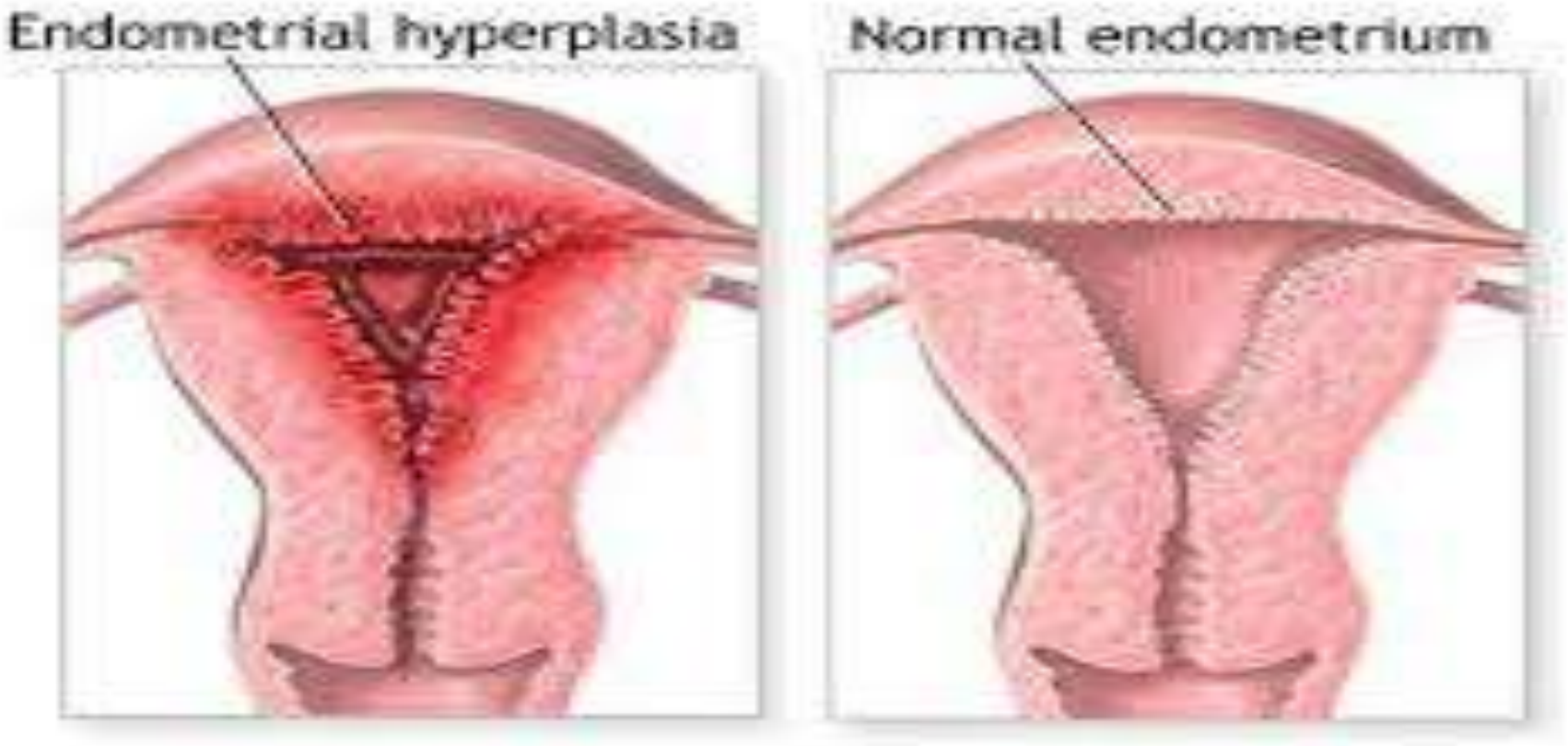
ENDOMETRIAL HYPERPLASIA AND ENDOMETERIAL CARCINOMA

Ass. Prof. Dr. Sawsan Talib
Department of Obstetrics and Gynecology
College of medicine/ Diyala University


بسم الله الرحمن الرحيم

ENDOMETRIAL HYPERPLASIA



ENDOMETRIAL HYPERPLASIA

* Endometrial premalignant conditions are less easily diagnosed and followed up.
* Any hyperplastic condition raises the question of development of cancer and assessment of risk is important.
* Hyperplasia and carcinoma may coexist.
* Endometrial hyperplasia may be classified as simple, complex or atypical.
* Heavy and/or irregular vaginal bleeding are the presenting symptoms but its severity or frequency is not related to the degree of pathological change.

TABLE 22.7 RISK FACTORS

- Unopposed estrogen stimulation
- Delayed menopause
- PCOS
- Nulliparity
- Diabetes
- Obesity
- Hypertension
- Previous radiation therapy
- Family history of endometrial carcinoma, carcinoma of breast, ovary or colon
- Tamoxifen therapy

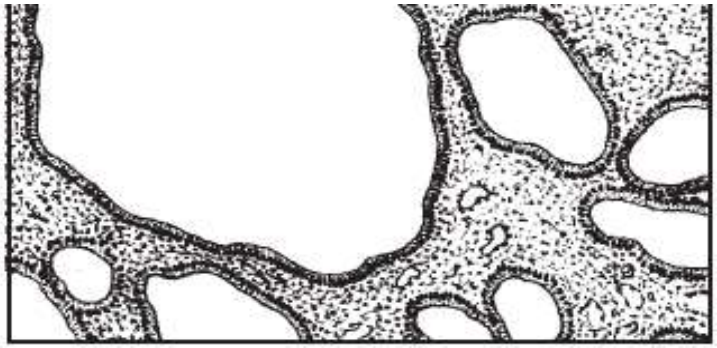
TABLE 22.8 PROTECTIVE FACTORS

- Multiparity
- Normal weight
- Combined oral contraceptive use
- Progestogen therapy
- Menopause <49 years

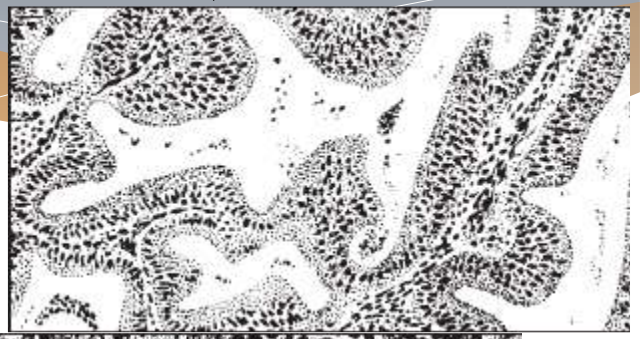
SIMPLE HYPERPLASIA

* This is the most common type. The endometrium has a characteristic appearance, often termed ‘Swiss cheese’ or cystic glandular hyperplasia.

* At low power magnification the pattern is a mixture of glands of varying sizes,
* a significant proportion of them being cystic.
* There is no crowding of the glands which are lined by cubical or columnar epithelium.
* Mitotic figures are present in small numbers.

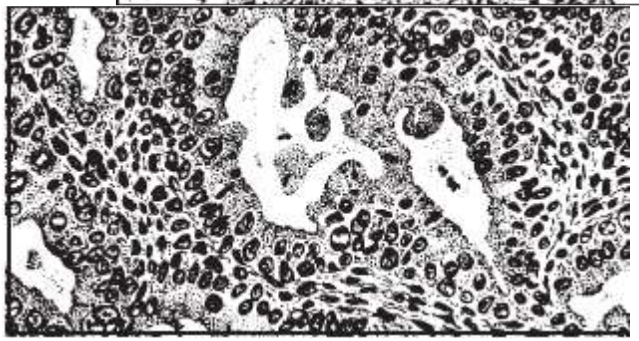


* COMPLEX HYPERPLASIA
* In this grade of hyperplasia the most striking feature is the quite obvious hyperplasia –
* crowding of glands so that they are back-to-back,
* the epithelium is stratified
* mitoses are relatively frequent.
* There is, however, no epithelial atypia.



ATYPICAL HYPERPLASIA

At this stage nuclear atypia is present.



* Intraglandular polypoid formations
* abnormal mitotic figures are seen.
* Severe cases may be indistinguishable from a carcinoma and adjacent areas of endometrial carcinoma may occur.

INVESTIGATION

1. Ultrasound
2. endometrial biopsy, with or without hysteroscopic assessment

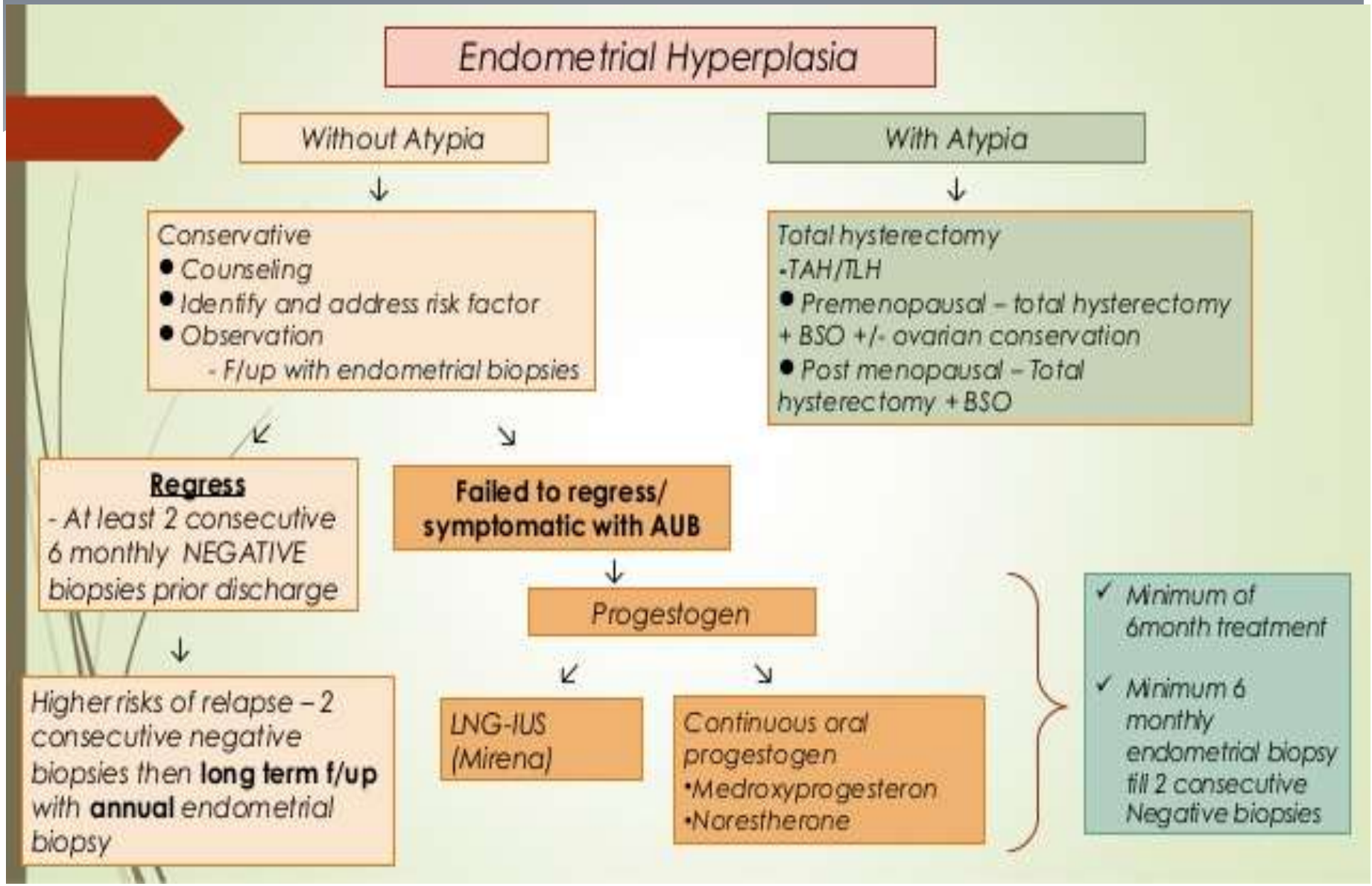
Investigation will usually be in an outpatient setting but inpatient general anaesthetic assessment may also be needed.

TREATMENT

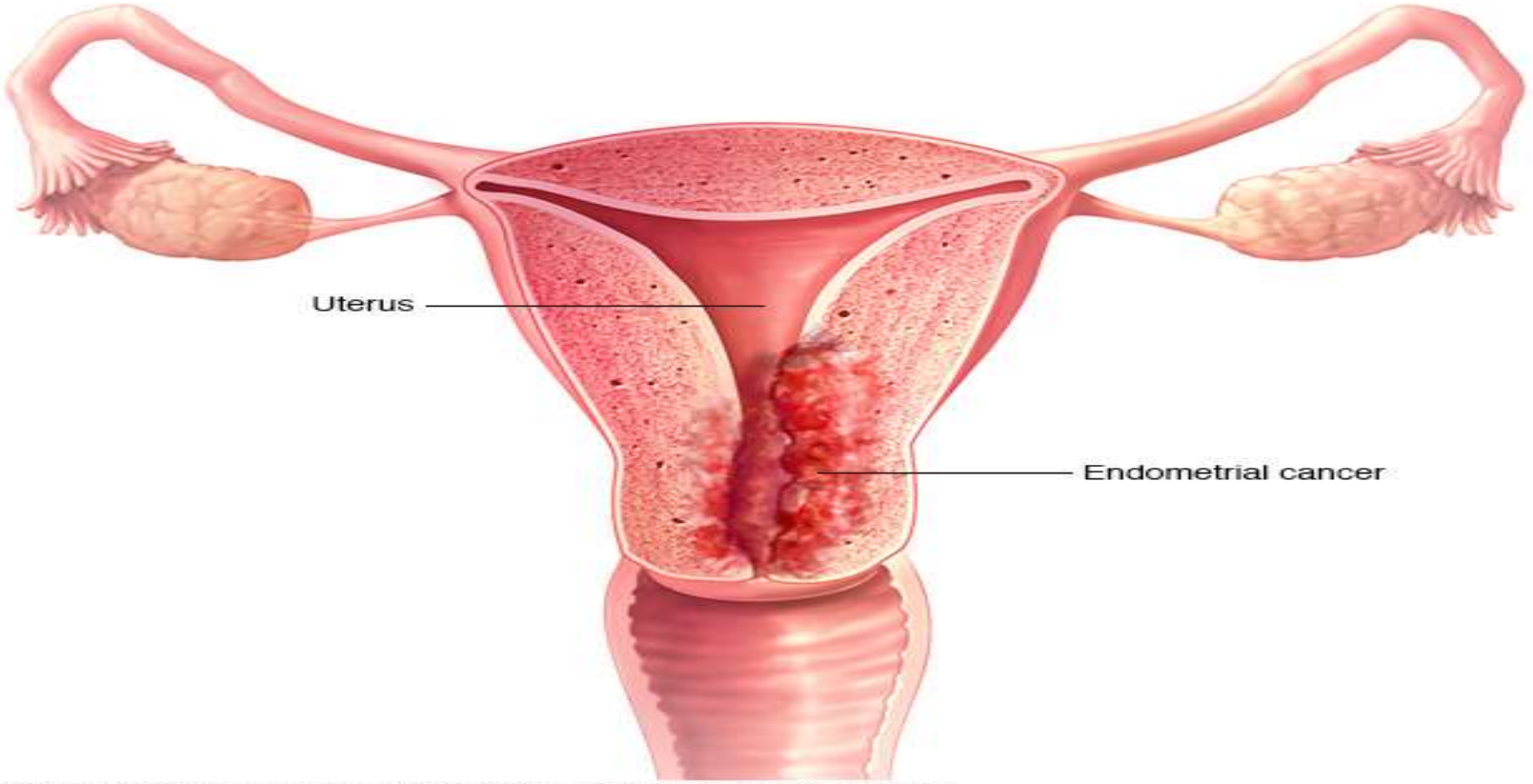
This depends principally on

1. The types of hyperplasia.
2. The age of the patient and
3. A desire to retain fertility are factors to be considered.

TREATMENT


Endometrial Hyperplasia
Without Atypia
With Atypia
Conservative
• Counseling
• Identify and address risk factor
• Observation
- F/up with endometrial biopsies
Total hysterectomy
-TAH/TLH
• Premenopausal – total hysterectomy + BSO +/- ovarian conservation
• Post menopausal – Total hysterectomy + BSO
Regress
- At least 2 consecutive 6 monthly NEGATIVE biopsies prior discharge
Failed to regress/ symptomatic with AUB
Progestogen
Higher risks of relapse – 2 consecutive negative biopsies then long term f/up with annual endometrial biopsy
LNG-IUS (Mirena)
Continuous oral progestogen
•Medroxyprogesteron
•Norestherone
✓ Minimum of 6month treatment
✓ Minimum 6 monthly endometrial biopsy till 2 consecutive Negative biopsies

CARCINOMA OF THE ENDOMETRIUM



CARCINOMA OF THE ENDOMETRIUM

One of the commonest gynaecological cancers

* it occurs most often in postmenopausal women (up to 80% of cases)
* less than 5% diagnosed under 40 years of age
* There is no effective screening programm, but postmenopausal bleeding may be a cardinal symptom prompting urgent investigation.

TABLE 23.13 'HIGH RISK' FACTORS FOR ENDOMETRIAL CANCER

- Late menopause
- Nulliparity
- Unopposed estrogen therapy
- History of persistent anovulation (PCOS)
- History of irregular and excessive premenopausal bleeding
- Obesity, diabetes, hypertension
- Personal or family history of breast, ovary, colon or endometrial cancer
- Atypical endometrial hyperplasia (p. 331)
- Tamoxifen therapy
- Radiation menopause.

PRESENTATION OF ENDOMETRIAL CA

* Abnormal vaginal bleeding ➡ most common 90%
* Premenopausal Pt ➡ usually c/o heavy flow at the time of menses

  may present with

  ➡ persistent intermenstrual bleeding

  ➡ pre or post menstrual spotting

  ➡ polymenorrhea that fails to respond to hormonal Rx
* Postmenopausal bleeding is the most common type of abnormal bleeding ➡ 12-15% due to E Ca

  ➡ 5-8% due to other cancers like uterine sarcoma, ovarian Ca, Cx, tubal or vaginal Ca
* Postmenopausal Pt ➡ commonly c/o intermittent spotting
* Postmenopausal vaginal discharge 10%

PRESENTATION OF ENDOMETRIAL CA

* Asymptomatic women with glandular abnormalities on routine PAP smear/ abnormalities found in 50% of Pt with E Ca
* Advanced disease ➡ symptoms due to local or distant metastases
* Sever cramps due to hematometra or pyometra ➡ occur in postmenopausal Pt with Cx stenosis ----10%
* At times, there is watery and offensive discharge due to pyometra.
* Pain is not uncommon. It may be colicky due to uterine contractions in an attempt to expel the polypoidal growth.
* Few patients (< 5%) remain asymptomatic.

* **Signs**:
* The patient presents with varying degrees of pallor.
* **Pelvic examination:**
* Speculum examination reveals the cervix looking healthy and the blood or purulent offensive discharge escapes out of the external os.
* Bimanual examination reveals—The uterus is either atrophic, normal or may be enlarged due to spread of the tumor, associated fibroid or pyometra. The uterus is usually mobile unless in late stage, when it becomes fixed.
* Rectal examination corroborates the bimanual findings. Regional lymph nodes and breasts are examined carefully.

Diagnosis

- Majority are diagnosed early, when surgery alone may be adequate for cure.

- History + Physical examination.

- CBC
- Transvaginal Ultrasound (endometrial thickness).
- Endometrial biopsy.
- Hysteroscopy & endometrial biopsy (Gold standard).

Where the endometrial thickness is measured to be less than 3 mm in women not on HRT

* and less than 5 mm in women taking HRT, there is an extremely low incidence of endometrial cancer and the patient can be reassured.
* In addition, careful inspection of the cervix, vulva and vagina should be undertaken to exclude these as a source of bleeding due to malignant change
* MRI is preferable to an US for the assessment of myometrial invasion and pelvic spread.
* To assess distal metastases (CT) scan of the chest, abdomen and pelvis may also be of value.

* **HISTOLOGY**
* **Distribution of Subtypes**
* Endometrioid 85%
* Adenosquamous 4%
* Serous carcinoma 4%
* Clear cell 3%

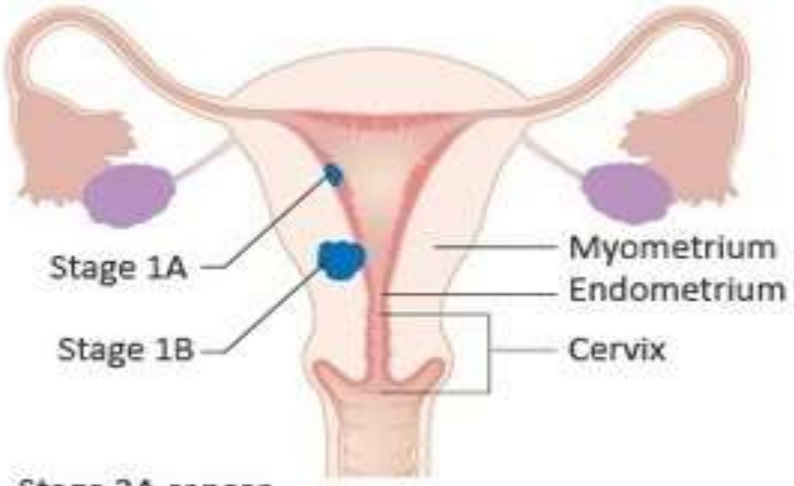
The majority of tumours are adenocarcinoma and they are divided into three groups according to the degree of glandular differentiation.

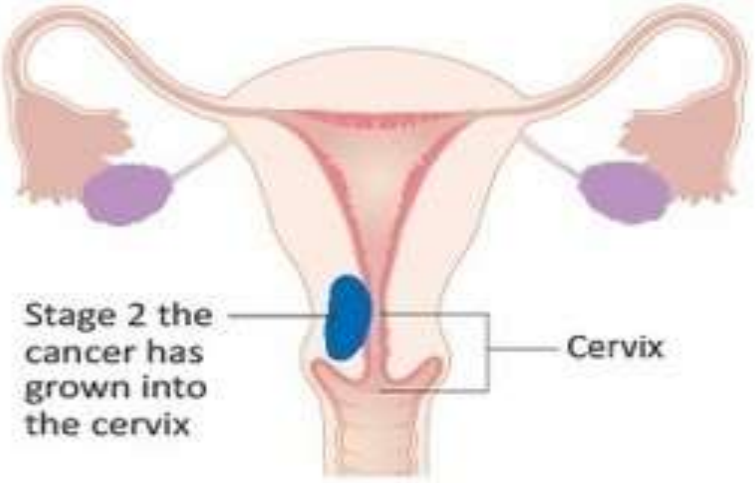
Grade 1 – Well differentiated

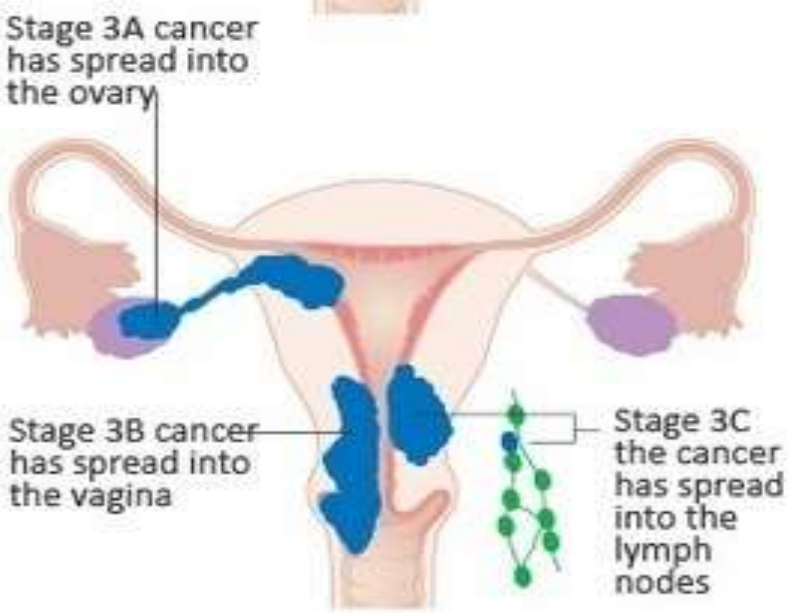
Grade 2 – Moderately differentiated

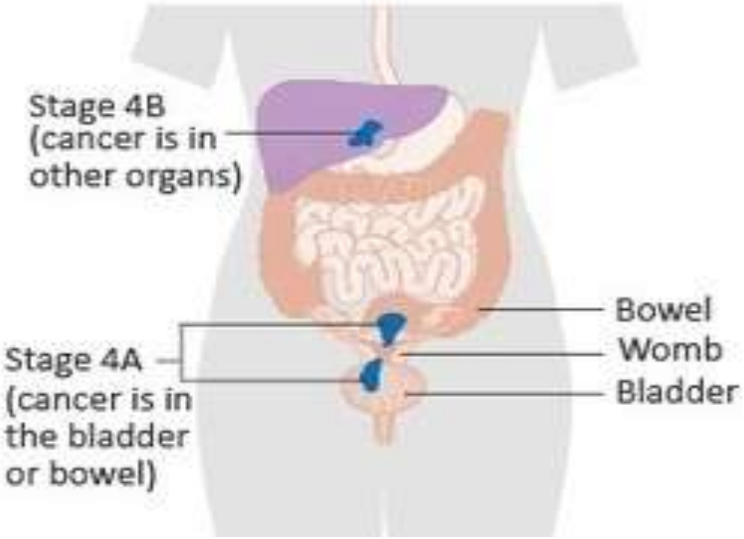
Grade 3 – Poorly differentiated. This type consists of solid masses of malignant cells of varying sizes and shapes with little or no stroma. Mitoses are numerous.

Stages of endometrial carcinoma









SPREAD OF ENDOMETRIAL CARCINOMA

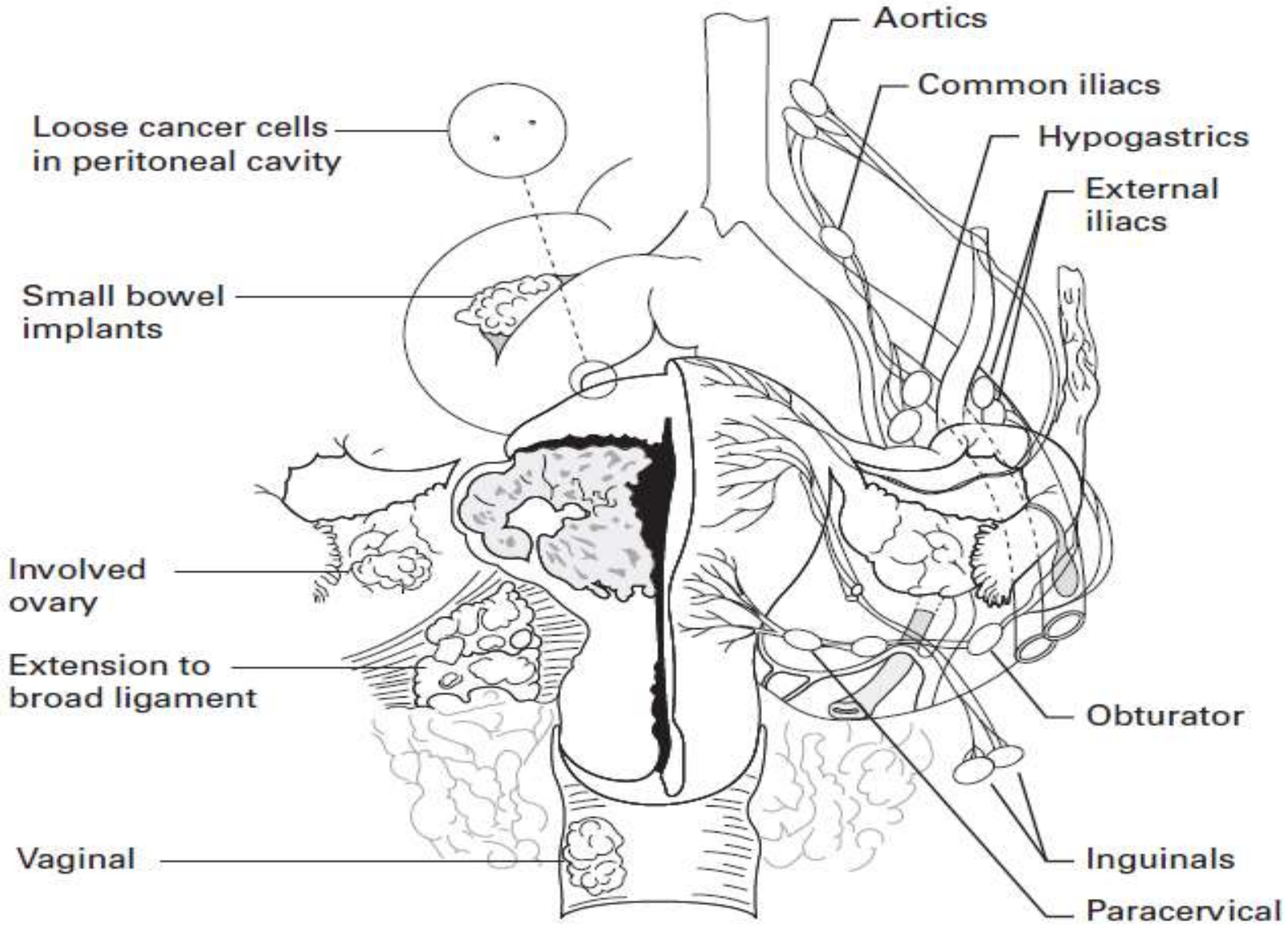
LOCAL SPREAD:

* Invasion of the myometrium and cervix is the commonest spread. It may produce considerable uterine enlargement.

LYMPHATIC SPREAD

* Lymphatic spread is more likely to occur when the tumour is poorly differentiated and the uterine wall is deeply invaded.
* The incidence of pelvic nodal metastases is in the region of 10%.
* Most metastases occur in the adjacent structures and in the peritoneum.
* In advanced cases, distant metastases do occur, most commonly in lung, but occasionally in liver, vertebrae or other bones and in the supraclavicular lymph nodes.

Pelvic organs	Lymph nodes



AETIOLOGICAL FACTORS IN ENDOMETRIAL CARCINOMA

* There are two suggested types of endometrial carcinoma, based on etiology.
* Type 1 – arising in patients with a background history of estrogen excess (have a better prognosis, better differentiation pattern, less invasive component)
* Type 2 – arising without evidence of estrogenic stimulation (including serous and clear cell cancers, arise from a atrophic type endometrium, aggressive phenotype with greater invasion, poorer differentiation, more metastatic disease, they carry a poorer prognosis)
* Hereditary non-polyposis colorectal cancer (Lynch II) syndrome is an inherited mutation in DNA mismatch repair genes. In those affected, the endometrial carcinoma occurs more frequently, together with breast and colon cancer.

PROGNOSIS OF ENDOMETRIAL CARCINOMA

The survival is affected by multiple prognostic factors including:

1. Stage at diagnosis
2. Histological grade
3. Depth of myometrial invasion
4. Lympho-vascular space involvement (LVSI)
5. Non-endometrioid type

Stage	*5-year survival (%)*
I	85
II	75
III	45
IV	25

Grading	5-year survival (%)
G1	92
G2	90
G3	81

TABLE 23.14 PREOPERATIVE EVALUATION

- Blood examination — complete hemogram, postprandial sugar, urea, creatinine and electrolytes.
- Liver and renal function tests.
- Urine — Routine examination for – protein, sugar and pus cells.
- ECG and X-ray chest for cardiopulmonary assessment.
- Abdominal and pelvic ultrasonography for ascites, metastasis (liver), pelvic/paraaortic nodes.
- MRI/CT imaging (optional) to assess the extrauterine spread of the disease and the degree of myometrial invasion.
- Steroid receptor status.

In stage I , surgery is the mainstay of treatment

1. TAH & BSO (uterus is opened at operating room for evaluation of size, extention and and myometrial invation)
2. Lymph node sampling of the following areas is done : (i) Common iliac (ii) External iliac (iii) Internal iliac (iv) Obturator and (v) Paraaortic.

* IN STAGE 2 CARCINOMA

Management options are:

*A. Radical hysterectomy BSO with pelvic and para-aortic lymphadenectomy.

*B. Combined radiation and surgery: Radiation (external and intracavitary) followed in 6 weeks by TAH and BSO. or

*C. Initial surgery (modified radical hysterectomy) followed by external and intravaginal radiation

STAGE III/IV

* Treatment of this stage is designed to control tumour growth and alleviate symptoms.
* Treatment will depend upon tumour burden at the preoperative assessment and imaging.
* Many cases may only be identified as Stage III, following surgical management.
* Surgery, radiation therapy, chemotherapy and adjuvant progestogen therapy all have a place.

SARCOMA OF THE UTERUS

* These are rare tumours and include:

1. Endometrial stromal sarcomas
2. Leiomyosarcomas
3. Carcinosarcomas

CLINICAL FEATURES

1. The patient is usually over 50 years old
2. Presents with a complaint of fairly heavy bleeding of recent origin Accompanied by pain.
3. Pelvic examination reveals a large intrauterine mass with friable tissue palpable through the os.
4. The tumour may originate from the vagina in younger women and from the cervix in the child; but these are, indeed, very rare conditions.
5. Sarcomatous change may occur in 0.1% of fibroids.

* Tumour tissue may infiltrate the whole myometrium and fill the uterine cavity or arise from a pedicle.
* This type often presents as a cervical or vaginal polyp.
* The tissues of origin are the connective tissue and muscle of the myometrium or leiomyoma, or the endometrial stroma.

ENDOMETRIAL STROMAL SARCOMAS

* These are tumours of the endometrial stromal cells and form two groups:

Low Grade Stromal Sarcomas

* The clinical course is often uncomplicated and cure may follow surgery. They can recur, often years later, and recurrence up to 25 years later has been reported.

High Grade Stromal Sarcoma

* This type of stromal tumour shows numerous mitoses and is infiltrative from the start.
* There is early recurrence and widespread metastases occur even if there has been little local invasion of the myometrium. The prognosis is poor.

CARCINOSARCOMA (MALIGNANT MIXED MESODERMAL TUMOUR)

In this variant, both epithelial and stromal elements are malignant.

1. It forms a soft polypoid mass that is usually haemorrhagic.
2. Microscopically, most of the growth is sarcomatous but there are foci of carcinoma – adeno, squamoid, undifferentiated or various mixtures of these.
3. The prognosis is poor.
4. Treatment is surgical with hysterectomy, bilateral salpingooophorectomy and pelvic lymphadenectomy

LEIOMYOSARCOMA

* Usually these cases do not present with postmenopausal bleeding and are found in patients thought to have a uterine fibroid.
* Fibroids of a very large size or those which increase rapidly in size should be suspected as having a higher chance of malignant change.
* Treatment is usually hysterectomy and bilateral salpingo-oophorectomy.
* It is often not suspected at diagnosis. If detected postoperatively, then CT scan of chest, abdomen and pelvis should be undertaken to look for metastases.
* 10% of cases at diagnosis may have pulmonary metastases. Haematogenous spread is most common

thank you!