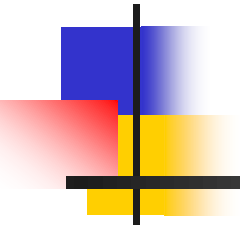


Cervical pathologies benign , premalignant and malignant cervical diseases

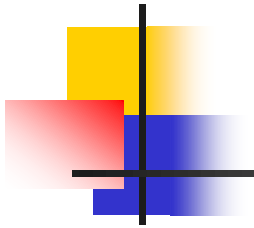
Introduction and learning objectives:

- squamocolumnar junction (SCJ)
- cervical metaplasia
- Transformation zone
- Nabothian follicle
- Polyp
- CIN??

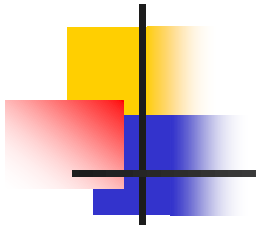
ENDOCERVICAL POLYPS

- endocervical polyps is common and usually increases with age up to the menopause.
- Occasionally these polyps will be symptomatic producing heavy vaginal discharge or bleeding upon coital contact.
- Histology of these polyps consist of columnar epithelium sometimes with squamous metaplasia across its tip
- Malignant change **is most unusual**. However, if these polyps are removed by polypectomy, tissue should be sent for histology.

PREMALIGNANT CONDITIONS OF THE CERVIX



- cervical cancer is a common cancer affecting women.
- the estimated prevalence of HPV in cervical cancers is 99.7 %.
- about 200 000 women die each year from the disease, most of them in developing countries?? Why?



- The disease has a relatively long natural history, and intervention and treatment in the premalignant phase is highly effective.
- The accessibility of the cervix and the availability of a simple test for the presence of pre-malignancy make it suitable for screening.

Terms and explanations:

Squamo-columnar junction (SCJ):

Where squamous and columnar tissue meet; this is not fixed, but is affected by metaplasia

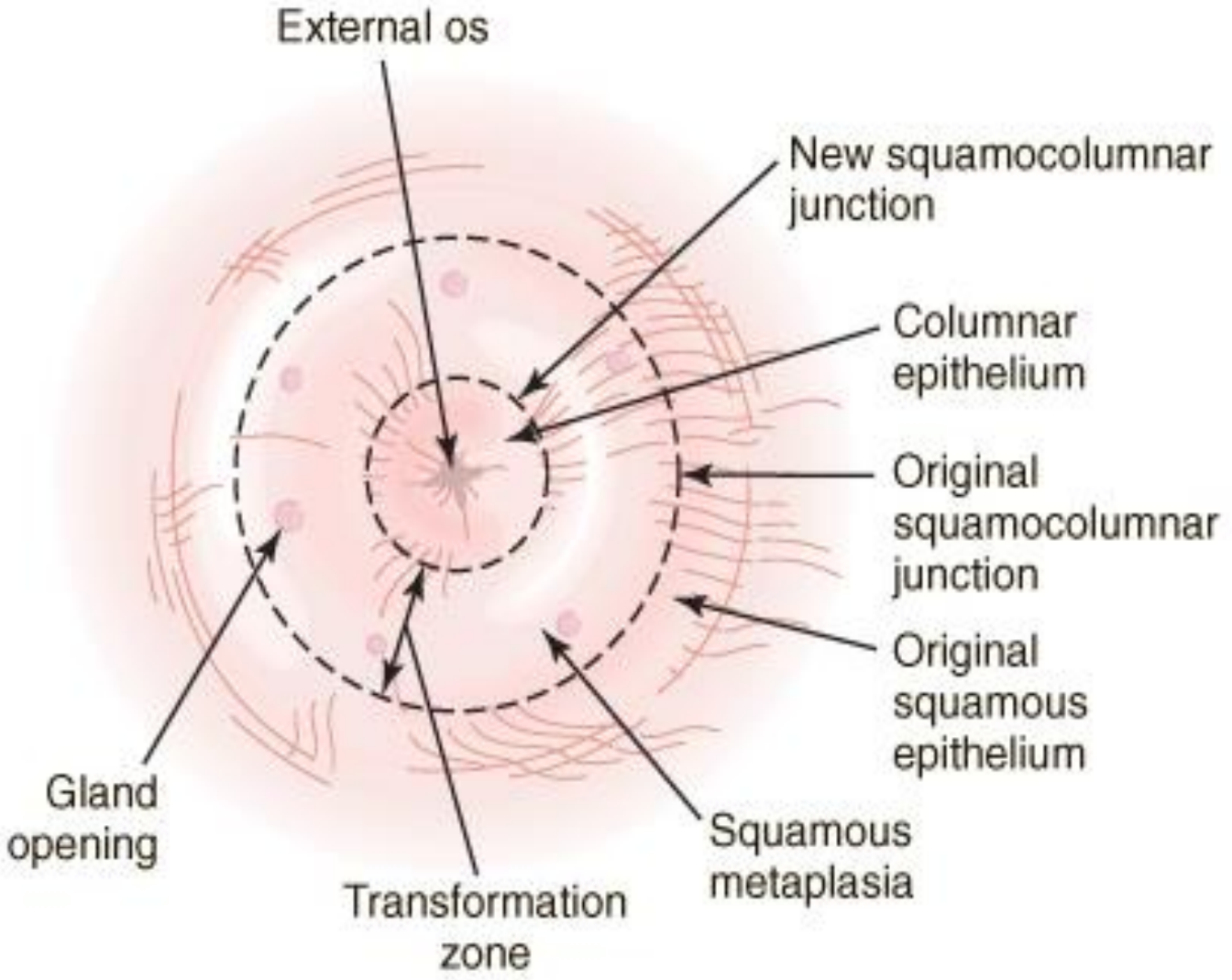
Metaplasia:

A physiological process whereby columnar epithelium is replaced by squamous tissue in response to the acid environment of the vagina

Transformation zone:

That area on the cervix that has undergone metaplasia; it is bounded by the original SCJ and the present SCJ

Transformation zone



TERMS AND DEFINITIONS:

Dyskaryosis:

A cytological term describing the cellular and nuclear abnormalities not synonymous with dysplasia

Dysplasia:

A histological term describing architectural abnormalities within tissue

CIN

Cervical intraepithelial neoplasia, graded 1–3 depending on severity: CIN I, CIN II, CIN III

LSIL

Low-grade squamous intraepithelial lesion – Bethesda system grade equating to CIN1

HSIL

High-grade squamous intraepithelial lesion – Bethesda system grade equating to moderate and severe / CIN2 and CIN3

premalignant cervical conditions (**dysplasia**) CIN

- The process of metaplasia can be disrupted by external influences and can lead to disordered squamous epithelium called dysplastic epithelium.
- Dysplastic epithelium lacks the normal maturation of cells as they move from the basal layer to the superficial layer.
- The nuclei tend to be larger, more variable in size and shape and more actively dividing than in healthy squamous epithelium.

aetiology

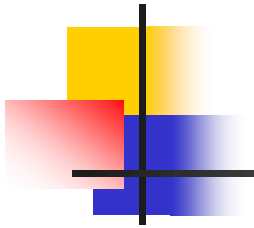
1- HPV is implicated in this process, although HPV infection alone does not appear to be sufficient to cause dysplasia,most of infections resolved spontaneously within 2 years.

2- Smoking?? Depressed local immunity

3- immune suppression appear to be additional factors which may act as co-agents, renal transplant and HIV.

HPV infection prevalence

- Genital HPV infection is extremely common with up to 80 per cent of sexually active women being HPV positive at some point during their lifetime.
- 90 % of women will clear the infection within two years depend on the host immunity



- With approximately 15 % prevalence of the oncogenic HPV types 16 and 18, 31, 33.
- The majority of HPV infections result in CIN 1 and 60 % of these will regress without the need for treatment, while approximately 10 per cent will progress to high-grade lesions.
- The estimated prevalence of HPV DNA in cervical cancers is 99.7 per cent.

Dysplasias (cervical intraepithelial neoplasia) (CIN):

They are graded as mild, moderate or severe, depending on the degree of cytological atypia and also the thickness of the epithelium involved.

CIN grades:

1- CIN I affects only the deepest third of the epithelium from the basal layer upwards, with maturation seen more superficial to that.

2- CIN II affects two-thirds of the thickness of the epithelium,

3- CIN III shows no maturation throughout the full thickness, it is severe dysplasia/ or called carcinoma in situ.

(risk factors for cervical carcinoma and need to be screened)

1- early marriage.

2- multiple sexual partners.

3- liberal sex.

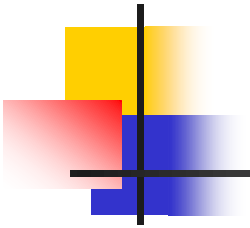
4- young age at 1st pregnancy.

5- high parity.

6- lower socioeconomic status.

7- smoking.

8- immune compromised women



How can we prevent or reduce the high grade disease and cervical cancer??

Cervical screening programs:

- a screening test is not diagnostic, but identifies a subgroup of the reference population at increased risk of the disease for which further tests should be carried out. Screening is always determined by sensitivity and specificity of screening tests. In this case, the reference population being screened comprises healthy, asymptomatic women.

Cervical screening programmes

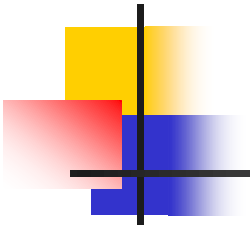
- in underdeveloped countries 75% of the cases of cervical cancer present with an advanced stage, while in the developed countries 75% of the cases present early and cure can be expected.
- the screening program should cover the at-risk population women between the ages of 25 and 64 to offer cervical cytology screening every 3–5 years.

HPV vaccination (to prevent cervical cancer)

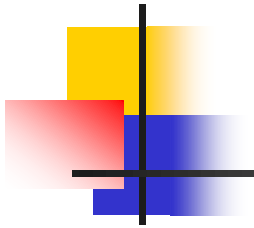
- up to 70 per cent of cervical cancers are the result of infections caused by either HPV16 or 18, there is an expectation that a vaccination programme, if systematically applied, will result in a significant reduction of invasive and pre-invasive disease
- Two types of vaccines, directed against HPV 6, 11, 16 and 18.
- both types of vaccine effectively increase specific IgG, reduce or eliminate HPV infection, and effectively eliminate pre-invasive disease.

Screening by cervical cytology (pap smear):

- technique developed by Papanicolaou to collect the cells that had been shed from the skin of the cervix, spread them on a glass slide and stain them using a specially developed technique.
- Exfoliated cells are collected by vaginal wash or by scraping the cervix by a wooden spatula (Eyre's)

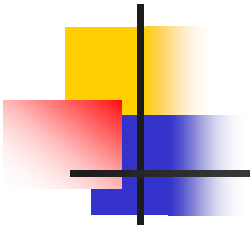


- the ‘Pap’ smear has been replaced by liquid-based cytology where a small brush is used to sample cells from the transformation zone and the brush head placed in a fixative
- This is then spun down and then the cellular aspect of the specimen examined cytologically.



- An abnormal smear can show cells in different degrees of maturity (dyskaryosis).
- cells can be classified as low grade (mild dyskaryosis and borderline change) or high grade (moderate and severe dyskaryosis)

- **The sensitivity of the cervical smear in picking up women with CIN is around 70 %;** however, as there is slow progression for most women with CIN to cancer, if a lesion is missed then this should be picked up on a subsequent smear.



- Liquid based cytology reduces the proportion of inadequate smears and increases the detection of true dyskaryosis.

Management of abnormal cervical smears

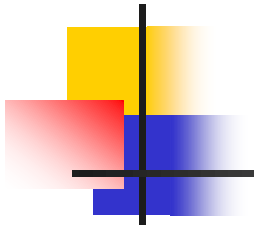
Ideally all women with abnormal cervical cytology should have colposcopic assessment.

- It was shown that the percentage of women found with high-grade CIN after a mild dyskaryotic smear is about 40 %.

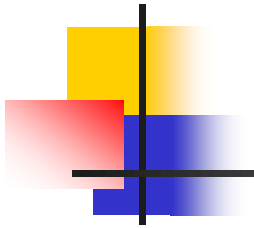
Colposcopy

Colposcopy is a system of low power magnification, (binocular operating microscope with magnification of between 5 and 20 times). **It has been used to examine the cervix in detail to identify CIN and pre-clinical invasive cancer**

- The cervix is first examined at low magnification (×4–6).
- A saline-soaked cotton-wool ball is then applied, which moistens the epithelium, allowing the underlying blood vessels to be examined under higher magnification (preferably ×16 or more).



- A green filter may be used as it makes the capillaries visible more clearly.
- The shapes of the capillaries are studied and the intercapillary distances estimated



Application of 3-5 percent acetic acid to the cervix highlights CIN areas as white areas compared to pinkish normal areas

(dehydration of cytoplasm or denaturation of nuclear protein)??

Schiller's test

- the application of Lugol's iodine solution to the ectocervix. The normal squamous epithelium will stain dark brown because it contains abundant glycogen, whereas columnar epithelium, abnormal squamous epithelium and immature normal squamous epithelium **will not stain brown (called Schiller positive)**

Abnormal colposcopic findings are: **(very important)**

1-Acetowhite epithelium

2-abnormal subepithelial capillary pattern

*mosaicism and punctation are features of CIN.

*Abnormal branching vessel Bezarre shape vessels are suggestive of micro invasive carcinoma.

Follow up of treated women

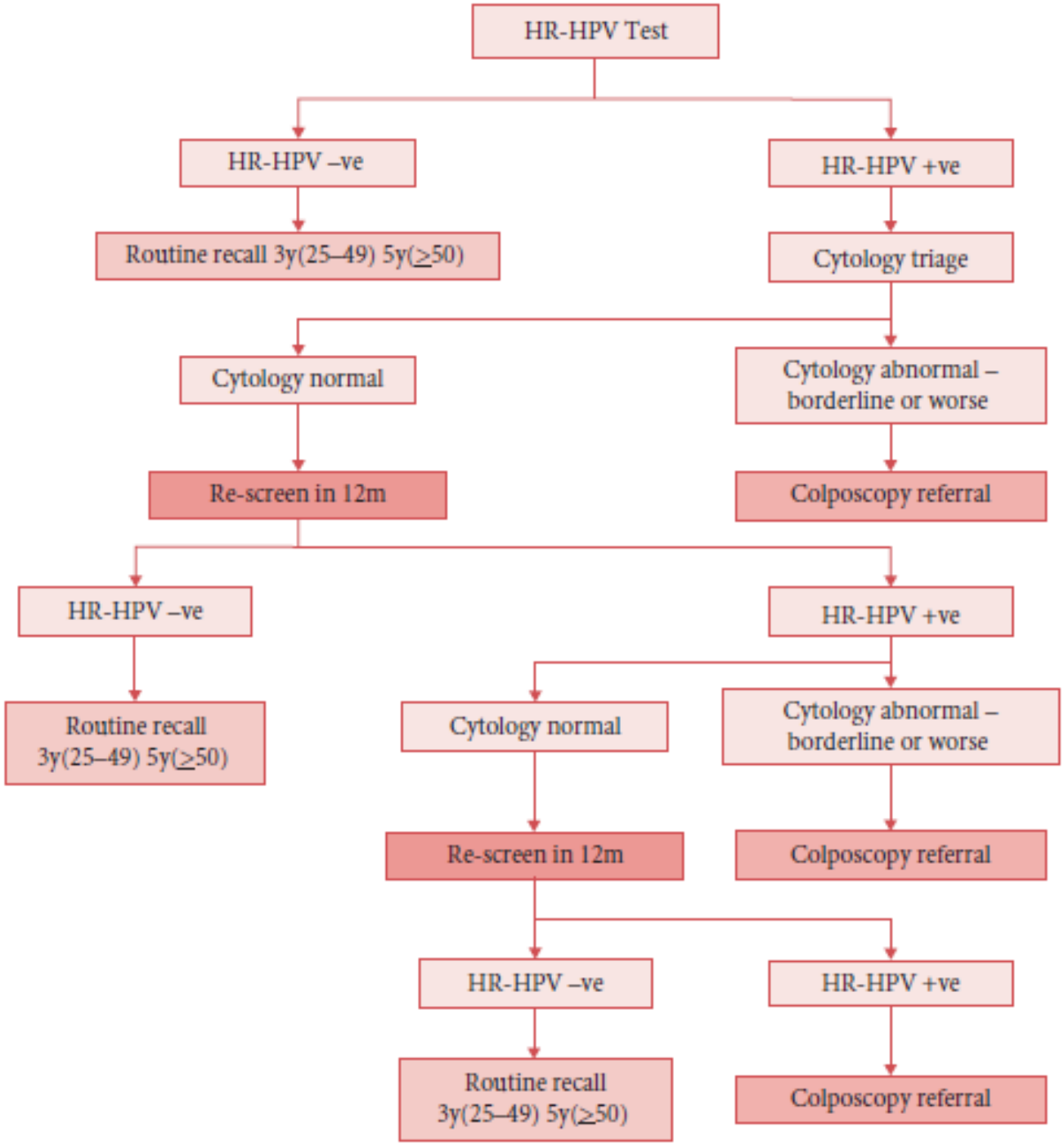
- Low-risk follow up: Women treated for low-grade disease require 6-, 12- and 24-month follow-up cytology. If all are negative, then the patient may be discharged to three to five-yearly routine screening cytology.

Follow up of untreated women

- the positive predictive value for distinguishing low- from high-grade lesions is only 57 per cent.
- Therefore, follow up is warranted as a result of the inherent poor colposcopic discrimination between high- and low-grade lesions

cervical screening programme: HPV primary screening algorithm

NHS



TREATMENT OF CIN

two main methods of treatment are:

1- ablative techniques

2- excisional techniques

The success of treatment is usually defined as negative cytology six months following intervention

the ablative and excisional methods achieve cure (or success) rates of 90–98%

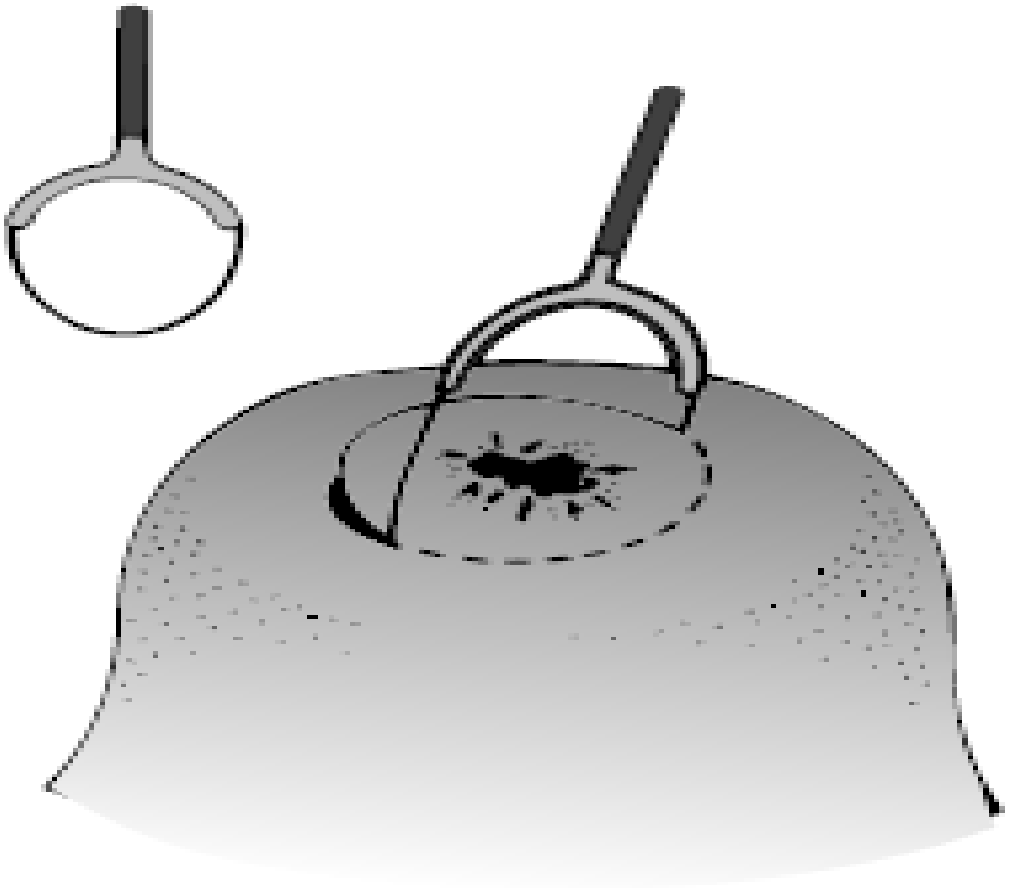
TREATMENT OF CIN

Excisional techniques	Ablative techniques
LLETZ – removal of the transformation zone using an electrodiathermy loop; requires local or general anaesthesia	**Radical electrodiathermy** – burning the transformation zone; usually requires general anaesthesia
Laser cone – removal of the transformation zone using the laser; requires local or general anaesthesia	**Cold coagulation** – destroying the transformation zone by applying a probe heated to 100–120°C; usually requires local anaesthesia
Knife cone biopsy – taking a cone with a knife; usually requires general anaesthesia	**Cryocautery** – freezing the tissue; does not require any anaesthesia
Hysterectomy – may be suitable if the woman has other gynaecological problems	**Laser** – vaporizing the tissue; requires local or general anaesthesia

Depth of destruction:

- The depth of destruction of any local treatment modality is important.
- Ablation to a depth of 5–8 mm has been recommended for erradication of the disease.

LLETZ

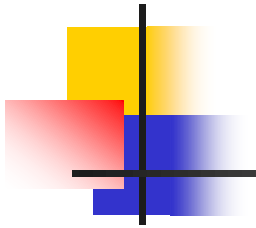


TREATMENT FAILURES

- The primary objective of treating women with CIN is to prevent invasive cervical cancer.
- women who have been treated for CIN need long-term follow-up.
- Colposcopic assessment is technically more difficult in those that have undergone previous treatment

Carcinoma of the cervix

By
Dr Suhaila Al-Shaikh



- Carcinoma of the cervix is the second commonest cancer among women worldwide, with only breast cancer occurring more commonly.
- cervical cancer accounts for about 500,000 new cases diagnosed and > 200,000 deaths every year.
- Of the new cases, 80% occur in the less developed countries

Aetiology

- Cervical cancer is of unknown aetiology
- HPV types 16 and 18 are the most commonly associated with cervical cancer
- The association between HPV infection and cervical cancer has led to the development of vaccines both to prevent and to treat this disorder and

risk factors for cervical carcinoma

- 1- HPV infection.
- 2- early marriage.
- 3- multiple sexual partners.
- 4- liberal sex.
- 5- young age at 1st pregnancy.
- 6- high parity.
- 7- lower socioeconomic status.
- 8- smoking.

Clinical presentation

*In early disease: asymptomatic 20%

*In more advanced disease:

1- post-coital bleeding,

2- intermenstrual or postmenopausal bleeding.

3- offensive blood- stained vaginal discharge (may be profuse).

4- If there is abnormal bleeding during pregnancy, then a cervical lesion needs to be excluded.

Clinical presentation:

In some women presenting with late disease: there may be

1- backache,

2- leg pain,

3- leg oedema,

4- haematuria,

5- bowel changes,

6- malaise,

7- weight loss.

Diagnosis

1- A full history

2- clinical examination.

atypical consistency on bimanual examination.

if the tumour is large it may look like a friable polyp or an ulcerated area that bled on contact, or If the referral is due to cervical cytology suspicious of invasion, then

3- a colposcopic examination should be performed.

4- Definite diagnosis is based on histological study of appropriately taken biopsies.

Suspicious features at colposcopy:

- 1- intense acetowhiteness,
- 2- atypical vessels,
- 3- raised/ulcerated surface.

Histology

1. **Squamous cell carcinoma (80–85%)**
2. **the remainder is adenocarcinoma,**

   and adenocarcinoma elements has been rising.

1. **Rarer histological types include clear cell, lymphomas**

   and sarcomas

Spread

Carcinoma of the cervix may spread by:

1- direct infiltration

2- via the lymphatic vessels.

The direct spread:

a- downwards into the vaginal wall,

b- forward into the bladder,

c- laterally into the parametrium

Lymphatic spread

- **Lymphatic spread occurs outwards in the parametrium to:**

1- the external and internal iliac nodes

2- the common iliac

3- and para-aortic nodes.

a- infra-mesenteric b- infra-renal

Blood spread occurs late in the disease.

Staging:

Staging is ***clinical process*** including assessment of disease extent and sites of spread. although early cancers are staged according to the ***surgical specimen.***

Why the disease is staged?

1) **the treatment can be planned appropriately.**
2) **give an idea of prognosis.**

Clinical assessment and investigations for evaluation of the stage:

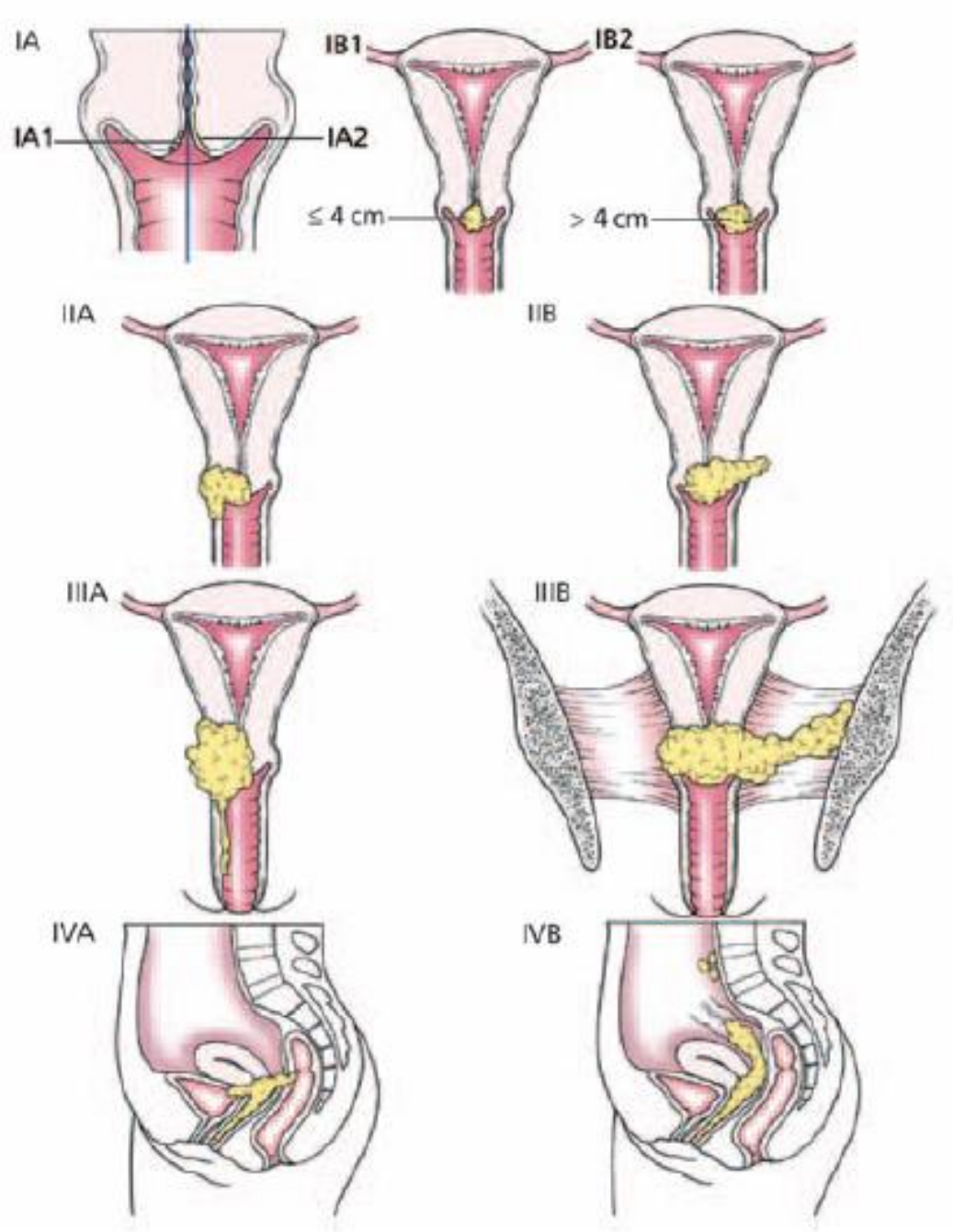
- **Examination under anaesthesia, a combined recto-vaginal assessment.**
- **Biopsy of the suspicious area.**

  1- wedge or

  2- cone shaped to obtain sufficient material for histological assessment.
- **Cystoscopy.**
- **Sigmoidoscopy.**
- **CXR and IVU.**
- **Other imaging as indicated such as:**

  Computerized axial tomography (CT) scan and Magnetic Resonance Imaging (MRI) Scan

stages

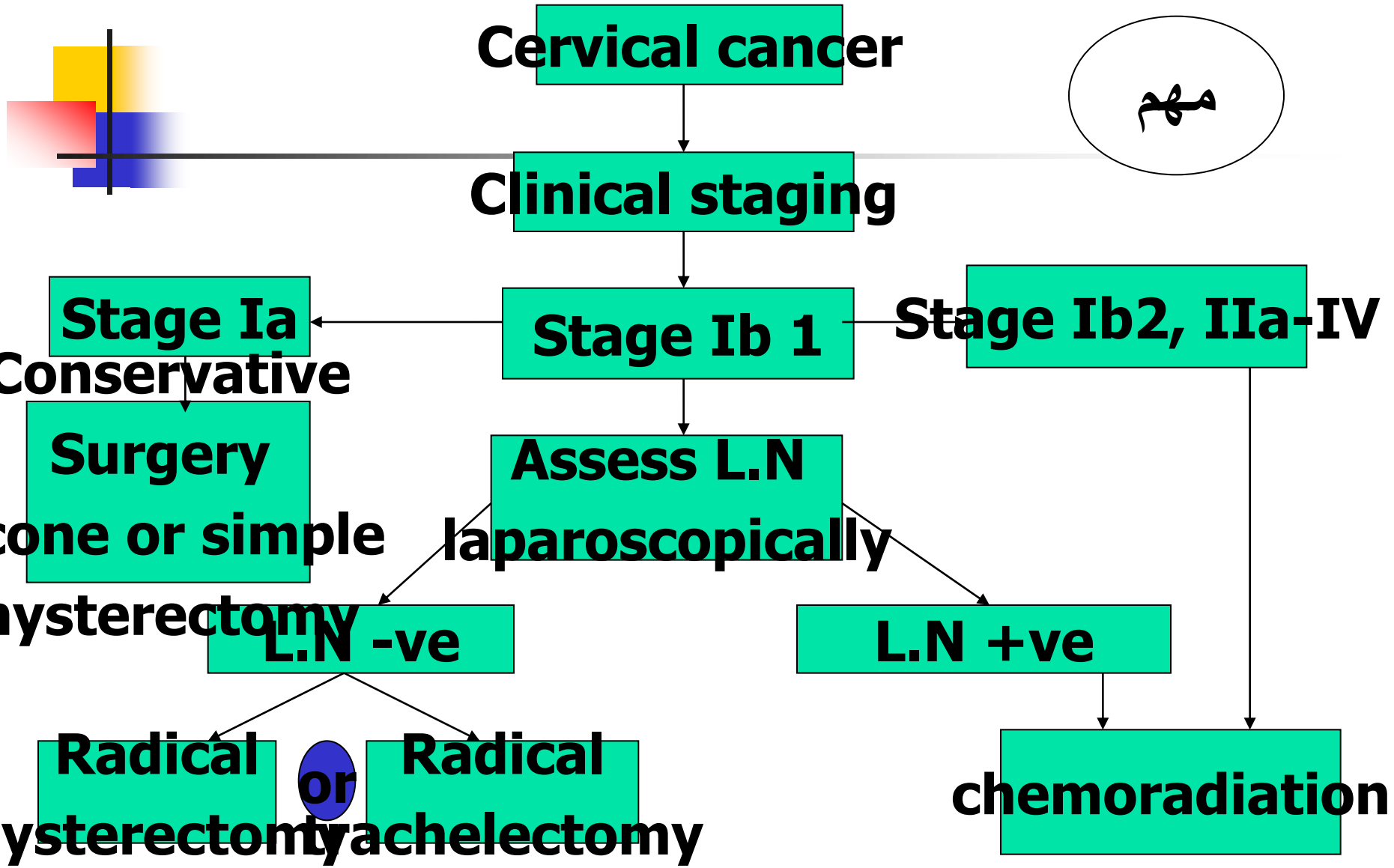


stages

- Stage 0 Carcinoma in situ, cervical intraepithelial neoplasia grade III
- Stage I The carcinoma is confined to the cervix.
- IA Invasive carcinoma (microscopical) stromal invasion is less than 5 mm and extension is less than 7 mm.
- IB Clinically visible lesions (macroscopical) or preclinical cancers greater than stage IA
- Stage II Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
- IIA No obvious parametrial involvement
- IIB Obvious parametrial involvement

- **Stage III The carcinoma has extended to the pelvic wall. On rectal examination, there is no cancer-free space between the tumour and the pelvic wall. The tumour involves the lower third of the vagina. All cases with hydronephrosis.**
- **IIIA Tumour 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**
- **Stage IV The carcinoma has extended beyond the true pelvis or has involved (biopsy-proven) the mucosa of the bladder or rectum.**
- **IVA Spread of the growth to adjacent organs**
- **IVB Spread to distant organs**

Flow chart showing management of cervical cancer



surgery

- **Cone surgery**
- **Simple hysterectomy**
- **Fertility sparing surgery (Radical trachelectomy) in those with L.N – ve :**

  removal of the cervix, parametrium, upper 1/3 of the vagina

Treatment:

- **For stage 0 local excision or ablation.**
- **stage 1 preclinical (microinvasive) the treatment is conservative by local excision (a colposcopically directed)**
- **If deep infiltration in > than (stage 1 a) more radical surgery or radical radiotherapy is needed.**
- **for premenopausal women, surgery offer lower morbidity (conserve the ovaries) and avoid sexual dysfunction.**
- **The optimal treatment is that obtain the highest cure rate and the least associated morbidity**

Surgery

Wertheim hysterectomy (radical hysterectomy):

which involves removal of (the uterus, the paracervical tissues surrounding the cervix, the upper vagina, the pelvic lymph nodes,

both tubes +\ - ovaries).

- **the ovaries may be conserved in young woman with SCC. Risk of metastasis is 1%**

Radiotherapy

involves the use of:

1- external beam therapy (teletherapy) to shrink the central carcinoma and also to treat the possible sites of regional metastasis.

2- Internal sources (brachytherapy) are then placed in the upper vagina and within the

Complications

1- some damage to the bladder and bowel is inevitable,

diarrhoea during treatment is usual, and is resolved after treatment is finished.

2- A radiation menopause is induced in premenopausal women.

3- some loss of elasticity within the vagina, may lead to loss of sexual

palliative treatment radiotherapy

In advanced cancer of the cervix, radiotherapy is palliative treatment:

1- to reduce pain, vaginal bleeding and discharge

2- to assist in local control of the disease.

Chemotherapy

Chemotherapy

(Platinum based) used as adjuvant therapy with other modalities in more advanced disease.

Carcinoma of the cervix and pregnancy

1- In early pregnancy, external irradiation may be given; abortion of a dead fetus will follow and then local irradiation with caesium can be given.

2- Later in pregnancy, the uterus must be emptied by hysterotomy or Caesarean section followed by radiotherapy.

Sometimes Wertheim hysterectomy at the time of Caesarean section is done

Survival

Survival is stage dependent and the advanced stages are associated with a poor prognosis. The relative survival rate for all women treated for invasive cervical cancer is 64%.

***The 5-year relative survival rates is:**

L.N +ve has 46% while L.V –ve has 90%

83% for stage I,

65% for stage II,

KEY POINTS

- Early micro-invasive disease can be treated by cone biopsy or excisional treatment alone [C].
- Surgery and radiotherapy for stage IB/IIA disease have similar five-year overall and disease-free survival rates, but women who have had surgery and adjuvant radiotherapy combined have significantly higher morbidity than those who have had either surgery or radiotherapy alone [B].
- Pre-operative imaging with MRI scans reduces the number of women undergoing both modalities of treatment [C].
- Chemoradiation increases survival over radiotherapy alone for advanced disease, but toxicity is increased [B].