Pathology of the Endometrium

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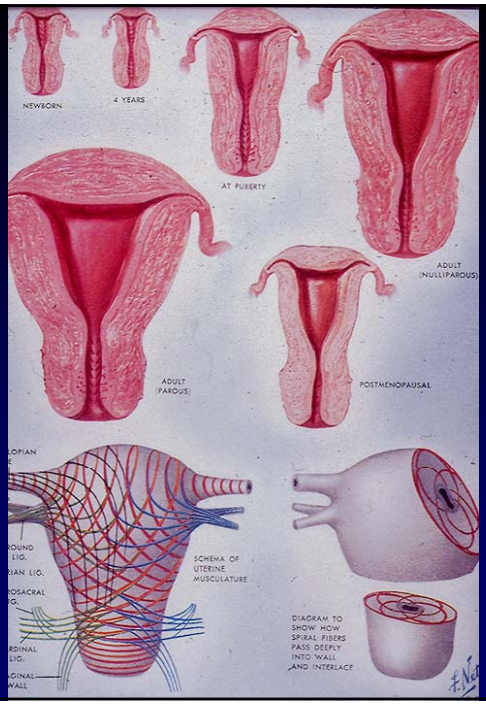


Changes in the Uterus

Thoughout life there are marked changes in the size of the uterus

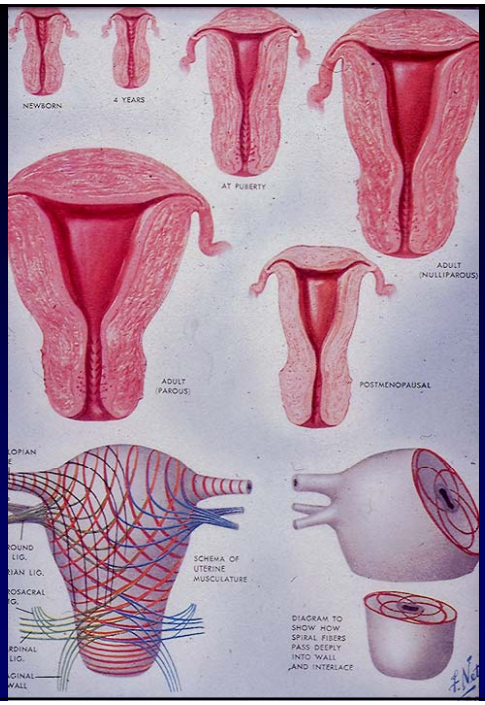
Endometrium

Most common diseases:

- Abnormal uterine bleeding
- Inflammatory conditions
- Benign neoplasms
- Endometrial cancer

Anatomical Regions

Corpus:	Responsive to hormones Thickness changes with cycle
LUS:	Thinner than corpus Less hormonally responsive Hybrid between endocervix and endometrium

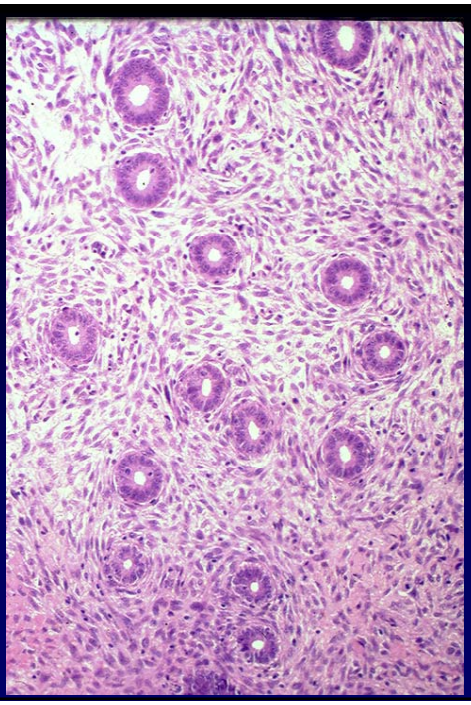


Changes in the Uterus

Thoughout life there are marked changes in the size of the uterus

Cellular Components

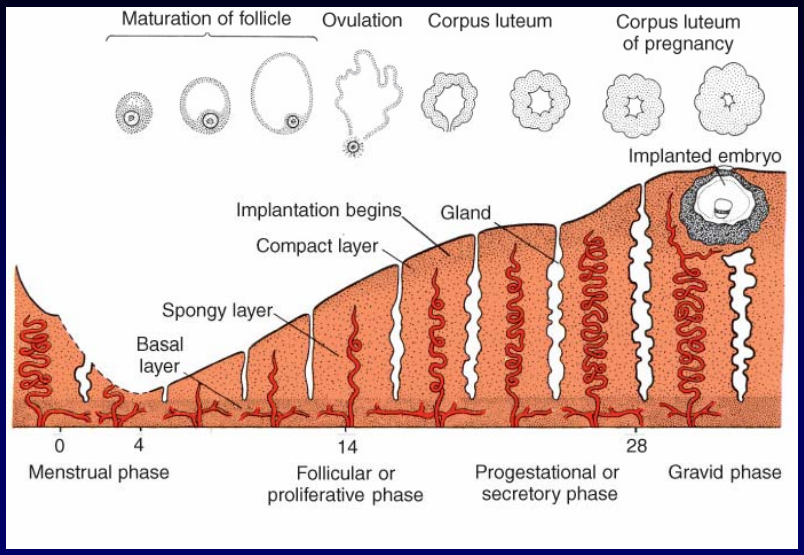
Epithelium:	Basalis-type cell Secretory cells Ciliated cells
Stroma:	Stromal cells Stromal granulocytes



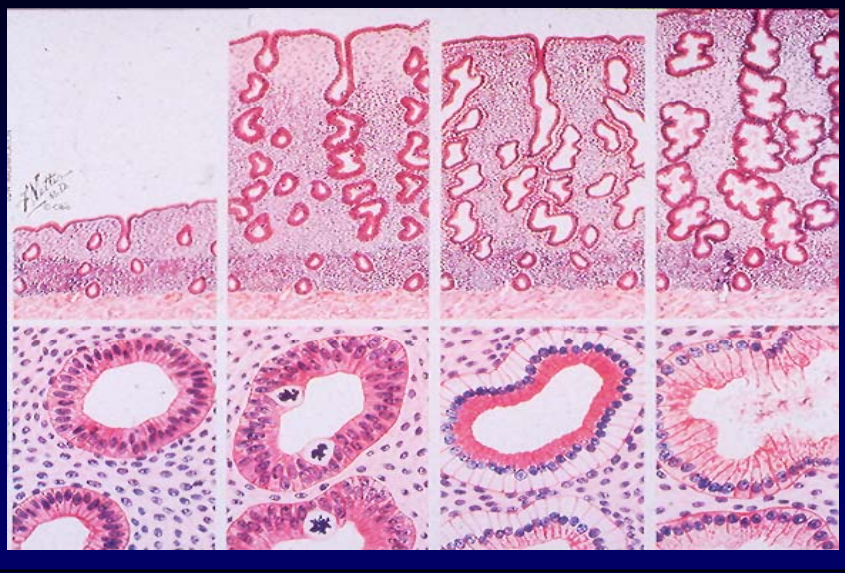
Endometrium

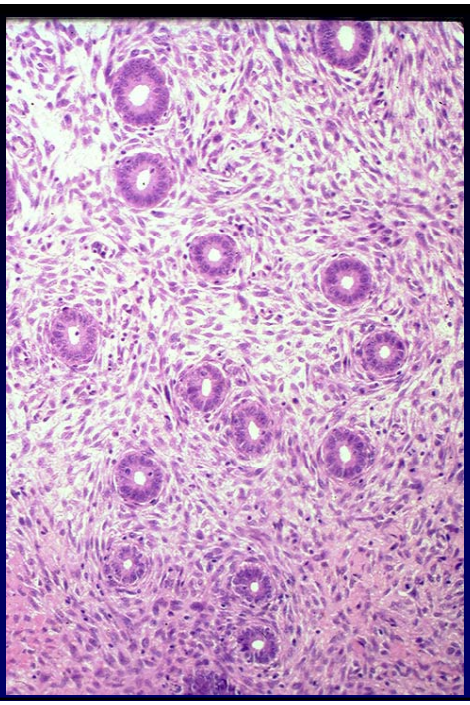
Composed of both glandular and stromal elements

Cyclical Changes in the Endometrium



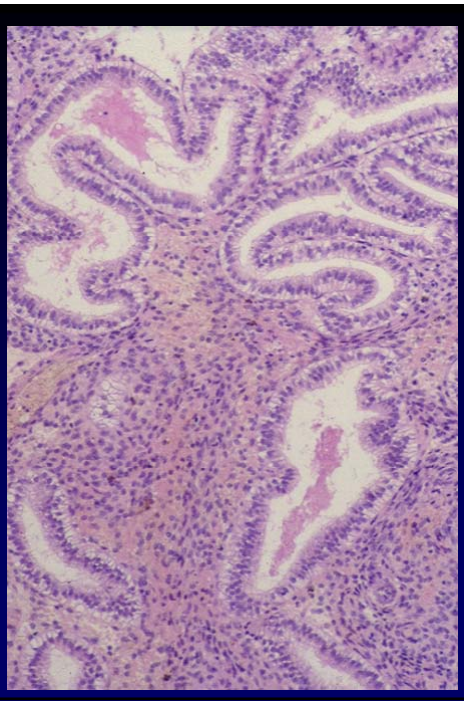
Cyclical Changes in the Endometrium





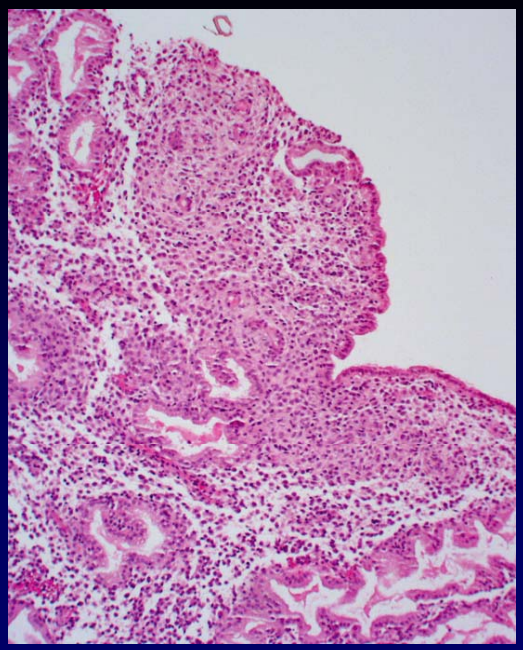
Early Proliferative Phase

Small circular glands with numerous mitoses are present.



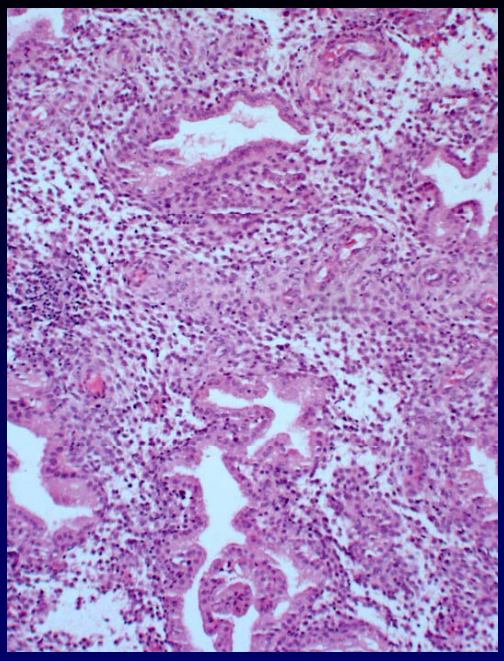
16 Day

- Glands are somewhat dilated with secretions
- Subnuclear vacuoles
- Many mitoses
- *Can't tell if ovulation has occurred*



23 Day

- Stroma shows prominent sprial arterioles with predecidual change adjacent to them
- Glands contain secretions



23 Day

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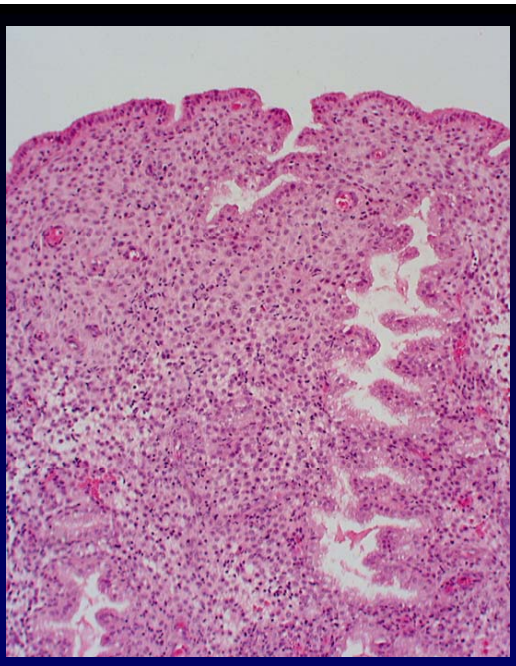
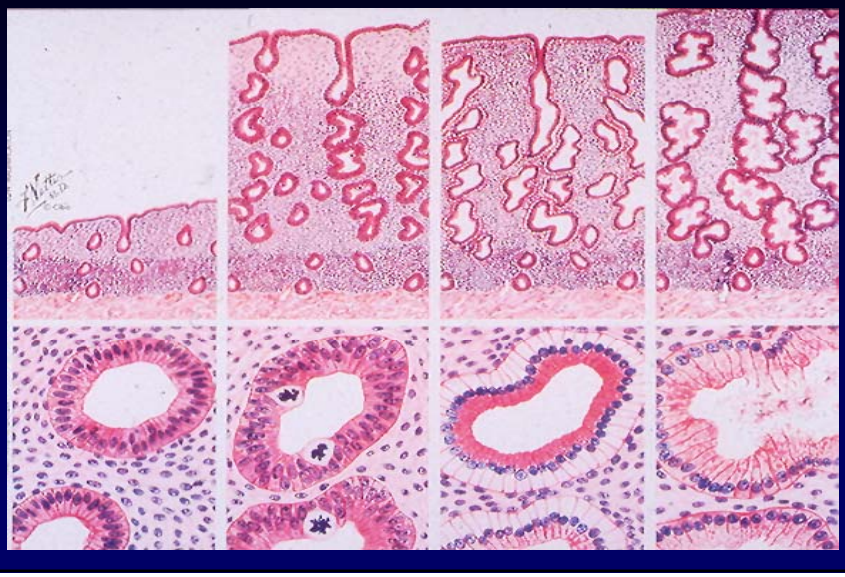


26 Day

Stroma shows predecidual change that bridges surface to spiral arterioles

Glands still contain secretions

Cyclical Changes in the Endometrium



Dysfunctional Bleeding

Definition:

- Abnormal bleeding - Dx of exclusion
- Most patients are anovulatory or short duration cycles
- Most common in postpubertal period and perimenopausal period
- Can be associated with PCO, stress

Dysfunctional Bleeding

Endometrium:

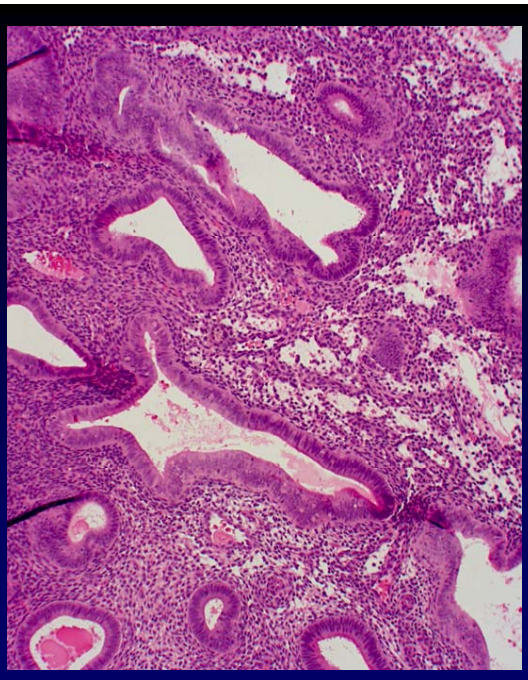
Weakly proliferative endometrium

Normal proliferative endometrium

Disordered proliferative

Endometrial hyperplasia

Asynchronously developed endometrium

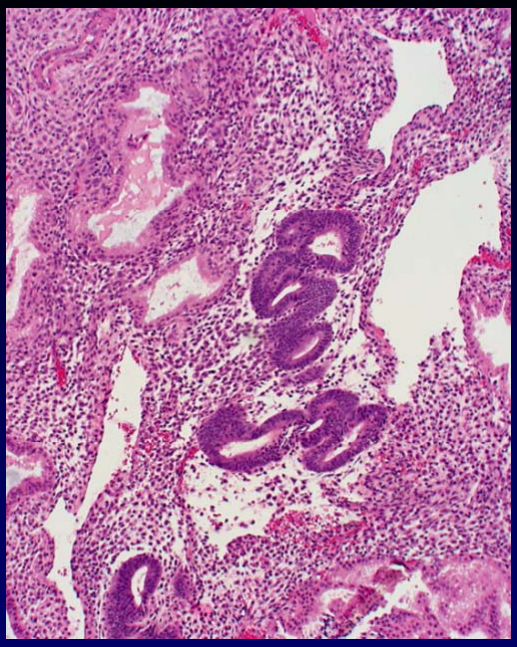


Persistent Proliferative

Dilated proliferative type glands, with pseudostratification

Focal breakdown common

Due to unopposed estrogen



Irregularly Developed

Secretory type glands co-exist with proliferative glands.

This pattern is sometimes seen in women with dysfunctional bleeding

Non-neoplastic Disorders

Iatrogenic endometrium

- Exogenous hormones
- Tamoxifin
- IUD's

Endometritis

Metaplasias

Hyperplasia

Progestational Agents

Marked pseudo-decidualization of stroma.

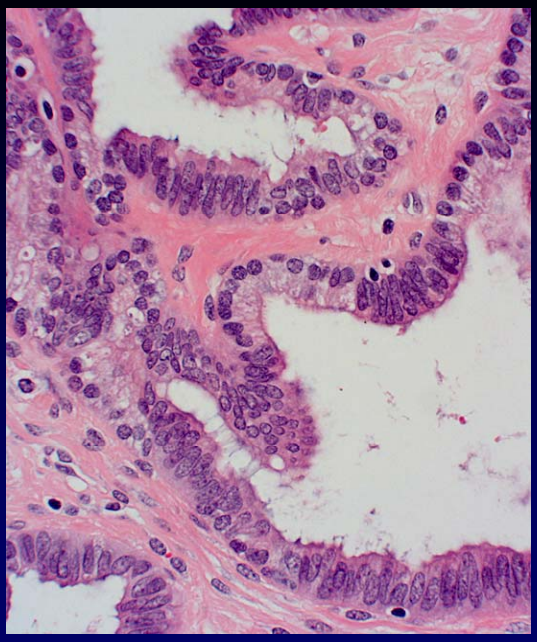
Glands are small with secretory exhaustion

Metaplasias

Tubal metaplasia occurs in setting of estrogen excess or postmenopausal.

Squamous metaplasia frequently occurs in hyperplasia, neoplasia, CEMI.

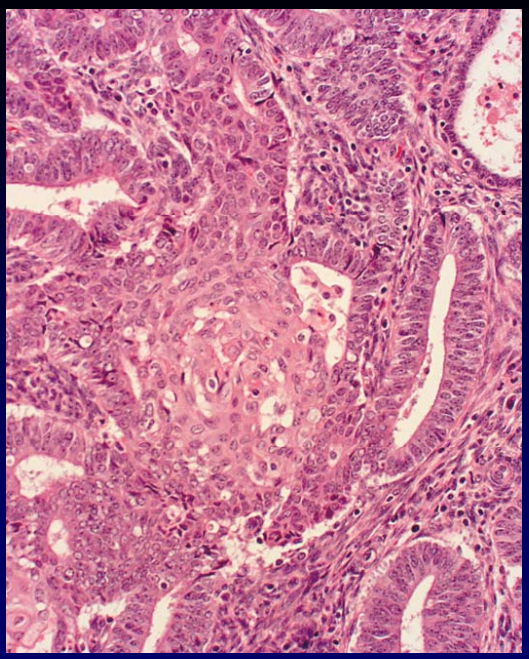
Mucinous, papillary and eosinophic types are less common



Tubal Metaplasia

The endometrium looks very much like the epithelium of the fallopian tube. Cilia are present.

Post-menopausal women with estrogen excess

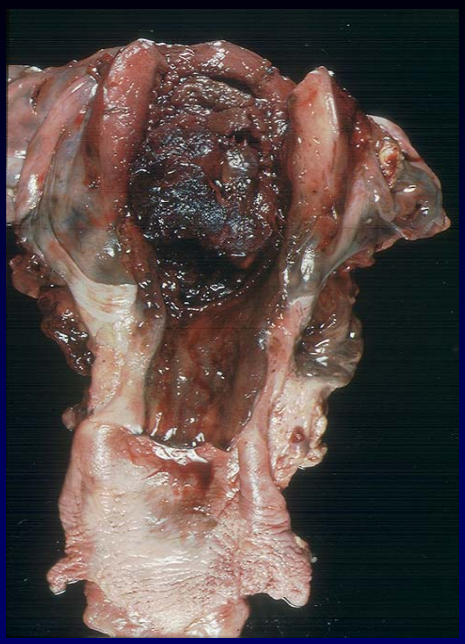


Squamous Metaplasia

A morule of squamous differentiation is present in the center of a group of glands with atypical hyperplasia

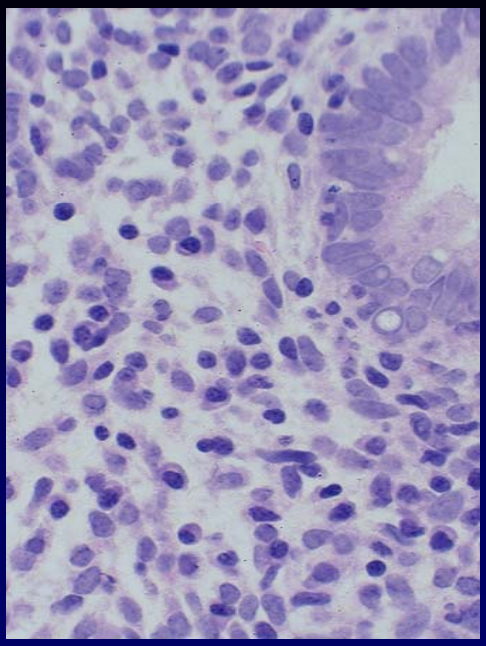
Endometritis

Acute:	Microabcesses - stroma / glands Classically postabortal Strep., Staphy., GC
Stroma:	Stromal cells Stromal granulocytes



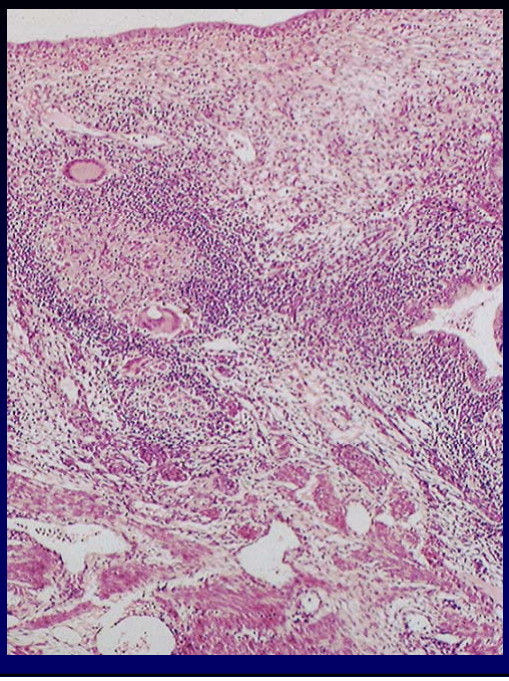
Acute Endometritis

This is a post-abortion septic uterus. Abortion was performed by non-medical personnel.



Chronic Endometritis

Multiple plasma cells are identified. These are not normally seen in the endometrium and when present indicate chronic endometritis



Tubercular Endometritis

A caseating granuloma is present with giant cells. TB of the endometrium is uncommon in the U.S. but is seen not infrequently in many areas of the world

Endometrial Hyperplasia

Abnormal proliferation of endometrial glandular epithelium (and often stroma) that lacks stromal invasion.

Endometrial Hyperplasia

Wide spectrum of patients

Associated with prolonged, unopposed exposure to estrogen

Therapy depends on type / patient / setting

Endometrial Hyperplasia

The endometrium is markedly thickened and is folded into prominent polypoid masses

Endometrial Hyperplasia

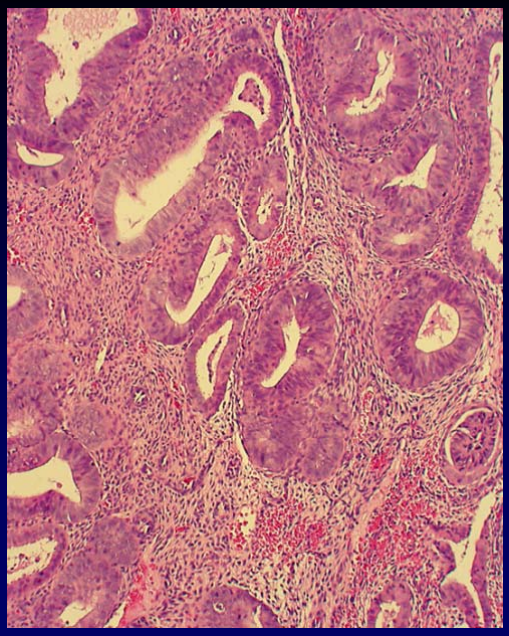
Current Terminology:

Simple hyperplasia

Complex hyperplasia *(adenomatous)*

Simple atypical hyperplasia

Complex atypical hyperplasia

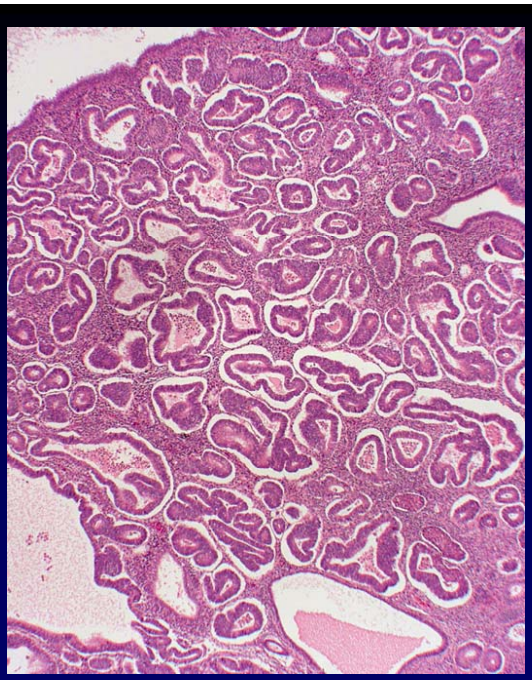


Simple Hyperplasia

Dilated proliferative type glands, with pseudostratification

Increased gland:stroma ratio and some "budding"

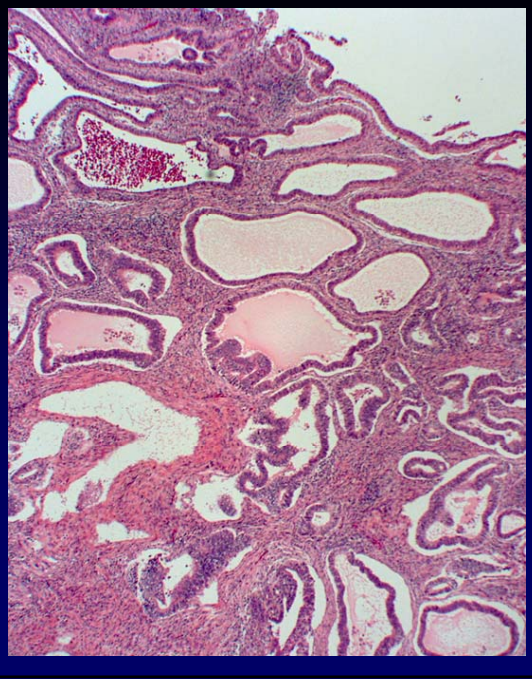
Due to unopposed estrogen



Complex Hyperplasia

The volume of glands is increased and the glands are "crowded"

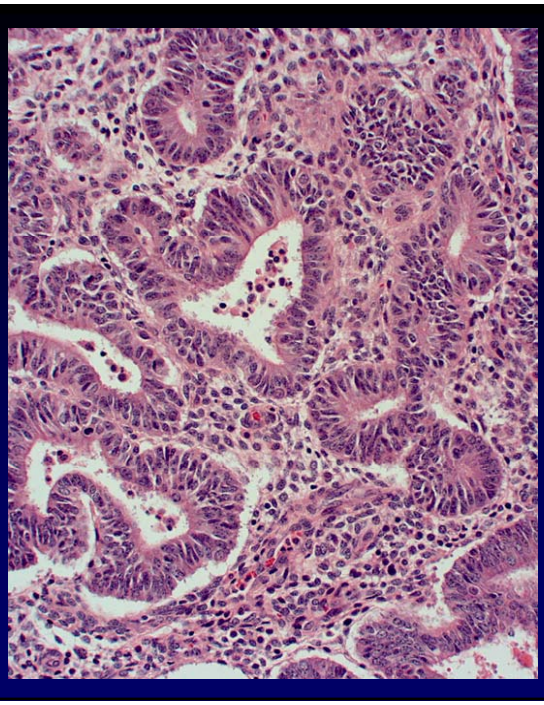
Glands are dilated and have irregular outlines



Complex Hyperplasia

Some glands have papillary projections into them

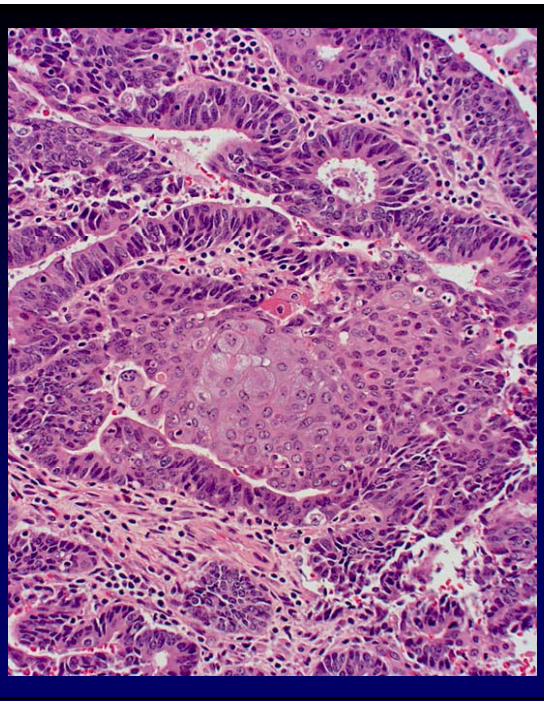
Outlines are complex



Atypical Hyperplasia

There is both cytological and architectural atypia present.

The architectural atypia is demonstrated by the cribiforming.



Atypical Hyperplasia

"Glands within glands" are seen.

There is squamous metaplasia in the center gland.

Endometrial Hyperplasia

Understanding its impact:

Early studies had lots of problems

Endometrium is histologically complex

Cytologic changes are difficult to judge

Can't follow without biopsy

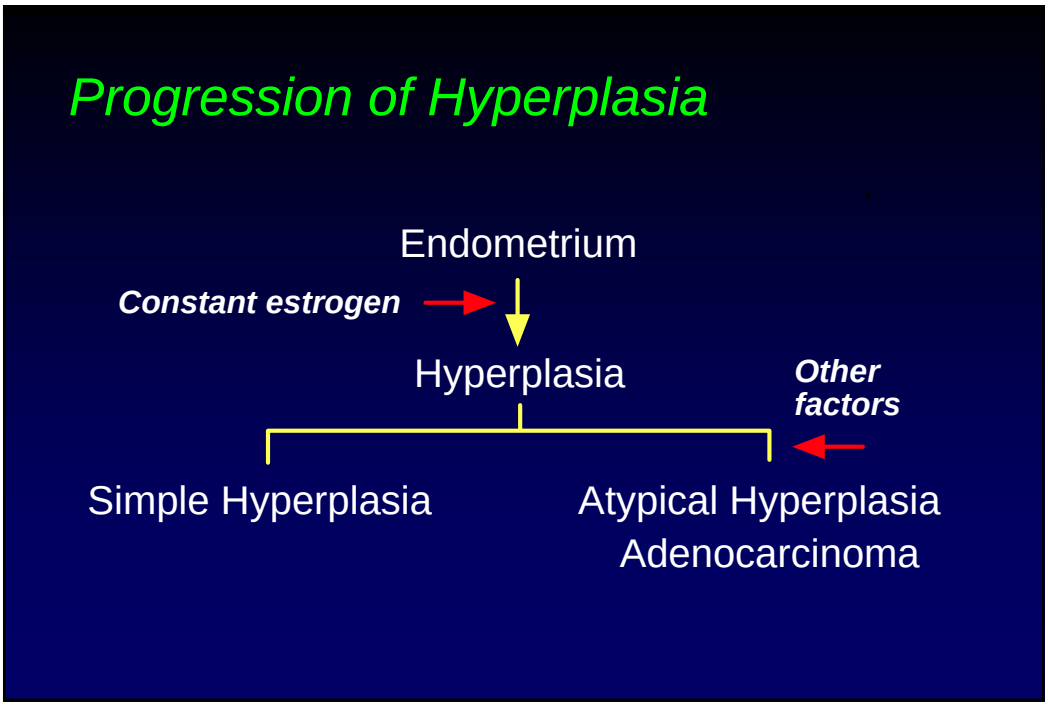
*Progression of Hyperplasia**

Type of Hyperplasia	*% to CA*
Simple ("Cystic")	13%
Complex ("Adenomatous")	27%
Atypical	75%
AdenoCA in situ	100%

Wentz, AJOG, 1984

Progression of Hyperplasia

Type	*Regress*	*Persist*	*CA*
Simple	80%	19%	1%
Complex	80%	17%	3%
Simple atypical	69%	23%	8%
Complex atyp.	57%	14%	29%



Neoplastic Disorders

Endometrial polyps
Endometrial stromal lesions
Endometrial carcinomas
Mesenchymal tumors
Mixed tumors

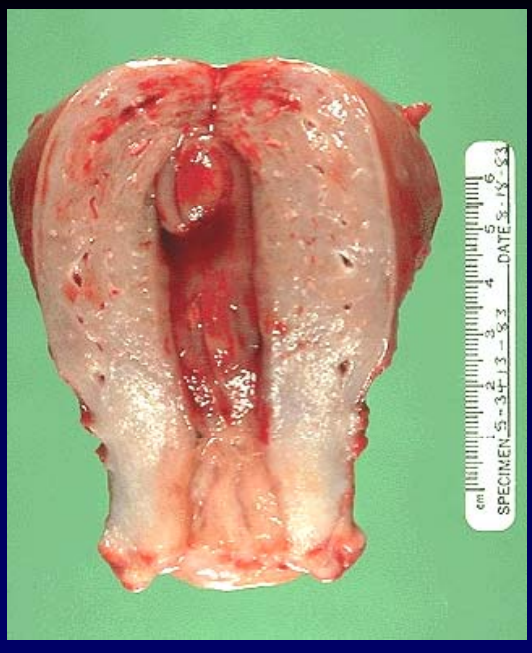
Endometrial Polyps

Are quite common, especially 40 - 50 yrs.

Develop as focal hyperplasia of basalis.

Four classic features:

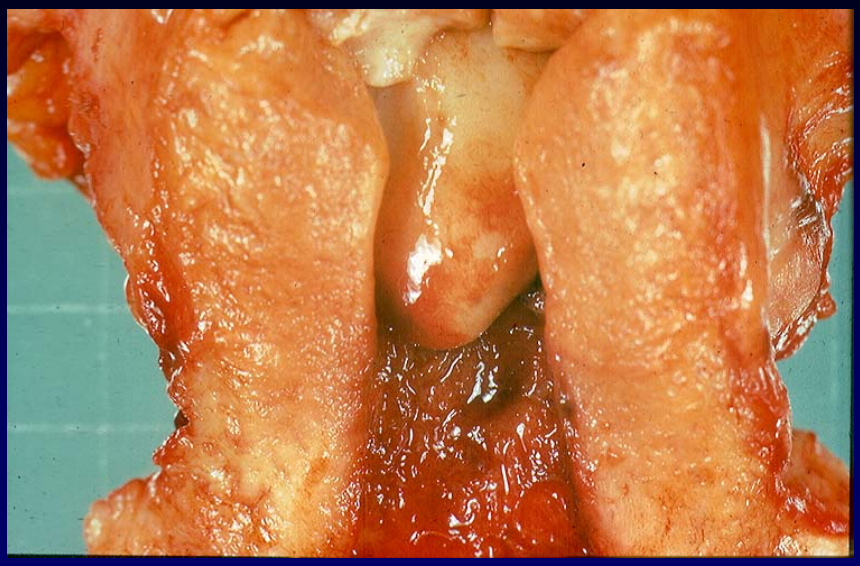
- *Fibrotic stroma*
- *Prominent vascularity*
- *Glands out of phase*
- *Irregular gland architecture*



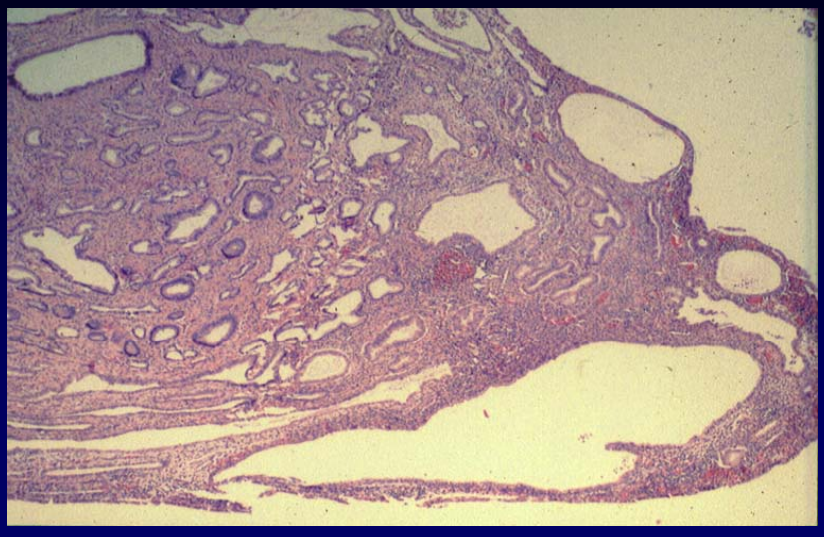
Endometrial Polyp

Small soft polyp arises from the fundus of the uterus

Endometrial Polyp



Endometrial Polyp



Uterine Leiomyoma

Proliferation of smooth muscle cells

Lesion of reproductive years

20 - 30% of women 30 years and older

More common in blacks

Present with bleeding, pain, pressure

Uterine Leiomyomas

Pathogenesis:

In reproductive yrs - rare after menopause

Contain estrogen / progesterone receptors

Hormones thought to play a role

Gonadotropin releasing hormone agonists cause regression

Uterine Leiomyomas

Pathogenesis:

Lesions are monoclonal - *G6PD or PCR*

Non-random chromosomal abnormalities quite common (40% of cases)

30% of abnormal karotypes involve region 12q14-15 (same area as involved in lipomas and rhabdosarcomas)

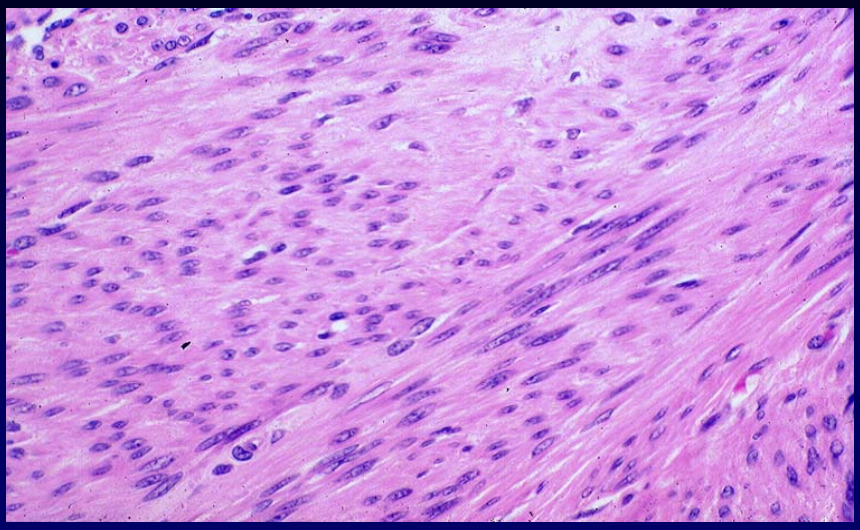
Fibroid Uterus

The uterus is distorted by multiple intramural leiomyomas.

Fibroid Uterus

Cut section through this leiomyoma shows a well-demarcated firm mass with a whorled appearance

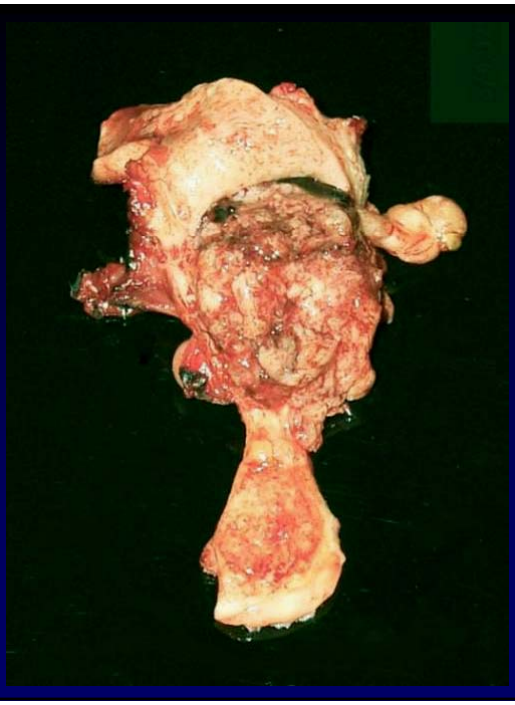
Leiomyoma of the Uterus



Endometrial Carcinomas

Clinical features:

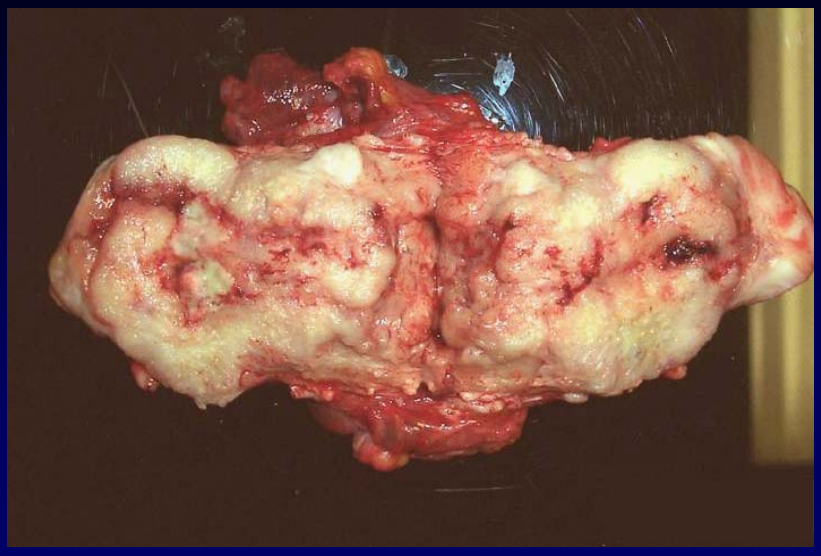
- Most common genital tract cancer
- High incidence in North America / Europe
- Associated with ERT, obesity, diabetes, hypertension, nulliparity, tamoxifin
- Two clinico-pathologic forms



Endometrial Adenocarcinoma

A necrotic mass arises from the posterior wall of the uterus and protudes into the endometrial cavity.

Extensive and Deeply Invasive Cancer

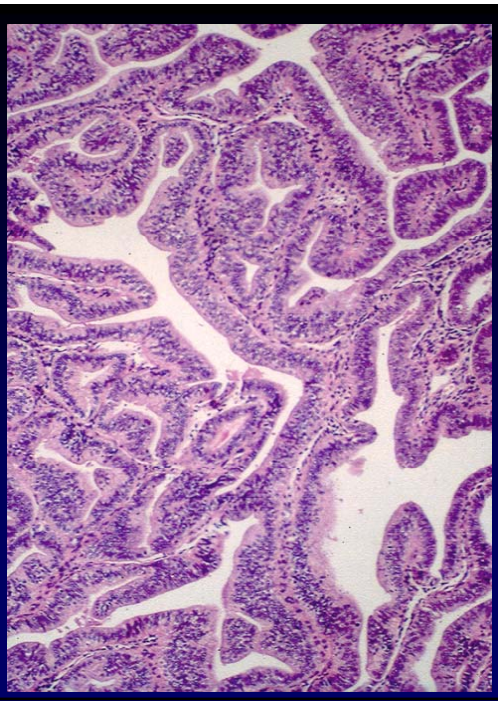


WHO Classification

Endometrioid carcinoma
Serous carcinoma
Clear cell adenocarcinoma
Mucinous adenocarcinoma
Squamous cell carcinoma
Mixed carcinoma
Undifferentiated carcinoma

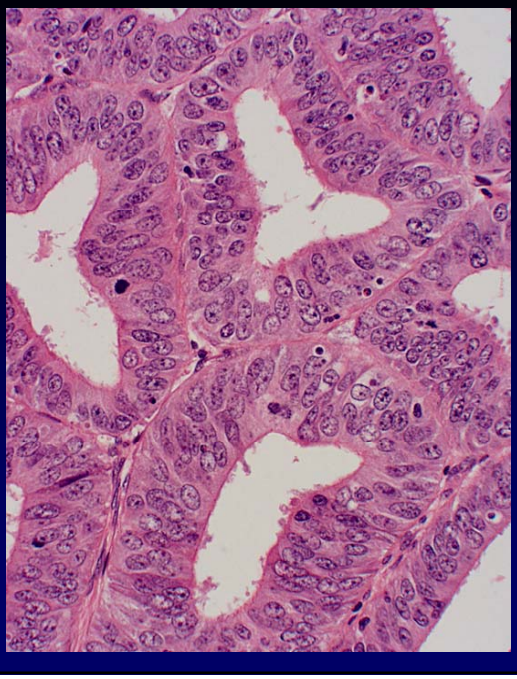
Endometrial Cancer - Types

	Type I	*Type II*
Age	Young	Old
Unopposed estrogen	Yes	No
Diabetes / obesity	Yes	No
Grade / stage	Low	High
Survival	Good	Poor



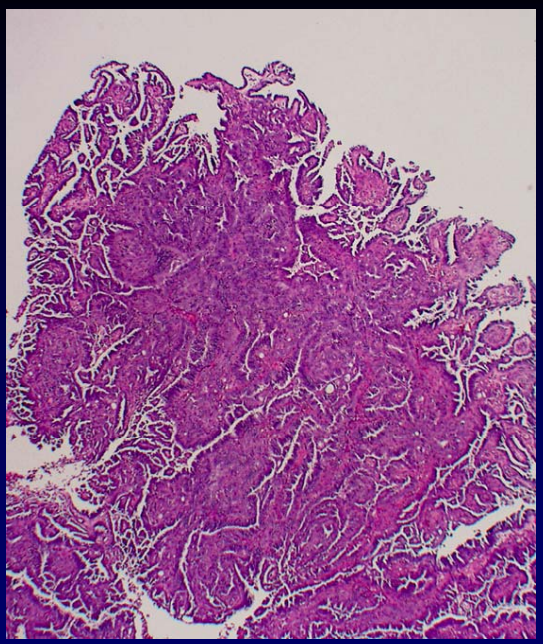
Endometrioid Adenocarcinoma

- This is a well-differentiated lesion
- Back-to-back glands with little intervening stroma
- No solid areas
- Difficult to identify "stromal invasion"



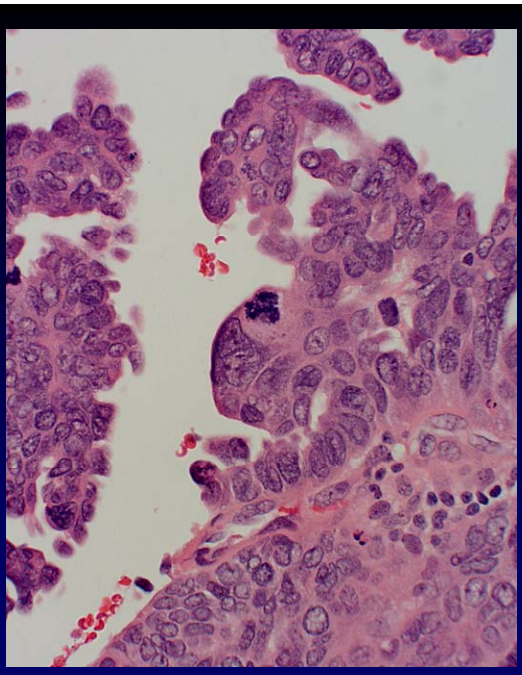
Endometrioid Adenocarcinoma

- Glands are pseudo-stratified with multiple layers
- Enlarged, round nuclei
- Coarse chromatin
- Prominent nucleoli



Uterine Serous Carcinoma

- Usually papillary
- Looks like ovarian CA
- High nuclear grade
- *Poor prognosis*



Uterine Serous Carcinoma

- Very high nuclear grade tumor
- Histology resembles that of ovarian papillary serous CA

Endometrial Cancer

Histological grading:

Based predominantly on architecture:

< 5% solid	*well-differentiated*
5 - 50% solid	*moderately diff*
> 50% solid	*poorly differentiated*

High nuclear grade can increase the grade

Endometrial Cancer

Prognostic features:

Age	Depth of invasion
Stage	Peritoneal cytology
Race	Vascular invasion
Grade	

FIGO Staging - Corpus Cancer

IA	Tumor limited to endometrium
IB	Invasion to <1/2 of myometrium
IC	Invasion to > 1/2 myometrium
II	Involvement of corpus and cervix
III	Extension outside of uterus, but not outside of true pelvis
IV	Extends outside true pelvis or involves mucosa of bladder or rectum

FIGO Stage: 5 Year Survival

	No.	*% Survival*
Stage 1	11,035	73%
Stage 2	2,014	56%
Stage 3	921	32%
Stage 4	409	11%