



Invasive Cancer of Uterine Cervix

SAMIR FOUAD ABD EL AZIZ MD
PROFESSOR OB.GYN
AL-AZHAR UNIVERSITY
PRESIDENT
WWW.ARABICOBGYN.NET

Invasive Cancer of Uterine Cervix

- ∞ **Cervical cancer is one of the most common cancers, accounting for 6% of all malignancies in women.**
- ∞ **Worldwide, cervical cancer is second only to breast cancer in incidence and mortality.**
- ∞ **More than 471,000 new cases are diagnosed each year**

Incidence

- ∞ In white women the incidence varies between 8.7/100.000 for women younger than 50 years to 17.7/100.000 for those above 50 years.
- ∞ In black women the incidence varies between 6.9 to 36.9/100.000.
- ∞ This racial difference is poorly understood

Mortality

- ∞ Mortality in white women ranged between 3 to 8.4/100.000
- ∞ In black women mortality ranged between 2.6 to 20.5/100.000

Survival

∞ The overall survival rate is 67%. The highest survival rates are among young white women aged under 50 years while the lowest survival rates are among black women older than 50 years

Risk Factors

- ⌚ **Strong risk factors for cervical cancer**
- ⌚ **Early age at first intercourse(<16ys)**
- ⌚ **history of multiple sexual partners**
- ⌚ **history of genital HPV infection or other STD**
- ⌚ **prior squamous intraepithelial lesion**

Risk Factors (cont.)

- ∩ Additional risk factors include:
- ∩ active or passive smoking
- ∩ Oral contraceptive pills
- ∩ Immunodeficiency or HIV positivity
- ∩ poor nutrition

Smoking and cervical cancer

- ∩ Cancer cervix increase 2-fold in women actively or passively exposed to environmental smoking
- ∩ biochemical evidence
- ∩ Molecular studies
 - ∩ 1)direct carcinogenic
 - ∩ 2)cocarcinogenic
 - ∩ 3)Local immunosuppressive effect

Oral Contraceptive and cervical cancer

- ∴ There is some evidence that long-term use of OCs may increase the risk of cervical cancer.
- ∴ Studies conducted by NCI and other centers support a relationship between extended use of pill (5 or more years) and a slightly increased risk of cervical cancer

Ocs and cancer cervix (cont.)

- ∞ The exact nature of the association between Ocs and cervical cancer still unclear.
- ∞ Oral contraceptive products have been revised to warn of the possible risk of cervical cancer
- ∞ Women taking Ocs are advised to have Pap smear annually

Nutritional Factors

- ∞ **Nutritional factors have been implicated in 60% of cancers in females and 40% of cancers in males**
- ∞ **Some studies showed decreased incidence of cancer cervix with increased dietary intake of vit.A, carotenoids, vit.C, folic acid.**

Reproductive Factors

∞ No association between the risk of cancer cervix and reproductive parameters including: age at menarche, age at menopause, age at 1st. live birth, age at last live birth, no. of abortions

Human papiloma Virus

More than 80 types of HPV are known and some of them are associated with high incidence of cancer cervix e.g. types 16, 18, 34.. And usually cause flat papiloma which could not be seen by naked eye, unlike the benign warty lesions caused by types 6 and 11.

Cellular Classification

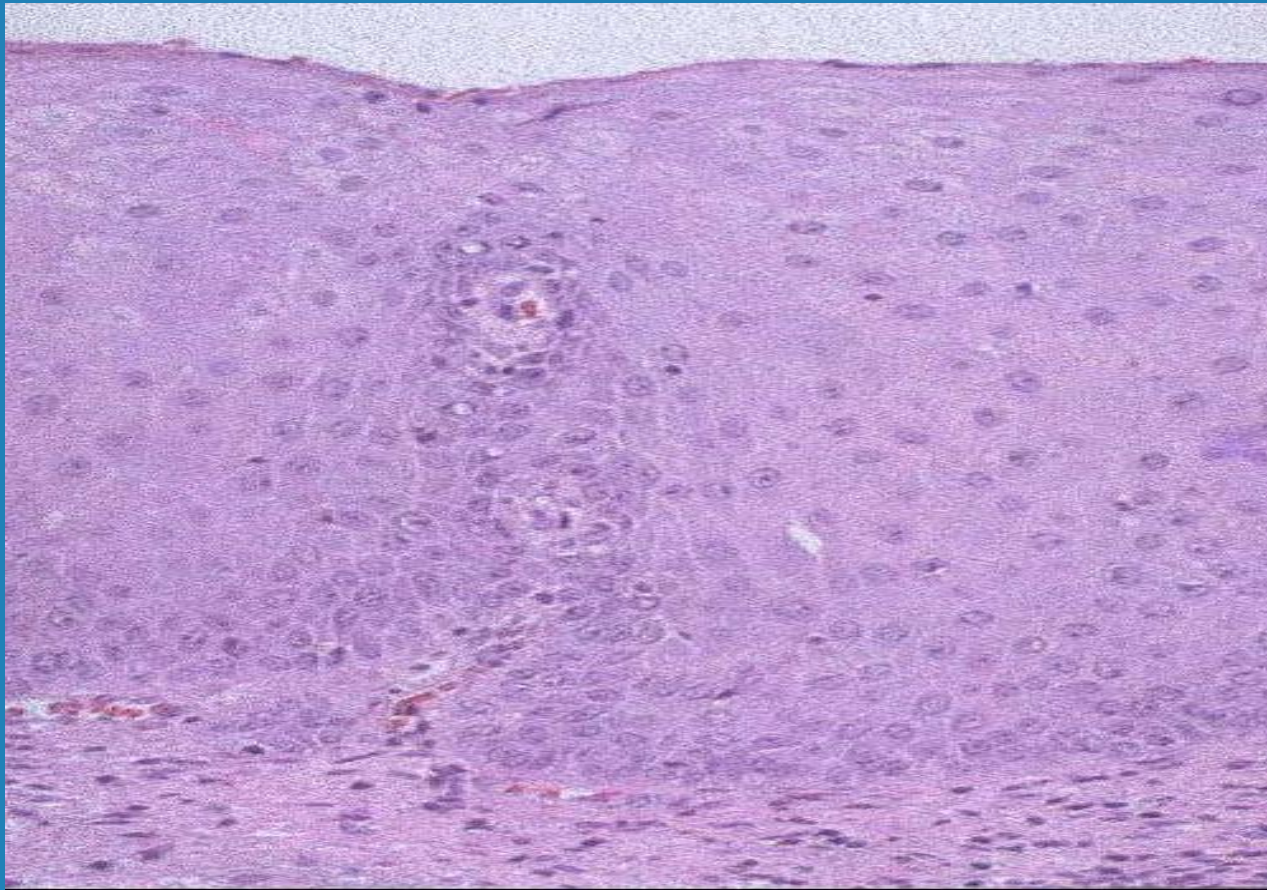
- ∞ Squamous cell carcinoma comprises 90% of cases and adenocarcinoma comprises about 10%.
- ∞ adenosquamous, small cell carcinoma are rare tumors,
- ∞ sarcoma and lymphoma occasionally reported

Origin of cancer cervix

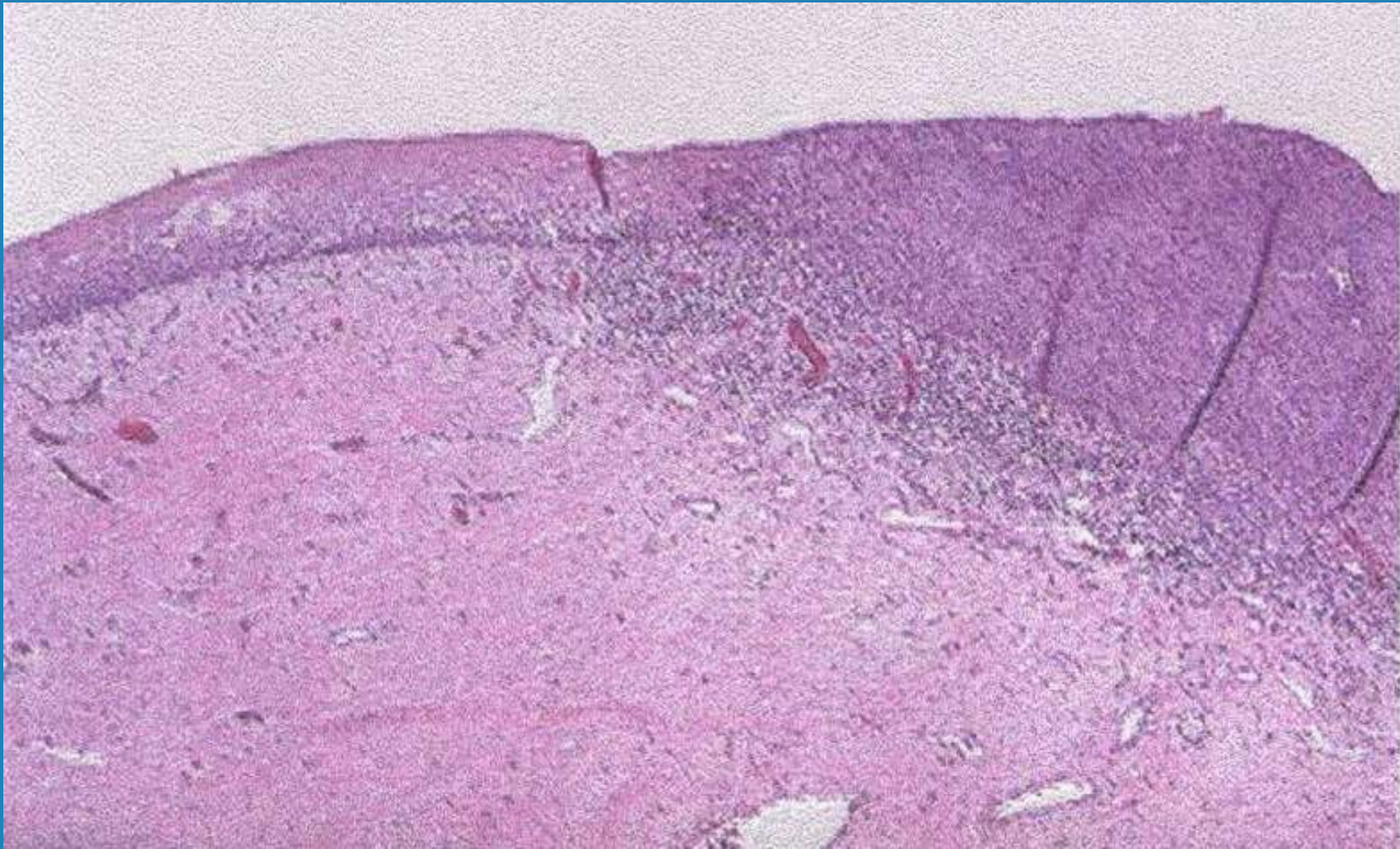
∞ The squamous cell carcinoma originate at the SCJ . The precursor lesion is CIS which if untreated develop into invasive cancer in 30-70% (over 10-12 years). However, in 10% of cases CIS develop into invasive cancer in less than one year

M.P. Normal SQ.Epith

♂ Normal sq.cell



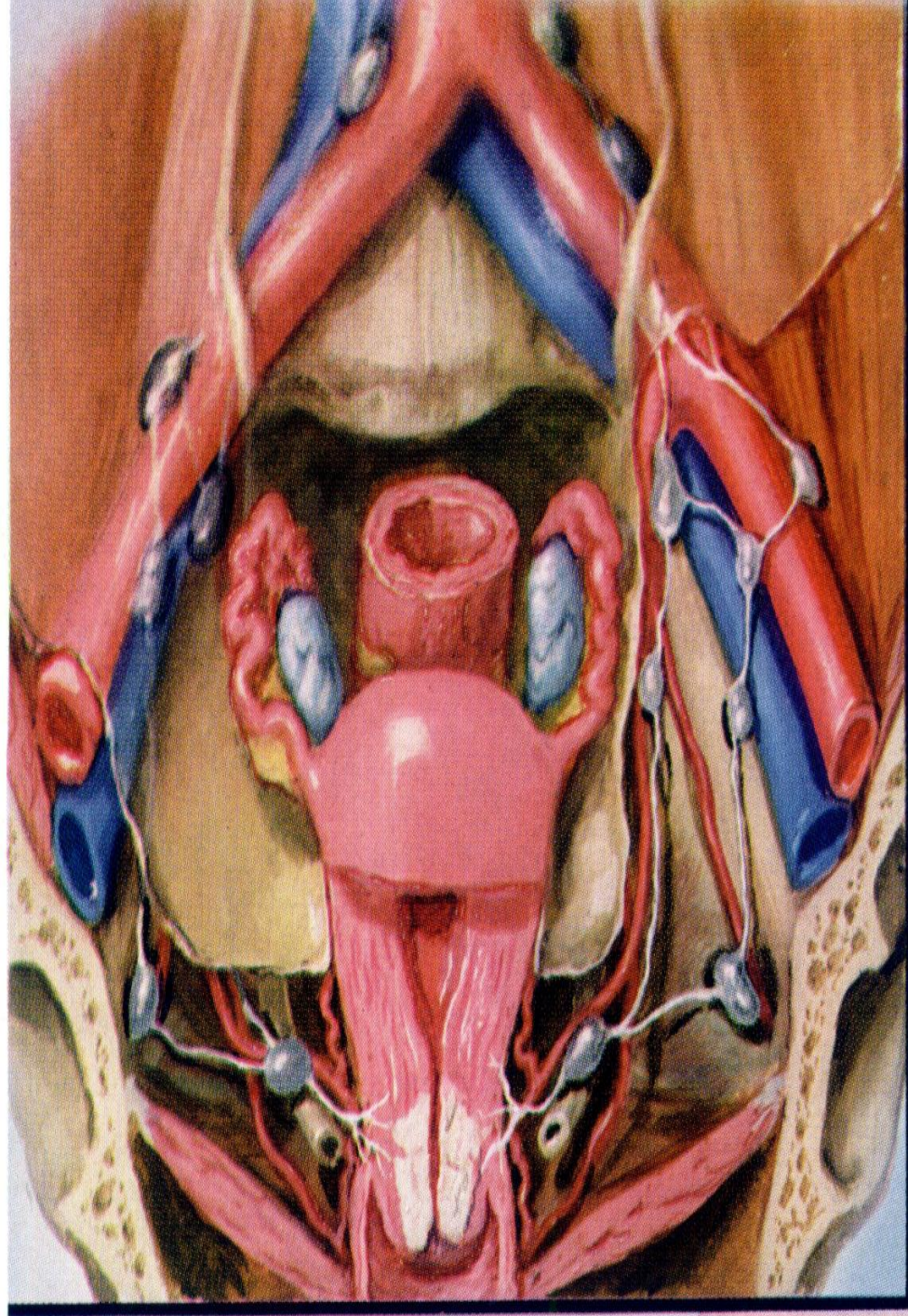
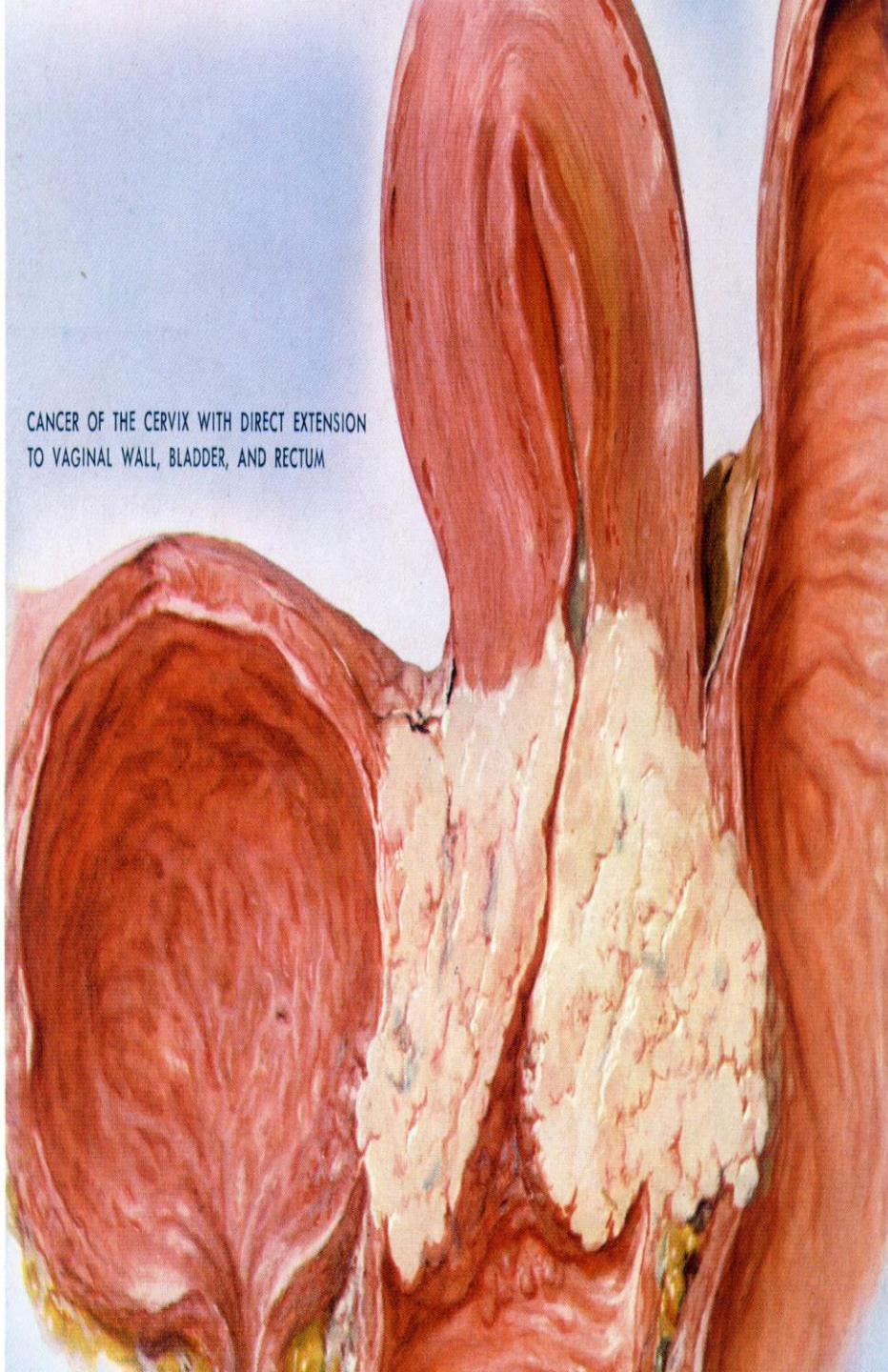
Normal and Dysplastic cells



Spread of cancer cervix

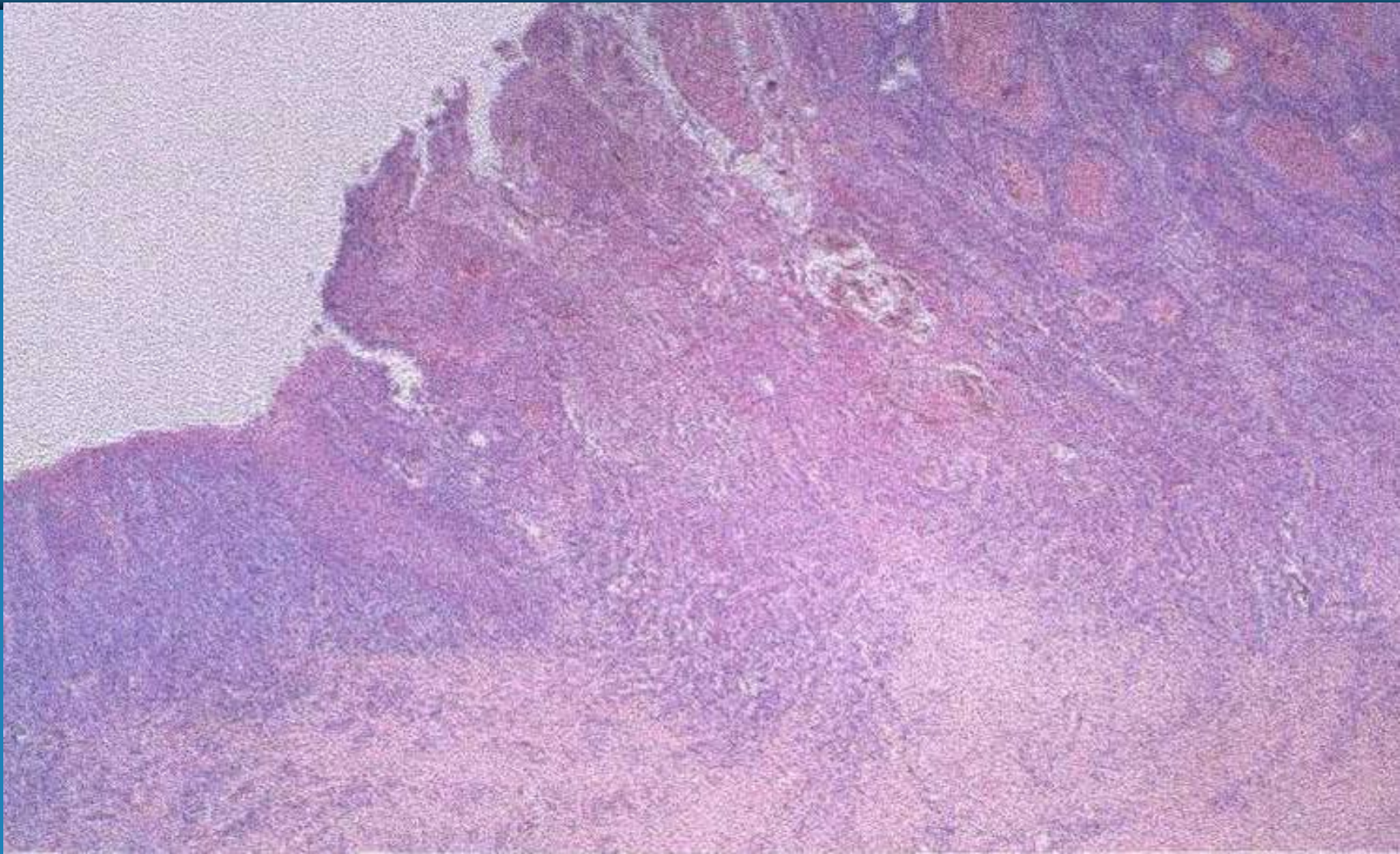
- ∩ As it become invasive , the tumor breaks through the basement membrane and invades cervical stroma and then spread through:
- ∩ Direct extension
- ∩ Lymphatics
- ∩ Blood

CANCER OF THE CERVIX WITH DIRECT EXTENSION
TO VAGINAL WALL, BLADDER, AND RECTUM

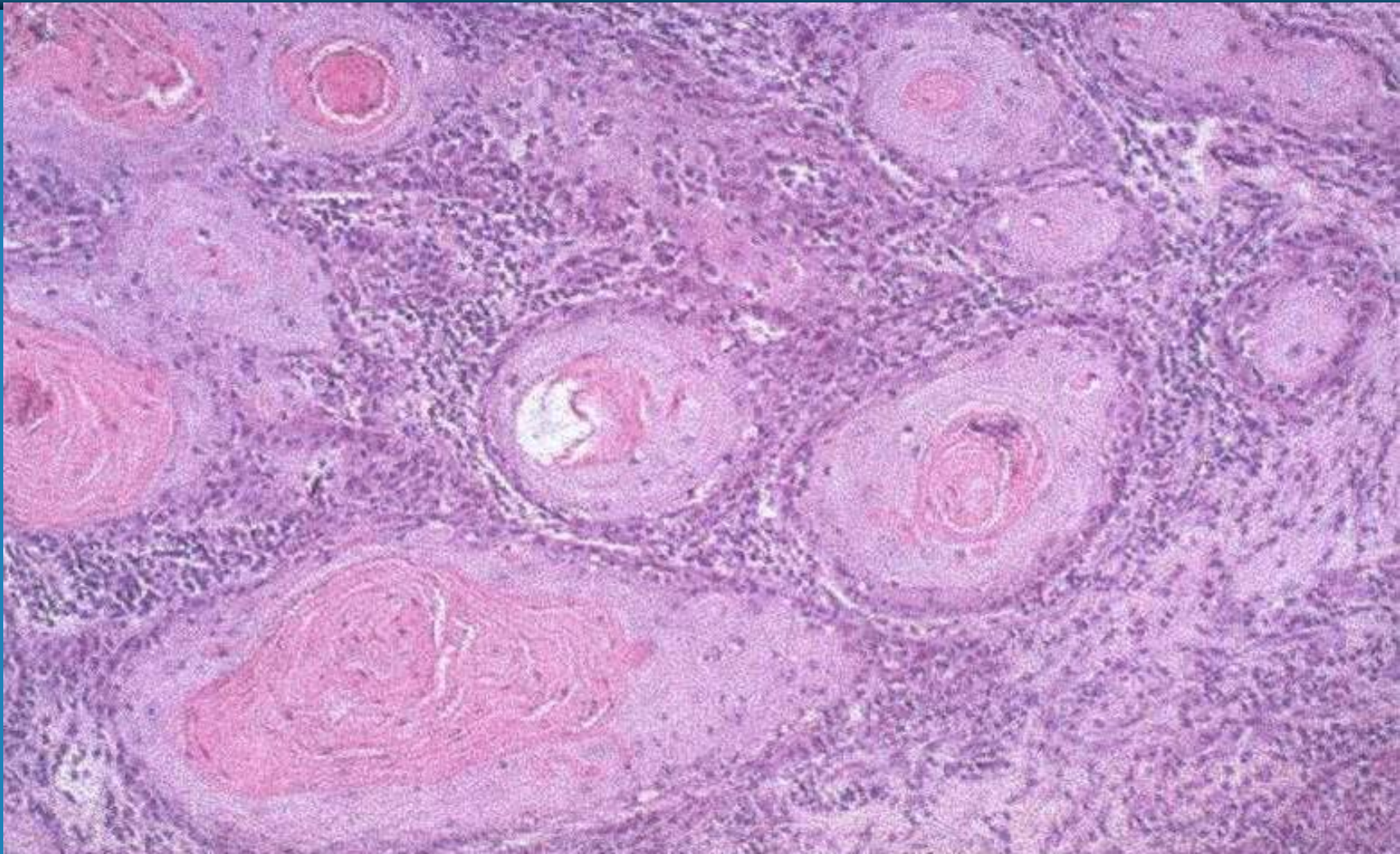


Sq.Cell Carcinoma

M.P.(LPF)



Sq.Cell Carcinoma M.P (HPF)



Stages of Cancer Cervix

∞ The Federation International of Gynecology and Obstetrics adopted clinical stages for cancer cervix with classification into four stages beside the intraepithelial lesion

General rules for staging

- ⌚ Staging must be completed before definitive therapy
- ⌚ Clinical examination, preferably under anesthesia, is the basis for staging
- ⌚ Regardless of error or subsequent findings, the Stage cannot be changed at a later date.

General rules for staging

- ⌚ **WHEN DOUBT EXISTS AS TO WHICH STAGE A CASE SHOULD BE ALLOTTED, THE EARLIER STAGE MUST BE DESIGNATED**
- ⌚ **ONLY EXAMINATIONS AND TESTS AVAILABLE AT ANY HOSPITAL CAN BE UTILIZED**

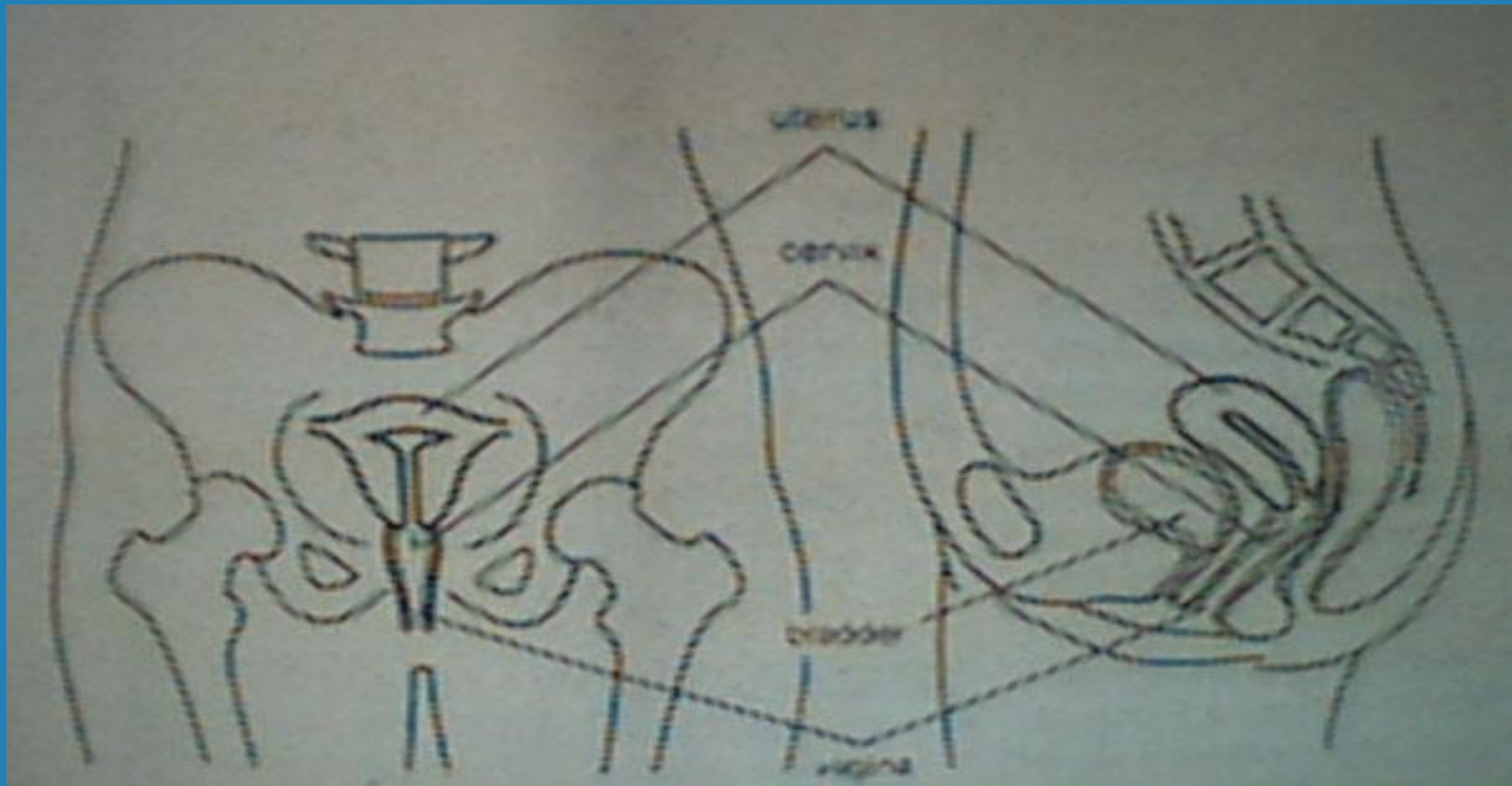
Stage 0 Disease

- ∞ This refers to the intraepithelial lesion ranging from CIN I to CIS
- ∞ This should not be included in any therapeutic statistics for invasive carcinoma

Stage I cancer cervix

- ∴ Carcinoma is strictly confined to the cervix. Classified into
- ∴ Stage IA...this is a microscopic disease which is classified into Stage Ia1 and IA2.
- ∴ Stage IB..is clinical disease or microscopic disease greater than IA2..classified into IB1 and IB2.

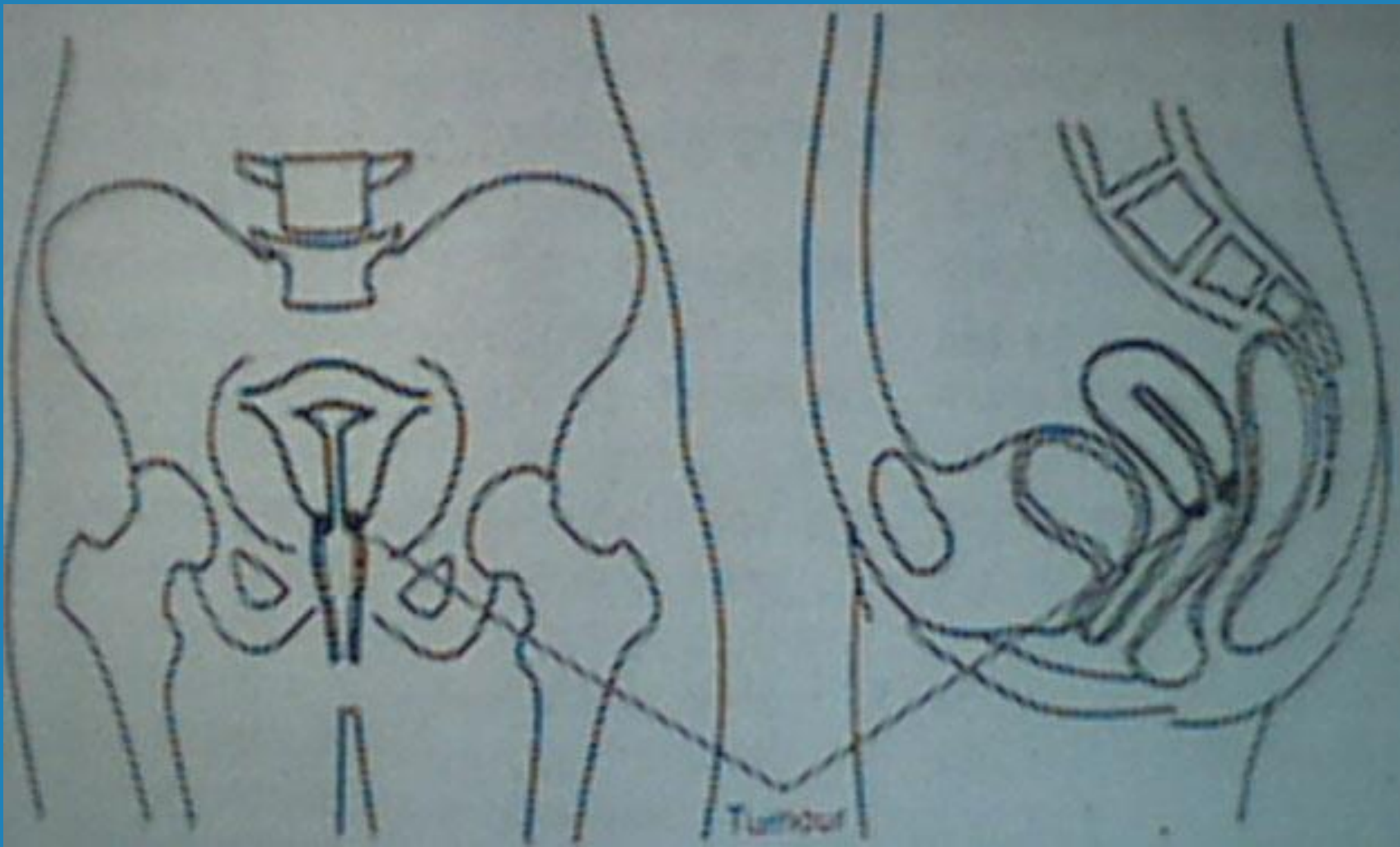
Normal view



Stage II cancer cervix

- ∩ Carcinoma extends beyond the cervix but not reaching lateral pelvic wall. Involvement of the vagina but not reaching lower 1/3.....further classified into:
 - ∩ IIA..no obvious parametrial invasion
 - ∩ IIB..obvious parametrial invasion

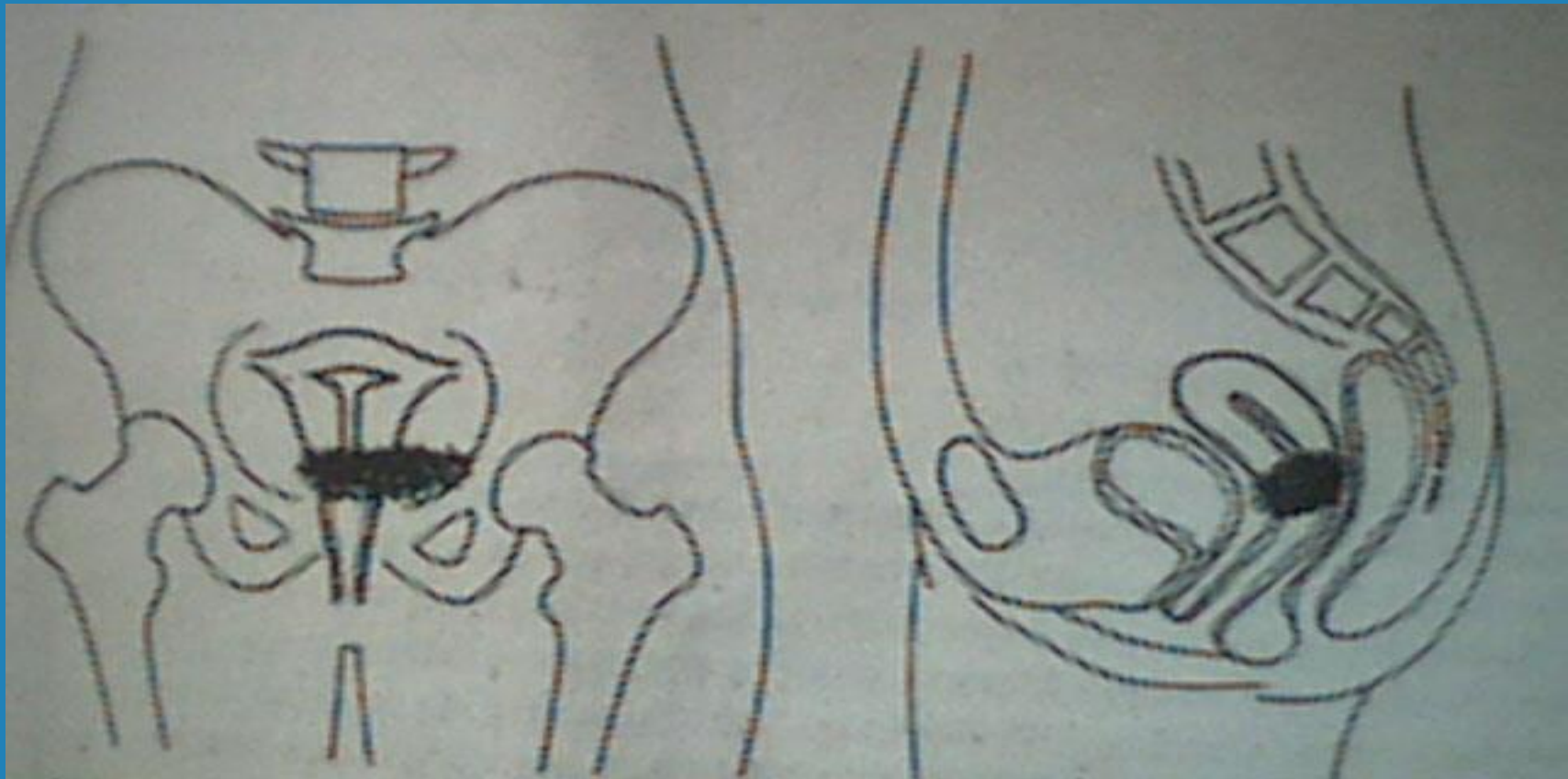
View stage II



Stage III cancer cervix

- ∩ The Carcinoma extend to the pelvic wall.
- ∩ The tumor involves the lower third of vagina
- ∩ All cases of hydronephrosis or nonfunctioning kidney
- ∩ classified into IIIA and IIIB

View stag III



Stage IV cancer cervix

- ∩ Carcinoma extends beyond the true pelvis or clinically involved the mucosa of the bladder or rectum..classified into:
- ∩ IV A.spread of growth to adjacent organs
- ∩ IV B..spread to distant organs



Distribution of patients by stage

Stage I	32%
Stage II	37%
Stage III	27%
Stage IV	4%

Surgical Staging

- ⌚ Clinical staging is inaccurate with up to 25% of stage I lesions and 50% of higher stage lesions being understaged.
- ⌚ Many institutions recommend a pretreatment surgical staging procedure. However, no survival benefit gained.

Additional Investigations

∞ LYMPHANGIOGRAPHY

∞ COMPUTED TOMOGRAPHY

∞ MAGNETIC RESONANCE IMAGING

∞ LAPAROSCOPIC L.N sampling

Prognostic Factors

- ∩ Stage
- ∩ Grade
- ∩ Volume of tumor
- ∩ Lymphatic involvement
- ∩ vascular invasion



Survival in relation to stage

Stage I	80%
Stage II	65%
Stage III	30%
Stage IV	15%

Lymph Node Metastases

- ∞ THE INCIDENCE OF L.N METASTASES RELATES PREDOMINANTLY TO THE TUMOR VOLUME (BOTH DEPTH AND PENETRATION AND OVERALL SIZE)
- ∞ SURVIVAL OF PATIENTS WITH NEGATIVE AND POSITIVE NODE IS APPROXIMATELY 90% AND 55% RESPECTIVELY

Incidence of L.N. Involvement

Stage	No.	Pelvic	Para-aortic
IAi	23	0	0
IA2			
1-3mm	156	0.6%	0
3-5mm	84	4.8%	<1%
Ib	1926	15.9%	2.2%



Incidence of L.N. Involvement

IIA	110	24.5%	11%
IIB	324	31.4%	19%
III	125	44.8%	30%
IV	23	55%	40%

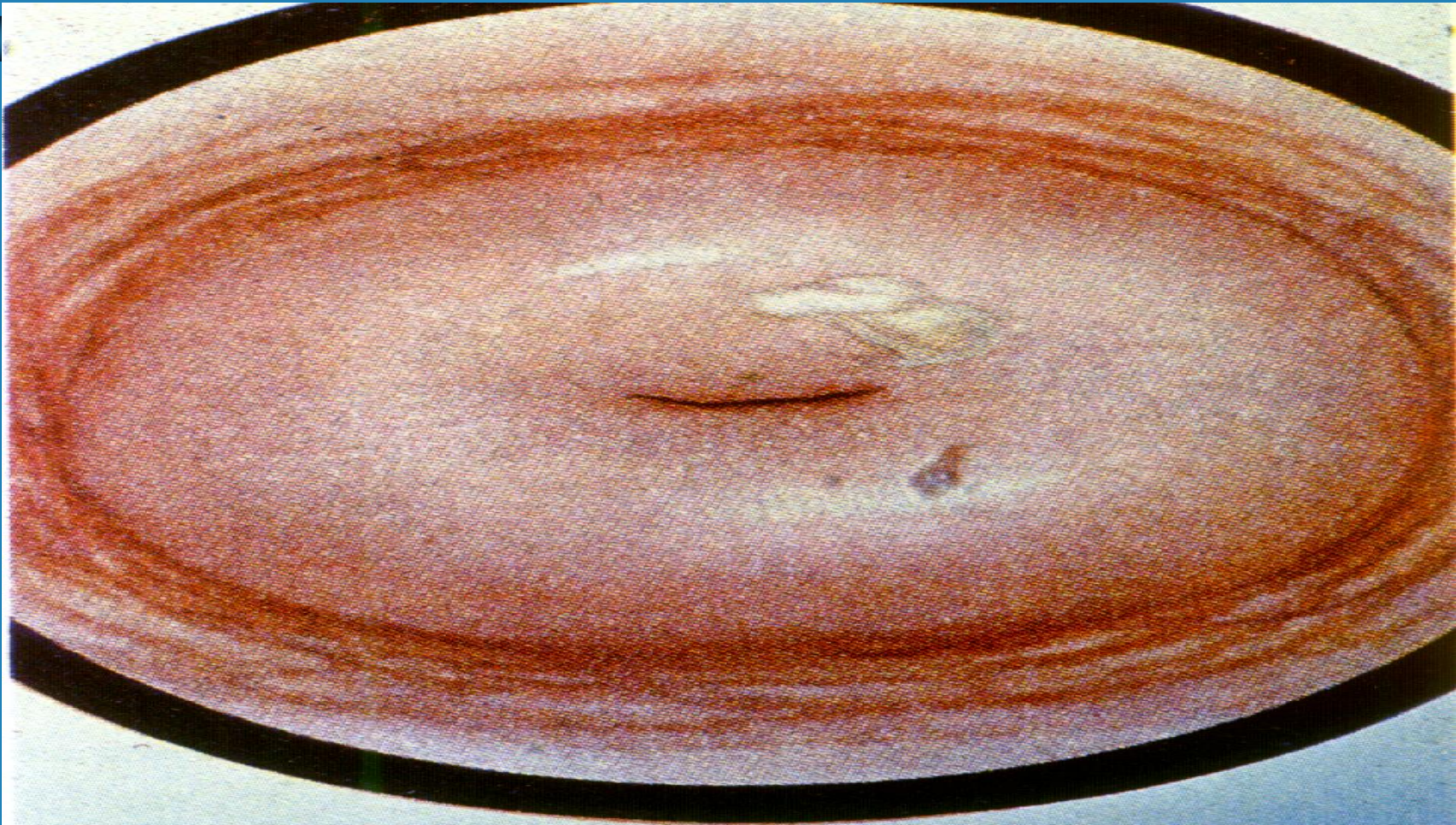
Serologic markers

- ∴ The measurement of serum tumor markers in patients with cervical cancer has not been found to be of clear benefit.
- ∴ CA 125 was reported to be more common in adenocarcinoma than Sq.Cell Carcinoma
- ∴ Sq.Cell Carcinoma antigen was positive in up to 67%

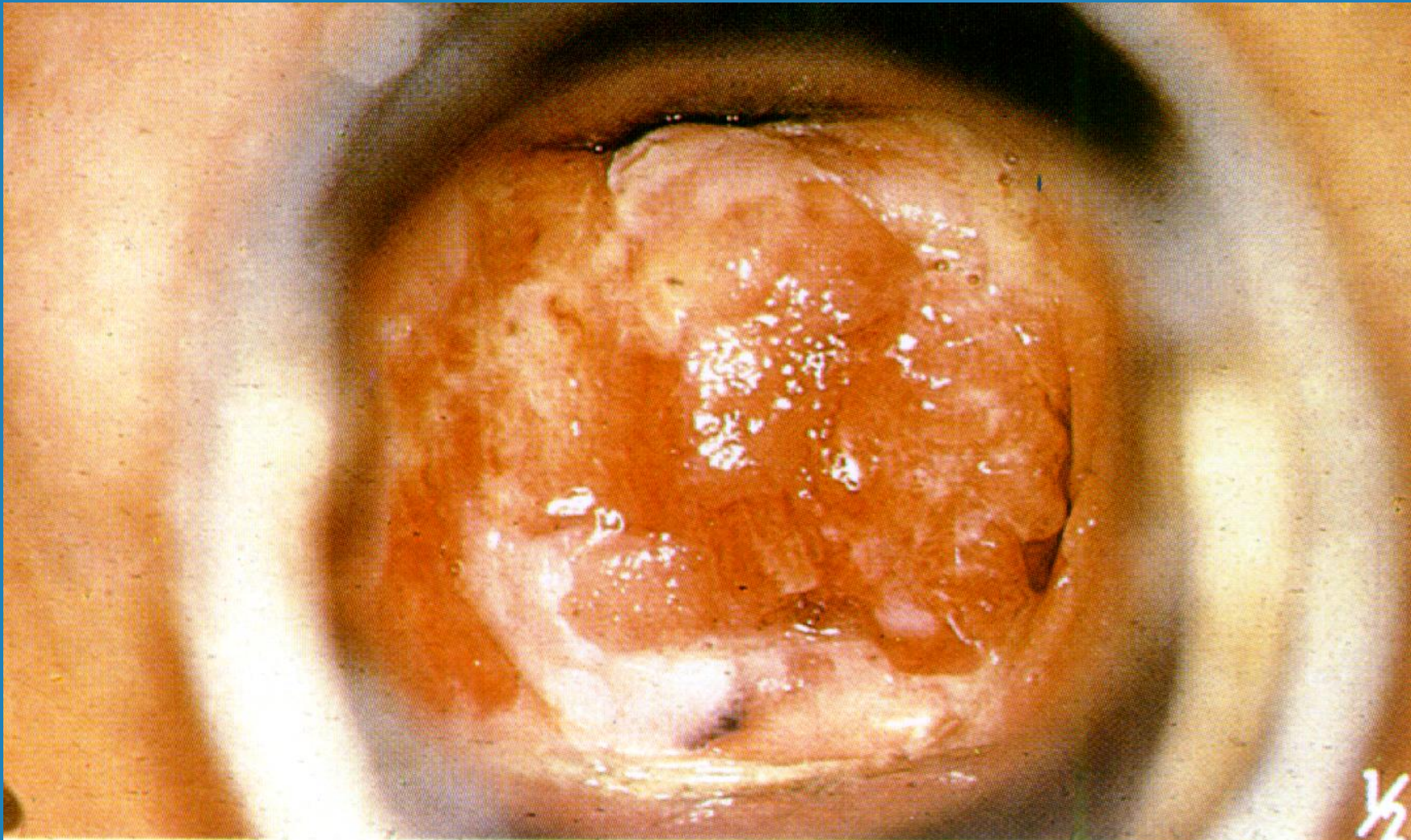
Presentation

- ∩ **Asymptomatic**
- ∩ **Vaginal discharge**
- ∩ **Abnormal Vaginal Bleeding...**
irregular, postcoital,
menorrhagia, postmenopausal
- ∩ **Pain, weight loss, anaemia ..late**
- ∩ **symptoms due to metastasis**

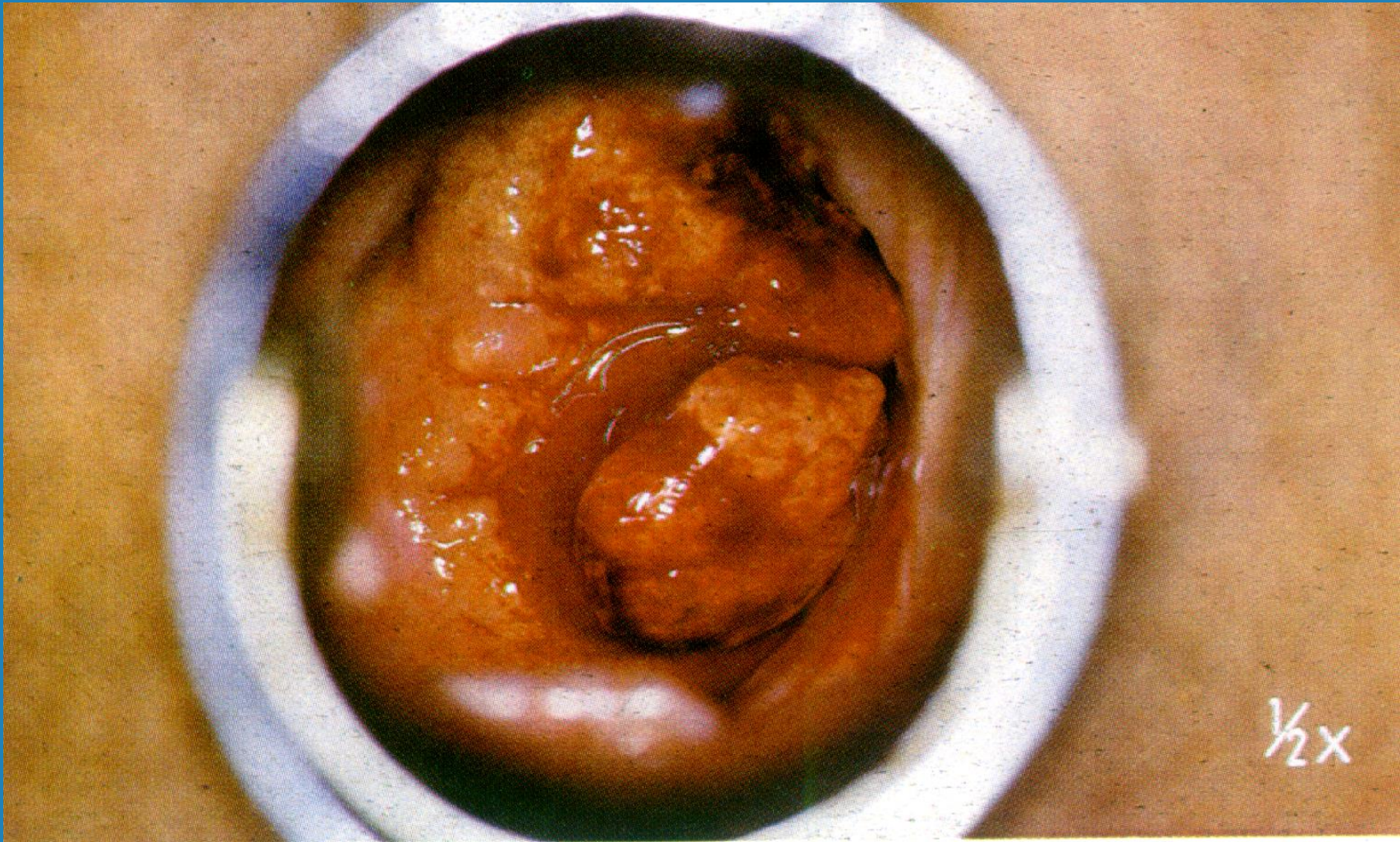
Normal Cervix



Cervical Cancer ..Gross



Cervical Cancer..Gross



Evaluation

- ∩ Physical Examination
- ∩ Pelvic Examination..EUA
- ∩ Cystoscopy
- ∩ Proctoscopy
- ∩ I.V.U.
- ∩ X-ray chest and skeleton

Treatment of Cervical Cancer

- ∩ The two primary treatment for cervical carcinoma are
 - ∩ Surgery
 - ∩ Radiation Therapy
 - ∩ Radiation therapy can be used in all stages, while surgery is used in stages I or IIA

Surgical Management

Stage	Stromal Invasion	Surgery
IA1	1-3mm	Conization, Type I Hyst.
	3-5mm + lymphovascular	Type I or II ?Pelvic L.N

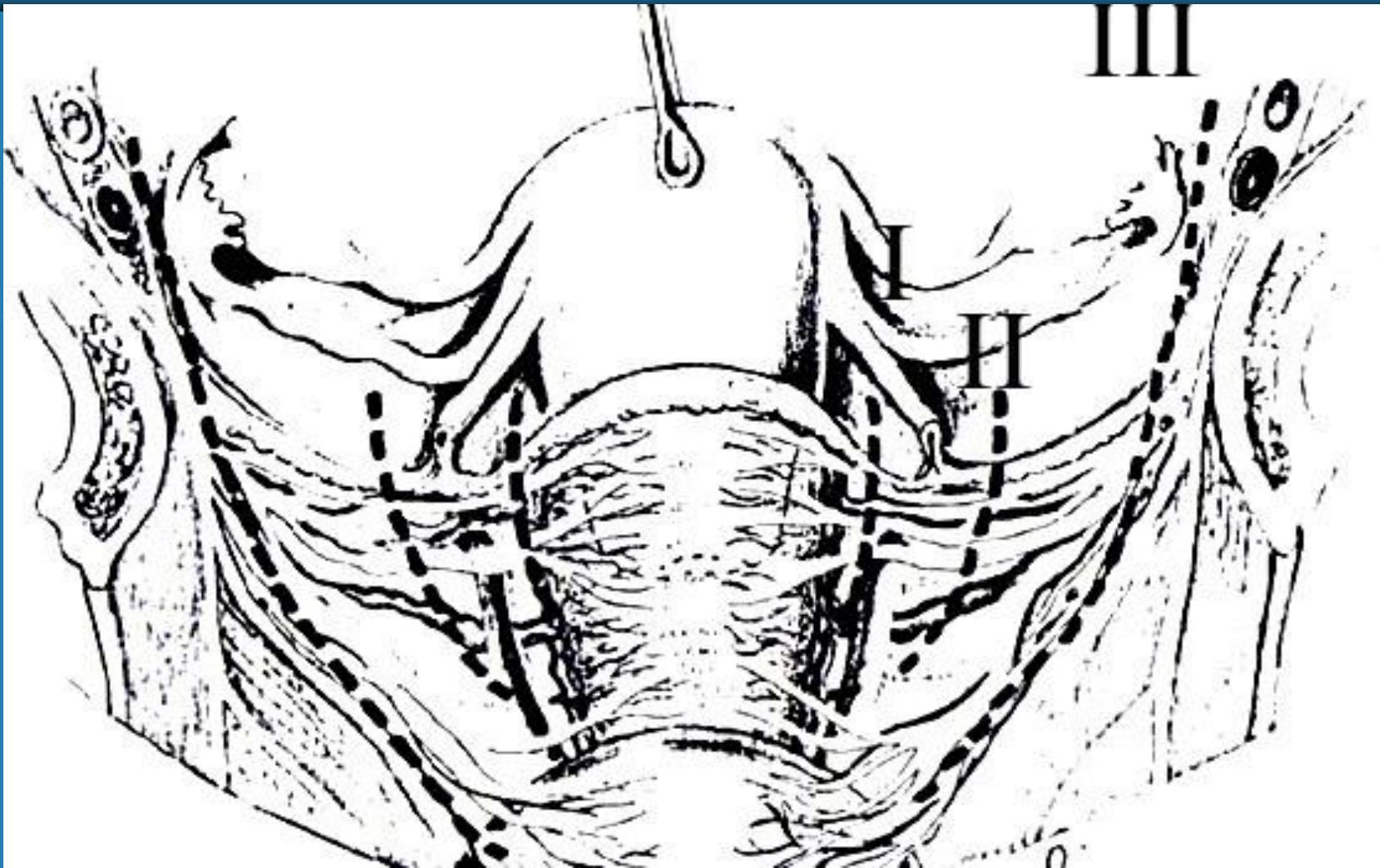
Surgical Management (cont.)

Stage	Stromal Invasion	Surgery
IA2	3-5mm, <1cm wide	Type II Hist. + pelvic L.N
	3-5mm, >1cm Wide	Type III Hist. + pelvic.N
Ib/Ila	>5mm, <3cm wide	Type III Hist. + pelvic L.N

Types of Hysterectomy

Vaginal cuff ureters	Small rim Not mobilized	Proximal 1-2cm Unroofed in uerteric canal	Upper 1/3-1/2 Compl etely mobili zed
Cardinal ligaments	Resected medial to ureters	At level of ureters	At pelvic sidew all
Uterosacra l ligaments	At level of cervix	Partially resected	At postp elvic

Types of Hysterectomy



Radiation Therapy

⌚ **ENTAILS THE USE OF VARIOUS
DOSES DELIVERED TO DIFFERENT
PROPORTIONS OF THE PATIENT
PELVIS, DEPENDING ON THE
EXTENT OF THE DISEASE**

Teletherapy (External Radiation)

∞ Consists of portals encompassing the whole pelvis and additional boost to the parametria. The later is provided with midline shielding to reduce bladder and sigmoid toxicity

Brachytherapy (Intracavitary)

- ∞ Provided by inserting a hollow applicator into the uterine cavity. Radioactive pellets are then loaded into it in a tandem.
- ∞ Ovoids containing radioactive material are placed at the cervix and fornices to increase radiation dose to the cervix and upper vagina

Brachytherapy (cont.)

- ∴ Two reference points are used in expressing the dose of radiation.
- ∴ Point A is 2 cm lateral and superior to the external os.
- ∴ Point B is 3 cm lateral to point A
- ∴ The sum of radiation doses required for central tumor control is 6000-9000 cGy to point A and 6500cGy to B

Applicators for RT tandem



Tandem and ovoids

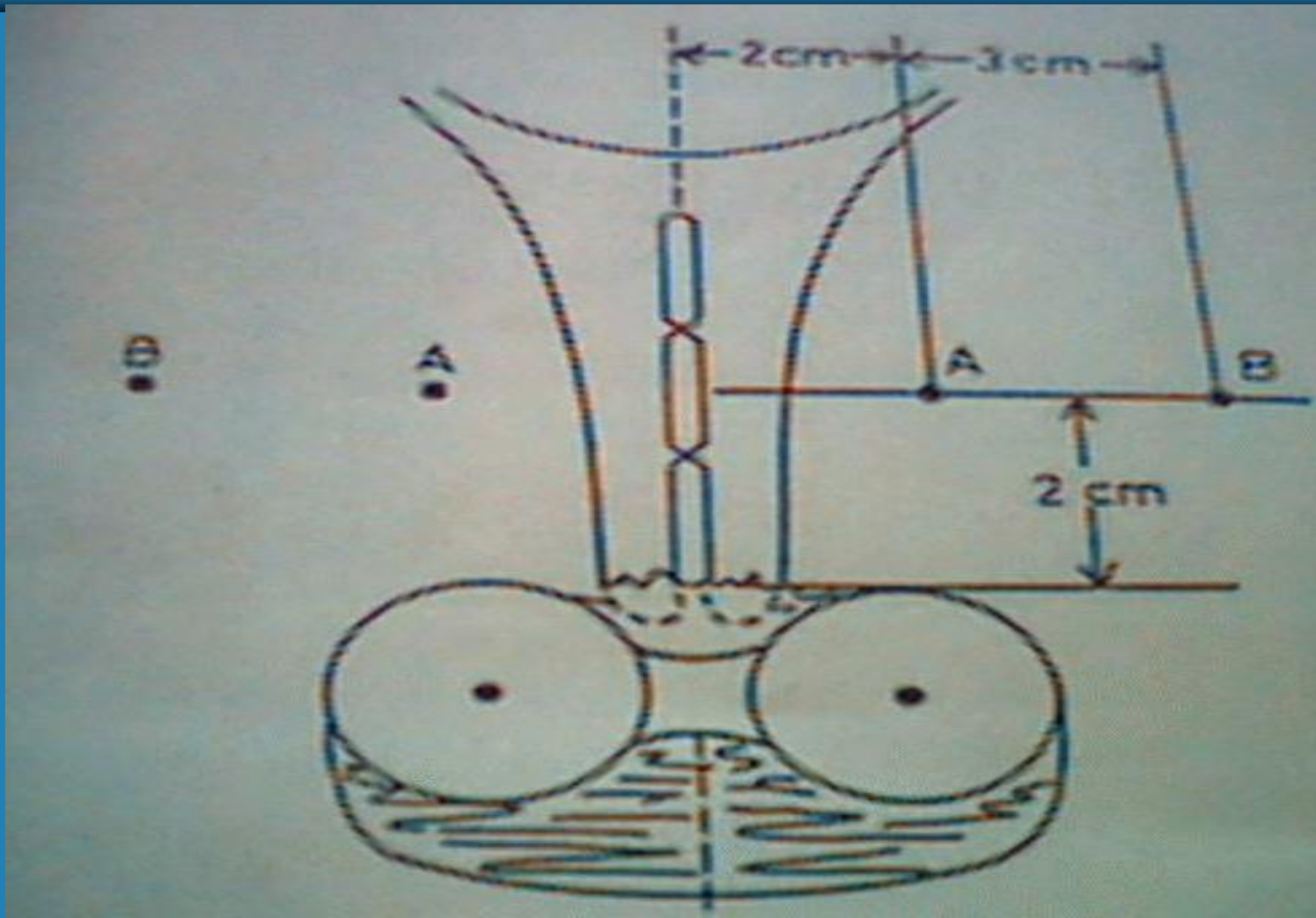


Prof.Dr. Samir Khalaf

X-ray after application



Reference points



Distribution of radiation



Disease control & survival after Radiotherapy alone

FIGO	No.Pt.	Pelvic cont.	surviv al
ST.I	229	93%	89%
St.IIA	315	88%	85%
St.IIB	314	80%	76%
St.IIIA	266	63%	62%
St.IIIB	216	57%	50%
St.IV	43	18%	20%

Surgery Vs Radiotherapy

Criterion	Surgery	Radioth.
Survival	85%	85%
Serious complications	Urologic fistula 1-2%	Intest.&urologic stricture 1.4-1.5%
Vagina	Gradually become long	Fibrosis and possible stenosis

Surgery Vs Radiotherapy

Ovaries	Can be preserved	Destroyed
Chronic effect	Bladder atony 3%	Radiation fibrosis of bowel & bladder 6%
Surgical mortality applicability	1% <65ys., <200 lb., surgically fit	<1%, thromboembolism All patients are potential candidates

Chemotherapy

- ⌚ **IN EARLY DISEASE**
- ⌚ **NEOADJUVANT CHEMOTHERAPY BEFORE PLANNED RADIATION OR SURGICAL THERAPY ARE UNDERWAY, BUT TILL NOW NO BENEFIT WAS GAINED**

Chemotherapy

- ∩ In Advanced Stage
- ∩ Several study designs used:
- ∩ Neoadjuvant
- ∩ Concomitant with radiotherapy
- ∩ Adjuvant after radiotherapy
- ∩ Cisplatin was most active, response rate 18-31% for 5 months

Concurrent Chemotherapy and Radiation Therapy

On February 22nd, 1999 the NCI announced the results of five large randomized clinical trials using Cisplatin and Fluorouracil in conjunction to radiotherapy in Risky patients with resultant decrease mortality by 30% to 50% in the group treated with chemoradiation

Palliative Therapy

- ∞ This is appropriate for patients with symptomatic disease.
- ∞ Palliation of pelvic symptoms can be achieved by radiation..also for bone metastases.
- ∞ Systemic chemotherapy although the benefit is of short duration.
- ∞ Palliative surgery for fistula

Post-therapy Surveillance

Regression after radiotherapy continue for 3 months, so patients should be evaluated monthly during this period. After that every 3 month visits for the first 2 years. Then biannual visits for 3 years and after this period patient should be seen annually.

Post-therapy

- ∞ At each visit physical examination should include palpation of supraclavicular L.N, breast and rectovaginal examination
- ∞ Annual Pap smear and chest x-ray
- ∞ No contraindication for HRT
premarin+provera if uterus intact
and premarin only if uterus removed