

# Pathology of female reproductive system- 2

Dr Hiroshi Silva

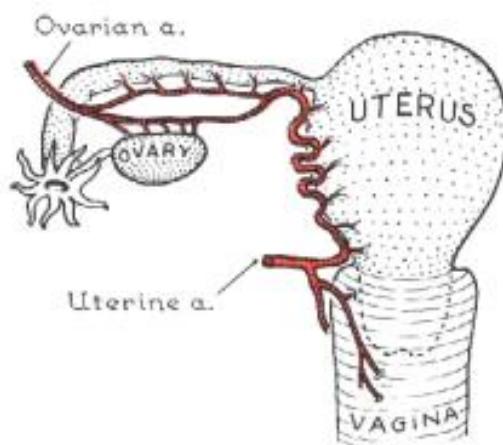
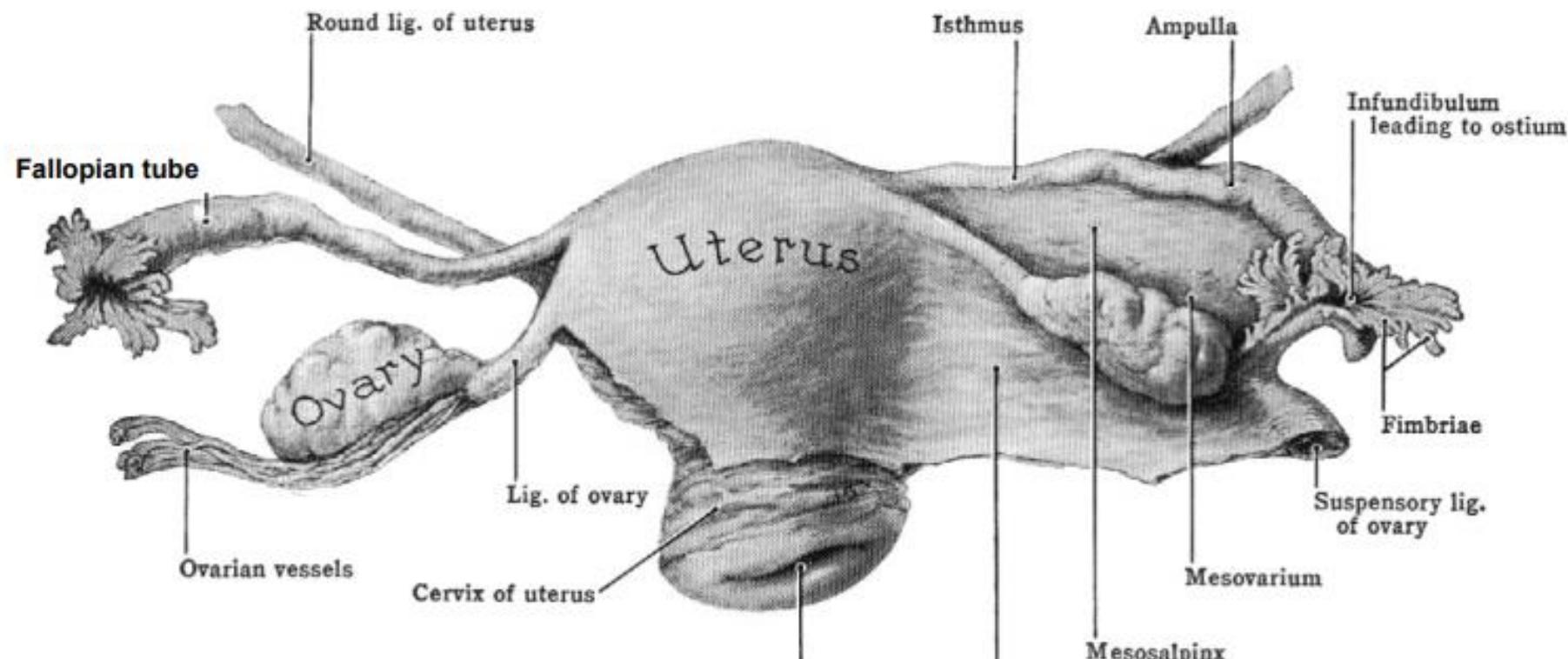
Department of pathology

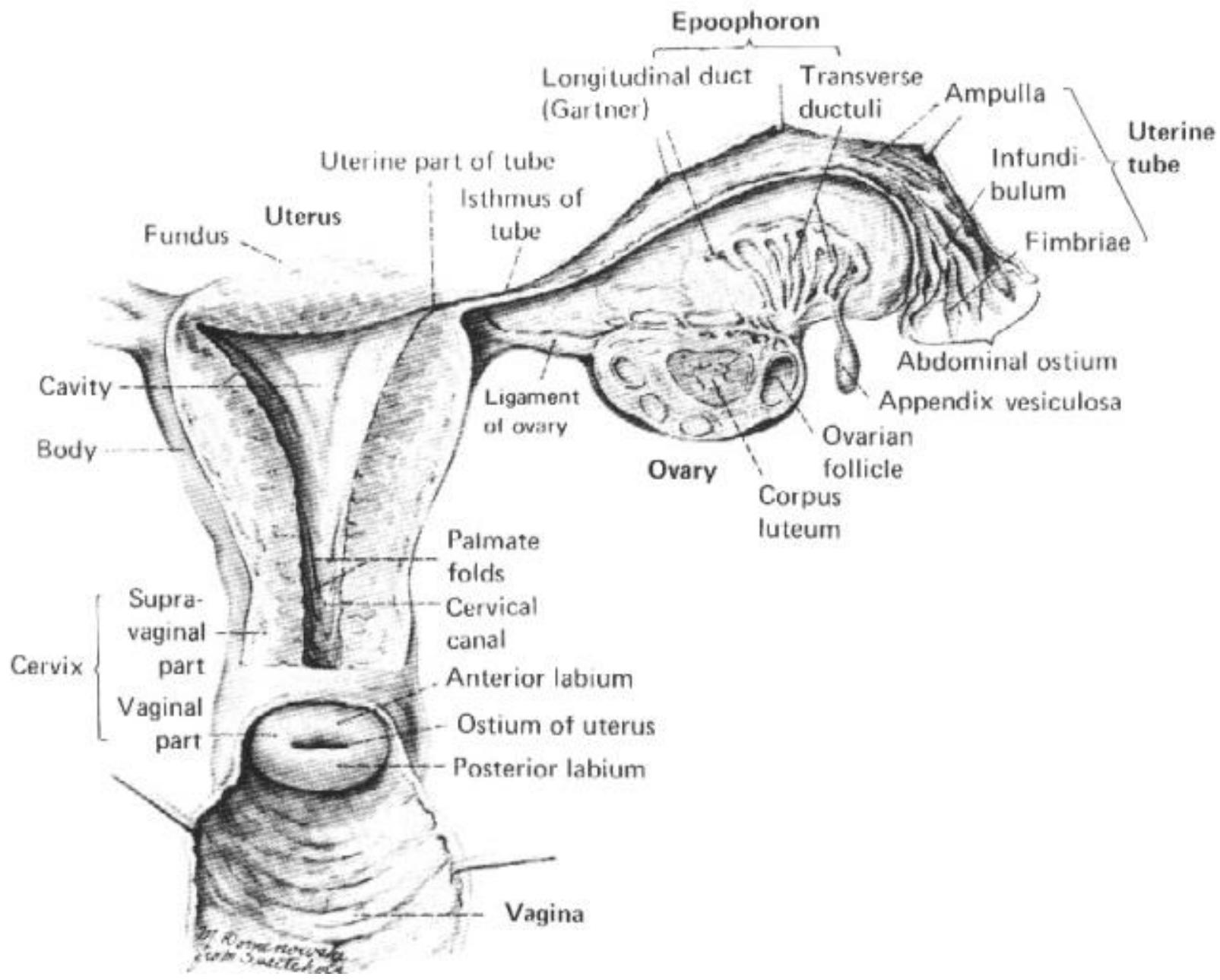
University of Kelaniya

# Objectives

At the end of this lecture, student should be able to

- Briefly describe the non- neoplastic lesions of the endometrium
- Describe the pathological changes in endometrial hyperplasia
- Discuss pathogenesis and morphology of carcinoma of the endometrium
- Describe the non-neoplastic and neoplastic lesions of the myometrium





# Uterine corpus

- Endometrium  
made up of endometrial glands surrounded by stroma
- Myometrium  
made up of smooth muscle bundles

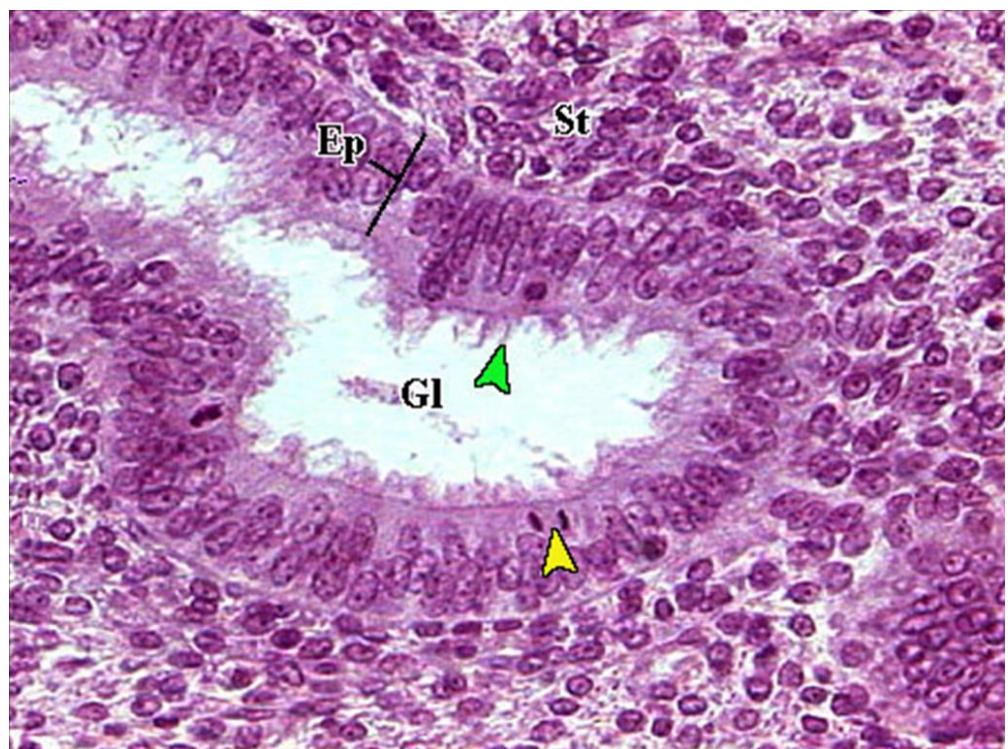
# Endometrium

Both glands and stroma responsive to hormonal influence

## Deep: basal layer

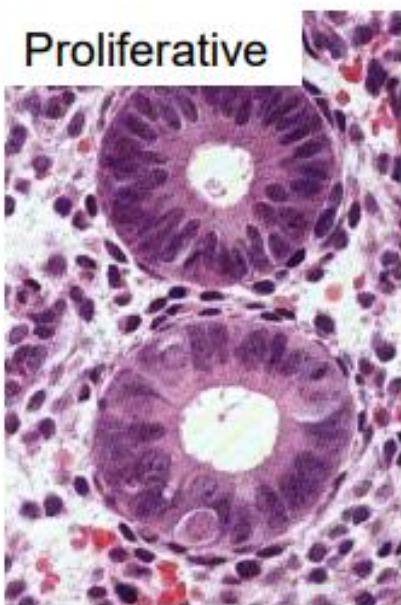
Responsible for regeneration following menstruation.

**Superficial: functional layer**  
undergoes sequential changes during the ovulatory cycle.

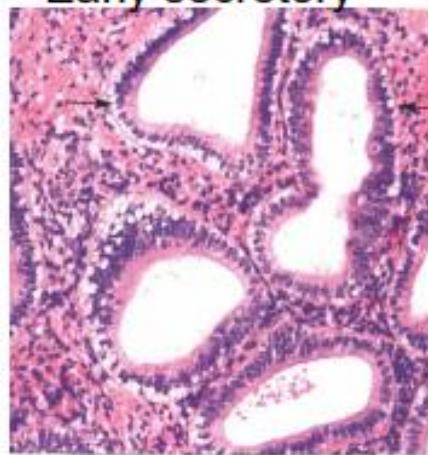


# The human menstrual cycle

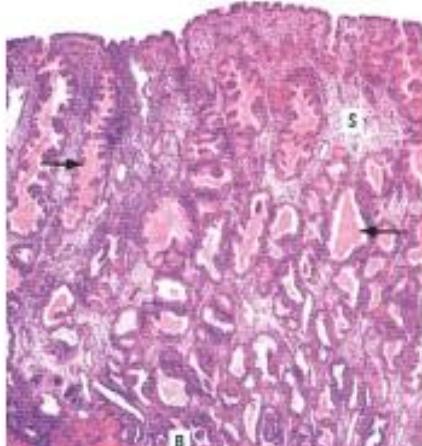
Proliferative



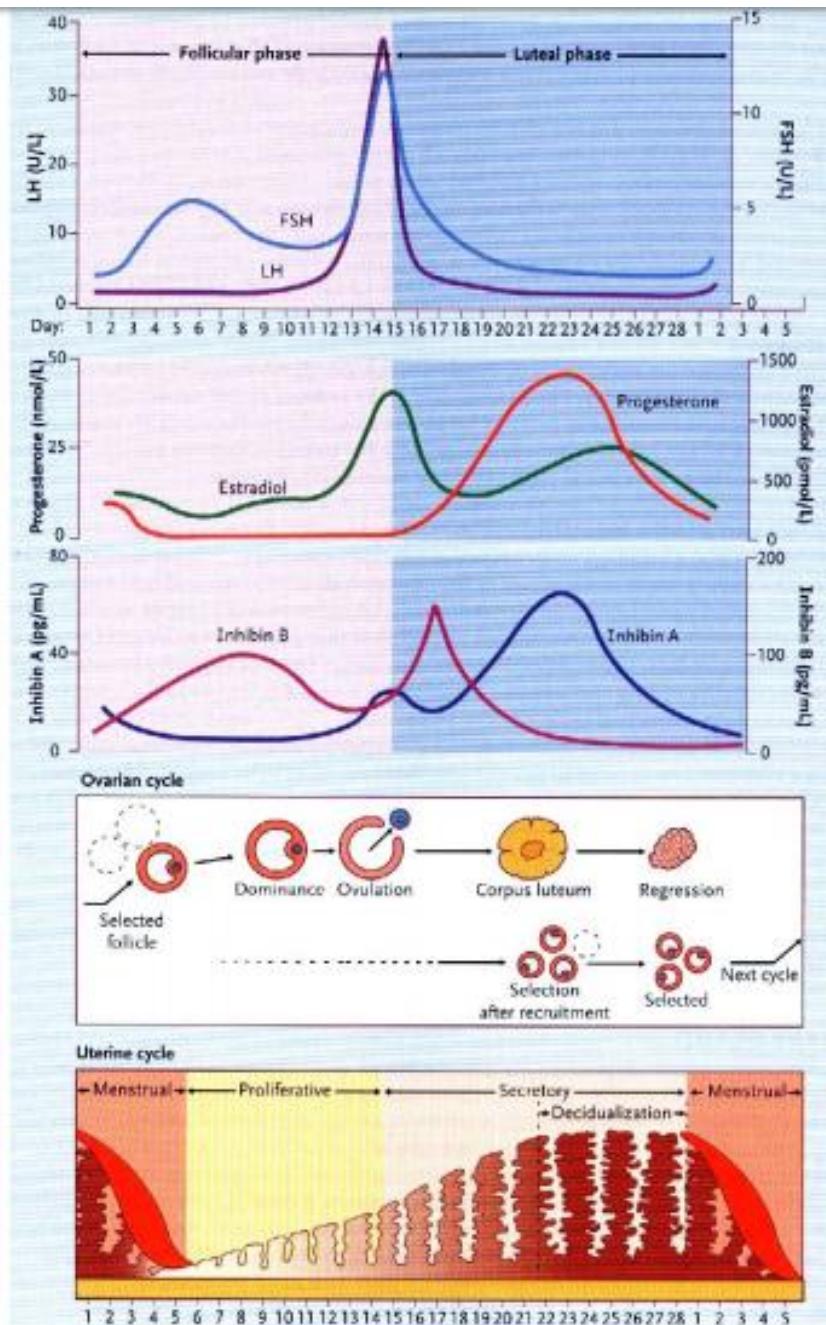
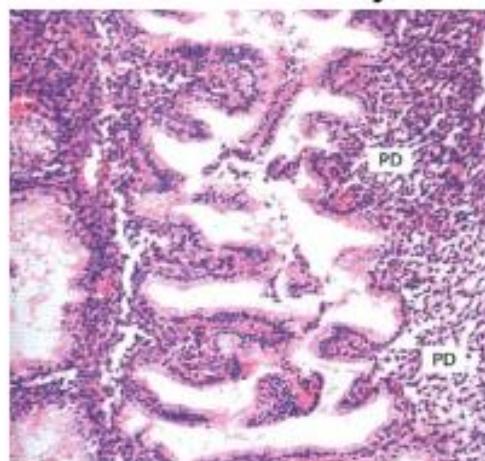
Early secretory

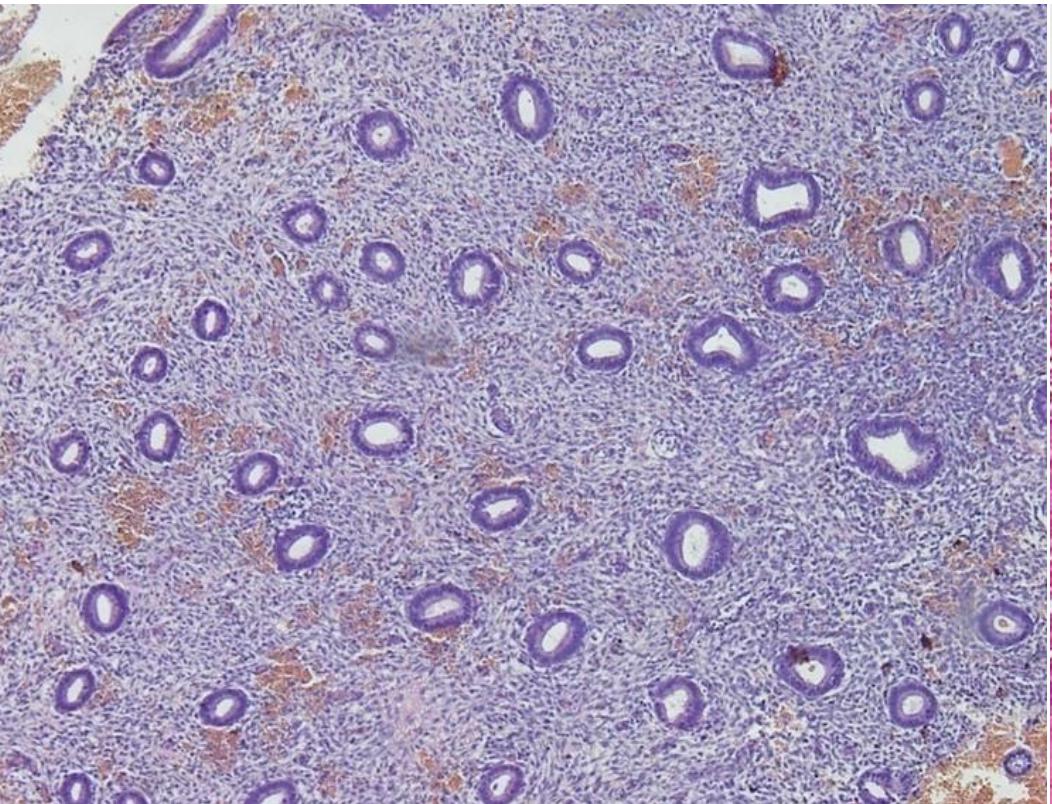


Mid Secretory



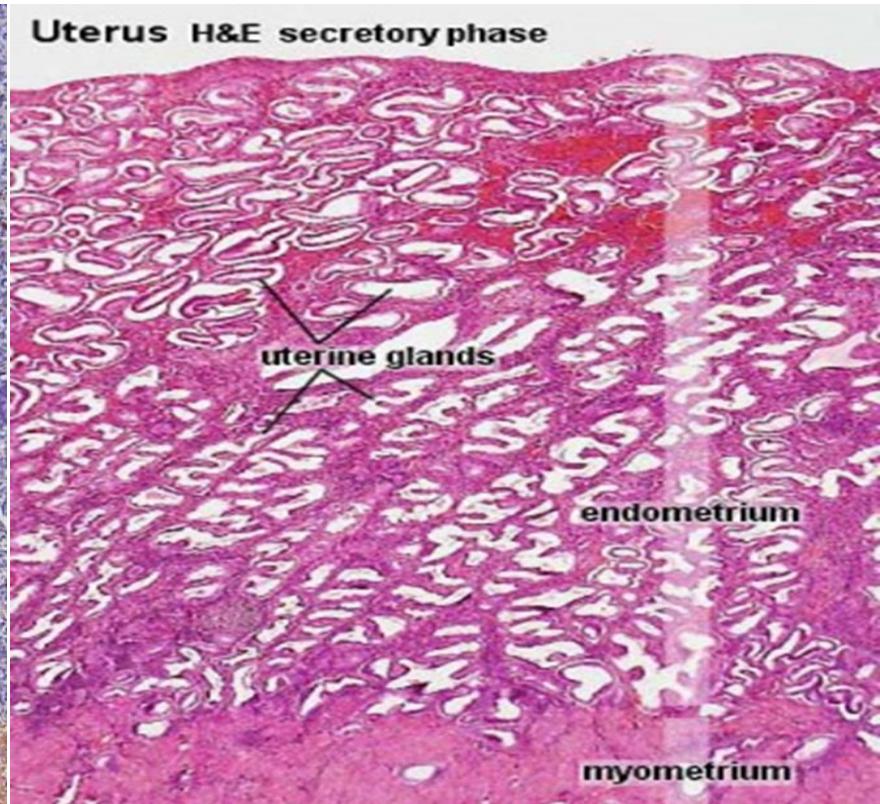
Late secretory





### Proliferative phase

Regular tubular glands.  
Columnar cells with mitoses  
Compact stroma



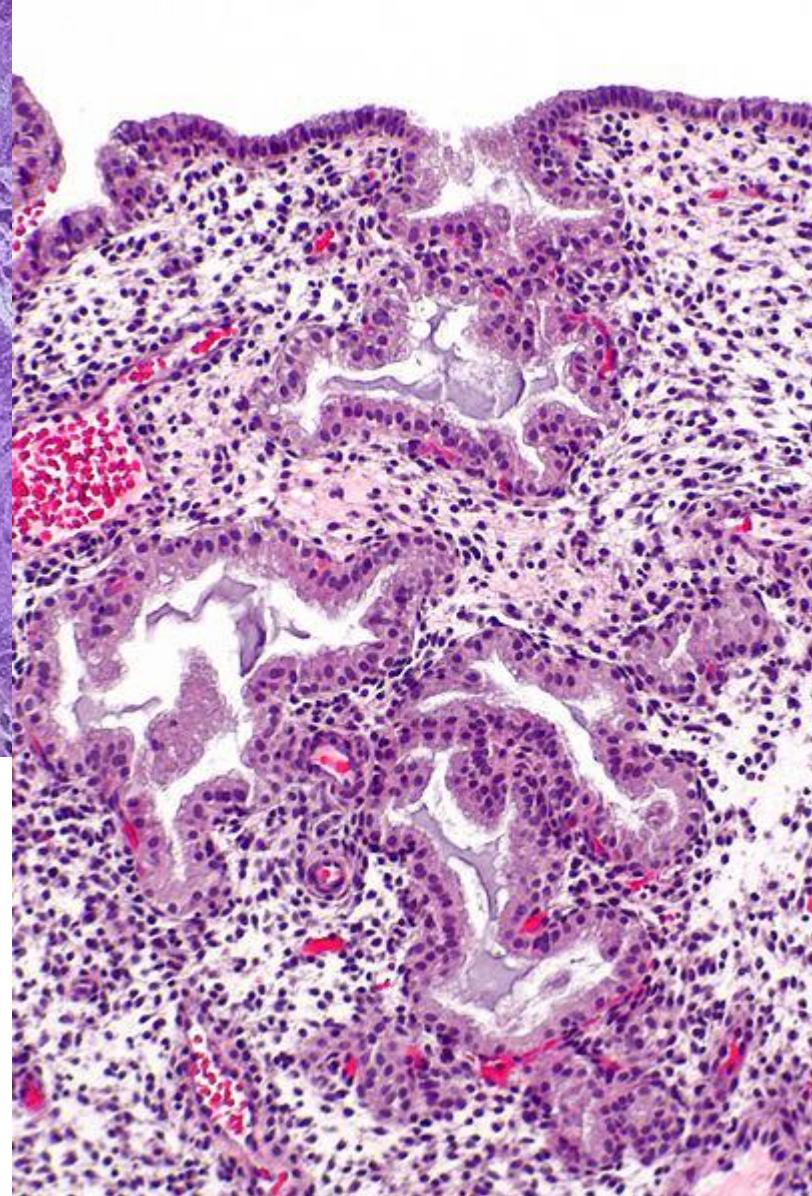
### Secretory phase

Dilated tortuous glands  
Sub/supra nuclear vacuoles,  
secretions  
Pre decidua  
Neutrophils, spiral arterioles

# Endometrium - Microscopy



Arrow-Mitoses(Proliferative activity)



# Objectives

At the end of this lecture the student should be able to

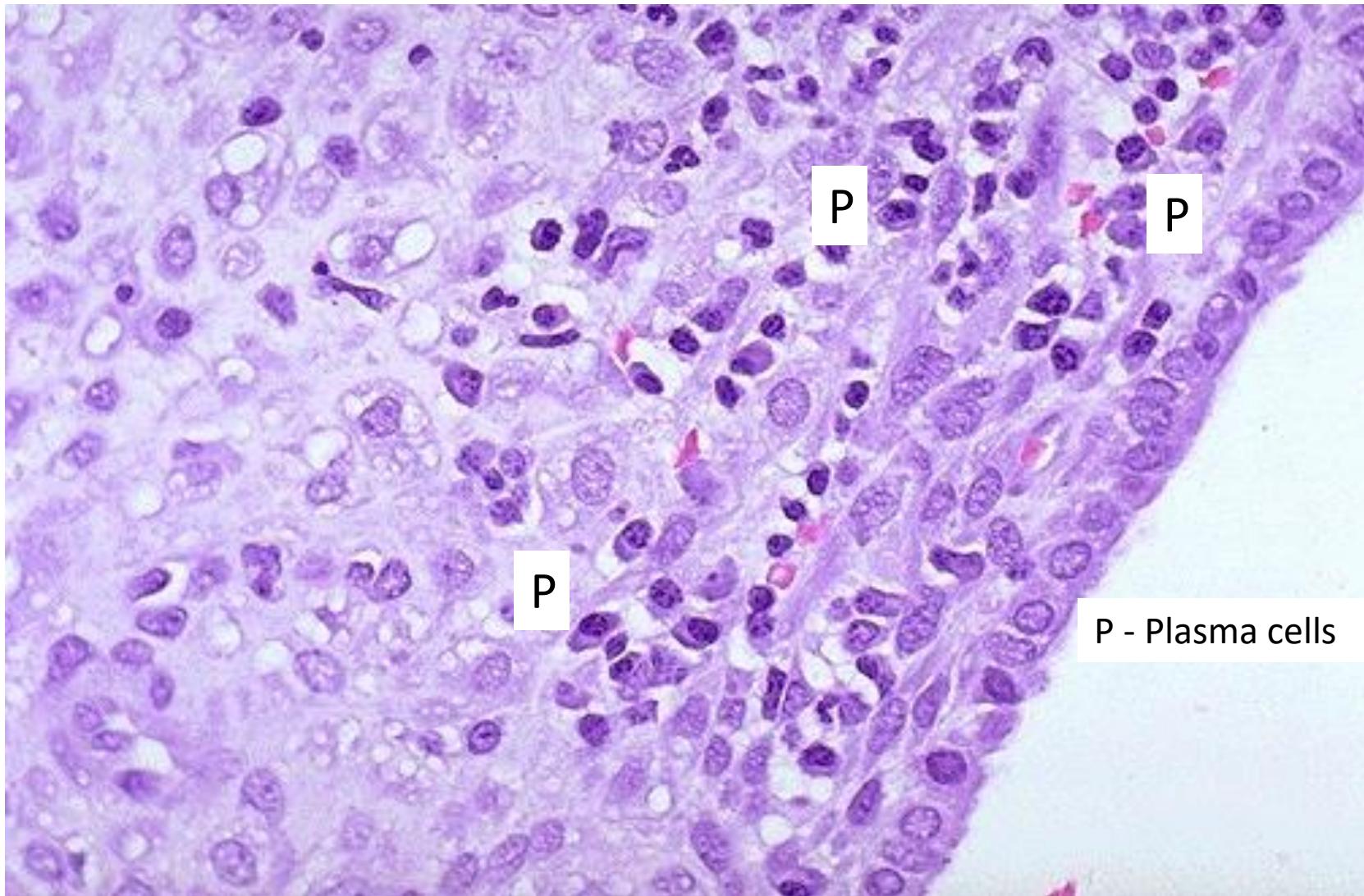
- Briefly describe the non- neoplastic lesions of the endometrium
- describe the pathological changes in endometrial hyperplasia
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- describe the non-neoplastic and neoplastic lesions of the myometrium

# Inflammation

- **Acute endometritis** is uncommon
  - limited to bacterial infections after delivery, miscarriage, abortion, instrumentation
- **Chronic endometritis** occurs secondary to
  - chronic PID
  - retained products of gestation
  - intrauterine contraceptive devices
  - tuberculosis (rare)

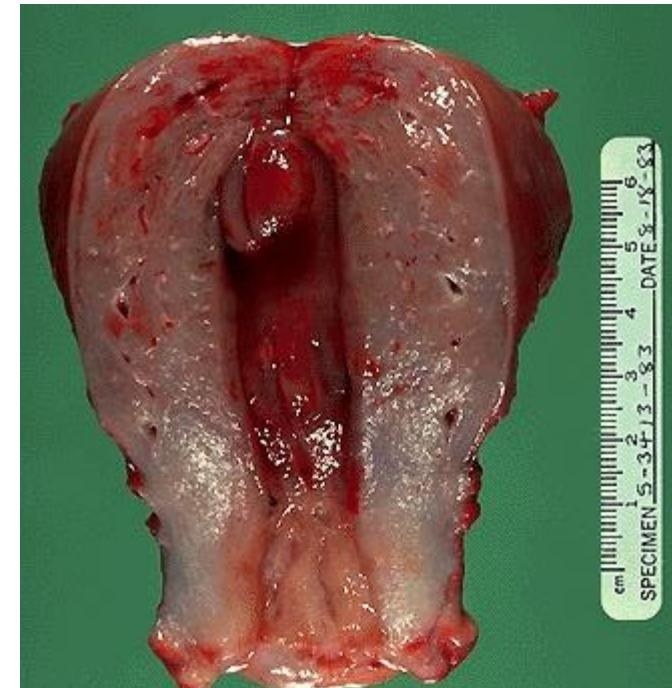
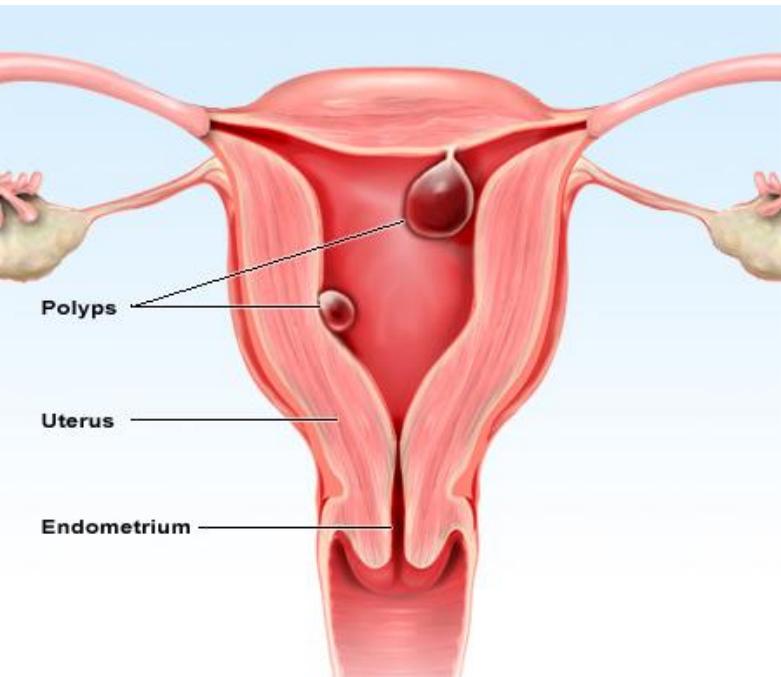
Myometrium is usually not involved; unless the inflammation is very severe

# Chronic endometritis



# Endometrial polyps

- Polypoidal masses protruding into the endometrial cavity
- May be single or multiple
- Usually sessile but may be pedunculated
- Rarely adenocarcinomas may arise within polyps



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# **Endometrial hyperplasia**

**Increased proliferation of endometrial glands relative to the endometrial stroma.**

**A precursor of endometrial carcinoma.**

Associated with prolonged unopposed oestrogenic stimulation of endometrium

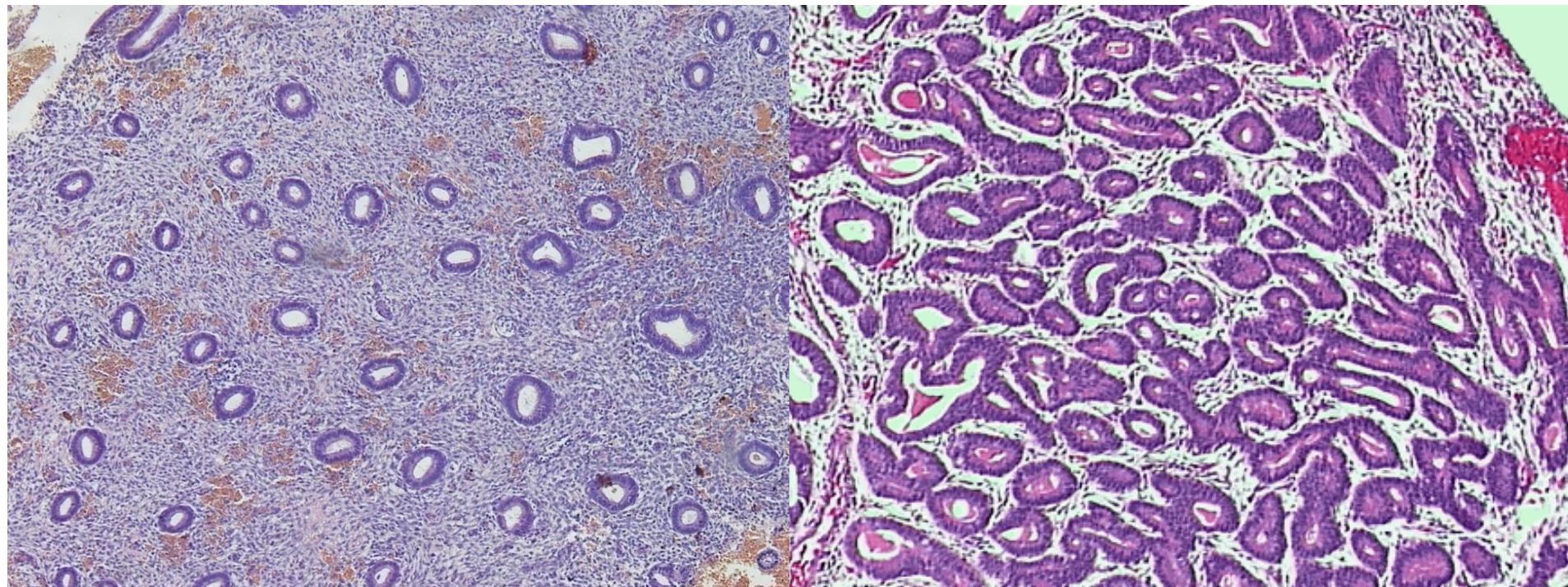
- Anovulatory cycles
  - Perimenarcheal and perimenopausal period
- Oestrogen administration
- Polycystic ovarian disease (PCOD), Obesity
- Oestrogen secreting tumours (granulosa theca cell tumours of ovary)

# Endometrial hyperplasia - Macroscopy

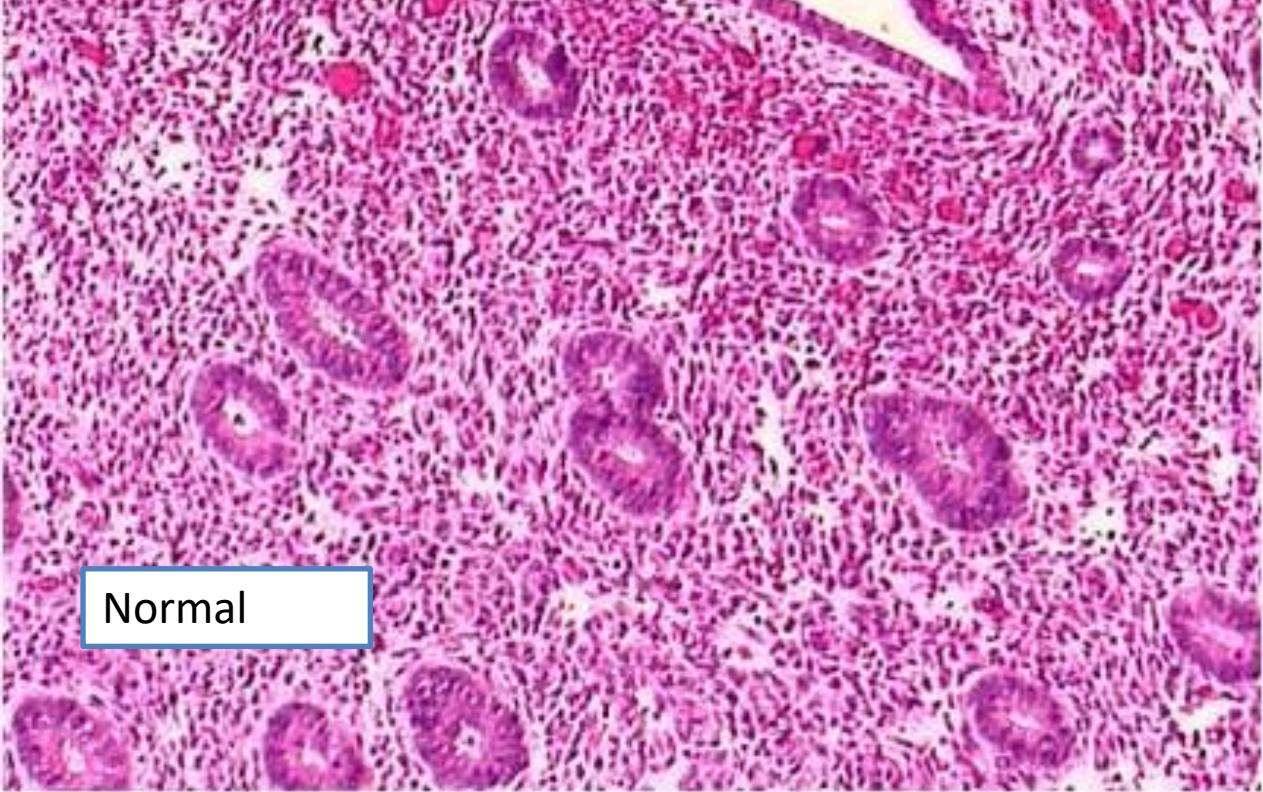


Note the increased thickness of the endometrium

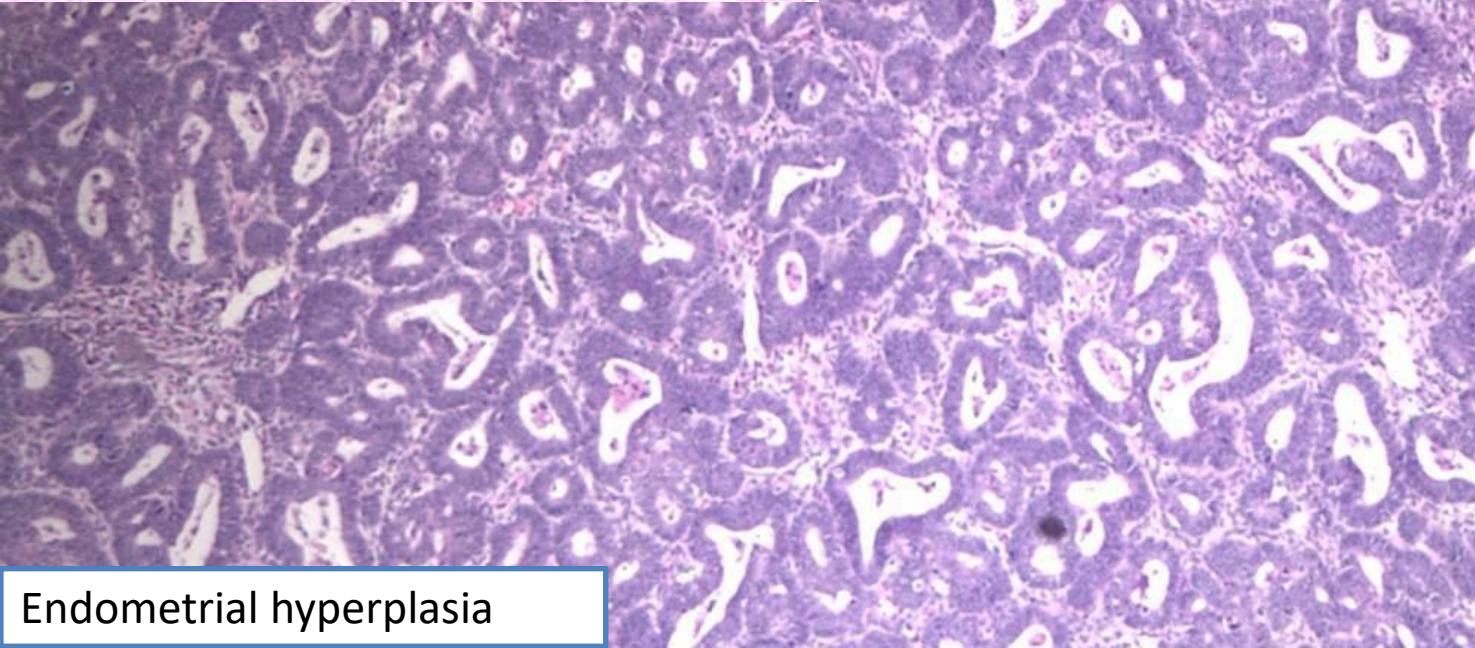
# Endometrial hyperplasia



Proliferative phase endometrium

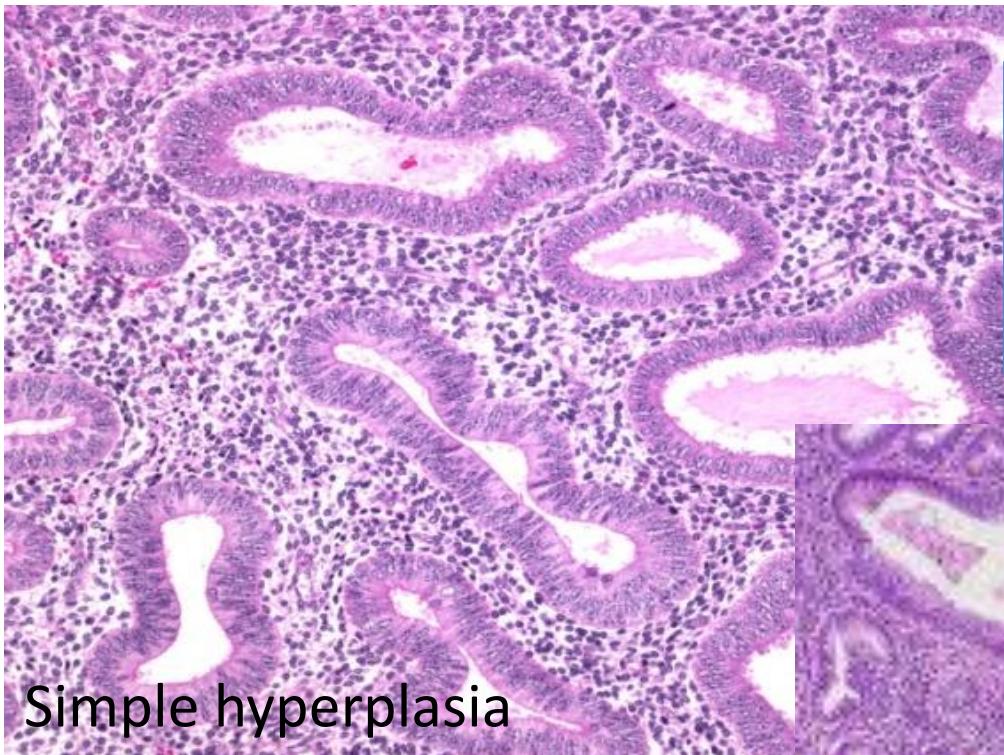


Normal



Endometrial hyperplasia

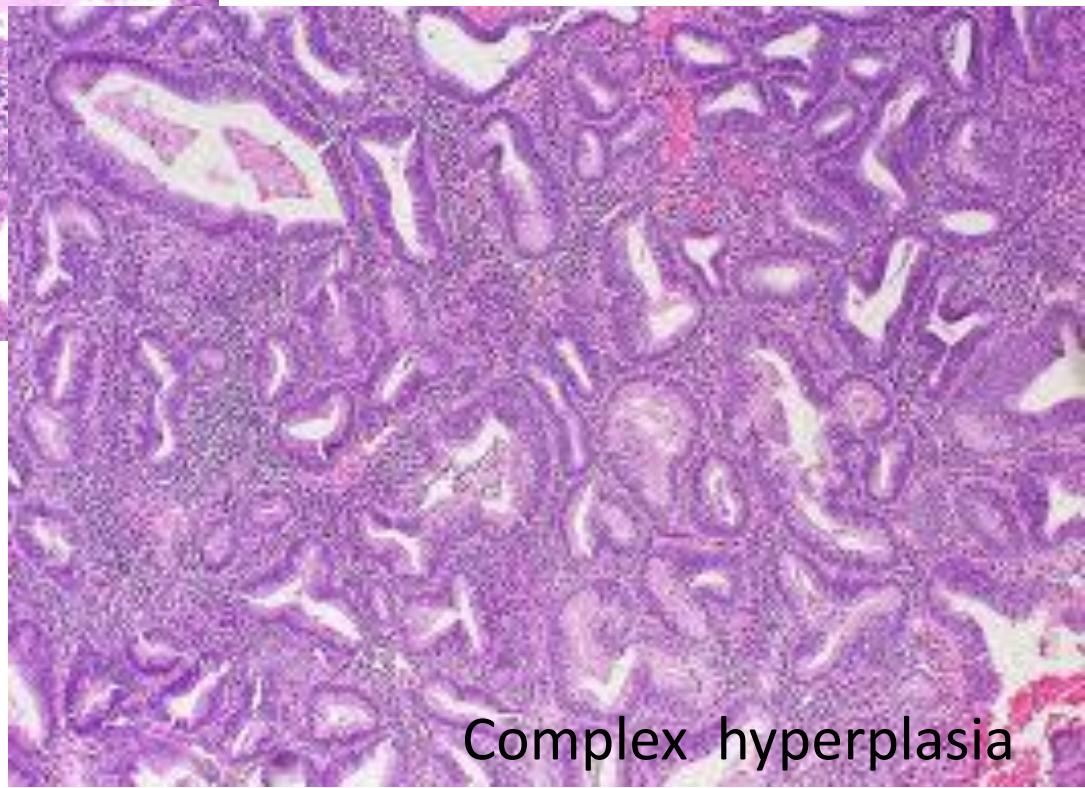
# Endometrial hyperplasia - Microscopy



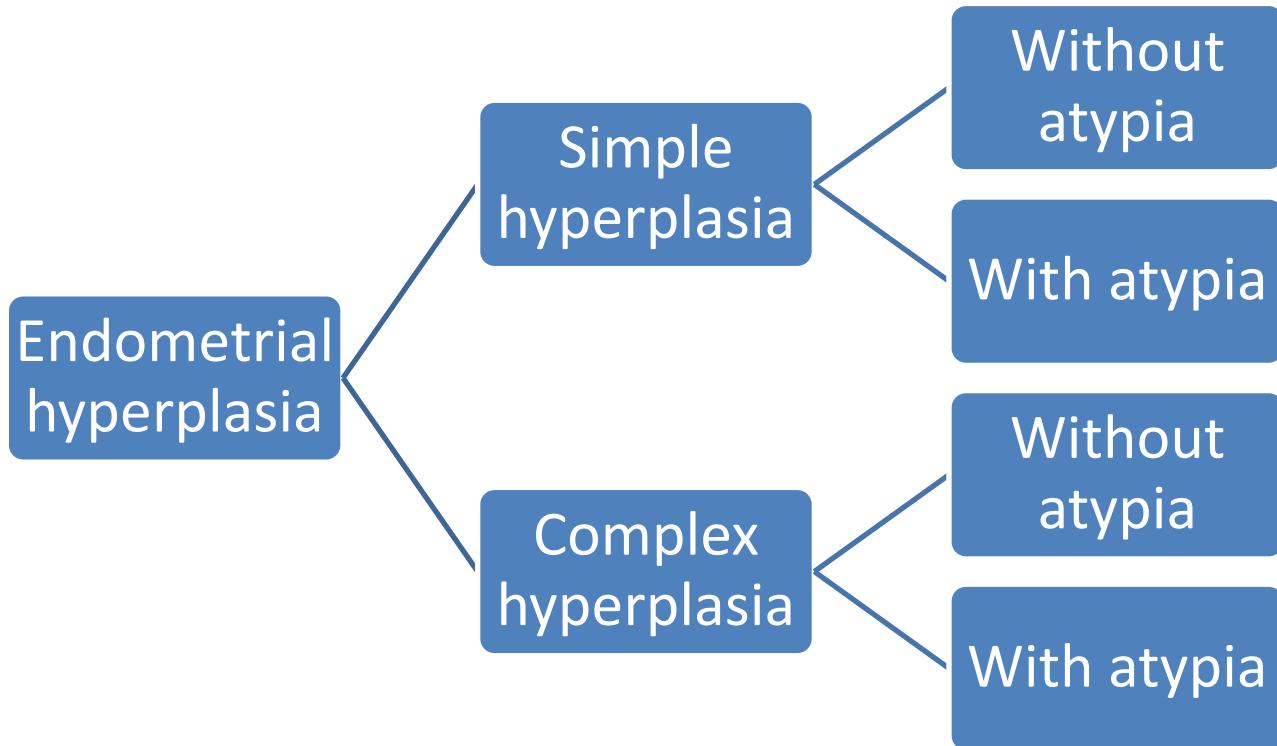
Simple hyperplasia

## Complex vs Simple hyperplasia

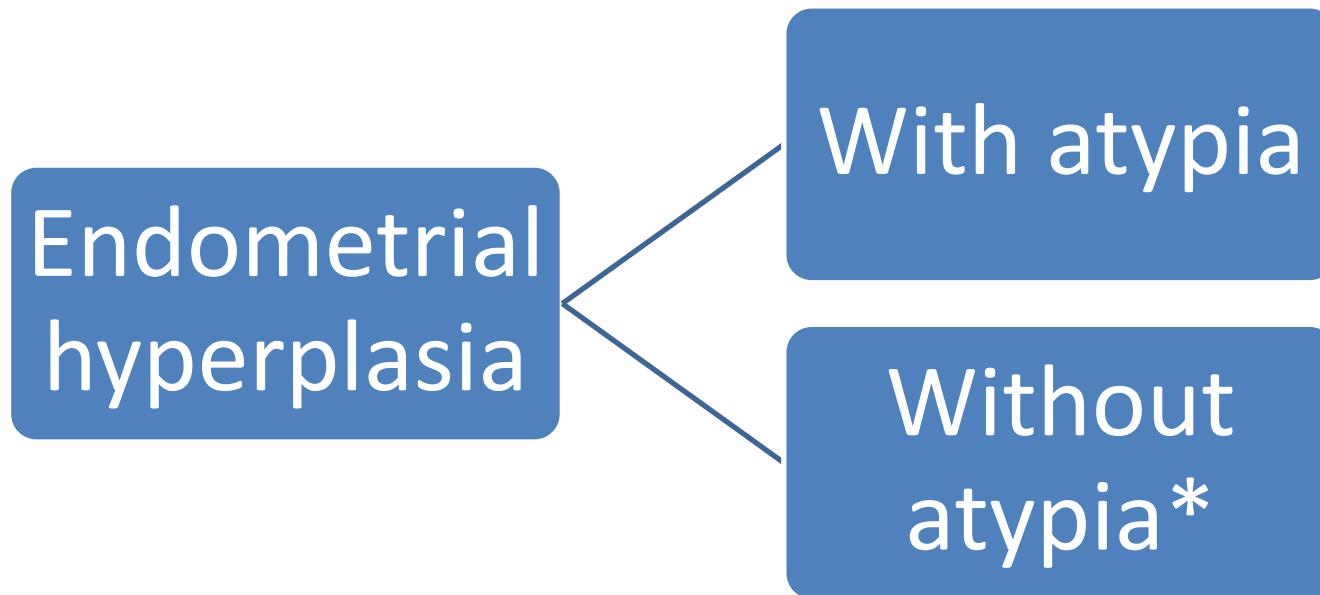
Based on the architectural crowding;  
Closely packed single glands vs nests of glands



Complex hyperplasia



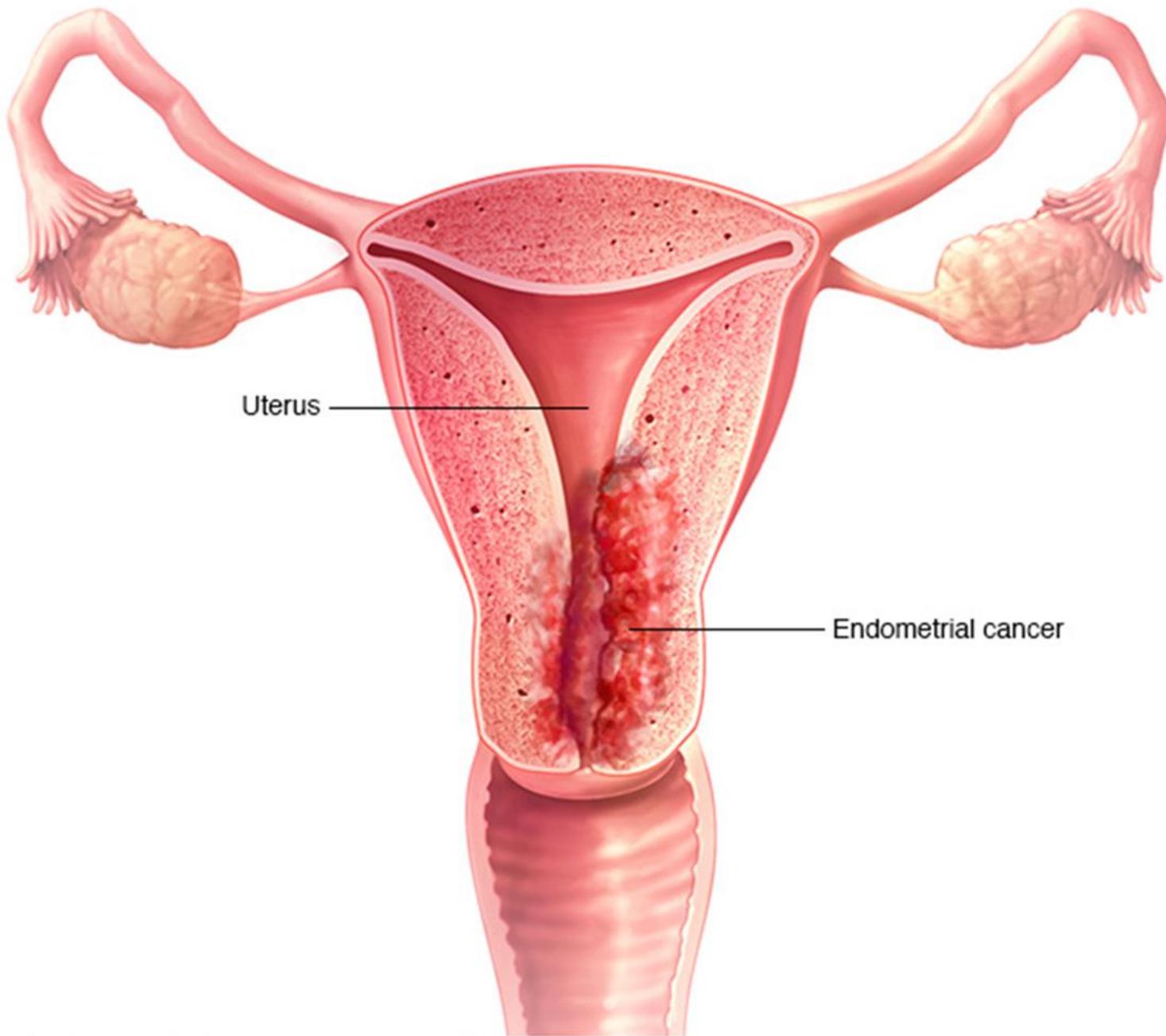
# 2014 WHO classification of endometrial hyperplasia



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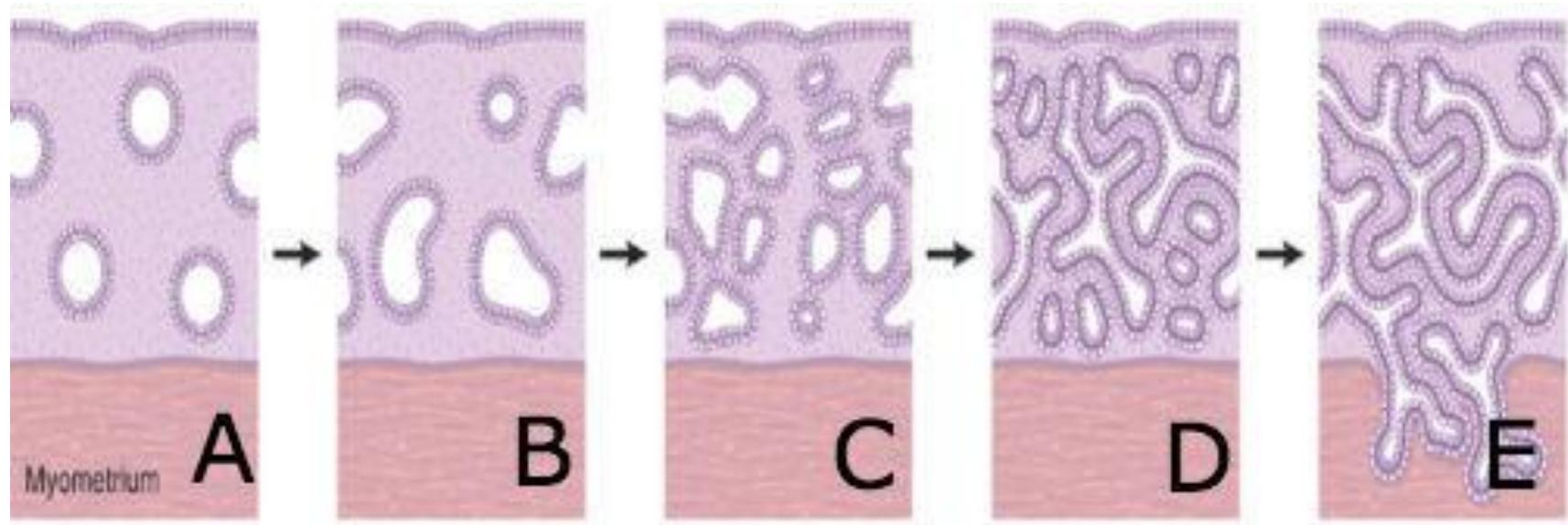


# Endometrial carcinoma (ECA)

- Common
- Mainly in post menopausal women
- Two broad categories

Characteristics	Type I	Type II
Age	55-65 years	65-75 years
Clinical setting	Unopposed oestrogen activity obesity, hypertension, diabetes	Atrophic endometrium
Tumour morphology	Endometrioid carcinoma	Serous carcinoma Clear cell carcinoma
Precursor	<b>Endometrial hyperplasia</b>	<b>Endometrial intraepithelial carcinoma</b>
Molecular genetics	Mutations in PTEN, KRAS, MSI	Mutations in TP53
Behaviour	Indolent	Aggressive

# Development of Type I ECA



Proliferative  
endometrium

Simple  
hyperplasia

Complex  
hyperplasia

Grade I uterine  
endometrial  
carcinoma

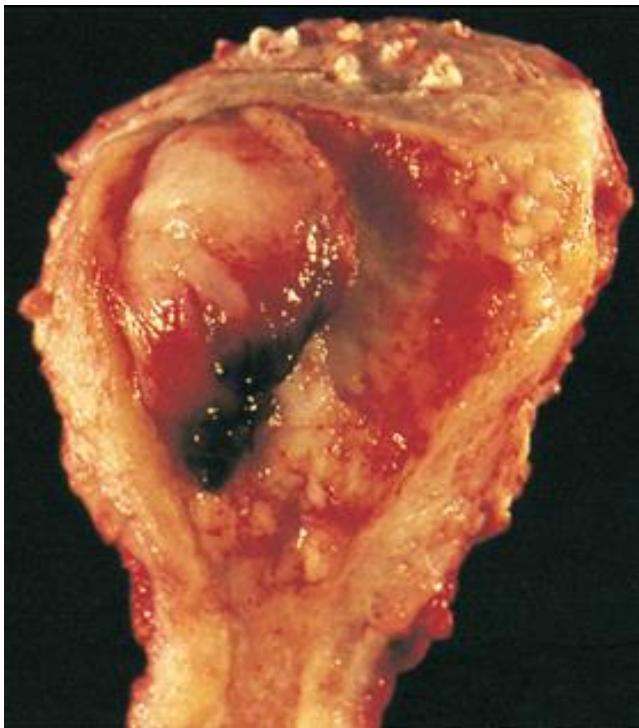
Inactivation of PTEN  
(Tumour suppressor gene)

hMLH1

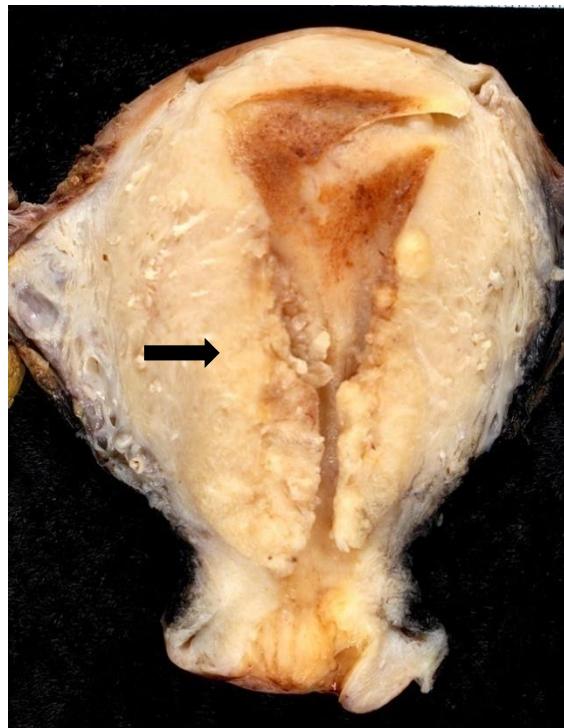
KRAS  
MI

B catenin  
PIK3CA

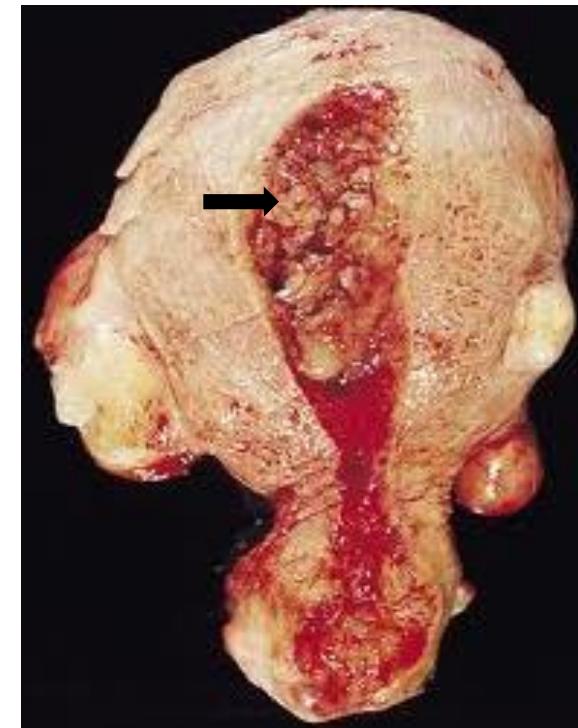
# Endometrial carcinoma - Macroscopy



Polyp



Endometrial  
thickening and  
infiltration



Polypoidal  
Growth

# Endometrial carcinoma - Macroscopy

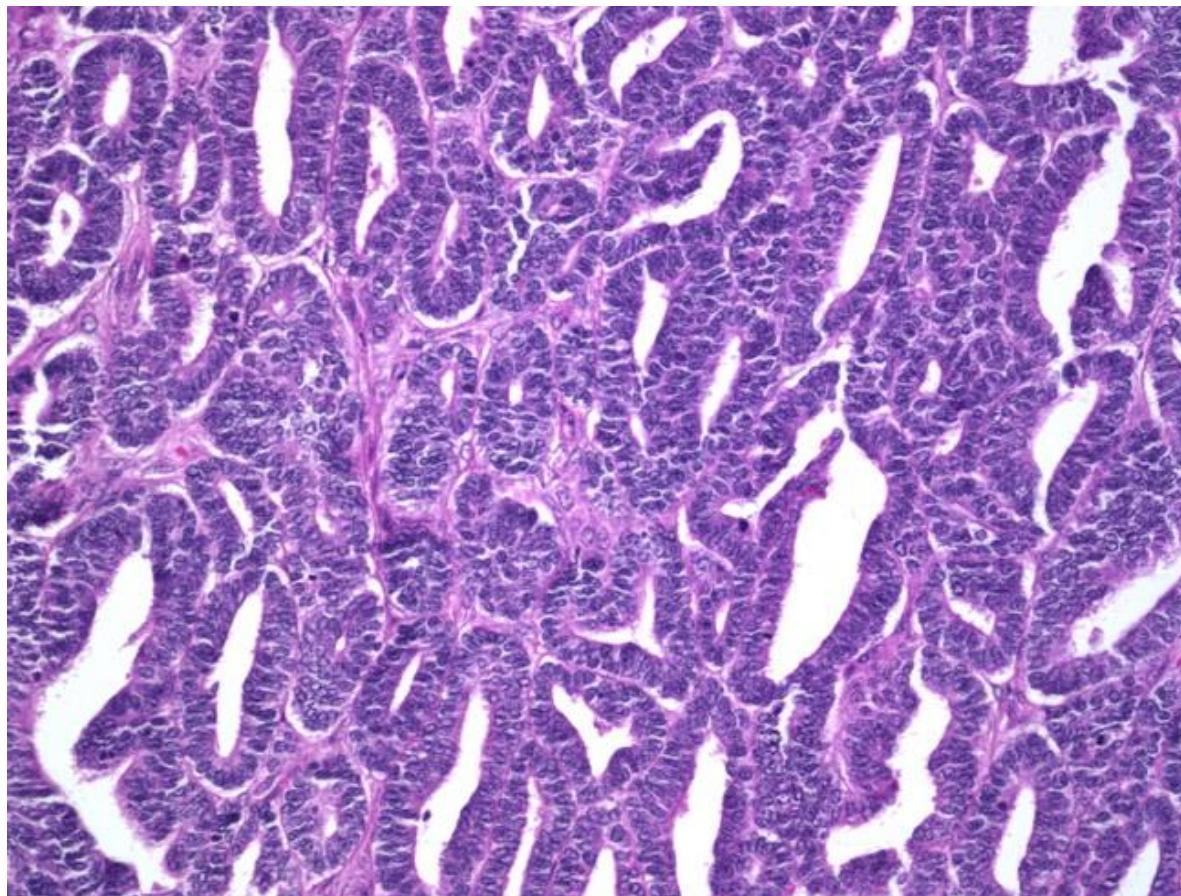


Solid, friable mass within the  
uterine cavity  
The cut surface shows  
Necrosis and haemorrhage

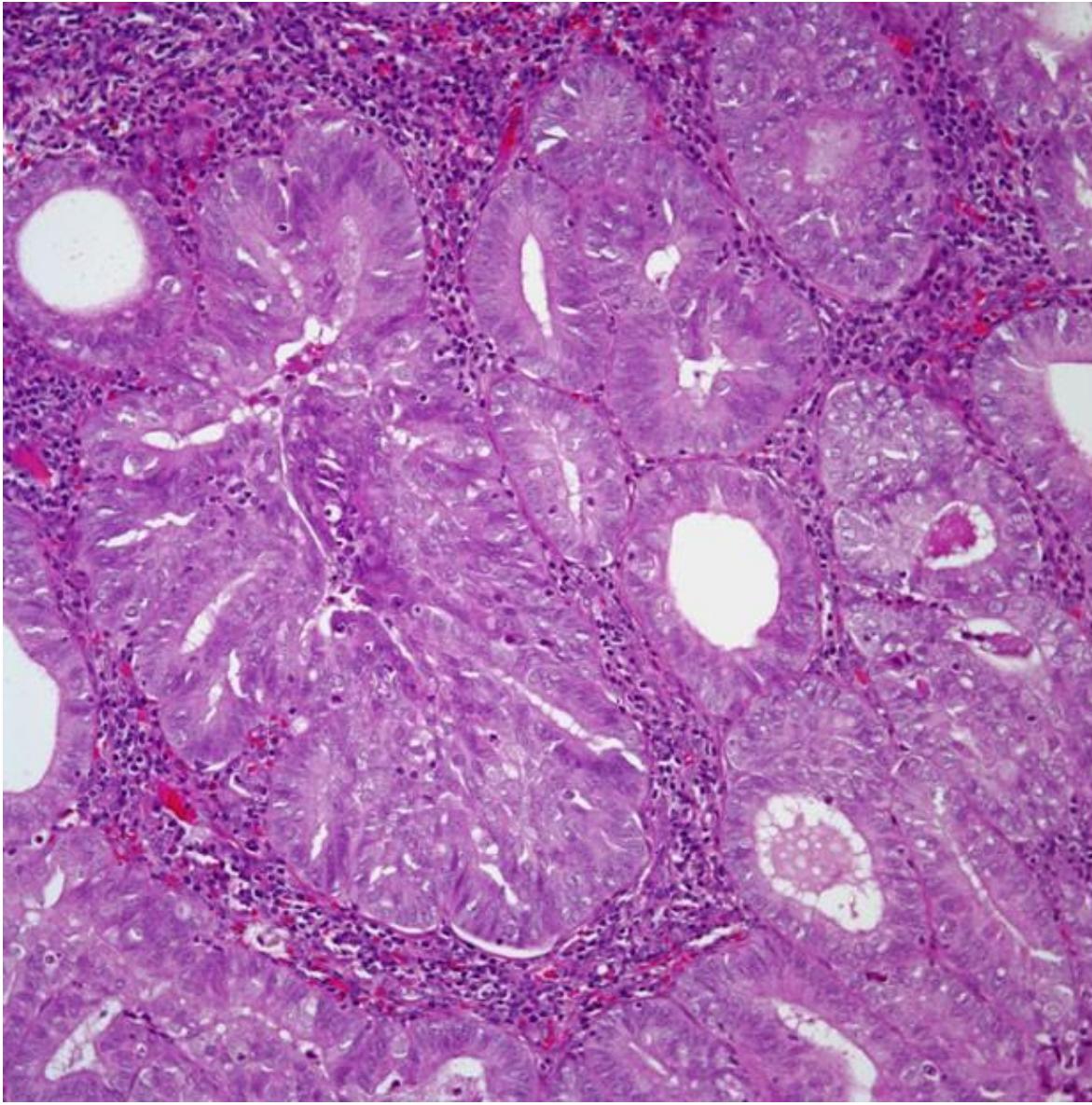
# Endometrial carcinoma

Microscopy

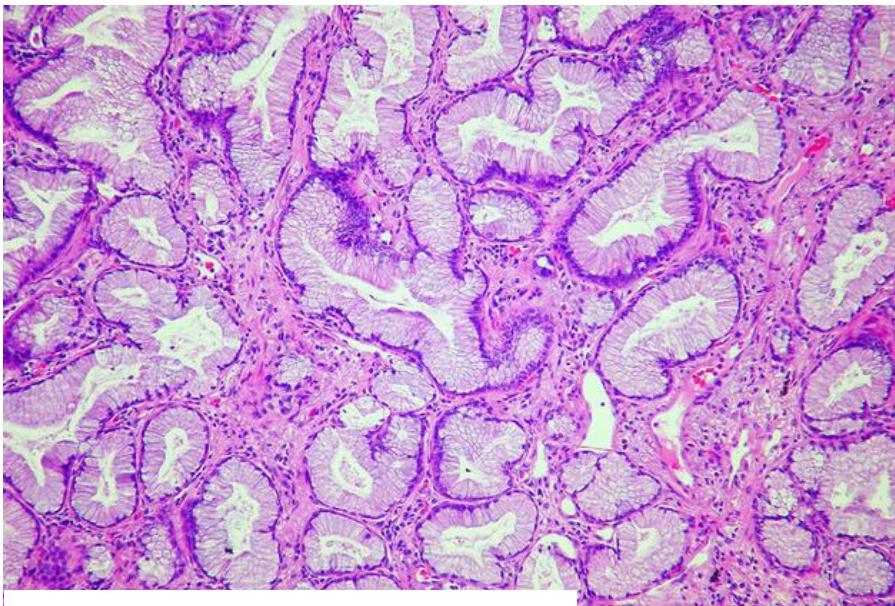
Commonest type - Adenocarcinoma



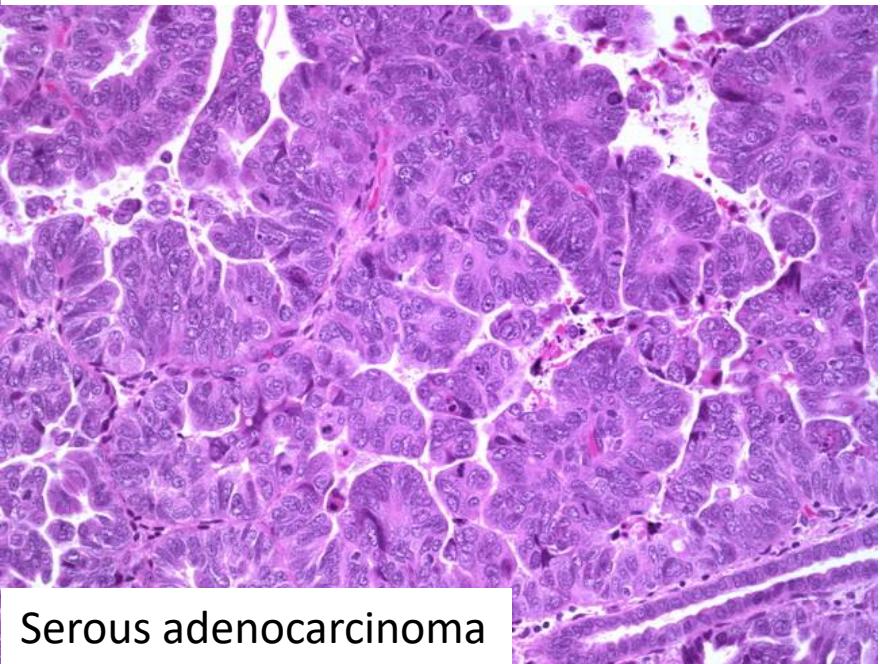
**Note: Gland formation in the tumour. Lack of stroma between glands.**



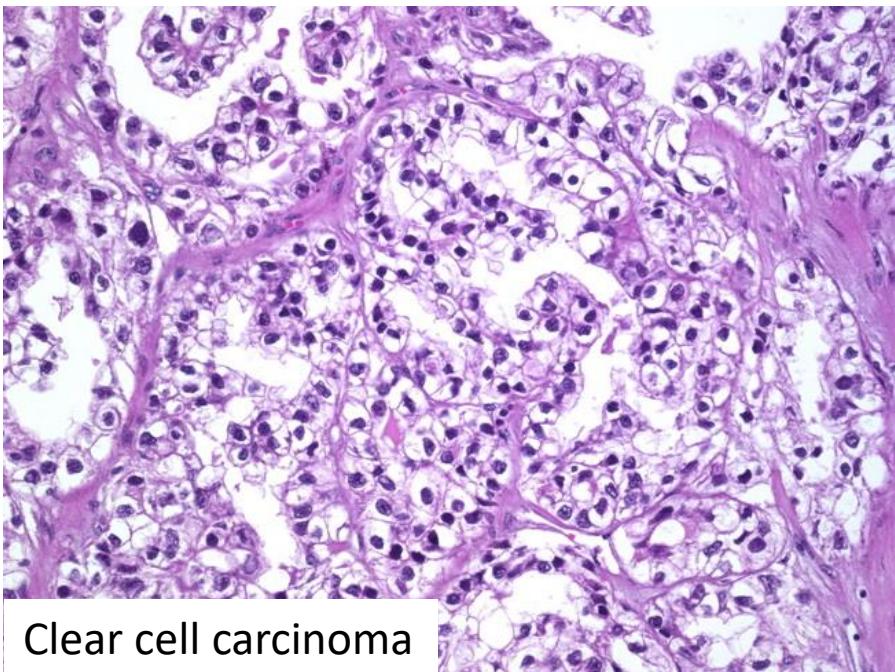
Commonest type - Endometrioid type adenocarcinoma



Mucinous adenocarcinoma



Serous adenocarcinoma



Clear cell carcinoma

Other histological types of  
endometrial  
adenocarcinomas

# Endometrial adenocarcinoma

- Locally invades myometrium, cervix, parametrium, POD and along fallopian tubes, ovaries and broad ligament
- Lymphatic - Para-aortic nodes
- Venous - Other organs

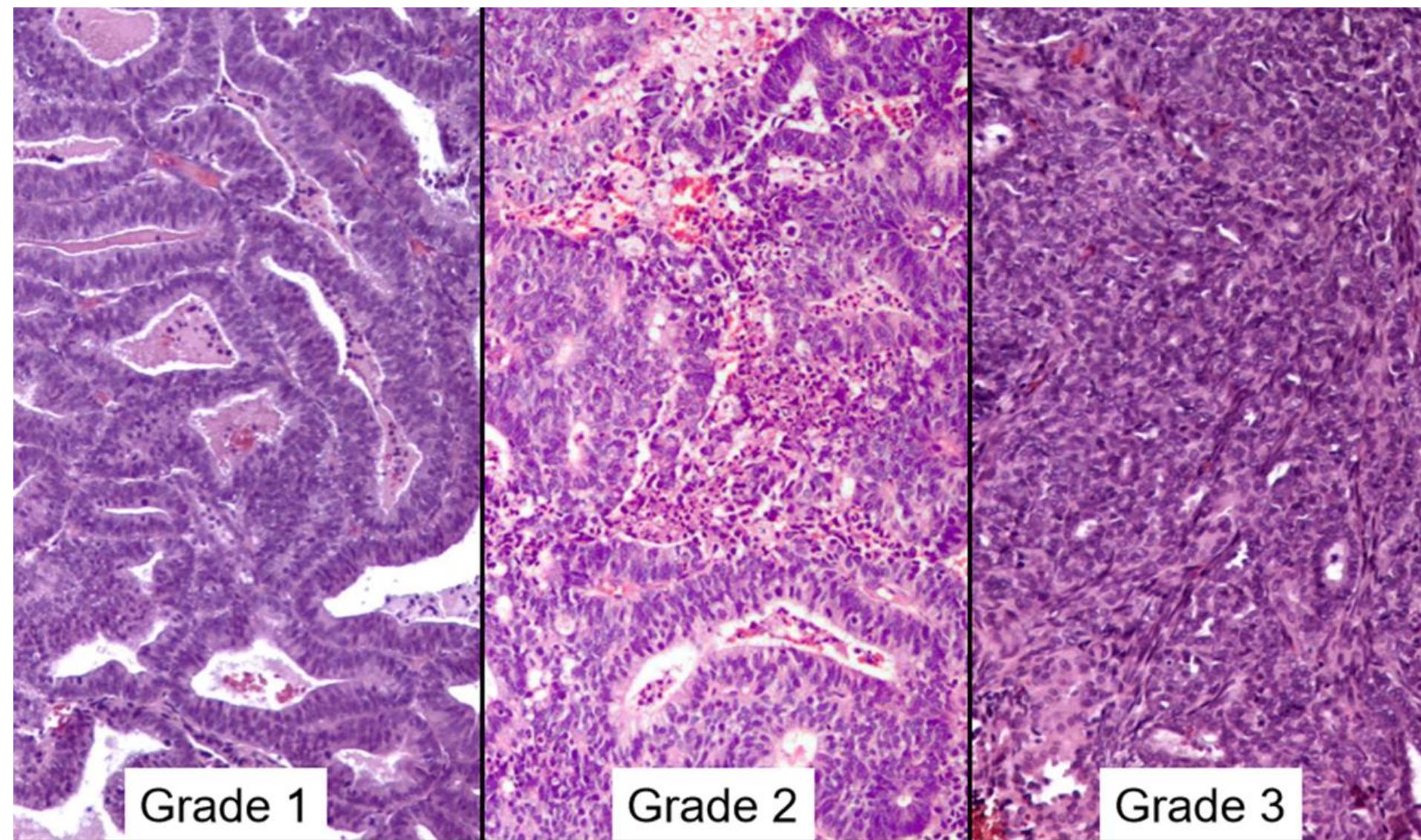
# Grading of endometrial adenocarcinoma

**G1** - Well-differentiated adenocarcinoma

**G2** - Differentiated adenocarcinoma with partly solid (less than 50%) areas

**G3** - Predominantly solid or entirely undifferentiated carcinoma

Serous and clear cell carcinomas are automatically classified as grade 3



# Staging of endometrial adenocarcinoma

**Stage I** - Carcinoma is confined to the corpus uteri

**Stage II**- Carcinoma has involved the corpus and the cervix

**Stage III**- Carcinoma has extended outside the uterus but not outside the true pelvis

**Stage IV**- Carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or the rectum

Stage is the most important factor in outcome

Any other tumours other than  
what we discussed already?

# WHO histological classification of tumours of the uterine corpus

<b>Epithelial tumours and related lesions</b>	
Endometrial carcinoma	Dissecting leiomyoma
Endometrioid adenocarcinoma	Intravenous leiomyomatosis 8890/1
Variant with squamous differentiation	Metastasizing leiomyoma 8898/1
Villoglandular variant	Miscellaneous mesenchymal tumours
Secretory variant	Mixed endometrial stromal and smooth muscle tumour
Ciliated cell variant	Perivascular epithelioid cell tumour
Mucinous adenocarcinoma	Adenomatoid tumour 9054/0
Serous adenocarcinoma	Other malignant mesenchymal tumours
Clear cell adenocarcinoma	Other benign mesenchymal tumours
Mixed cell adenocarcinoma	
Squamous cell carcinoma	
Transitional cell carcinoma	
Small cell carcinoma	
Undifferentiated carcinoma	
Others	
Endometrial hyperplasia	<b>Mixed epithelial and mesenchymal tumours</b>
Nonatypical hyperplasia	Carcinosarcoma (malignant müllerian mixed tumour; metaplastic carcinoma) 8980/3
Simple	Adenosarcoma 8933/3
Complex (adenomatous)	Carcinofibroma 8934/3
Atypical hyperplasia	Adenofibroma 9013/0
Simple	Adenomyoma 8932/0
Complex	Atypical polypoid variant 8932/0
Endometrial polyp	
Tamoxifen-related lesions	
<b>Mesenchymal tumours</b>	
Endometrial stromal and related tumours	<b>Gestational trophoblastic disease</b>
Endometrial stromal sarcoma, low grade	Trophoblastic neoplasms
Endometrial stromal nodule	Choriocarcinoma 9100/3
Undifferentiated endometrial sarcoma	Placental site trophoblastic tumour 9104/1
Smooth muscle tumours	Epithelioid trophoblastic tumour 9105/3
Leiomyosarcoma	Molar pregnancies
Epithelioid variant	Hydatidiform mole 9100/0
Myxoid variant	Complete 9100/0
Smooth muscle tumour of uncertain malignant potential	Partial 9103/0
Leiomyoma, not otherwise specified	Invasive 9100/1
Histological variants	Metastatic 9100/1
Mitotically active variant	Non-neoplastic, non-molar trophoblastic lesions
Cellular variant	Placental site nodule and plaque
Haemorrhagic cellular variant	Exaggerated placental site
Epithelioid variant	
Myxoid	
Atypical variant	
Lipoleiomyoma variant	
Growth pattern variants	<b>Miscellaneous tumours</b>
Diffuse leiomyomatosis	Sex cord-like tumours
	Neuroectodermal tumours
	Melanotic paraganglioma
	Tumours of germ cell type
	Others
	<b>Lymphoid and haematopoietic tumours</b>
	Malignant lymphoma (specify type)
	Leukaemia (specify type)
	<b>Secondary tumours</b>

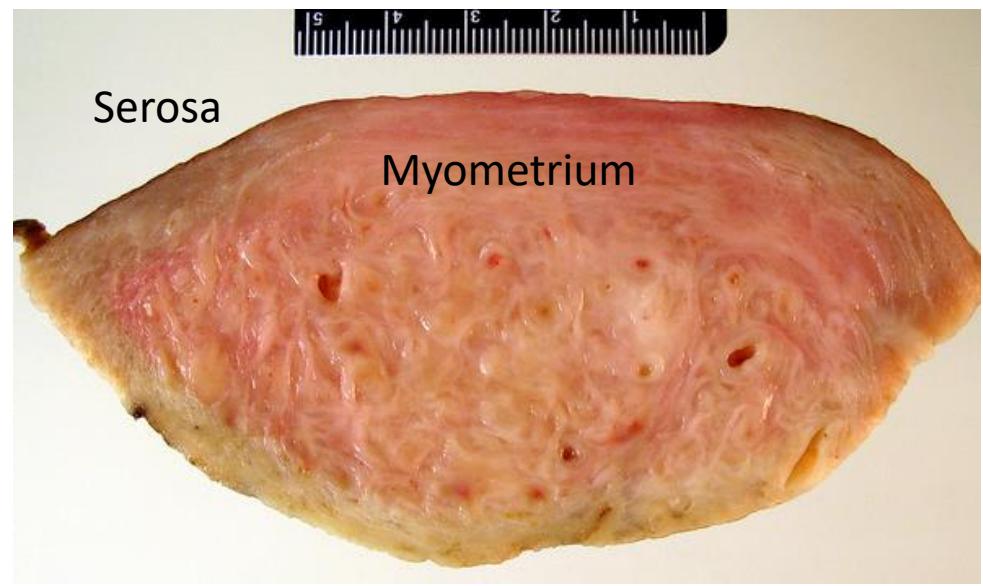
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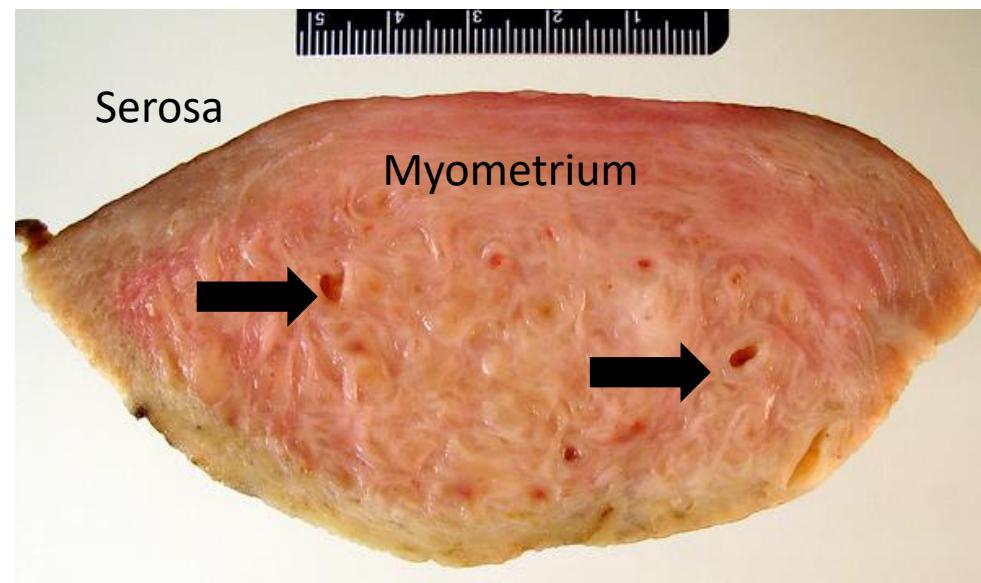
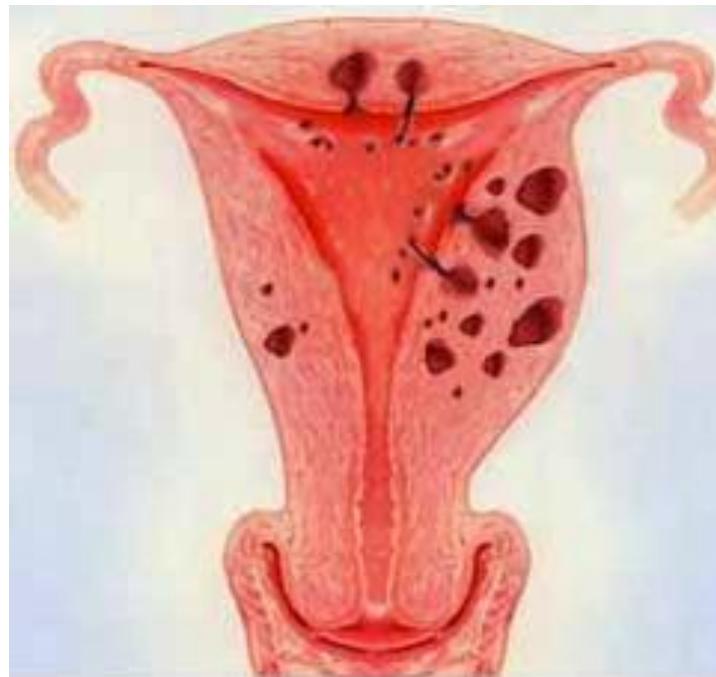
# Adenomyosis

- Presence of endometrial tissue in the uterine wall (myometrium)
- Closely related to endometriosis
- Macroscopy - Foci of haemorrhagic cysts of variable size within the myometrium



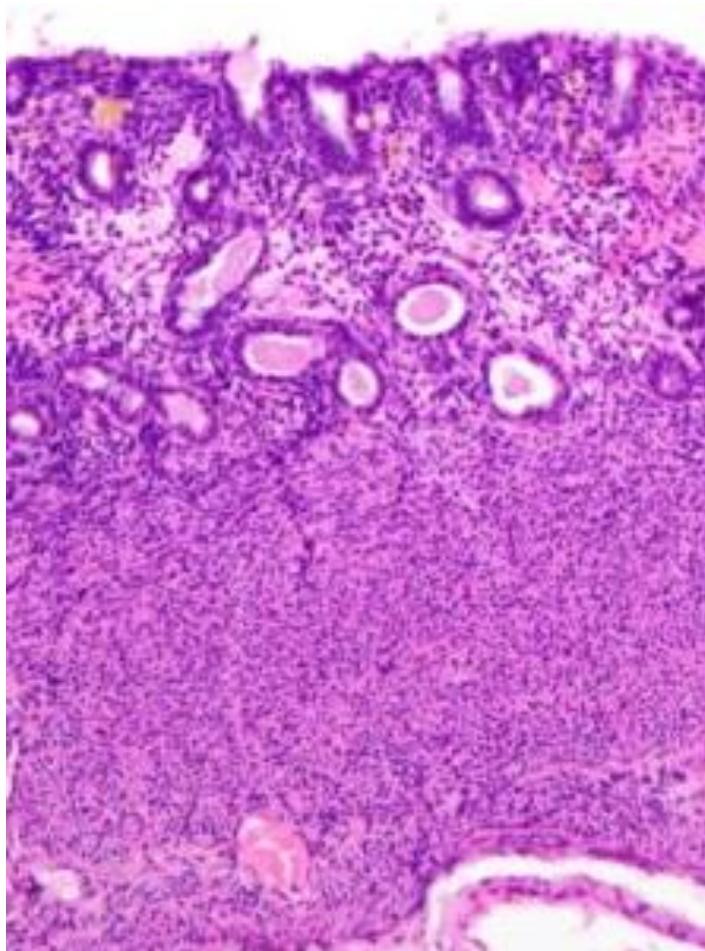
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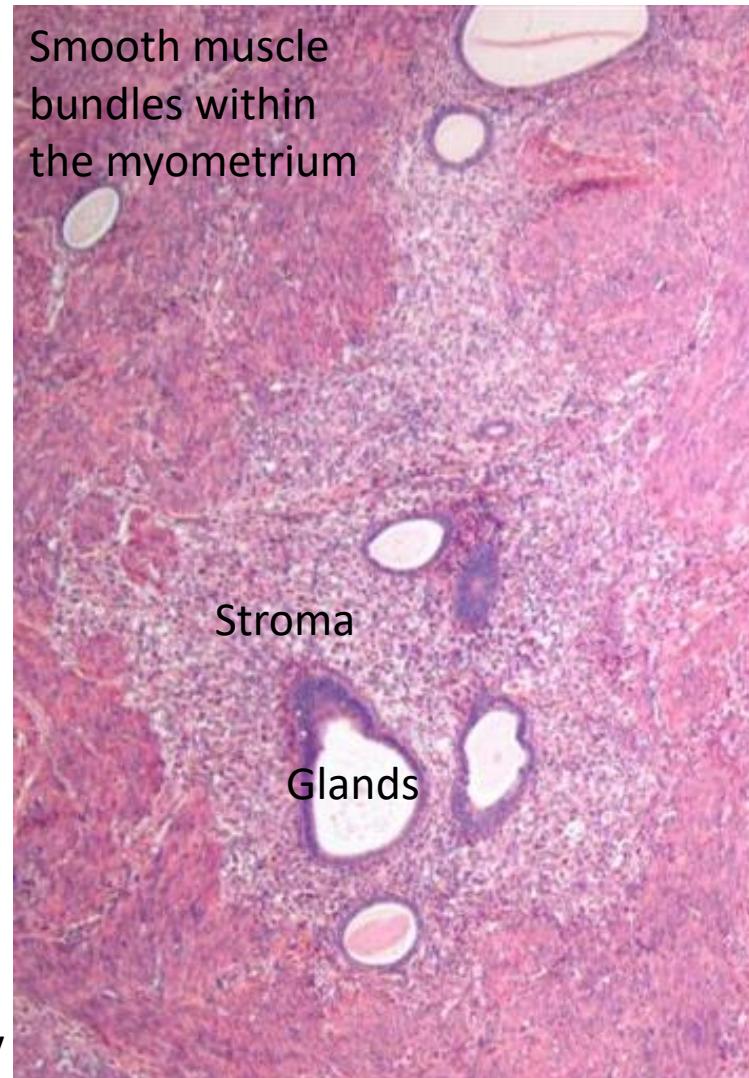


# Adenomyosis - Microscopy

- Endometrial tissue within the myometrium



Normal endometrial lining of the uterine cavity



# Benign tumours

- Benign tumours

Leiomyoma (fibroid)

Common

Origin - smooth muscle

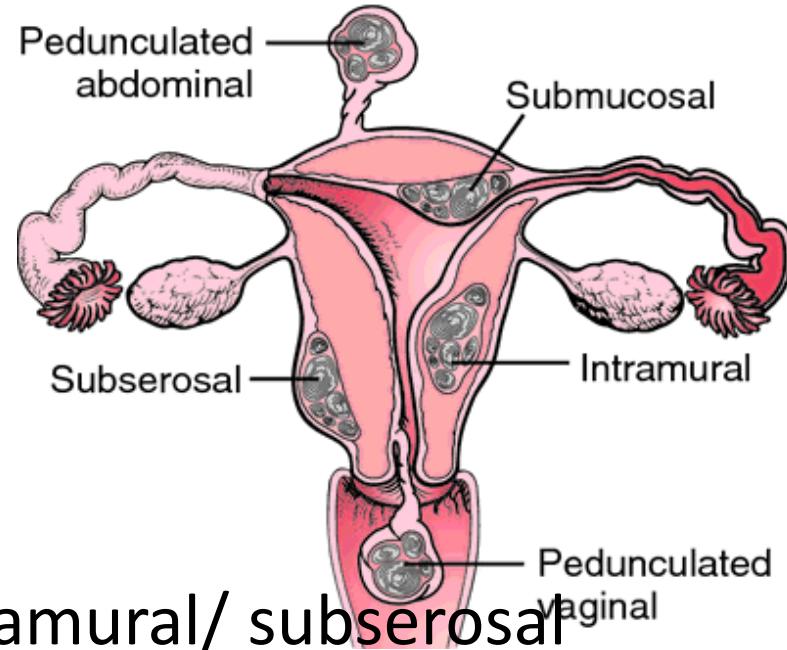
Single / multiple

Location – submucosal/ intramural/ subserosal

Partly hormone dependant

Enlarge with OCP and pregnancy

Regress/ calcify after menopause



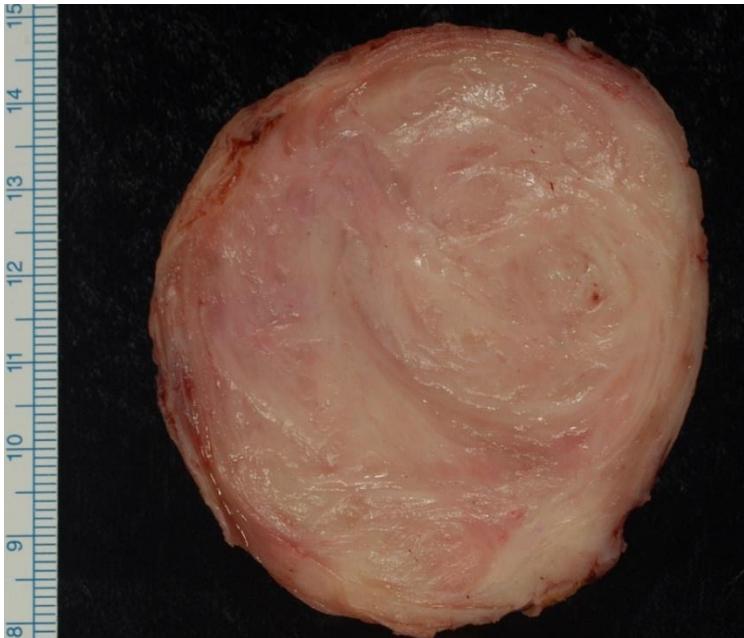
# Leiomyoma - Macroscopy

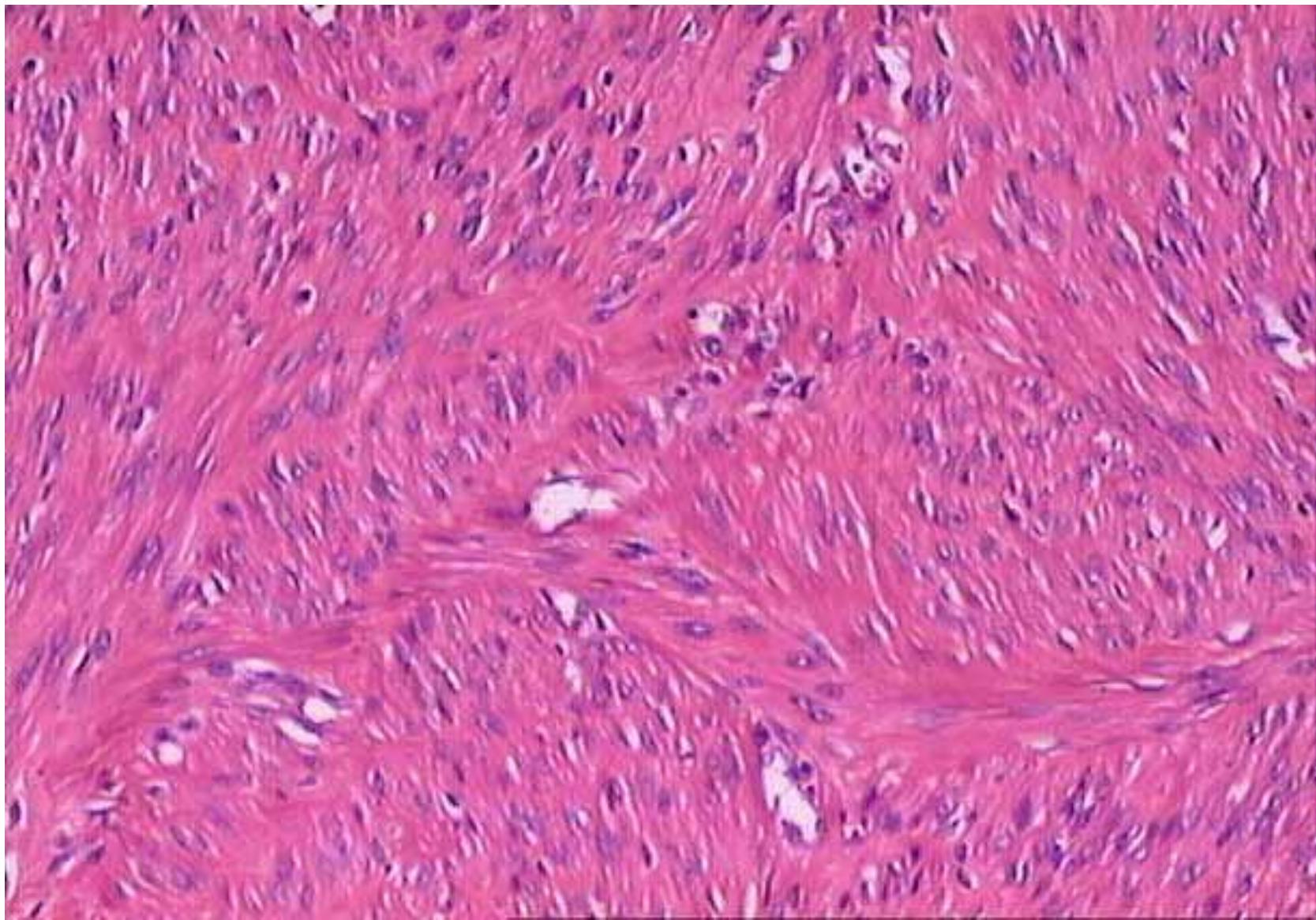


- Well defined nodules
  - Smooth, regular outlines
  - Firm/ hard/ calcified
- 
- Cut surface
- Usually grey-white in colour  
Whorled appearance  
No necrosis



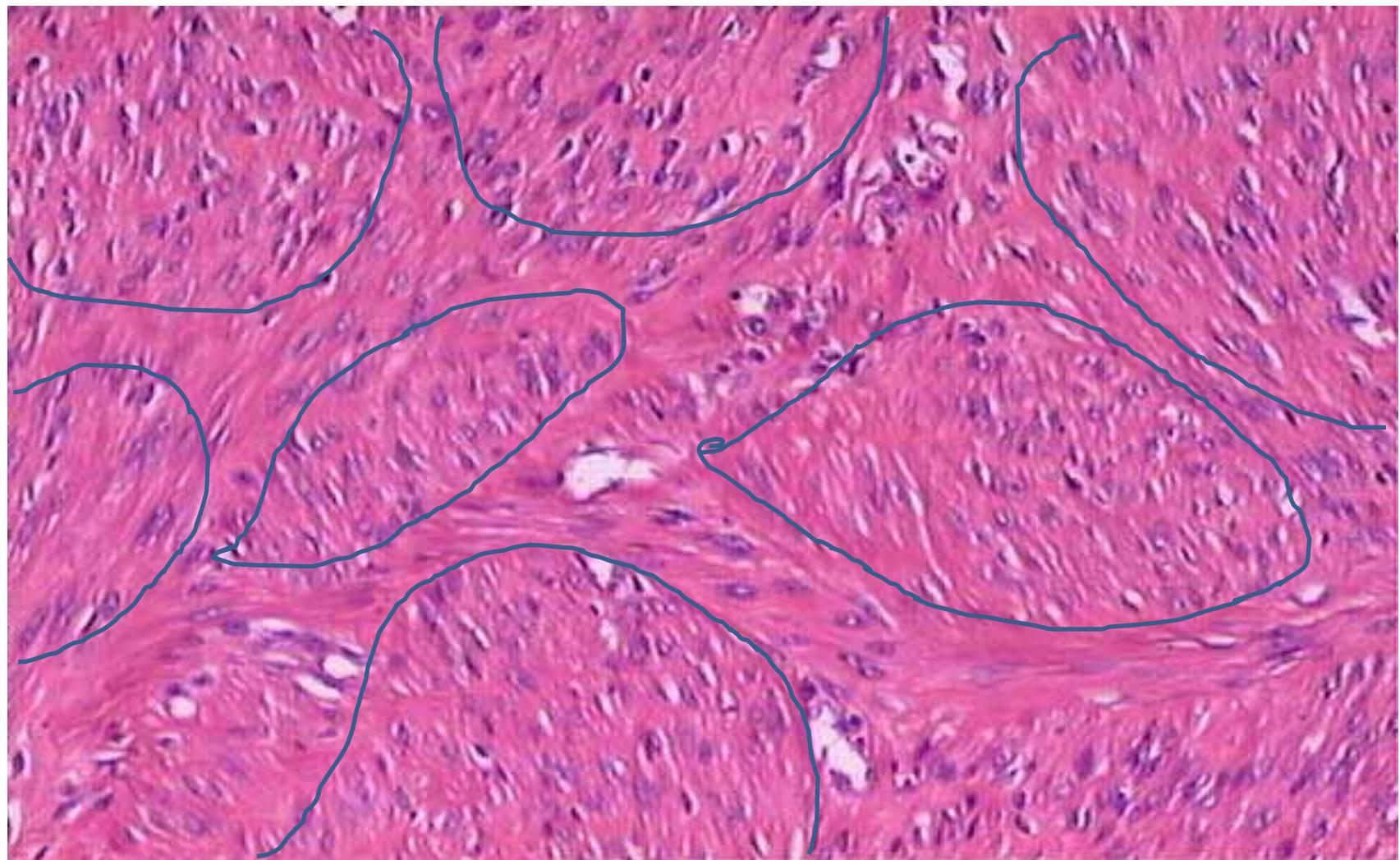
# Cut surface - whorled appearance

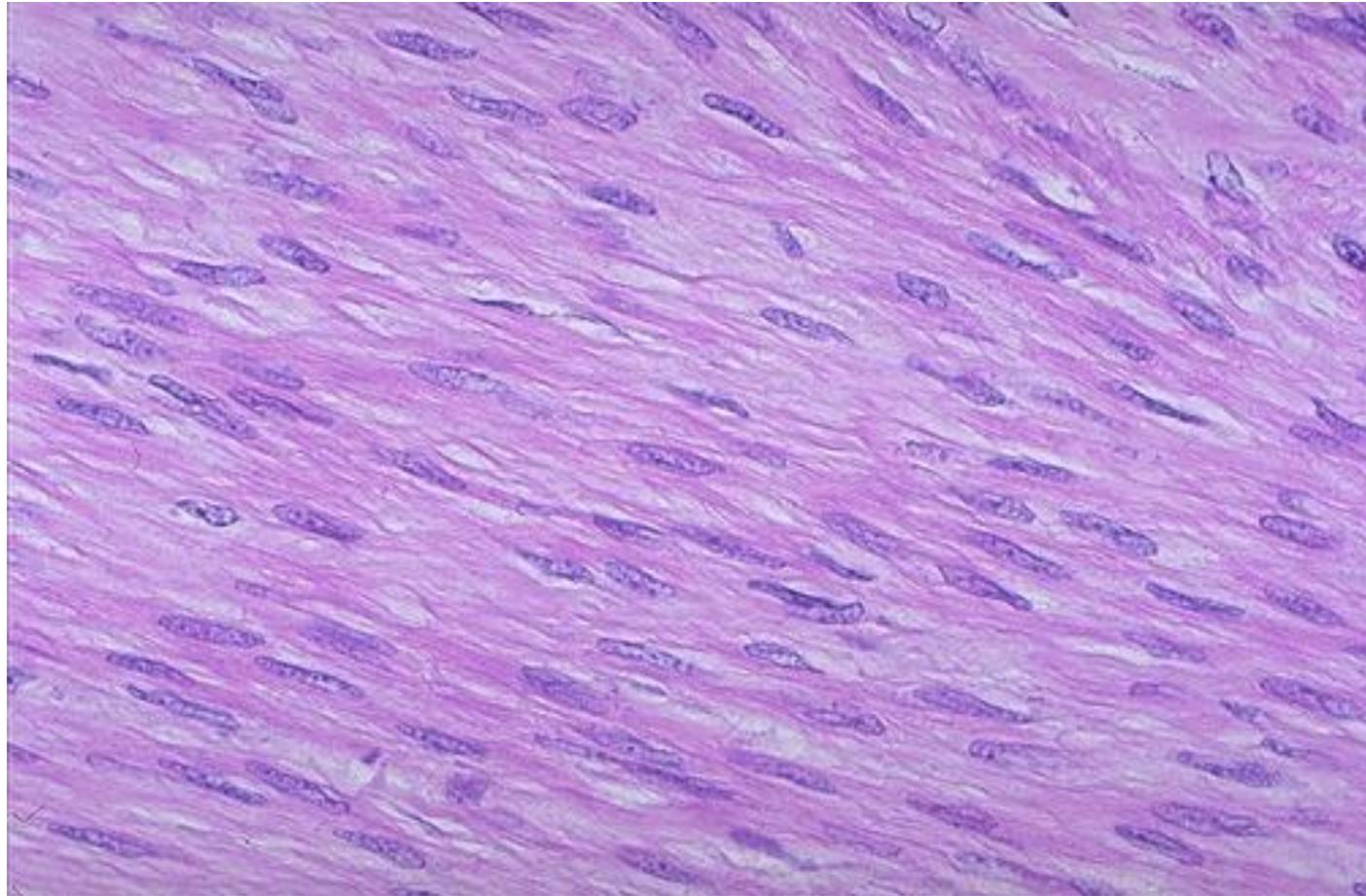




**Interlacing bundles of smooth muscles**

# Interlacing bundles of smooth muscles



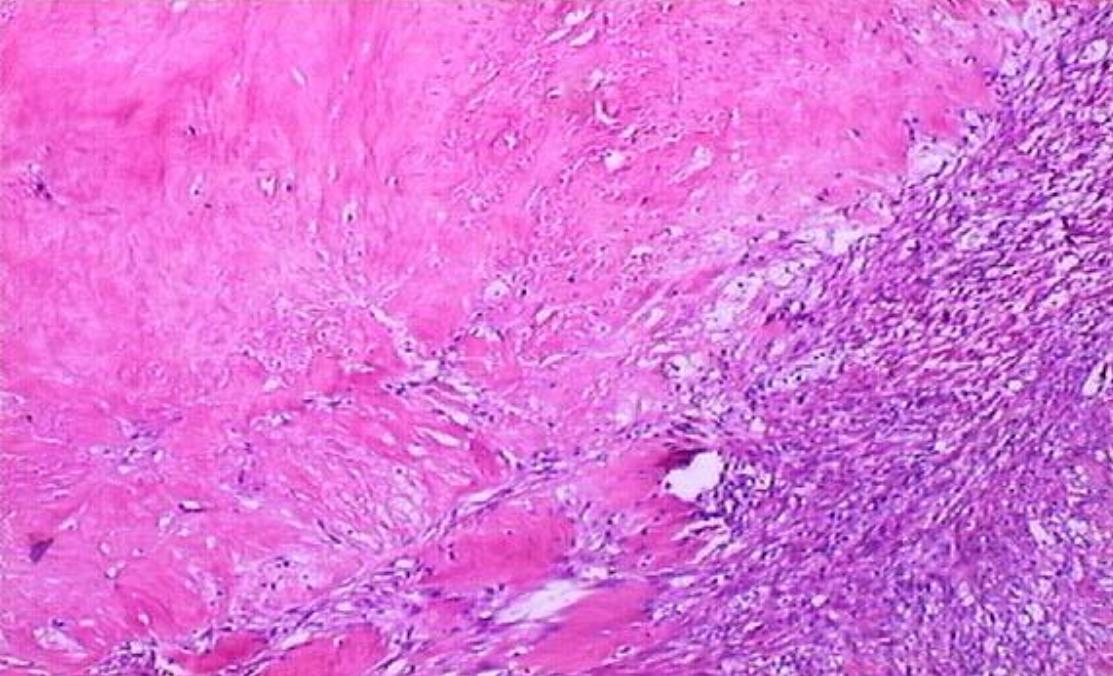


## **Leiomyoma - smooth muscle cells**

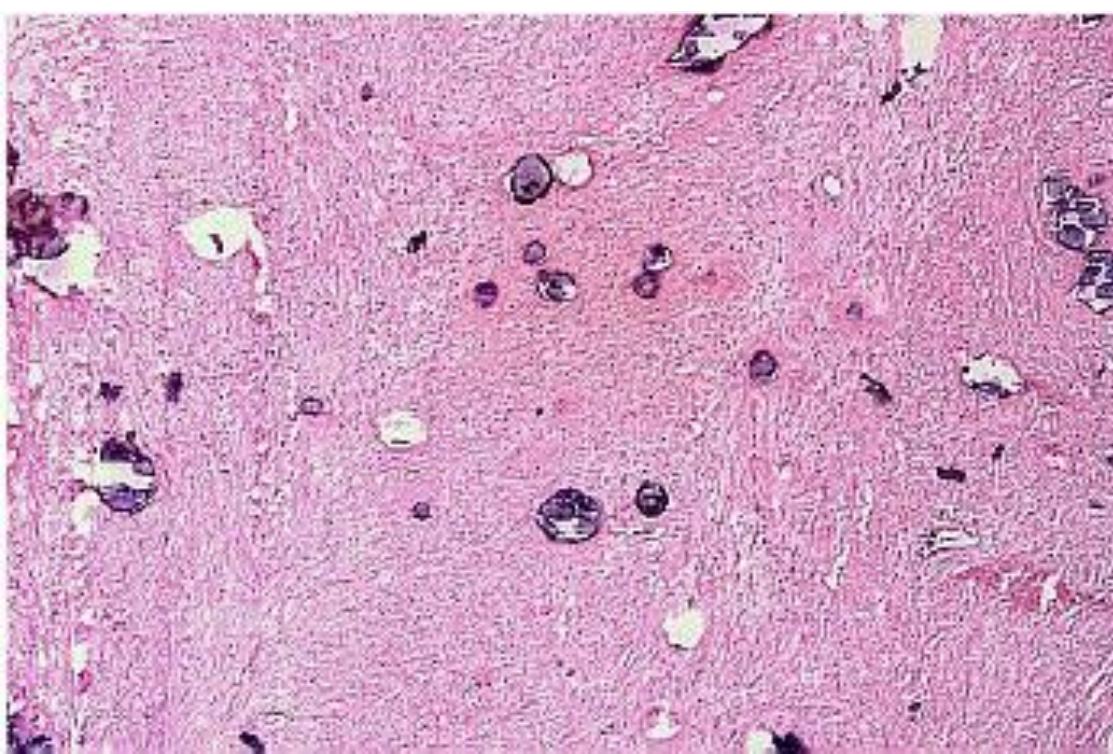
Bland spindle cells

Cigar shaped elongated nuclei with blunt ends.

Poorly defined eosinophilic cytoplasm.

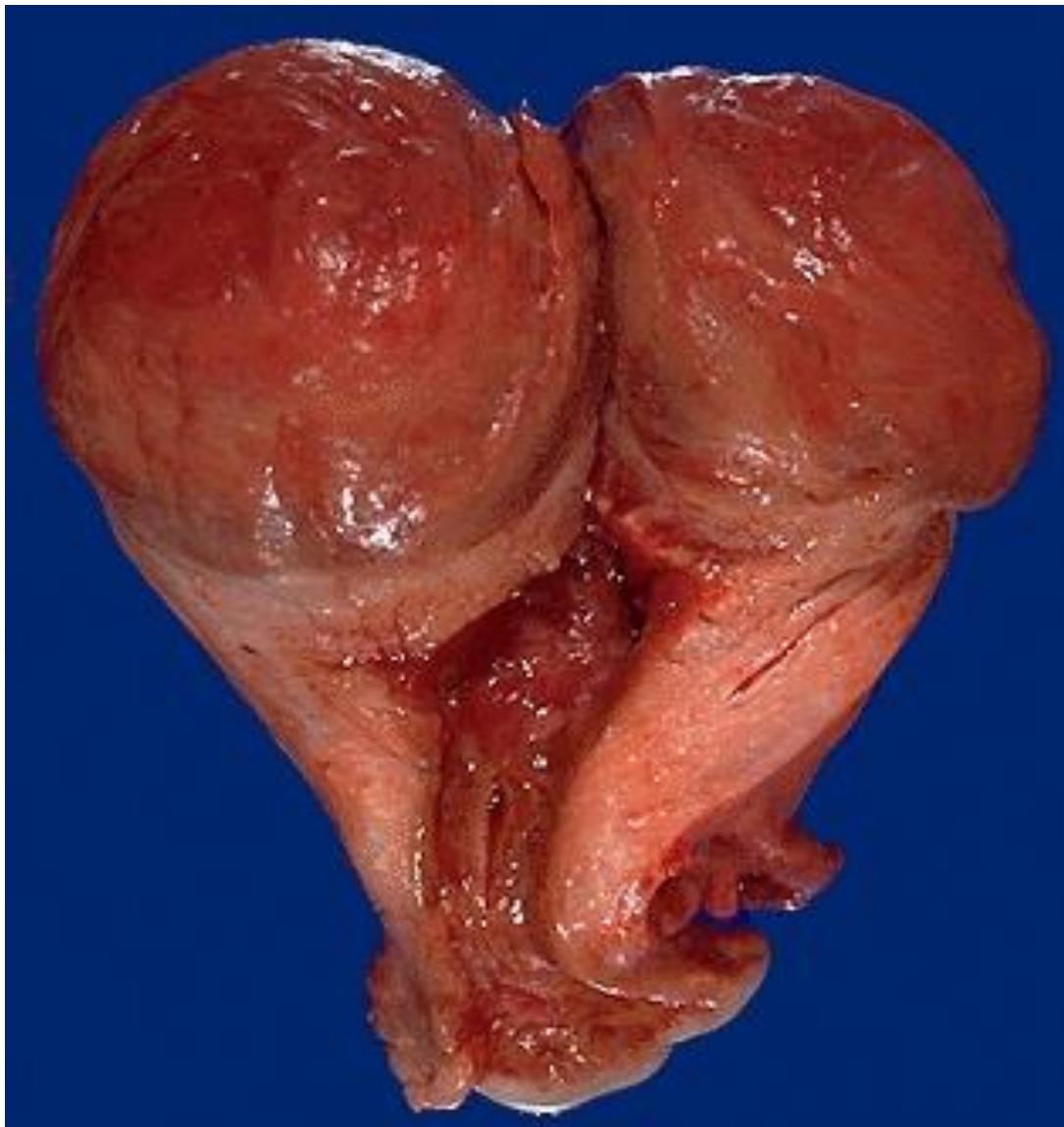


Leiomyoma with  
hyaline change



Leiomyoma with  
calcification

# Leiomyoma-Red degeneration



What is red  
degeneration of a  
leiomyoma?

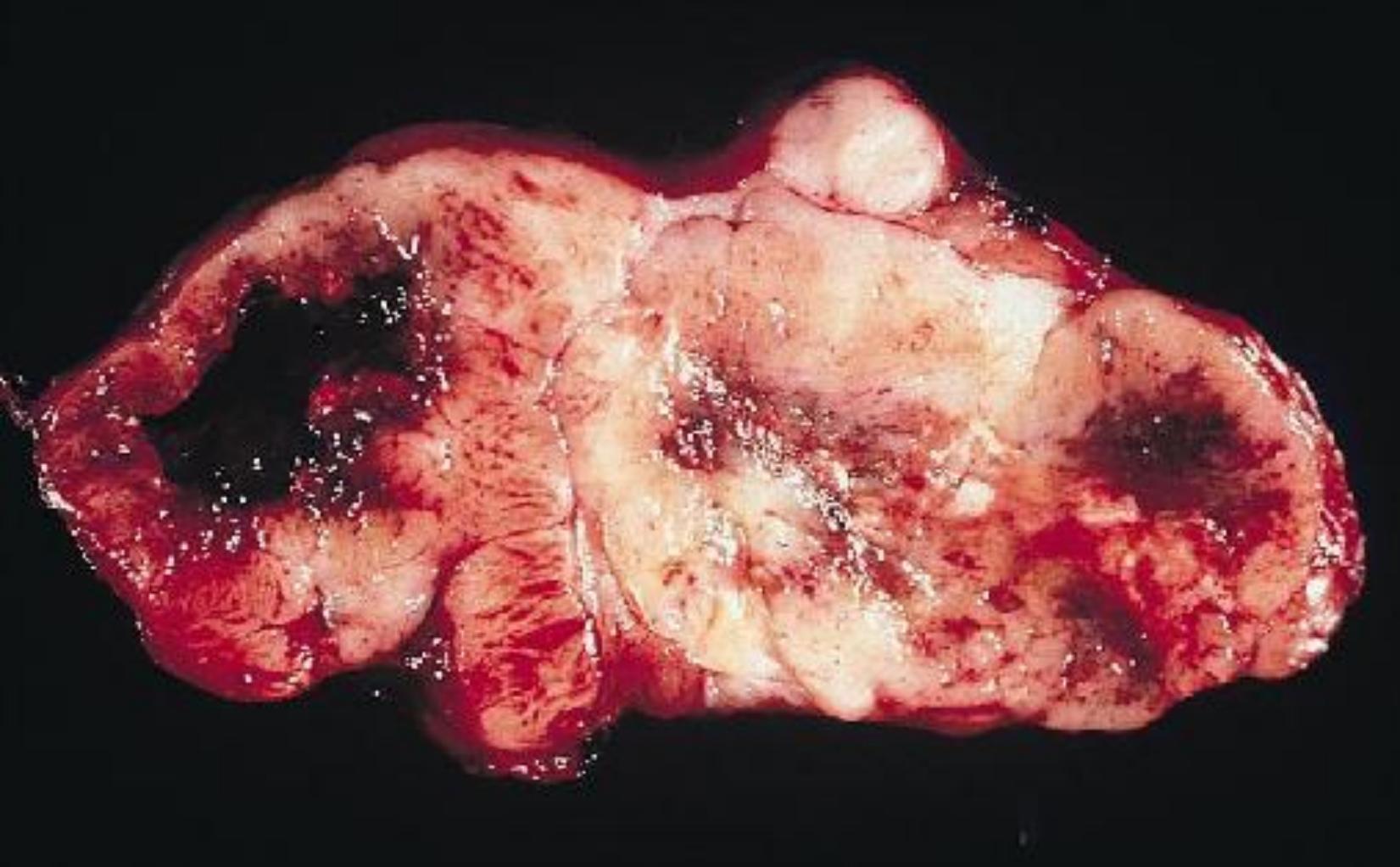
**Leiomyoma**



**Leiomyosarcoma**



Leiomyosarcoma



## Malignant tumours - Leiomyosarcoma

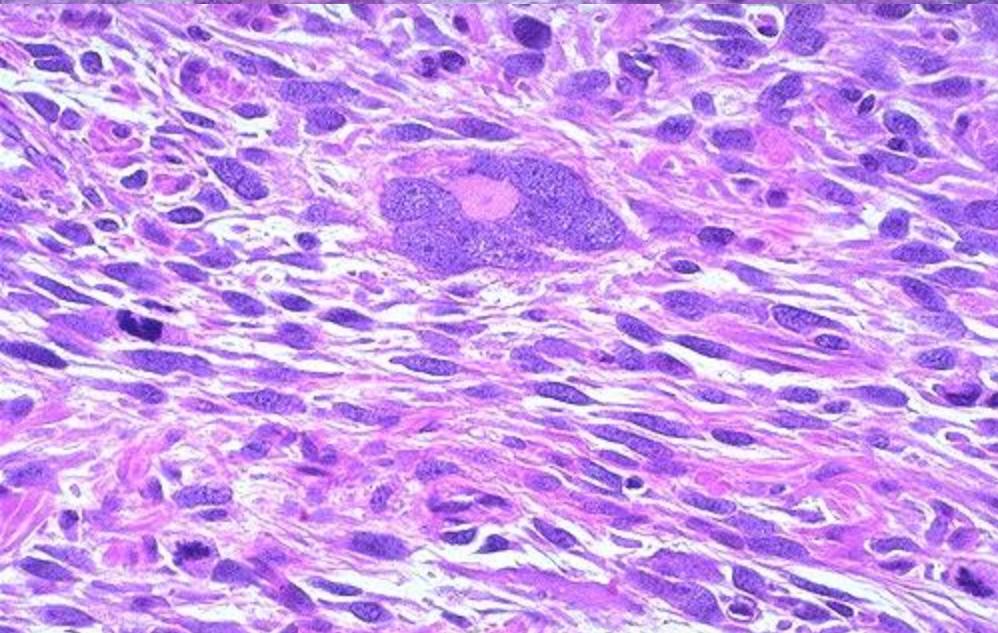
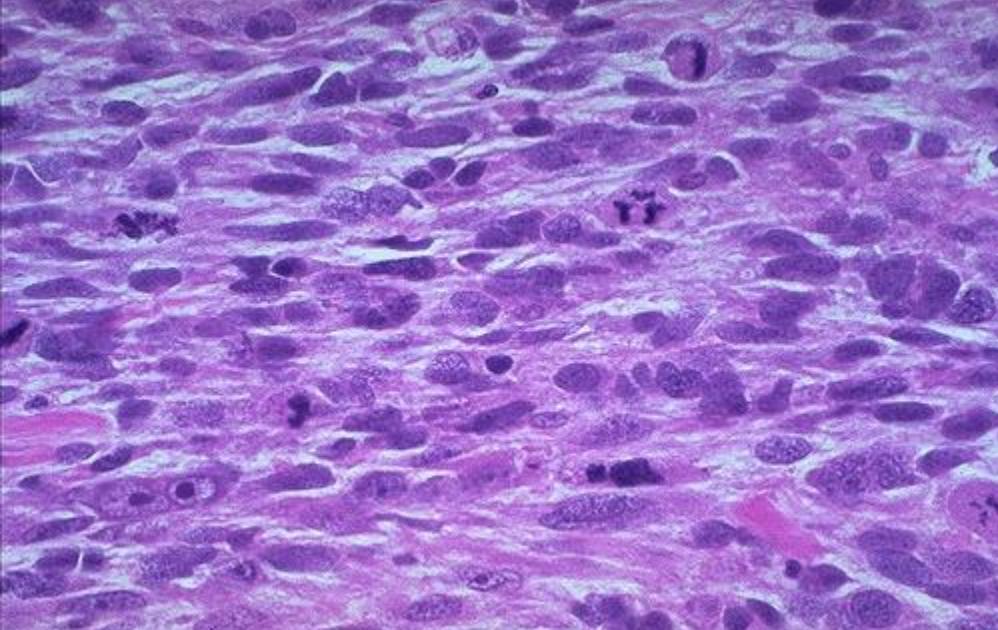
Arise de novo

Almost always solitary

Cut surface of a leiomyosarcoma

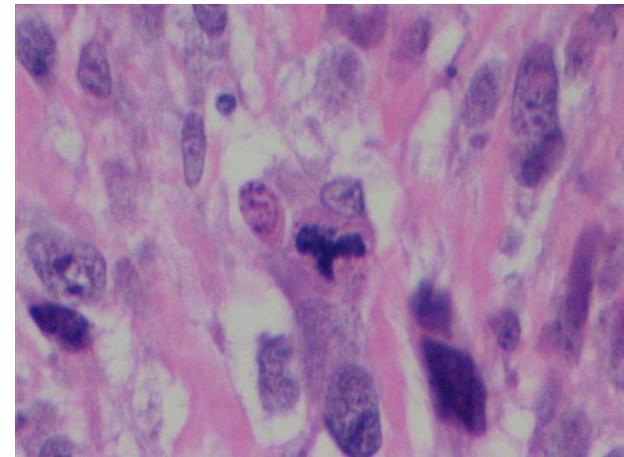
- Haemorrhagic and necrotic areas

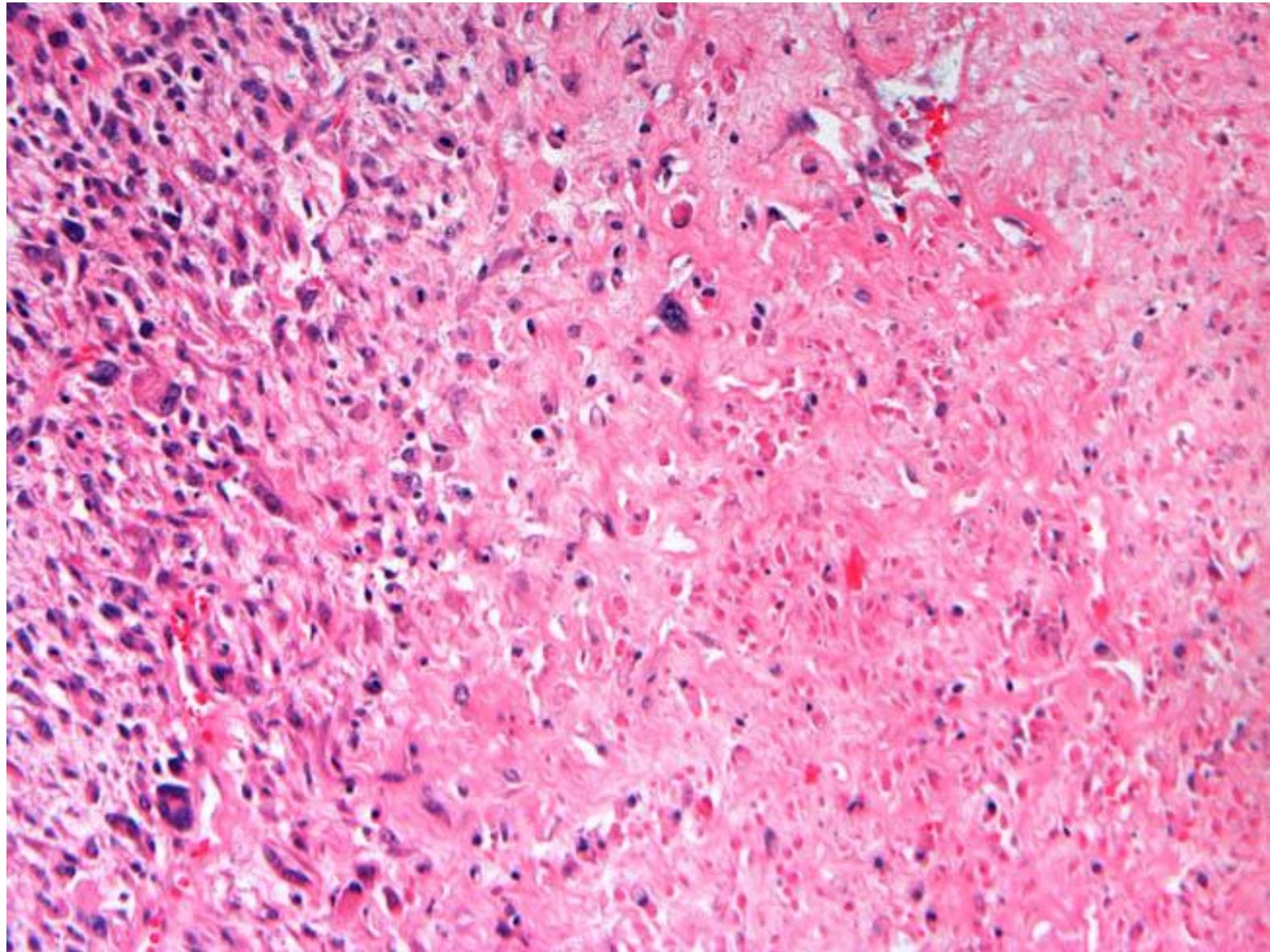
# Leiomyosarcoma - Microscopy



Bundles of atypical  
spindle cells

- Pleiomorphic cells
- Hyperchromatic nuclei
- Increased and  
abnormal mitoses





Necrosis in leiomyosarcoma

Any other tumours?

# WHO histological classification of tumours of the uterine corpus

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Endometrial carcinoma	Dissecting leiomyoma
Endometrioid adenocarcinoma	Intravenous leiomyomatosis
Variant with squamous differentiation	Metastasizing leiomyoma
Villoglandular variant	
Secretory variant	Miscellaneous mesenchymal tumours
Ciliated cell variant	Mixed endometrial stromal and smooth muscle tumour
Mucinous adenocarcinoma	Perivascular epithelioid cell tumour
Serous adenocarcinoma	Adenomatoid tumour
Clear cell adenocarcinoma	Other malignant mesenchymal tumours
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Complex	Atypical polypoid variant
Endometrial polyp	
Tamoxifen-related lesions	<b>Gestational trophoblastic disease</b>
	Trophoblastic neoplasms
	Choriocarcinoma
	Placental site trophoblastic tumour
	Epithelioid trophoblastic tumour
	Molar pregnancies
	Hydatidiform mole
	Complete
	Partial
	Invasive
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Cellular variant	
Haemorrhagic cellular variant	
Epithelioid variant	
Myxoid	
Atypical variant	
Lipoleiomyoma variant	
Growth pattern variants	<b>Secondary tumours</b>
Diffuse leiomyomatosis	

# Summary

- Normal anatomy, histology, physiology of uterus- Revise
- Non neoplastic lesions of the endometrium
- Pathological changes in endometrial hyperplasia
- Pathogenesis and morphology of endometrial carcinoma
- Non-neoplastic lesions of the myometrium
  - Adenomyosis
  - Leiomyoma
- Leiomyosarcoma morphology