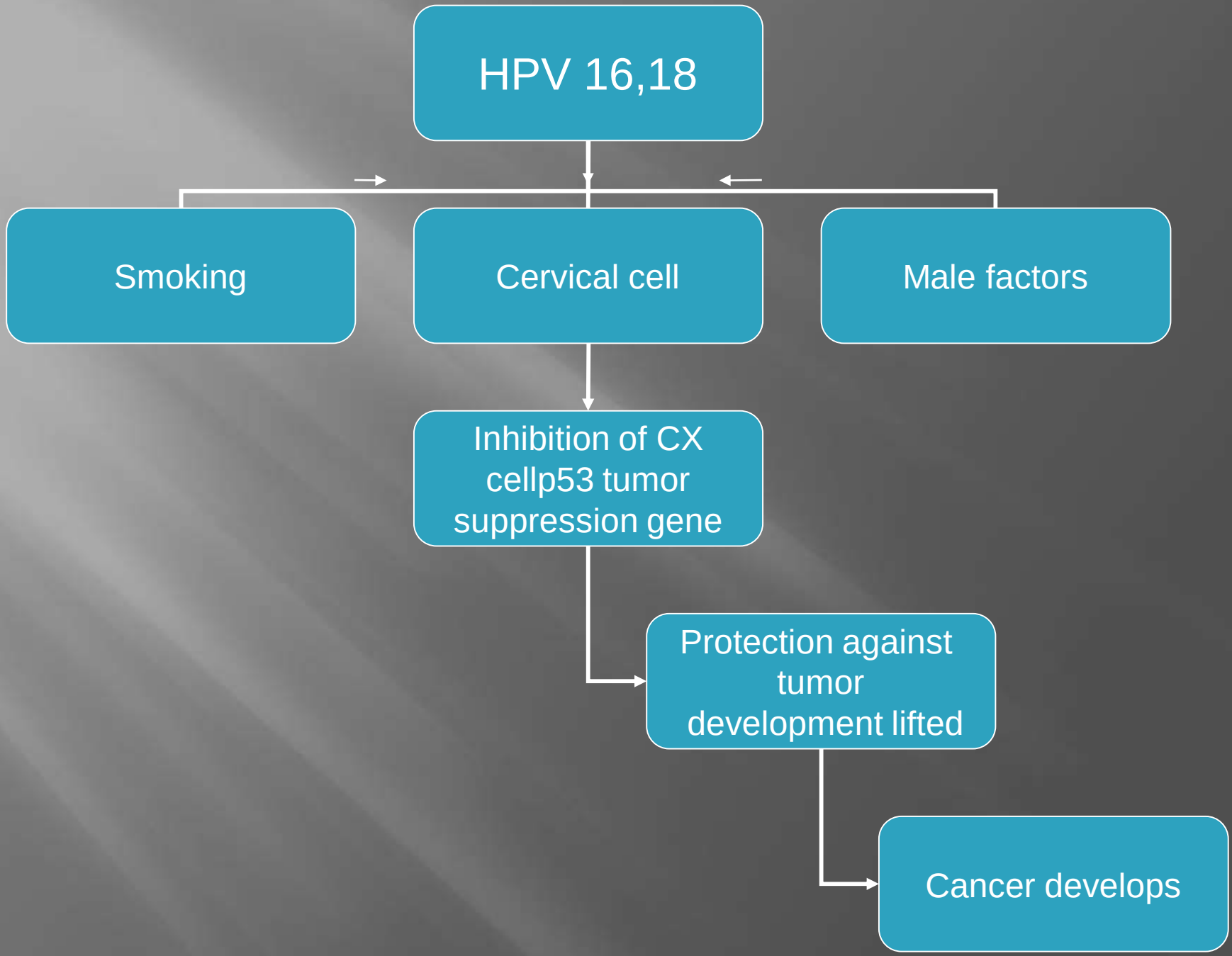
Risk Factors

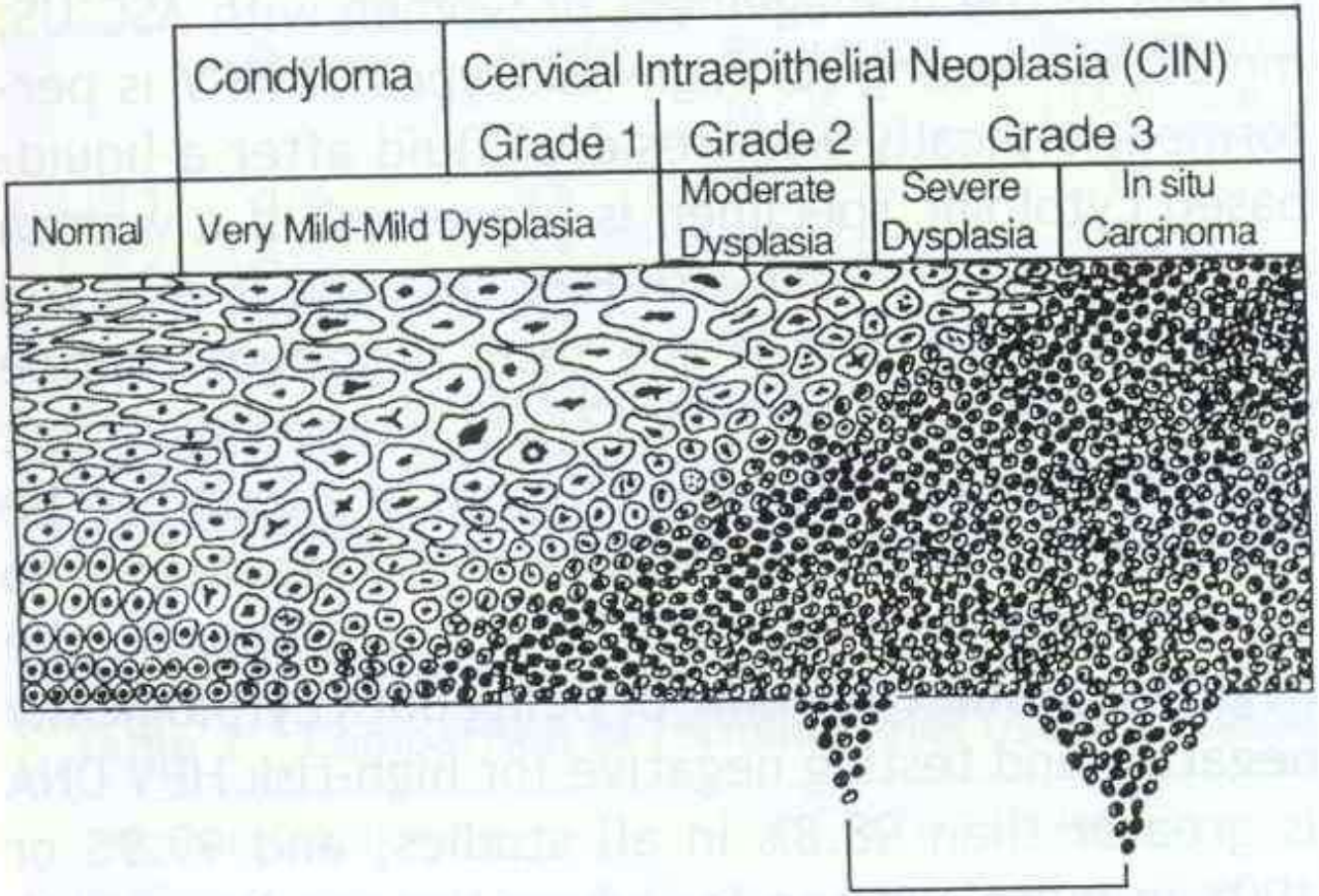
- Human papillomavirus infection (HPV) – Primary factor
  - HPV 16, HPV 18, HPV 31, HPV 33, HPV 45,,,,,,50% are caused by HPV 16 AND 18
- Sexual behavior
- Smoking
- HIV infection
- Chlamydia infection
- Diet
- Oral contraceptives
- Multiple pregnancies
- Low socioeconomic status
- Diethylstilbestrol (DES)
- Family history

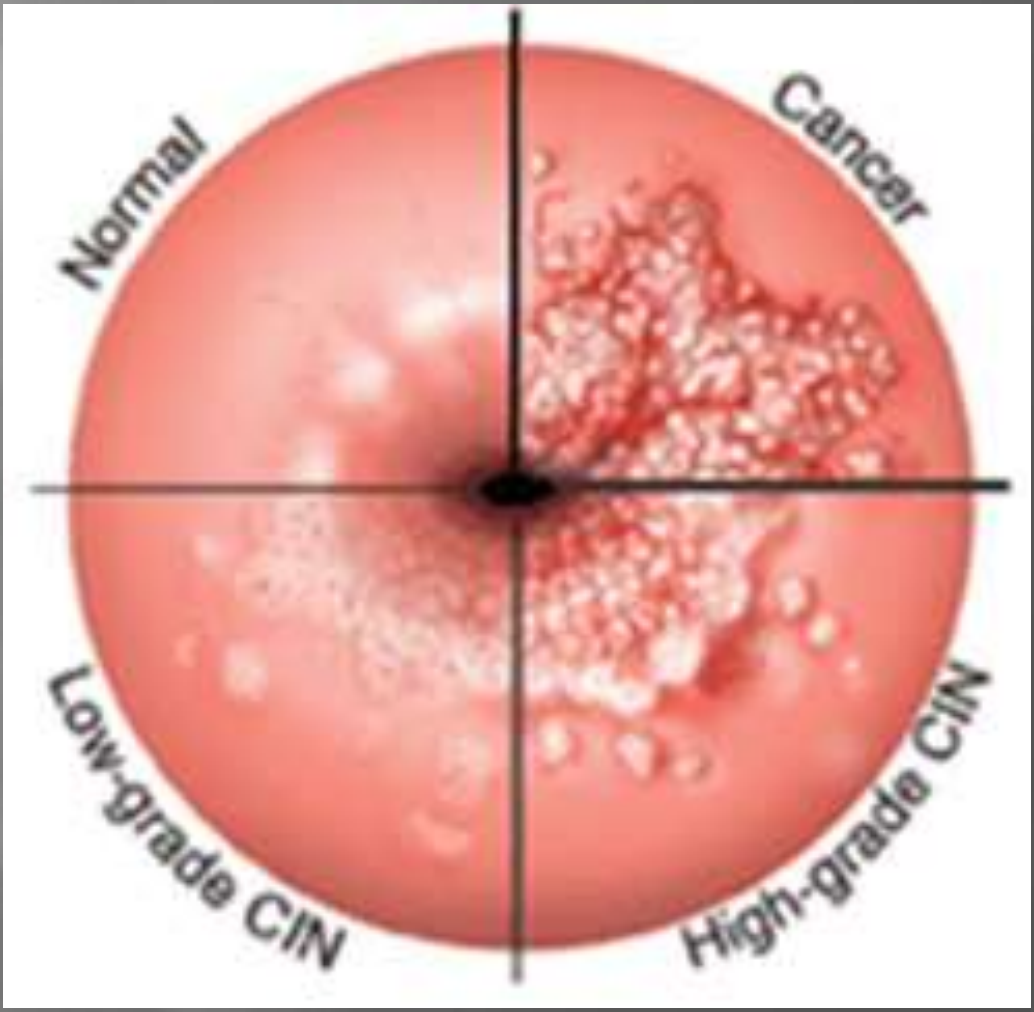
Risk of cervical cancer with human papillomavirus

High-risk (oncogenic or cancer-associated) types
Common types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 82
Low-risk (non-oncogenic) types
Common types: 6, 11, 40, 42, 43, 44, 54, 61, 72, 81

Data from: Centers for Disease Control and Prevention. National Cancer Institute Factsheet. Human papillomavirus and cancer: Questions and answers. Available at: www.cancer.gov/cancertopics/factsheet/Risk/HPV (Accessed on June 11, 2012).


HPV 16,18
Smoking
Cervical cell
Male factors
Inhibition of CX cellp53 tumor suppression gene
Protection against tumor development lifted
Cancer develops


Condyloma
Cervical Intraepithelial Neoplasia (CIN)
Grade 1
Grade 2
Grade 3
Normal
Very Mild-Mild Dysplasia
Moderate Dysplasia
Severe Dysplasia
In situ Carcinoma
Microinvasive Carcinoma


Normal
Cancer
Low-grade CIN
High-grade CIN

Normal cervix

Cervical dysplasia

Normal cervical cells

Cancerous or pre-cancerous cervical cells

Prevention

- Avoiding the risk factors
  - Especially HPV
  - Help for low-income women
- Having the Pap Test
  - 3 years after first vaginal intercourse or by age 21.
  - Have test annually

DETECTION

- Cervical Cytology (Pap Test)
  - Cells are removed from the cervix and examined under the microscope.
  - Can detect epithelial cell abnormalities
    - Atypical squamous cells
    - Squamous intraepithelial lesions
    - Squamous cell carcinoma (likely to be invasive)

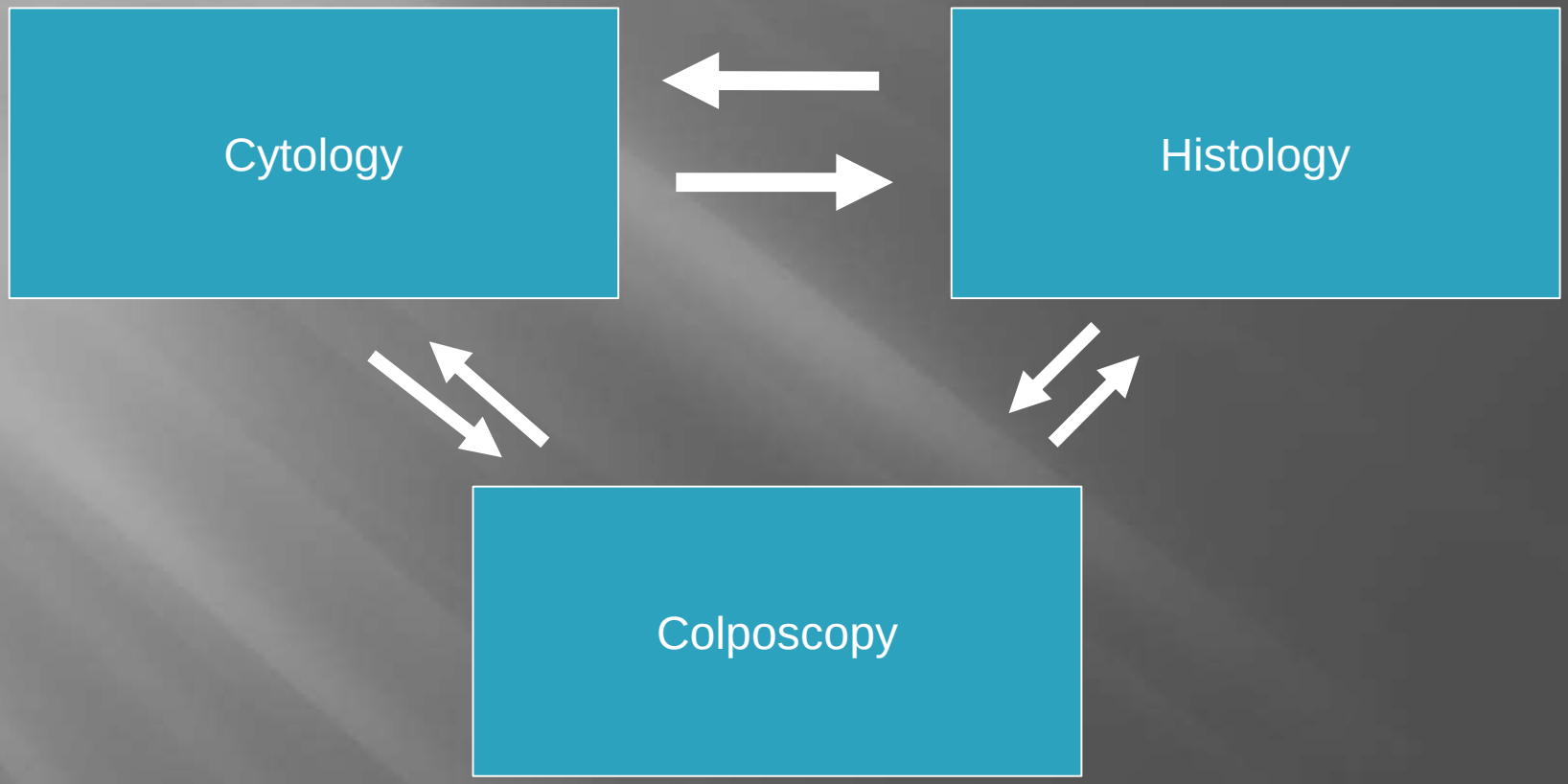
DIAGNOSIS

- 1- History.
- Many women are a symptomatic .
- Presented with abnormal routine cx smear
- Complain of abnormal vaginal bleeding
- I M bleeding
- post coital bleeding
- perimenopausal bleeding
- postmenopausal bleeding
- blood stain vaginal discharge

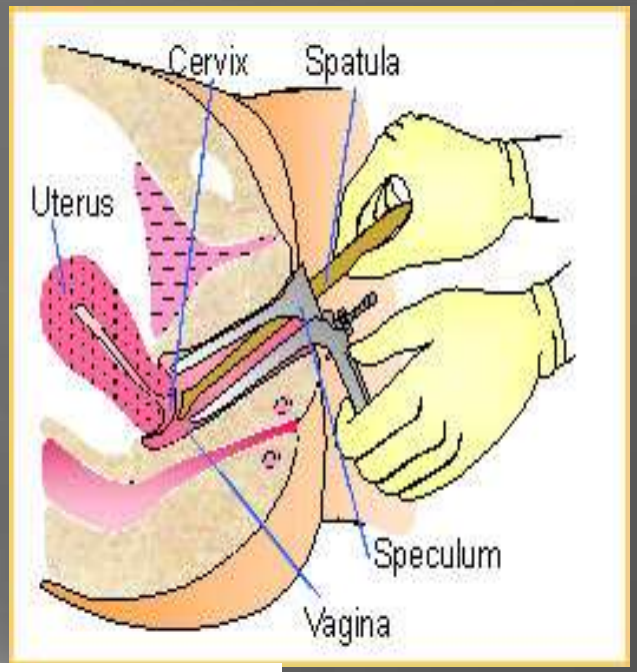
- 2- Examination:
- Mainly vaginal examination using cuscu's speculem nothing is found in early stage .
- Mass ,ulcerating fungating in the cervix
- P/V P/R is mandatory to determine the stage .

Diagnosis

- Colposcopy
  - Cervix is viewed through a colposcope and the surface of the cervix can be seen close and clear.
- Cervical Biopsies
  - Colposcopic biopsy – removal of small section of the abnormal area of the surface.
  - Endocervical curettage – removing some tissue lining from the endocervical canal.
  - Cone biopsy – cone-shaped piece of tissue is removed from the cervix


Cytology
Histology
Colposcopy


WelchAllyn ZoomScope


Cervix
Spatula
Uterus
Speculum
Vagina

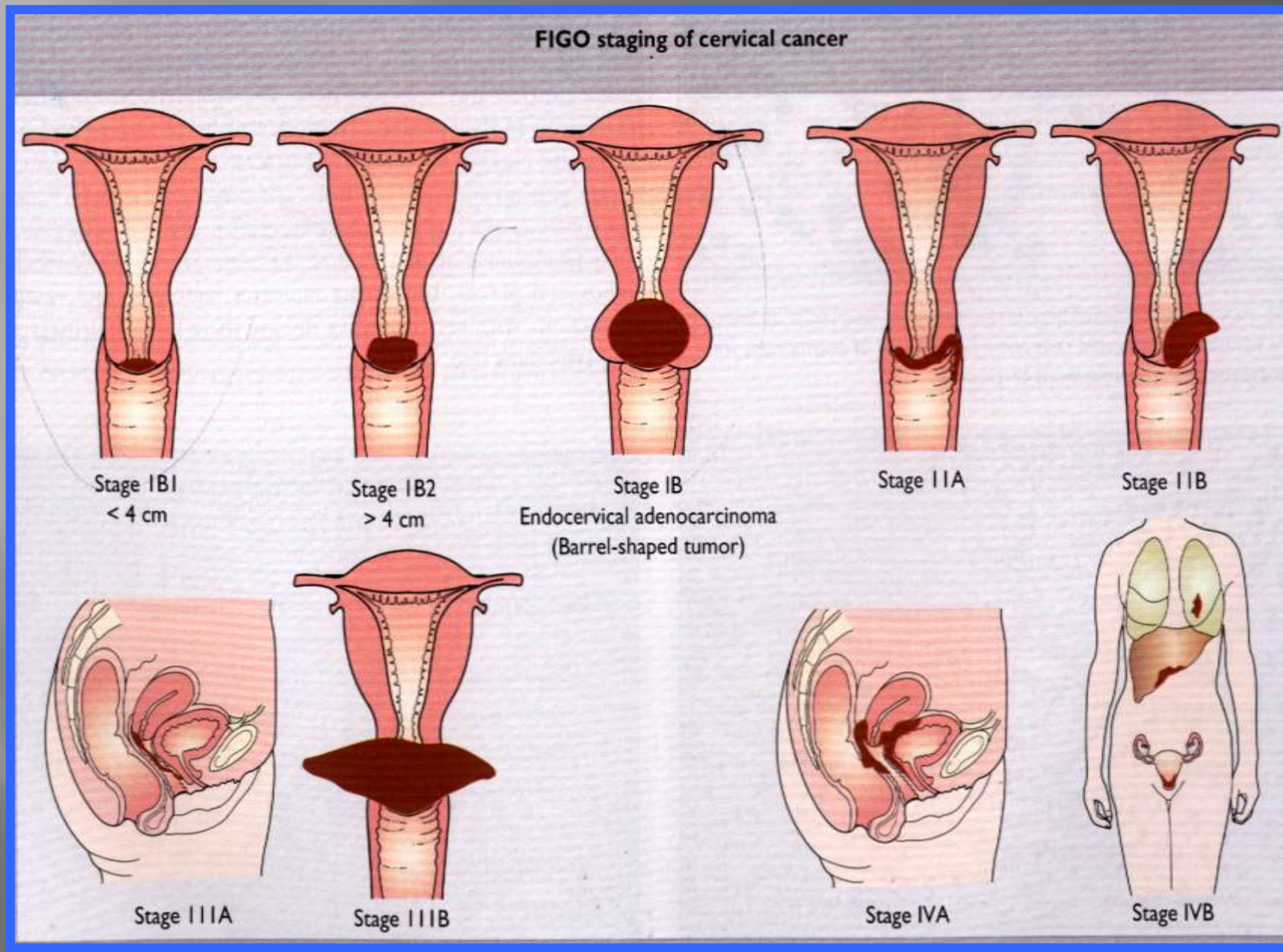
Staging is CLINICAL

- FIGO System (International Federation Of Gynecology and Obstetrics)
- Has five stages – 0 to 4
  - Stage 0 Carcinoma in situ
  - Stage 1 Invaded cervix, but has not spread.
  - Stage 2 Has spread to nearby areas, not leaving pelvic area.
  - Stage 3 Cancer has spread to the lower part of the vagina.
  - Stage 4 Cancer has spread to nearby organs; metastasis.

Staging

- Best to follow FIGO system.
- Examination under anaesthesia.
- Bimanual palpation.
- P/V, P/R.
- Cervical biopsy, uterine biopsy.
- Cystoscopy, Proctoscopy, if necessary.

- **Carcinoma of the Cervix**
- IA1 Confined to the cervix, diagnosed only by microscopy with invasion of < 3 mm in depth and lateral spread < 7 mm
- IA2 Confined to the cervix, diagnosed with microscopy with invasion of > 3 mm and < 5 mm with lateral spread < 7mm
- IB1 Clinically visible lesion or greater than A2, < 4 cm in greatest dimension
- IB2 Clinically visible lesion, > 4 cm in greatest dimension
- IIA1 Involvement of the upper two-thirds of the vagina, without parametrial invasion, < 4 cm in greatest dimension
- IIA2 > 4 cm in greatest dimension
- IIB With parametrial involvement
- IIIA/B Unchanged
- IVA/B Unchanged


FIGO staging of cervical cancer
Stage IB1
< 4 cm
Stage IB2
> 4 cm
Stage IB
Endocervical adenocarcinoma
(Barrel-shaped tumor)
Stage IIA
Stage IIB
Stage IIIA
Stage IIIB
Stage IVA
Stage IVB

Preoperative evaluation

- Review history.
- General examination:
  - Anaemia.
  - Lymphadenopathy-Supraclavicular LN.
  - Renal area.
  - Liver or any palpable mass.
  - Oedema.
- Laboratory tests:

- CBC, LFT, KFT, Urine analysis.
- Tumor markers.
- Chest X- ray, abdominal X- ray, IVU.
- CAT, MRI, if necessary.
- Ultrasound.
- Lymphography, if necessary.

SPREAD:

Direct	Lymphatic	Dissemination (late)
- Uterus. - Vagina. - Parametrium. - Bladder and rectum.	A- primary node: parametrial. Paracervical. Vesicovaginal. Rectovaginal. Hypogastric. Obturator and external iliac B-Secondary nodes: Common iliac Sacral Vaginal Paraortic Inguinal.	- Parametrial spread causes obstruction of the ureters, many deaths occur due to uremia. - Obstruction to the cervical canal results in pyometria.

Survival Rate

- 5-year survival rate is 92% for earliest stage
- 71% for all stages combined

Treatment

- Surgery
  - Pre-invasive cervical cancer
    - Cryosurgery
    - Laser surgery
    - Conization
  - Invasive cervical cancer
    - Simple hysterectomy
      - Removal of the body of the uterus and cervix.
    - Radical hysterectomy and pelvic lymph node dissection
- Radiation
- Chemotherapy

COMPLICATIONS OF SURGERY

- Haemorrhage: primary or secondary.
- Injury to the bladder, uerters.
- Bladder dysfunction.
- Fistula.
- Lymphocele.
- Shortening of the vagina.

The choice of treatment will depend on

- Fitness of the patients
- Age of the patients
- Stage of disease.
- Type of lesion
- Experience and the resources avalible.

Surgery offers several advantage

- It allows presentation of the ovaries (radiotherapy will destroy them).
- There is better chance of preserving sexual function.
- (vaginal stenosis occur in up 85% after radiation.
- Psychological feeling of removing the disease from the body .
- More accurate staging and prognosis

- INDICATIONS OF P/O XRT FOLLOWING WERTHEIM'S HYSTERECTOMY (STAGE I , IIa):

- Positive pelvic lymph nodes.
- Tumour close to resection margins and/or parametrial extension.

Radiotherapy

- Stage IIb and III
- Radical Radiotherapy
- External irradiation (Teletherapy).
- Intracavitary radiation (Brachytherapy).
- In some cases of stage IIa or b radio and chemotherapy to be given then followed by simple hysterectomy -------

PROGNOSIS

- Depends on:
  - Age of the patient.
  - Fitness of the patient.
  - Stage of the disease.
  - Type of the tumour.
  - Adequacy of treatment.

MANAGEMENT OF RECURRENT DISEASE

- 1. Local recurrence:
  - Radiation – if not used.
  - Pelvic exenturation.
- 2. Distant disease
  - Chemotherapy.

- Glandular tumours (adenocarcinomas) are not detectable by screening are associated with skip lesions and require radical surgery.

Follow up policy

- On completion of treatment all patients are given a vaginal dilator to use until vaginal mucosa healed, this prevents vaginal stenosis.
- Premenopausal patients commenced on HRT:
- post hysterectomy-Extraderm skin patches 50 meg twice weekly.
- No hysterectomy- Cycloprogyn 1mg daily.
- The patient to be seen 1/12 post-treatment.
- 3 monthly for 2 years.
- 4 monthly for 3rd year.
- 6 monthly until 5years.
- Then yearly all her life.
- Patients with stage I and II disease treated with radical radiotherapy will be assessed by EUA approximately 3 months after completing treatment.

- THE OVERALL 5 YEARS SURVIVAL FOLLOWING THERAPY:

- Stage I -------80%
- Stage II-------50-60%
- Stage III-------30-40%
- Stage IV-------4%

What's new in cervical cancer research and treatment?

- HPV test
- HPV vaccine
- Radical trachelectomy procedure
- Other clinical trials