Endometrial Pathology
Female genital tract Development

1. Ovary- Indifferent stage- Germ cells from yolk sac at $4^{th}$ week of gestation
2. Uterus and fallopian tubes from Mullerian ducts at $6^{th}$ week of gestation in absence of Mullerian Inhibiting substances.
3. Lower genital tract from urogenital sinus
Endometrial Pathology

- Normal Histology
- Indications for Biopsy
- Clinical history
- Interpretation of abnormalities
  - Hormone therapy
  - Products of conception
  - Abnormal uterine bleeding
Endometrium

- Normal Structure
- Surface epithelium
- Glands
- Stroma and blood vessels
- Inflammatory cells
Endometrium

- Functional
  - Incorporates surface epithelium
  - Superficial part
  - Undergoes cyclical changes
  - Fine blood vessels
  - Shed in menstruation

- Basal
  - Deep component
  - Does not show cyclical changes
  - Thick walled blood vessels
  - Retained post menstruation
Menstrual Cycle

- 0-4 menstrual phase
- 4-14 proliferative phase- Oestrogen driven
  - Early
  - Mid
  - late
- 14-28 secretory phase- Progesterone modulated-date specific features
Features for Endometrial Dating

- **Glandular changes**
  - Structure
  - Mitotic activity
  - Nuclear features
  - Cytoplasmic vacuolation
  - Luminal secretions
  - Apoptosis

- **Stromal changes**
  - Edema
  - Mitotic activity
  - Decidua
  - Inflammatory cells
Proliferative endometrium

- Growth of endometrium form 0.5 to 4 mm in thickness
- Glands and stroma show brisk mitotic activity
- Glands change from small tubular to tortuous
- Pseudostratified, oval nuclei
- Stromal edema
- Fine blood vessels
Secretory Endometrium

- Thickness up to 7 to 8 mm
- Day 16 to day 28 orderly sequence of changes in glands (first half) and stroma (second half)
- 36 to 48 hours after ovulation
- Ovarian luteal phase
- At least 50% cells and gland should show vacuolation
Secretory endometrium

- Stromal changes are characterised by predecidualisation, days 23 to 28
- Granular lymphocytes or NK cells, CD56 positive
- Apoptosis and nuclear dust appears at the base of glands
- Fibrin thrombi in blood vessels
Menstrual Endometrium

- Fibrin thrombi in small vessels
- Glandular and stromal breakdown
- Stromal Crumbling
- Haemorrhagic background
Indications for Biopsy

- Determining the cause of abnormal bleeding
- Status of endometrium in infertility analysis
- Products of conception
- Assessment of response to hormonal treatment
Variations

- Regional variations between Isthmic and corpus and functionalis and basalis
- Recognition of metaplastic epithelium such as ciliated cells, pink cells, papillary and squamous cells
- Cyclical
- Age related changes such as atrophic or inactive
Clinical history

- Any nonphysiological uterine bleeding
  - Dysfunctional/nonorganic abnormality
  - Pregnancy related
  - Organic lesion
- Age and menstrual menopausal status important for interpretation
  - Dysfunctional disorders seen in young patients
  - Polyp- 2 to 24%, in our study of PMB polyps accounted for 25%.
  - Hyperplasia- in peri or post menopausal patients upto 16%
  - Malignancy in 10% of women
Endometritis

- Disorder of reproductive years
- Features include Presence of plasma cells and eosinophils, lymphoid cells, neutrophil and lack of normal glandular development
- Infective aetiology includes Chlamydia and gonococcus infection
- Follows pelvic inflammatory disease, recent gestation, instrumentation
Endometrial Polyp

- Common cause of postmenopausal bleeding
- Focus of hyperplasia/true neoplasia/focus lacking in hormonal receptors
- Low proliferative potential
- Cystic glands, Fibrous stroma incorporating blood vessels
Endometrial Polyp

- **Histological features**
  - Glands
  - Stroma
  - Proliferative activity
  - Inflammatory component
  - Architectural abnormality
  - Cytological abnormality
  - Therapy related features i.e. Tamoxifen
Pregnancy related changes

• Miscarriage before 16th week of gestation
• Approximately 15% to 20% early pregnancies result in loss
  o Spontaneous abortion before 12 weeks and at least half are due to chromosomal abnormalities
  o Incomplete abortion- conceptus is incompletely passed
  o Missed abortion- retained products without bleeding after death of foetus
Pregnancy related changes- Early

- Implantation on day 20 or 21
- Within 10 to 15 days after implantation decidualised cells appear
- Stromal granulocytes persist
- Hypersecretory glands appear and persist
Pregnancy related changes

- Trophoblast and chorionic villi
- The implantation site
- Foetal tissue
Trophoblast and Chorionic villi

- Trophoblast is extra embryonic but foetal in origin
- Closely related to host/ maternal tissue
- Epithelial component of placenta
- Has 3 distinct populations
  - Cytotrophoblast - germinative cells
  - Syncytiotrophoblast
  - Intermediate Trophoblast
Chorionic Villi

- Villi appear from day 12 to 13 post fertilisation
- Surface Trophoblast and stroma
  - Cytotrophoblast and Syncytiotrophoblast grow in a polar fashion
  - Stroma has blood vessels and stromal cells including macrophages.
  - Embryonic nucleated blood of yolk sac derivation (first 2 months of pregnancy)
Endometrial Hyperplasia

- Disease of perimenopausal women
- Reflection of Anovulatory cycle
- May result in menorrhagia
- Ultra sound examination shows thickened endometrium

Subtypes
Simple- Cystic Hyperplasia
Complex Hyperplasia
Atypical Hyperplasia- EIN
Endometrial hyperplasia

- **Causes of Hyperplasia**
  - Anovulatory cycles
  - Prolonged exposure to oestrogen
  - Polycystic ovary disease
  - Functioning ovarian or adrenal tumours
Simple Cystic Hyperplasia

- Increased number of glands
- Increased amount of stroma
- Anovulatory cycles
- Causes irregular bleeding
- High levels of oestrogens
Atypical Hyperplasia

- EIN - Endometrial Intraepithelial Neoplasia
- Presence of cytological abnormality
- Risk of progression to Adenocarcinoma is 25%
- May regress in a proportion of patients with Progesterone therapy
Endometrial Carcinoma

- Most common malignant tumour of female genital tract in developed world
- Increased risk in women receiving unopposed oestrogen and with polycystic ovary syndrome.
- Risk factors include obesity, hypertension, diabetes mellitus
- Genetic factors- HNPCC 20-30% women develop endometrial cancer
- Two pathways
  - Type1 – Oestrogen dependant-80-85%
  - Type 2 Oestrogen independent 15-20%
Endometrial cancer 2

- Clinical presentation with postmenopausal bleeding
- Most tumours are low grade and low stage
- Commonest morphological type is Endometrioid
- Grading of tumour depends on gland formation and nuclear atypia
- Prognosis depends on grade and stage
- Spreads by lymphatic, direct and transtubal to peritoneum
Myometrium

- Smooth muscle cells supported by collagen
- Respond to progesterone
- Undergoes hypertrophy in pregnancy
Myometrial pathology

- Leiomyoma
- Adenomyosis
- Stromal tumours
- Leiomyosarcom
Take home message

- Mullerian tract incorporates different types of specialised epithelium which is capable of metaplastic changes and respond to hormones.
- There is a spectrum of age related, cyclical and regional variations in endometrium.
- Products of conception are routine specimen which require some considered reporting to be of clinical use.